Title	Towards a Risk Management Framework for Quality, Environmental and Health & Safety Management Systems in Regulated Environments
Author(s)	Kelly, Martina
Publication Date	2011-07-11
Item record	http://hdl.handle.net/10379/2622

Towards an Integrated Risk Management Framework for

Quality, Environmental and Health & Safety Management Systems

in

Regulated Environments

_____

Martina Kelly

Submitted for the degree of Doctor of Philosophy

to the

National University of Ireland, Galway

Research Supervisor:	Mr. Enda F. Fallon, Senior Lecturer in Industrial Engineering
Research Director:	Professor John Sheil
Location:	Mechanical and Biomedical Engineering
	College of Engineering & Informatics
	National University of Ireland, Galway
Date Submitted:	July, 2011

Table of Contents

List of Abbreviations

ACoP	Approved Code of Practice
AIMDD	Active Implantable Medical Devices
APIs	Active Pharmaceutical Ingredients
BAT	Best Available Techniques
BPR	Business Process Reengineering
BS	British Standard
CA	Competent Authority
CAPA	Corrective and Preventive Action
CDER	Center for Drug Evaluation and Research
CDRH	Center for Devices and Radiological Health
CE	Conformité Européene
CFR	Code of Federal Regulations
cGMP	Current Good Manufacturing Practice
DMAIC	Define opportunities, Measure performance, Analyse opportunities, Improve performance, Control performance
EC	European Commission
EC	European Council
EEE	Electrical and Electronic Equipment
EHS	Environment Health and Safety
EMAS	Eco-Management and Audit Scheme
EMEA	European Medicines Evaluation Agency
EPA	Environmental Protection Agency
ETS	Emission Trading Scheme
EU	European Union
EU	European Commission
FD&C	Food Drug & Cosmetics
FDA	Food and Drug Administration
FMEA	Failure Mode and Effects Analysis

GDP	Good Distribution Practice
GHTF	Global Harmonisation Task Force
GMP	Good Manufacturing Practice
H&S	Health and Safety
HSA	Health and Safety Authority
HSC	Health and Safety Commission
ICH	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
ICOMs	Inputs, Constraints, Outputs, Mechanisms
IDA	International Development Agency
IDEF∅	Integrated Definition for Function Modelling
IEC	International Electrotechnical Commission
IMB	Irish Medicines Board
IPC	Integrated Pollution Control
IPPC	Integrated Pollution Prevention Control
ISA	International Federation of the National Standardising Associations
ISO	International Organisation for Standardisation
IVDD	In-vitro Diagnostic Medical Devices Directive
MAPP	Major Accident Prevention Policy
MDD	Medical Devices Directive
MRA	Mutual Recognition Agreement
NSAI	National Standards Authority of Ireland
OHSAS	Occupational Health & Safety Assessment Series
OMG	Object Management Group
ORA	Office of Regulatory Affairs
PDCA	Plan Do Check Act
PoE	Protection of the Environment
PQS	Pharmaceutical Quality System
QA	Quality Assurance

QC	Quality Control
QEH&S	Quality Environment and Health & Safety
QMS	Quality Management System
QRM	Quality Risk Management
QSIT	Quality System Inspection Technique
QSR	Quality System Regulation
REACH	Registration Evaluation Authorisation and Restriction of Chemicals
S.I.	Statutory Instrument
SHWWA	Safety Health and Welfare at Work Act
SMART	Specific, Measureable, Achievable, Relevant, Time-bound
SMS	Safety Management System
SOPs	Standard Operating Procedures
SysML	System Modeling Language
TC	Technical Committee
TQM	Total Quality Management
UML	Unified Modeling Language
VDU	Visual Display Unit
WCB	World Class Business
WCM	World Class Manufacturer
WEEE	Waste Electrical and Electronic Equipment

List of Figures

List of Tables

Declaration

I hereby declare that, except where duly acknowledged, the work presented in this thesis is my own, and that it has not been submitted in full or partial fulfilment of the requirement for any other award in the National University of Ireland or any other University.

_____

Martina Kelly, July 2011

Abstract

Whilst large-scale manufacturing in Ireland has seen a general decline in recent years, exceptions to this rule have been the medical device and pharmaceutical sectors which have seen continual growth. These sectors differ from traditional manufacturing in that many of the products they produce are viewed not just as industrial goods, but also a tool of public health. Because of this, the Industries are highly regulated. In order for a company to receive product approval, it must undergo stringent auditing of its quality management system.

In addition to their quality systems, companies are under increasing pressure to control, improve and maintain their environmental systems and their health & safety systems. Traditionally, manufacturing companies have been structured as a hierarchy of functional units. The difficulty with this type of structure is that problems that occur at the interfaces, or at function boundaries, are often given less priority than the short-term goals of the functional unit. Integrating quality, environmental, and health & safety management systems may provide a solution. However, because medical devices and pharmaceutical companies manufacture under strong regulatory oversight of their Quality Management System, this oversight has led many companies to reject integration in the belief that integrating their environmental and health & safety systems with their quality system will jeopardise approval by regulatory authorities. The difficulty is, that if these systems operate independently of each other, then the barriers between them will not be crossed. Corrective actions will be focused on the system concerned, and therefore will result in little benefit to the organisation as a whole. Moreover, as part of its risk control measures in one system, the organisation many actually create risk in another.

This thesis details the development of a risk-based framework by which companies operating in such highly regulated environments can resolve this problem. Based on the evidence from a detailed literature review and the data gathered by means of survey and case studies, the corrective and preventive

action (CAPA) component of the management system was found to be the most significant common element throughout the regulations and standards governing these companies. The proposed framework supports an integrated approach to the management of environmental, quality and health & safety systems, which is developed around this CAPA process. IDEFØ, (Integration Definition Function Modeling) is the functional modelling methodology used to describe the analysis and development of the framework. The framework was then validated via expert reviewers some of the main end-users of the framework.

Published Work Associated with this Thesis

Peer-reviewed Papers

Kelly, M. (2008). Identifying opportunities for the Integration of Quality, Environmental, and Health & Safety Management Systems in the Medical Device Sector. In Karwowski, W. and Salvendy, G. (Eds.). *Proceedings of the 2nd International Conference on Applied Human Factors and Ergonomics,* Las Vegas, Nevada, USA.

Kelly, M., Donnellan P. and Velazco Figueroa, I. J., (2005). Integration of Management Systems in the Irish Medical Device and Pharmaceutical Sectors. *IMC 2, 2005.*

Kelly, M. (2003). Remodelling the Safety Function using IDEFØ. In Bagnara, S., Rizzo, A., Pozzi, S., Rizzo, F. and Save, L. (Eds.). *Proceedings of the 8th International Conference on Human Aspects of Advanced Manufacturing; Agility & Hybrid Automation,* Rome, Italy.

Acknowledgements

I would like to sincerely thank all who contributed to this work:

- My research supervisors, Mr. Enda Fallon and Professor John Sheil for their invaluable help and support throughout the period of this research

- The manufacturing companies who allowed me into their factories and gave me virtually unlimited access to their extensive knowledge and documentation

- All those who responded to the questionnaire survey and to Ignacio for his help with this

- The members of the expert review panel who were gracious with their feedback, and generous with their time

- Liam and Rachel for their expertise in Microsoft Word

- Vincent, for the comprehensive editing job

- All my wonderful colleagues in Industrial Engineering, Nun's Island.

- My family - immediate and extended

- A final word to my parents-in-law – I'm sorry I hadn't it finished in time to give you your day out!

Dedication

Dedicated to Vincent, Bronagh and Eanna

Chapter 1:   Introduction

1.1 Background to Risk Management in Regulated Enterprises

This thesis focuses on the development of a Framework which can be adopted by highly regulated medical devices and pharmaceutical manufacturers to provide an integrated approach to managing their quality, environmental and health & safety systems. Despite the many benefits to be accrued from an integrated management approach, there is a tendency for these companies to resist integration of their management systems due to unique regulatory constraints. This study will identify these constraints and present a Framework which will not only ensure regulatory and legislative compliance but will provide the opportunity for continuous improvement.

In the last few decades, Ireland has experienced an economic boom and bust cycle characterised by alternating periods of economic growth and contraction. From chronic unemployment and massive emigration during the 1980's, the 1990's saw remarkable economic achievements, earning Ireland an international reputation as the 'Celtic Tiger'. However, before the end of the following decade, the Tiger economy collapsed and Ireland is currently facing an economic crisis. Ireland is being repositioned as a knowledge economy, and this has changed the profile of investment targets in recent years. Despite many comments that the manufacturing sector is in decline, manufacturing remains critically important to the country. The export sector, on which manufacturing is highly dependent, has been the driving force of the Irish economy during the recent crisis and according to one economist it "must continue to perform robustly to counterbalance the continued weakness in the domestic economy, which will enable the economy to better absorb the forthcoming fiscal cuts." (Devine, B. 2010).

Competitiveness is also critical to Ireland's continued success and its future development. Whereas in the past, competitiveness in its broadest sense meant low costs (in wages, services etc), today it means much more. The Industrial

Development Authority (IDA) contends that the continued success of the Irish economy will not be about "making more things" as it has been in the past, but about "making things better and making better things" (Industrial Development Authority, 2002). Historically the key to making things better and making better things has been through the use of quality systems and the manufacturing sector has wholeheartedly adopted concepts such as Total Quality Management (TQM) and World Class Business (WCB) to help them in this regard. However, having streamlined their quality systems, companies are under increasing pressure to control, maintain and improve their environmental systems and their health & safety systems. The increasing cost of maintaining such systems has brought much focus to bear on the integration of management systems. Much of the literature expounds the benefits of integrated management systems in terms of reducing documentation, avoiding duplication of effort, and improved cooperation and communication etc. (Bamber et al, 2000; Wilkinson and Dale, 2001; Honkasalo, 2000; Karapetrovic, 2003). However, this thesis contends that there are unique barriers to integrating management systems within two of Ireland's most important manufacturing sectors; namely, the medical device and pharmaceutical sectors.

This contention has arisen from an investigation into human and safety issues in advanced manufacturing systems in Ireland and an attempt to develop a methodology to ensure that health and safety is given equal status with other key business elements. While modelling the safety management system of a Food and Drug Administration (FDA) regulated medical device company in the investigation, it became apparent to the author that the quality department controlled all process changes and hence all changes to standard operating procedures (SOPs) - even those changes required for health & safety reasons. In effect, health & safety activities were constrained by the quality department. Further investigation exposed the rationale behind these constraints. The FDA conducts stringent auditing of medical device companies' quality systems.

Approval of the quality system is critical to a company as without this approval they cannot sell their products in United States markets. If a company integrates its safety management system with its quality system this will allow an FDA audit on the complete integrated system. From a company perspective, this increases the possibility of failing an audit and the failure may result not from a quality non-conformance but a safety non-conformance for instance. If existing research states the benefits of integrating management systems but ignores those companies regulated by the FDA, does this mean that those companies are bereft of all the advantages outlined in the literature?

1.2 Research Objectives

The aim of this research is to develop a framework whereby highly regulated medical device and pharmaceutical companies can adopt an integrated approach to managing their quality, environmental and health & safety systems (QEH&S) whilst assuring compliance with regulatory requirements. It is proposed that the adoption of this framework will ensure a cycle of continuous improvement while offering protection for the people, the process, and the environment.

The research aim will be achieved by meeting the following objectives:
1. To determine the prevalence of integrated QEH&S management systems within the Irish medical device and pharmaceutical sectors.
2. To determine the extent to which these companies believe integration is desirable and feasible.
3. Where integration does not exist or where companies believe it is not feasible, to determine the barriers to integration.
4. To identify the regulatory requirements on medical device and pharmaceutical companies and other requirements that may constrain the management of their activities (e.g. legislative, corporate requirements).

5. Informed by the results of 1 to 4 above, to develop a framework to assist companies in adopting an integrated approach to managing their QEH&S systems.

1.3 Scope of the Study

Quality, Environment and Health & Safety are all very large topics in their own right, as is the whole field of management and the philosophies of management. A great deal of research, spanning many decades, has been undertaken in each of these areas. It is therefore necessary to define the scope of the research undertaken in this dissertation. This study focuses on bringing together the critical elements of managing Quality, Environmental and Health & Safety issues in a manner which will ensure that each system is given due recognition within the business model adopted. It will concentrate on identifying the main legislative and regulatory requirements as well as best practice in managing QEH&S in specific, highly regulated industrial sectors. The main focus is on developing a methodology to facilitate an integrated approach to managing risk across each system. The work must reflect best practice in shifting from a functionally orientated management model to a process based approach. Implementation of the approach will be considered, as will the development of tools to support this implementation. Consideration will also be given to its implementation and to how the methodology (application framework) may be modified via an iterative cycle of implementation – feedback – redesign cycle, although the rollout of this cycle is not possible within the timeframe of the research. However, a validation of the proposed framework is presented.

1.4 Research Methodology

In order to achieve the objectives set out above, a series of specific steps are undertaken. An extensive review of the literature addressing issues relating to the management of quality, environmental, and health & safety systems is undertaken. This includes regulatory and legislative requirements, standards,

and best practice, as well as integrated management systems and system audits. An exploratory case study elicits reasons why a particular company is not willing to integrate its management systems. On foot of the results of this case study, a questionnaire-based survey of medical device and pharmaceutical manufacturers is conducted in order to examine the extent of integration of Quality, Environment and Health & Safety management systems within these sectors. As well as determining the extent of integration of QEH&S management systems, the survey seeks to determine if such companies believe integration is desirable and feasible. Where integration does not exist or is not deemed desirable or feasible, the survey endeavours to elicit the perceived barriers to integration.

In order to gain a deeper understanding of the issues and to identify the needs and requirements of these manufacturing organisations, further case studies are conducted. A business process modelling tool (IDEFØ) is used to generate the current state of the organisations studied. Together with the data obtained from the questionnaire, case studies and the literature, IDEFØ is also used to generate a framework for the proposed future state of Integrated QEH&S management within these manufacturing sectors.

1.5   Thesis Structure

This thesis is structured as follows:

This introductory chapter outlines the rationale for the research, its aims and objectives, and briefly outlines the research approach adopted.

Chapters two, three, four and five contain reviews of the pertinent literature. Chapter two provides a brief history of the quality movement before proceeding to a review of specific quality regulations governing medical device and pharmaceutical manufacture. Chapter three presents a review of the literature on safety and safety systems, whilst chapter four is focussed on environmental

concerns. Chapter five extends these reviews to include the literature on integrated management systems.

Chapter six details the fieldwork and analytical methodologies employed. It describes the rationale for using both survey and case study methodologies and it describes the use of the IDEFØ modelling language as a tool for mapping the case study data.

Chapter seven presents the results of the field work undertaken. Analysis of the survey data provides an overview of the state-of-play within the Irish medical device and pharmaceutical sectors with respect to the level of integration of their Quality, Environmental, and Health & Safety management systems. This chapter also details the outcomes from the case studies undertaken.

Based on key findings from the literature review and outcomes from the work reported in chapter seven, chapter eight lays out a framework for systems integration. This framework identifies how a highly regulated organisation can adopt an integrated risk management approach within its corrective and preventive action (CAPA) system, which will ensure protection for the product, the process and the environment. Chapter nine offers a validation for this framework.

Finally, chapter ten presents a discussion and provides a conclusion to the research undertaken. An overview of the work completed is provided, together with a brief summary of the more significant findings. Limitations of the research and recommendations for future research are also given.

Chapter 2:   **Literature Review - Focus on Quality**

2.1 Introduction

This chapter will present the requirements on medical devices and pharmaceutical manufacturers in relation to the management of quality. Pharmaceutical and medical device manufacturers must ensure that their products are fit for use and do not place patients at risk due to inadequate safety, quality or efficacy. The means by which this is achieved is through the implementation of rigorous quality systems which are a legislative and regulatory requirement. As part of the product approval process, firms must undergo stringent auditing of their quality management systems. This chapter outlines for the reader the main regulatory requirements on companies in these sectors in respect of managing quality. Because many firms use international standards to meet these requirements, the reader is also introduced to the main elements and recent changes to the ISO 9001 standard for quality management systems.

2.2 The Quality Movement

Quality is often defined as "fitness for use" and/or "conformance to requirements". The quality revolution as we know it today, began in the United States during the 1920's under Walter A. Shewart, gaining momentum during World War 2, only to witness a demise during the strong economic activity after the war. At the end of World War 2, the quality movement again gained prominence, but this time in Japan. Devastated by the war, the United States offered assistance to the Japanese to rebuild their nation. Part of this assistance was in the form of classes in industrial and scientific management. Initially led by W. Edwards Deming's teachings on statistical methods and later complimented by the provision of Joseph J. Juran's management tools, the Japanese generated a paradigm shift which saw their manufacturing base move from one of cheap, shoddy production to one synonymous with producing innovative, quality products. The Japanese used the ideas of Deming and Juran as the foundation for

their system of quality management which led to Japan and the Pacific Rim countries becoming major economic powers.

Since its inception many tools have been developed to support the 'quality approach'; the core one being the Plan, Do, Check, Act (PDCA) cycle. The components of this cycle are described as follows:

- **Plan:** establish objectives and processes necessary to deliver the required results.

- **Do:** implement the processes.

- **Check:** monitor and measure processes against policy, objectives, targets, legal and other requirements, and report these results.

- **Act:** take actions to continually improve performance of the quality management system.

This system can be represented graphically as per Figure 1.
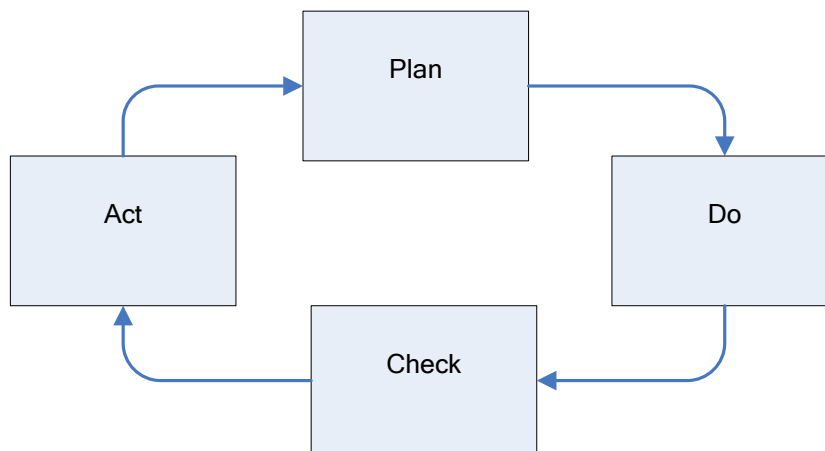
Figure 1. The Plan, Do, Check, Act Cycle

According to Dennis (1997), this cycle is based on an objective assessment of the current status; a clear understanding of the desired state and the gap between the two; and a plan to bridge that gap. The PDCA cycle is supported by quality tools such as flowcharts, check sheets, Ishikawa diagrams and control charts

through to a host of other approaches such as benchmarking, teamwork, the 5 S's, Six Sigma and World Class Manufacturing (WCM).

2.3   International Standardisation

Quality has become a universal concern for all businesses and organisations. The adoption of quality system standards such as ISO 9000 has been widespread globally. The International Organisation for Standardisation (ISO) began operations in 1947 having been preceded by the International Electrotechnical Commission (IEC) and the International Federation of the National Standardising Associations (ISA). ISO is a non-governmental organization. The objective of ISO is "to facilitate the international coordination and unification of industrial standards". Consensus agreements are achieved between national delegations representing all the economic stakeholders concerned - suppliers, government regulators and other interest groups. They agree on specifications and criteria to be applied consistently in the classification of materials, in the manufacture and supply of products, in testing and analysis, in terminology and in the provision of services. In this way, international standards provide a reference framework, or a common technological language, between suppliers and their customers - which facilitates trade and the transfer of technology. ISO standards and guidelines form the basis of many management systems. ISO is the world's largest developer of standards, having a total portfolio at the end of 2009 of 18,000 international standards (ISO, 2008). One of the most well-known of these is the ISO 9000 family of quality management systems standards.

2.4   ISO 9000 and the Process Approach

The ISO 9000 family of standards comprises of four components:
   (1) ISO 9000, *Quality management systems – Fundamentals and vocabulary.* This standard introduces fundamental concepts relating to quality management, such as the rationale for a quality management system (QMS); the quality management systems approach; quality policy and

objectives; and the need for QMS evaluation. The standard also outlines the vocabulary used in the ISO 9000 family of standards and provides definitions of terms used.

(2) ISO 9001, *Quality management systems – Requirements.* This standard specifies requirements for quality management systems in terms of general requirements, requirements for documentation, the responsibilities of management, management of resources, product realisation, as well as the measurement, analysis and improvement of processes.

(3) ISO 9004, *Quality management systems – Guidelines for performance improvements.* This standard provides guidelines which go beyond the requirements of ISO 9001 above, in order to consider both the effectiveness and efficiency of a QMS and hence the potential for improvement of an organisation's performance.

(4) ISO 19011, *Guidelines for quality and/or environmental management systems auditing*. This standard provides guidance on the principles of auditing, managing audit programmes, conducting quality management system audits and environmental management system audits. The overlap between the quality management system and the environmental management system is evident in these guidelines, which provide guidance on the competence of quality and environmental management system auditors.

ISO 9001, the operational standard from manufacturing organisations, was first published in 1987 and revised in 1994. These two editions focused on enabling an organisation to produce the same quality of products every time by specifying the policy, procedures and job instructions in a quality manual.

The ISO 9000 family of International standards saw a major revision with the publication of ISO 9000:2000 (withdrawn and superseded by ISO 9000:2005).

According to the International Organisation for Standardisation, the reasons for the revisions were to:

- Emphasise the need to monitor customer satisfaction

- Meet the need for user-friendly documents

- Assure consistency between quality management system requirements and guidelines

- Promote the use of generic quality management principles by organisations, and enhance their compatibility with ISO 14001, the environmental standard.

2.4.1 Quality Management Principles

Whereas earlier editions of ISO 9001 included twenty quality management principles, the revised standard reduced these to eight.

1. Customer focus

"Organisations depend on their customers and therefore should understand current and future customer needs, should meet customer requirements and strive to exceed customer expectations."

2. Leadership

"Leaders establish unity of purpose and direction of the organisation. They should create and maintain the internal environment in which people can become fully involved in achieving the organisation's objectives."

3. Involvement of people

"People at all levels are the essence of an organisation and their full involvement enables their abilities to be used for the organisation's benefit."

4. Process approach

"A desired result is achieved more efficiently when activities and related resources are managed as a process." This principle will be dealt with in more detail later in this chapter as it is key to the development of the framework proposed at the end of this work.

5. Systems approach to management

"Identifying, understanding and managing interrelated processes as a system contributes to the organisation's effectiveness and efficiency in achieving its objectives."

6. Continual improvement

"Continual improvement of the organisation's overall performance should be a permanent objective of the organisation."

7. Factual approach to decision making

"Effective decisions are based on the analysis of data and information."

8. Mutually beneficial supplier relationships

"An organisation and its suppliers are interdependent and a mutually beneficial relationship enhances the ability of both to create value."

Subsequent revision of the Standard to its current ISO9000:2005 maintains these principles. (ISO 9000:2000 and ISO 9000:2005).

According to Hoyle and Thompson (2001) the main contrasts between the older and newer approaches may be delineated as follows (Table 1):

Table 1. Contrast between the old and new approaches of ISO 9001

Old Approach	New Approach
No clearly defined and communicated organisational purpose and objectives	Everyone understands the organisation's purpose and objectives and is motivated and supported to achieve them
No marketing process and customer satisfaction measurement within the QMS	Marketing process integrated in QMS and customer satisfaction regularly monitored
People are just another resource to be used to achieve the results	People are valued, developed and results achieved through team work
There is a set of random task based	Processes are designed to achieve

procedures that are independent of the business objectives	defined objectives and are continually measured, reviewed and improved
The system for achieving quality is defined by the 20 elements of ISO 9001:1994	Delivering business results is achieved through a coherent management system of integrated processes
Continual improvement is perceived as correcting mistakes only	Continual improvement is perceived as proactively seeking opportunities to improve performance at all levels and in all aspects
Data generated by the QMS creates records that are not used to make decisions	Decisions are based on performance data generated by the processes of the management system
Key decisions are made in an arbitrary and unilateral manner with purchasing decisions being based primarily on lowest price	Key decisions take into account the different stakeholders and the impact of these decisions are considered

One of the major changes in emphasis between ISO 2001, as published in 1994 and ISO 9000:2005 relates to the introduction in Principle 4 of the so-called 'process approach'. This principle is based on the premise that a desired result is achieved more efficiently when activities and related resources are managed as a process. ISO 9000:2005 clause 3.4.1 defines a "Process" as a "set of interrelated or interacting activities which transforms inputs into outputs". The ISO 9000:2005 Standard provides the following model of a process-based quality management system (Figure 2).

Figure Removed for Copyright Reasons

Figure 2. Model of a Process-based Quality Management System

(Source: ISO 9000:2005)

The rationale for the process approach is that organisations have traditionally been structured into a hierarchy of functional units. They are usually managed vertically, with responsibility for the intended outputs being divided among these functional units. The end customer or other interested party is not always visible to everyone involved. Consequently, problems that occur at unit interfaces are often given less priority than the short-term goals of the units. This leads to little or no improvement for the interested party, as actions are usually focused on the unit, rather than on any overall benefit to the organisation. The process approach introduces horizontal management, crossing the barriers between different functional units and unifying their focus to the main goals of the organisation. This approach is what ISO terms a "systems approach" to management (ISO/TC 176/SC 2/N544R2). Figure 3 compares the old approach based on functional units with the new process-based approach.

Figure Removed for Copyright Reasons

Figure 3. Process Linkages across Departments in an Organisation

(Modified from ISO/TC ISO 9000 Guidance on the Concept and Use of the Process Approach for management systems).

The benefits of the process approach, according to ISO, are;

1. The integration and alignment of processes to enable the achievement of planned results.

2. The ability to focus effort on process effectiveness and efficiency.

3. Providing confidence to customers, and other interested parties, about the consistent performance of the organisation.

4. Making operations transparent within the organisation.

5. Lowering costs and creating shorter cycle times, through the effective use of resources.

6. Achieving improved, consistent and predictable results.

7. Providing opportunities for focused and prioritised improvement initiatives.

8. Encouraging the involvement of people and the clarification of their responsibilities.

The ISO intend the process approach to be applicable to any management system including management systems for Environment and Occupational Health and Safety.

The Process Approach to managing systems is central to the way ISO requires quality systems to be managed. The approach recognises that all work is performed to achieve some objective and this objective is realised more efficiently when resources and activities are managed not as discrete entities but as an integrated process. An earlier emphasis on documentation has been replaced by an emphasis on meeting business objectives. Each organisation determines the extent of documentation now required, which is dependent on the type and size of the organisation; the complexity of products; customer requirements; the applicable regulatory requirements; as well as the ability of personnel and the extent to which it is necessary to demonstrate fulfilment of quality management system requirements. It is a significant departure from the earlier notion of 'document what you do and do what you document' and therefore presents new challenges for organisations.

These considerations are key to the framework developed in this dissertation. This will be demonstrated as the requirements on medical device and

pharmaceutical companies to rigorously manage their quality systems becomes evident in subsequent sections.

2.5 Regulatory Requirements in the Pharmaceutical Industry

The pharmaceutical industry differs from general manufacturing industries because the products are viewed not just as industrial goods, but also as a tool of public health. Because of this the industry is highly regulated. Pharmaceutical manufacturers must ensure that products are fit for their intended use and do not place patients at risk due to inadequate safety, quality or efficacy. The means by which this is achieved is through the implementation of rigorous quality systems which are required by legislative and regulatory authorities and overseen by these authorities. However, as an industry sector it must remain competitive, without compromising patients' access to medicines at an affordable cost. According to the European Commission in 2003 (Commission of the European Communities, 2003), "Europe is lagging behind [the USA] in its ability to generate, organise and sustain innovative processes".

This section outlines for the reader the quality requirements on pharmaceutical manufacturers in Ireland. As Ireland comes within the remit of European legislation, European Union requirements will be outlined. Many pharmaceutical manufacturers in Ireland are either part of a United States multinational or are exporting into the U.S., or both, and therefore US requirements are also outlined.

2.5.1 European Union Regulatory Requirements

As already stated, pharmaceutical manufacturers must ensure that products are fit for their intended use and do not place patients at risk due to inadequate safety, quality or efficacy. The first European Community pharmaceutical directive was issued in 1965 and has since been built upon with the aim of ensuring that medicinal products for human use maintain a high level of

protection for public health. Much of the impetus behind the original directive stemmed from a determination to prevent a recurrence of the thalidomide disaster in the early 1960's, when thousands of babies were born with limb deformities as a result of their mothers taking thalidomide as a sedative during pregnancy. It was decided that in order to safeguard public health, medicinal products would never again be marketed without prior authorisation. Directives which followed, whilst striving to safeguard public health, also sought to create (in line with European objectives) a single market for pharmaceutical products. The mechanism adopted to achieve this was via the imposition of an authorisation process. Two routes exist for authorisation of medicinal products: one is mutual recognition of national marketing authorisations; the other is a centralised procedure where applications are made directly to the European Agency for the Evaluation of Medicinal Products (more commonly known as the European Medicines Evaluation Agency – EMEA).

The EMEA is a decentralised body of the European Union with headquarters in London. As stated above, it provides for a mutual recognition procedure for authorising medicinal products. Its key aims are the protection and promotion of public health by providing safe and effective medicines for human and veterinary use whilst at the same time harmonising scientific requirements so that pharmaceutical research worldwide can be optimised. Following the EMEA's success in harmonising regulatory requirements within the European Union (EU), the International Conference on Harmonisation of Technical Requirements for the Registration of Pharmaceuticals for Human Use (ICH) was established in 1990. This broadened the scope of harmonisation to include the United States and Japan as well as the European Union. To date, technical requirements for demonstrating the quality, safety and efficacy of new medicines have been almost fully harmonised throughout these three regions.

This section however, will focus on European regulation. Within the European Union, a series of rules exist which govern medicinal products. This series of rules

is called Eudralex. There are four volumes in the series covering medicinal products for human use and three covering veterinary medicinal products. The fourth volume in the series is concerned with medicinal products for Human Use: Good Manufacturing Practices, commonly referred to as GMP. According to this, in order to achieve the required quality reliably there must be a comprehensively designed and correctly implemented system of Quality Assurance (QA) incorporating Good Manufacturing Practice (GMP), Quality Control (QC), and Quality Risk Management.

These basic concepts and allied activities are inter-related and are described as follows:

Quality Assurance: Quality Assurance is a wide-ranging concept which covers all matters influencing the quality of a product. It is the sum total of all arrangements made with the objective of ensuring that products are of the quality required for their intended use. It therefore incorporates Good Manufacturing Practice.

Good Manufacturing Practice (GMP): Good Manufacturing Practice (GMP) is that part of Quality Assurance which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use. GMP is concerned with both production and quality control. It has its legislative basis in EU Directive 2003/94/EC (Medicinal Products for Human and Veterinary Use: Good Manufacturing Practice). The basic requirements are that;

- All manufacturing processes are clearly defined and systematically reviewed to ensure consistent manufacturing of products to the required quality;
- Critical steps of the manufacturing processes and significant changes to the process are validated;
- All necessary facilities for GMP are provided, including:

- o appropriately qualified and trained personnel;

- o adequate premises and space;

- o suitable equipment and services;

- o correct materials, containers and labels;

- o approved procedures and instructions;

- o suitable storage and transport;

- Instructions and procedures are clear and unambiguous;

- Operators are trained to carry out procedures correctly;

- Records are made during manufacture which demonstrate that all the steps required by the procedures and instructions were in fact taken and that the quantity and quality of the product were as expected. Any significant deviations are fully recorded and investigated;

- Records of manufacture are retained to facilitate traceability;

- The distribution of the product is controlled to minimise any risk to its quality;

- A product recall system is in place;

- Complaints about marketed products are examined, the causes of quality defects investigated and appropriate measures taken in respect of the defective products and to prevent reoccurrence.

Quality control: Quality Control is the part of GMP concerned with sampling, specifications and testing. Documentation and release procedures ensure the necessary tests are carried out so that products are not released for sale or supply, until their quality has been judged to be satisfactory. Quality Control is not confined to laboratory operations but must be involved in all decisions which may concern the quality of the product. The independence of Quality Control from Production is considered fundamental to the satisfactory operation of Quality Control (Eudralex Vol. 4 Chp. 1: Quality Management).

Quality Risk Management: Quality Risk Management is described as a systematic process for the assessment, control, communication and review of risks to the quality of the medicinal product. It can be applied both proactively and retrospectively. The Quality risk management system should ensure that the evaluation of the risk to quality is based on scientific knowledge, experience with the process and that the level of effort, formality and documentation of the quality risk process is commensurate with the level of risk. (European Commission, 2008).

2.5.2   Irish Regulatory Requirements

Within Ireland, the Irish Medicines Board (IMB) regulates pharmaceutical companies. The objective of the Irish Medicines Board is to ensure the quality, safety and efficacy of medicines available in Ireland and to collaborate within the European Union. Before a medicinal product can be authorised for use, an application must be made to the Irish Medicines Board and this must contain all of the necessary data supporting its quality, safety and efficacy. There are two main areas where the IMB are involved: product licensing and establishment licensing. A facility wishing to manufacture or wholesale medicinal products for human use may do so only if it is in possession of a Manufacturer's Licence or a Wholesale Licence which has been issued by the IMB. The EU has issued guidance documents for the conduct of activities by manufacturers or wholesalers of medicinal products, known as the Good Manufacturing Practice (GMP) guidelines (detailed previously), and Good Distribution Practice (GDP) guidelines, respectively. The Inspectorate of the IMB inspects facilities to ensure their operations comply with these GMP/GDP guidelines. The Compliance Department of the IMB also inspects facilities which produce Investigational Medicinal Products (IMPs) and those producing Active Pharmaceutical Ingredients (APIs). It also inspects Contract Laboratories which perform tests for medicinal product manufacturers. Manufacturers of IMPs must hold a Manufacturer's Licence from the IMB just as those involved in the manufacture

or wholesale of medicinal products. Although the API manufacturer's and contract laboratories do not require a manufacturing authorisation, the Irish Medicines Board will only issue a certificate of compliance following a successful inspection.

The Compliance Department of the IMB requires sufficient initial information from the manufacturer or wholesaler to enable them to perform an assessment of the application with respect to its potential adequacy and suitability. If an inspection of the applicant's premises and/or Quality System is deemed necessary to process the application, an inspection is carried out, documented and reported. Generally, an inspection is *always* performed for an application for a new licence, *occasionally* for an application for a variation to a licence, and *generally not* for an application to renew a licence unless a recent general re-inspection has not been performed. This inspection is conducted by the Compliance Department to establish compliance with GMP and/or GDP requirements, as defined in European legislation and guidelines.

If the inspection concludes that the manufacturer or wholesaler is operating in compliance with the appropriate EU legislation and guidelines, a recommendation for approval of the application is referred to the Management Committee of the IMB. In addition, manufacturers of medicinal products in non-EU countries (known as "third countries"), from which medicinal products are imported into the state, may be inspected to assess compliance with GMP requirements. Inspections may also be performed in another EU country, or non-EU third country, on the request of the European Medicines Agency (EMEA) where a pre-authorisation GMP inspection of a manufacturer of a medicinal product is considered necessary (Irish Medicines Board, 2010).

2.5.3   Mutual Recognition Agreements (MRAs)

Mutual Recognition Agreements (MRAs) are used to facilitate transatlantic trade whilst reducing costs for compliance with regulatory requirements. MRAs work on the basis of determining the equivalence of regulatory requirements. Once equivalence has been determined, either party to an MRA should be able to recognise the other party's assessment. The underlying premise behind all MRAs for GMP compliance certification is that it can be demonstrated that the EC member states and the third party countries have equivalent GMP compliance programmes. If a Certificate of Manufacturing Authorisation/Licence is issued by the authority in one country, this is the only evidence required for accepting that facility as being compliant by the other country. Again, a compliance programme will include regulatory requirements, standards, processes, and quality systems. The general principles governing Mutual Recognition Agreements are detailed in European Directive 2001/83/EC. The EU commission has also published guidance documentation in 'The Rules Governing Medicinal Products in the European Community. The Notice to Applicants, Volume 2A Procedures for Marketing Authorisation (European Commission, 2007).

2.5.4   United States Requirements on Pharmaceutical Companies

As stated previously, many Irish pharmaceutical manufacturers come within the remit of United States regulation. The Food and Drug Administration (FDA) is the United States' scientific, regulatory, and public health agency that oversees the manufacture of food products (other than meat and poultry), human and animal drugs, therapeutic agents of biological origin, medical devices, radiation-emitting products for consumer, medical and occupational use, cosmetics, and animal feed (Swann, J., 1998). As a law enforcement organisation it dates back to 1906. In 1927 the United States Congress authorised the formation of the Food, Drug, and Insecticide Administration whose name was shortened to Food and Drug Administration in 1930. Following a series of moves between government

departments, the FDA now finds its home within the Department of Health and Human Services.

One of the landmark U.S. pieces of legislation was the Food and Drugs Act 1906. This law was enacted on foot of serious problems in the supply of food and drugs. Shortcomings in the law however, were still evident even after its enactment, and so in 1938 the law was replaced by the Food, Drug, and Cosmetic Act, which remains the basic law in force today. This Act differed from previous acts in that it mandated that all new drugs be proved safe before marketing. It also expanded its scope to include therapeutic devices and cosmetics and it mandated that standards of identity and quality be instituted for foods. The law also formalised the FDA's right to conduct factory inspections. Over the following decades numerous acts and amendments broadened the FDA's responsibilities and included provisions for testing insulin and antibiotics; regulation of chemical pesticides; distinction between prescription and non-prescription medications; regulation of drug efficacy; and ensuring good manufacturing practices (Swann, J., 1998). Within the FDA, the Center for Drug Evaluation and Research (CDER) oversees the pharmaceutical industry. CDER is involved in four major activities: new drug development and review; generic drug review; over-the-counter drug review; and post drug approval activities. The array of regulated products extends over 300,000 facilities in more than 150 countries. http://www.fda.gov/About FD/ReportsManualsForms/Reports/ucm227527.htm

2.5.5   FDA Approval

The approach used by the FDA to oversee the quality of drug products involves both a review of information submitted in applications as well as the inspection of manufacturing facilities to ensure they conform to current Good Manufacturing Practice (cGMP) requirements. However, over the last two decades, significant changes have occurred in the regulatory environment which has led to the FDA seeking new approaches to approval. Recent years have seen

an increased number of pharmaceutical products and a greater role for medicines in health care. However, this increase in pharmaceutical production has not been matched by an equivalent increase in resources available for pharmaceutical manufacturing inspections and so the frequency of FDA manufacturing inspections has decreased. The increasing complexity of pharmaceutical sciences such as complex drug and drug delivery systems, biotechnology, nanotechnology, and drug-device combinations etc., has placed an even greater strain on resources. Furthermore, advances in the science and management of quality, together with the FDA's own experience in regulating product quality, has led the FDA to undertake a systematic reappraisal of its approach to product quality regulation. The main purpose of this reappraisal is to ensure that the most up-to-date quality systems approaches are utilised to ensure product quality. Guiding the implementation of the FDA reappraisal are:

- *Science-based policies and standards;* FDA aim to undertake a thorough evaluation of advances in the pharmaceutical sciences and manufacturing technologies to ensure product quality regulation and contribute to the assessment of risk.

- *Integrated quality systems orientation;* principles from various innovative approaches to manufacturing quality will be evaluated as well as current Good Manufacturing Practices (cGMP) requirements and pre-approval requirements.

- *International cooperation;* the globalisation of pharmaceutical manufacturing requires a global approach to regulation and so FDA will collaborate with other regulatory authorities.

- *Strong Public Health Protection;* FDA's approach, which aims to strengthen public health protection, will not interfere with the enforcement of existing regulatory requirements.

- *A Risk-based orientation;* FDA must match its level of effort against the magnitude of risk.

Matching the level of effort against the magnitude of risk is important as resource limitations prevent uniformly intensive coverage of all products and production. Although the agency already implements risk-based programmes, they are working towards developing a more systematic and rigourous risk-based approach. This new risk-based orientation was first emphasised in a report produced by the FDA titled "Pharmaceutical cGMPs for the 21st century – a risk-based approach". (FDA, 2004). This report was prompted by the fact that the last major revision of the cGMP regulations was published in 1978 and although many advances had been made in manufacturing technologies and in quality systems, these were not reflected in the regulations. Furthermore, pharmaceutical manufacturing was becoming increasingly costly and inefficient. Static manufacturing processes, and a focus on testing as opposed to "quality by design", was keeping the system in a corrective action mode. The industry has been hesitant to introduce innovative systems (such as new technological advances and modern quality management techniques) into the manufacturing sector due to the perception that the existing regulatory system is rigid and unfavourable to innovation. Regulatory policies were not keeping pace with technological advances and the time to market for new and essential drugs was increasing. The aim of the new initiative is to incorporate the most up-to-date concepts of quality systems and risk management approaches into pharmaceutical manufacture. This initiative is based on the realisation that quality cannot be tested into a product but it must be assured through "quality by design". The FDA has recently issued its strategic priorities for 2011-2015 (FDA, 2010). In this document, they again emphasise how the growing challenges of globalisation have far outstripped their capacity for inspection and quality monitoring as well as an inability to maintain adequate oversight. They realise how this will lead to the potential for risk to consumers. The FDA emphasise that addressing these challenges will require a paradigm shift – to a focus on prevention. This must be based on more detailed information about product supply chains and regulatory standards which will foster corporate

responsibility to identify, protect and control risks. This will, according to the report, require updated systems and novel and updated enforcement tools.

2.5.6   FDA and Quality Systems

The FDA has adopted the concepts of 'modern' quality systems. These include the following:

- *Quality* – i.e. the quality characteristics of the product which ensure required levels of safety and effectiveness.

- *Quality by Design and Product Development* – i.e. consistency attaining a predefined quality.

- *Quality Risk Management* – which will mitigate the risk of changing a process or specification and which will determine the extent of discrepancy investigations and corrective actions.

- *CAPA (Corrective and Preventive Action)* – this is threefold: remedial corrections of an identified problem; root cause analysis; and preventive action to avert recurrence.

- *Change control* – managing change to prevent unintended consequences.

- *The Quality Unit* – dividing responsibility between quality control (QC), generally associated with the product; and quality assurance (QA), generally associated with procedures.

At the end of September 2006, the FDA issued a guidance document entitled "Guidance for Industry: Quality Systems Approach to Pharmaceutical Current Good Manufacturing Practice Regulations" in which the FDA set out its intent to integrate quality systems and risk management approaches into existing programmes. The guidance document does not recommend new regulatory requirements; rather it outlines a quality systems model which will allow manufacturers to operate a robust, modern quality system which is fully compliant with cGMP regulations (21 Code of Federal Regulations parts 210 and 211). It is a systems-based approach to inspection, with the underlying

philosophy being one of Quality by Design i.e. "Quality should be built into the product, and testing alone cannot be relied on to ensure product quality". In this document the FDA describes the relationship between the quality system and five other 'manufacturing' systems. It presents the production, facilities and equipment, laboratory control, materials and the packaging and labelling systems as overlapping systems with the quality system overriding all of these. The six systems are described as follows:

- *Quality System* – which assures overall compliance with cGMPs (Mandatory inspection).

- *Facilities and Equipment System* – which includes the physical environment and resources used in the production of the drugs.

- *Materials System* – which includes measures and activities to control finished products or components that are incorporated into the product or its containers.

- *Production System* – which includes measures and activities to control the manufacture of the drugs.

- *Packaging and Labelling System* – which includes measures and activities that control the packaging and labelling of the drugs.

- *Laboratory Control System* – which includes activities related to laboratory procedures, testing, validation etc.

The FDA's representation of the Quality Systems Model is shown in Figure 4.

Figure Removed for Copyright Purposes

Figure 4. FDA Six-System Inspection Model

(Source: Food and Drug Administration, Guidance for Industry: Quality Systems Approach to Pharmaceutical Current Good Manufacturing Practice Regulations, September 2006)

The diagram illustrates the inter-relationship between the six systems - the quality system and the five manufacturing systems. The quality system provides the foundation for the manufacturing systems controls that are linked and function within it. The quality system model described in this FDA guidance document does not consider the five manufacturing systems as discrete entities, but instead integrates them. The systems-based approach to inspection advocates the auditing of two or more of the systems, with mandatory inspection of the Quality System. This should allow an organisation assess whether each of the systems is in a state of control.

Within this quality systems model, the concept of risk management and risk assessment is a major focus. Risk management can guide the setting of specifications and process parameters; risk assessment can determine the need for discrepancy investigations and corrective actions. The quality systems model is organised around four main sections: management responsibilities; resources; manufacturing operations; and evaluation activities. This is outlined in Figure 5 below.

Figure Removed for Copyright Reasons

Figure 5. FDA Quality Systems Model

(Compiled from: Food and Drug Administration, Guidance for Industry: Quality Systems Approach to Pharmaceutical Current Good Manufacturing Practice Regulations, September 2006)

This new approach derives from the FDA's conclusion that modern quality systems, when coupled with manufacturing process and product knowledge, can handle many types of changes to facilities, equipment, and process without the need for a regulatory submission. Manufacturers with appropriate process

knowledge and a robust quality system should be able to implement many types of improvements without the need for a prior regulator filing. In addition, an effective quality system, by lowering the risk of manufacturing problems, may result in shorter and fewer FDA inspections. Surveillance inspections can be Full Inspections, Abbreviated Inspections, or Compliance Inspections. *Full Inspections* are carried out where little or no information is known about a firm's cGMP compliance (e.g. new firms); or for firms where there is doubt about their cGMP compliance (e.g. history of short-lived compliance and recidivism). A Full Inspection will normally include an inspection audit of at least four of the systems, of which one must be the Quality System. An *Abbreviated Inspection* is conducted to provide an updated evaluation of a firm's cGMP. This is generally conducted when a firm has a record of satisfactory cGMP compliance, with no significant recall or product defect and little shift in its manufacturing profile within the previous two years. The Abbreviated Inspection Option will normally include an inspection audit of at least two of the systems, one of which must be the Quality System. A *Compliance Inspection* is undertaken to evaluate or verify compliance corrective actions after a regulatory action has been taken. It must cover the areas found deficient and subject to corrective actions. A Full Inspection should be used for compliance inspection. As part of its corrective action plan, the firm is expected to address not just the deficiencies noted in the FDA report, but all of its operations.

The FDA also realises the importance of harmonising cGMPs with other widely used quality management systems including ISO 9000 and quality system regulations governing medical devices production. Recognising how crucial it is to have international harmonisation of quality standards, the FDA collaborates with the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).

2.5.7 International Pharmaceutical Regulation

Whilst national registration of new drug products is critical in bringing important and often life-saving treatments to patients, a single set of technical requirements will streamline the development process and ensure that these products and treatments will reach patients faster. The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) comprises the regulatory authorities of the European Union, the United States and Japan, as well as experts from the pharmaceutical industry in these three regions. The underlying philosophy of the ICH is that by achieving greater harmonisation in the interpretation and application of technical guidelines and requirements for product registration, the need for the duplication of tests in each region will be reduced or removed. Companies will therefore reduce drug development time, reduce resource requirements and improve their competitiveness.

One of the major areas addressed for harmonisation by ICH is quality, as it is believed that setting a common quality standard will help companies streamline their "time/resource/quality triangle" (ICH, 2000 Value and Benefits). To aid manufacturers in improving their quality systems, the ICH have issued a series of four documents;

- Q7 Good Manufacturing Practice Guide for Active Pharmaceuticals (2000)
- Q8 (R2) Pharmaceutical Development (2009)
- Q9 Quality Risk Management (2005)
- Q10 Pharmaceutical Quality System (2009)

Q7 Good Manufacturing Practice Guide for Active Pharmaceuticals is intended to provide guidance regarding good manufacturing practice (GMP) for the manufacturing of active pharmaceutical ingredients (APIs) under an appropriate system for managing quality. It is also intended to help ensure that APIs meet the requirements for quality and purity that they purport or are represented to

possess. It outlines quality management principles and the responsibilities of the quality units i.e. quality control and quality assurance (these units to be independent of production).

Q8 (R2) Pharmaceutical Development sets out the basic philosophy of pharmaceutical development where the aim is to design a quality product and a manufacturing process which will consistently deliver the intended performance from the product. Quality cannot be tested into products but should be built in by design. Information from pharmaceutical development studies can be a basis for Quality Risk Management. This guidance is supported by Q9, the main principles of which are detailed as follows.

Q9 Quality Risk Management is based on the systematic application of quality management policies, procedures and practices to the tasks of assessing, controlling, communicating and reviewing risk. This approach will ensure that both industry and regulators have a common understanding of Quality Risk Management (QRM) and it will facilitate communication and transparency. It will also help move away form 'fire fighting' to management of risk. A further benefit is that QRM can add value. As risk and the assessment of risk are central to this dissertation, this document will be dealt with in greater detail in the next section.

Q10 Pharmaceutical Quality System, the most recent ICH document, supports Q9 in reflecting a harmonised pharmaceutical quality system applicable across the lifecycle of the product. It also emphasises an integrated approach to quality risk management and science, particularly within the areas of

1. Management Responsibility
2. Continual Improvement of Process Performance and Product Quality
3. Continual Improvement of the Pharmaceutical Quality System

Q10 identifies Quality Risk Management and Knowledge Management as enablers to support the goals of the Pharmaceutical Quality System (PQS). These goals are identified as: achieving product realisation; establishing and maintaining a state of control; and facilitating continual improvement. The elements of the PQS include process performance and product quality monitoring; system corrective action and preventive action system (CAPA), change management system, and management review.

2.6   Quality Risk Management

Returning to the quality risk management, Q9 Quality Risk Management (ICH, 2005) outlines two primary principles of quality risk management to assist manufacturers. The first principle is that the evaluation of risk to quality should ultimately link to the protection of the patient. Secondly, that the level of effort, formality and documentation of the quality risk management process should be commensurate with the level of risk and should be based on scientific knowledge. The Q9 document presents a general quality risk management process with an emphasis on risk assessment, risk control, and management review. This is represented in Figure 6.

Figure Removed for Copyright Reasons

Figure 6. Overview of Quality Risk Management Process (ICH Q9)
(Source: ICH, 2005)

ICH Q9 states that risk management activities are usually, but not always, undertaken by interdisciplinary teams. Teams formed for quality risk management activities should include experts from the appropriate areas involved in addition to individuals who are knowledgeable of the quality risk

management process. According to Q9, in initiating a quality risk management process, possible steps might be:

- Define the problem and/or risk question, including pertinent assumptions identifying the potential for risk;

- Assemble background information and data on the potential hazard, harm or human health impact relevant to the risk assessment;

- Define how decision makers will use the information, assessment and conclusions;

- Identify a leader and necessary resources;

- Specify a timeline and deliverables for the risk management process.

As detailed in figure 6, risk management includes risk assessment, risk control, risk communication and risk review.

- **Risk assessment** consists of the identification of hazards and the analysis and evaluation of risks associated with exposure to those hazards. It attempts to answer the following questions:

  What might go wrong?

  What is the likelihood (probability) it will go wrong?

  What are the consequences (severity) if it does go wrong?

- **Risk control** includes decision making to reduce and/or accept risks. The purpose of risk control is to reduce the risk to an acceptable level. The following questions can be addressed:

  Is the risk above an acceptable level?

  What can be done to reduce, control or eliminate risks?

  What is the appropriate balance among benefits, risks and resources?

  Are new risks introduced as a result of the identified risks being controlled?

- **Risk communication** is the exchange or sharing of information about risk and its management between the decision makers and others. This communication could include the existence of the risk, its nature and

form, the probability of it happening and its likely severity should it happen, its detectability, acceptability, treatment etc. The output of the quality risk management process should be documented when a formal process has been utilised.

- **Risk Review** suggests that the output of the risk management process should be reviewed to take into account new knowledge and experience. This review should consider events that are planned (e.g. results of product review, inspections, audits, change control) and events which are unplanned (e.g. root cause analyses from failure investigations, recall etc.). Reviews should take place periodically, the frequency to be determined by the level of risk.

2.7   Key Findings: Quality in the Pharmaceutical Sector

The greater role of medicines in health care and the associated increase in the number of pharmaceutical products coupled with the increasing complexity of pharmaceutical science is presenting new challenges to both manufacturers and regulators. The compliance system in this sector is seen to inhibit or prevent innovation, and quality improvements are often not implemented due to compliance concerns. The FDA has recognised these constraints and has been to the forefront in proposing a new risk-based approach to quality management. This approach is built on the FDA's conclusion that modern quality systems, when coupled with manufacturing processes and product knowledge, can handle many types of changes to facilities, equipment, and processes without the need for a regulatory submission. Manufacturers with appropriate process knowledge and a robust quality system should be able to implement many types of improvements without the need for a prior regulatory filing. In addition, an effective quality system, by lowering the risk of manufacturing problems, may result in shorter and fewer FDA inspections. The FDA also realises the importance of harmonising cGMPs with other widely used quality management systems including ISO 9000 and the FDA's medical device quality system

regulations. The ICH has also recognised that setting a common quality standard will help companies streamline their "time/resource/quality triangle". They propose an interdisciplinary quality risk-management process based on risk assessment, risk control and management review. The new quality paradigm is based on a sound combination of science (enhanced scientific knowledge), use of risk management tools and the establishment of an efficient Quality System.

2.8 Quality Requirements in the Medical Device Industry

In a similar vein to the previous section, the following paragraphs outline for the reader the quality requirements for medical device manufacture in Ireland. Again, EU and US requirements are described.

A medical device is defined in European legislation as any instrument, apparatus, appliance, material or other article, whether used alone or in combination, together with any accessories, including the software intended by its manufacturer to be used specifically for diagnostic and/or therapeutic purposes and necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of:

- Diagnosis, prevention, monitoring, treatment or alleviation of disease
- Diagnosis, monitoring, treatment, alleviation of, or compensation for an injury or handicap
- Investigation, replacement or modification of the anatomy, or of a physiological process
- Control of conception (Directive 2007/47/EC).

2.8.1 European Union Regulations Governing Medical Devices

Within the European Union the manufacture of general medical devices is governed by a number of Directives. Directive 2007/47/EC (commonly referred to as the Medical Devices Directive or MDD) is concerned with General Medical Devices. This Directive classifies medical devices into three classes corresponding to their risk category - low, medium, and high risk categories.

- **Class 1** – these devices are those that pose a low risk to the patient and generally do not enter into contact or interact with the body.

- **Class 11a** – these devices are of a medium risk and are invasive in their interaction with the human body, but the methods of invasion are limited to natural body orifices.

- **Class 11b** – these devices are of medium risk and are either partially or totally implantable within the human body and may modify the biological or chemical composition of body fluids.

- **Class 111** – these devices are of high risk and require design/clinical trial reviews. They generally affect the functioning of vital organs and/or life-support systems.

This and subsequent Directives such as the Active Implantable Medical Devices Directive (AIMDD) and the *In-vitro* Diagnostic Medical Devices Directive (IVDD), are intended to ensure the safety and performance of medical devices and to prohibit the marketing of devices, which may compromise the health and safety of patients and users. The means by which this is to be achieved is stated in the Medical Devices Directive and includes:

- Specifying "Essential Requirements" which must be met before the device is put on the market
- Introducing safety, performance, specification, design, manufacture and packaging controls
- Evaluating adverse incidents
- Empowering a Competent Authority to designate "Notified Bodies" who check and verify that devices meet the relevant essential requirements. (Council Directive 2007/47/EC)

Within Ireland, the Competent Authority (CA) is the Irish Medicines Board. This body (established under the Irish Medicines Board Act 1995) has the authority to act on behalf of the government to ensure compliance with the requirements of

the Medical Devices Directives. The CA designates a Notified Body as part of the regulatory system. Such bodies are usually certification bodies with expertise in the relevant area. Within Ireland, for example, a designated Notified Body is the National Standards Authority of Ireland (NSAI). The Directives have been transposed into Irish Law through Statutory Instruments (S.I.'s). In relation to controlling quality, the designation of the Notified Body covers the following schedules and annexes (Table 2). These are expressed with reference to the Irish Statutory Instruments (Schedule), and the EU legislative equivalent (Annex to Directive).

Table 2. Schedules and Annexes Designated to Notified Body

 (Source: IMB Guidance Note 1. About the Medical Devices Department of the Irish Medicines Board, 2004)

EU Directive	Irish Statutory Instrument Schedule /EU Annex
MDD (General Medical Devices)	*Schedule 2*. EC Declaration of Conformity (Full quality assurance system) Corresponding to Annex 2 of Directive *Schedule 5*. EC Declaration of Conformity (Production quality assurance) Corresponding to Annex 5 of Directive *Schedule 6*. EC Declaration of Conformity (Product quality assurance) Corresponding to Annex 6 of Directive
AIMDD (Active Implantable Medical Devices)	Schedule 2. EC Declaration of Conformity (Complete quality assurance system) Corresponding to Annex 2 of Directive Schedule 5. EC Declaration of Conformity to type (Assurance of production quality) Corresponding to Annex 5 of Directive
IVDD (*In-vitro* Diagnostic	Annex 11 List A Virology Products (e.g. reagents and products for HIV I and II, hepatitis B, C and D) Annex 11 List B Products (e.g. reagents and products for testing

Medical Devices)	of rubella, toxoplasmosis, as well as devices for self-testing for blood sugar levels) Self Test Devices (e.g. those used by lay persons in a home environment)

These schedules lay down specific requirements for the manufacturer's quality system. These must include a description of the manufacturer's quality objectives, including the organisational structures and the responsibilities and authority of managerial staff. The methods of monitoring the quality system and the control of nonconforming product must be identified. The quality system must also address techniques of quality control and quality assurance during the production stage. The notified body audits the manufacturer's quality system and periodically carries out inspections and evaluations to ensure the approved quality system is being applied.

Devices meeting the essential requirements are entitled to carry the CE mark, which indicates conformance with the appropriate Directive. Once CE marked, these devices can be freely marketed anywhere in the European Union and European Economic Area. The main purpose of the Directives is to harmonise controls for regulating the safety and performance of devices throughout Europe by placing explicit obligations on manufacturers.

2.8.2   United States Regulations for Medical Devices

In the United States, the Food and Drug Administration (FDA) Center (*sic*) for Devices and Radiological Health (CDRH) is responsible for regulating firms who manufacture, repackage, relabel, and/or import medical devices sold in the United States. CDRH is responsible for ensuring the safety and effectiveness of medical devices and eliminating unnecessary human exposure to man-made radiation from not only medical but also occupational and consumer products. There are thousands of types of medical devices, from heart pacemakers to

contact lenses. Radiation-emitting products regulated by FDA include microwave ovens, video display terminals, and medical ultrasound and x-ray machines. The centre accomplishes its mission by:

- reviewing requests to research or market medical devices

- collecting, analyzing, and acting on information about injuries and other experiences in the use of medical devices and radiation-emitting electronic products

- setting and enforcing good manufacturing practice regulations and performance standards

- monitoring compliance and surveillance programs

- providing technical and other non-financial assistance to small manufacturers of medical devices.

The main Act governing Medical Devices in the United States is the Federal Drug and Cosmetic Act (FD&C Act) 1938. The 1976 Medical Device Amendments to this Act established three regulatory classes for medical devices. The three classes are based on the degree of control necessary to assure the various types of devices are safe and effective.

- **Class 1** – These devices present minimal potential for harm to the user and are often simpler in design that Class 11 or Class 111 devices. Examples include crutches and band aids. 47% of medical devices fall under this category and 95% of these are exempt from the regulatory process.

- **Class 11** – 43% of medical devices fall under this category. Examples include powered wheelchairs and some pregnancy test kits.

- **Class 111** – These medical devices usually sustain or support life, are implanted, or present potential unreasonable risk of illness or injury.

Examples of Class 111 devices include implantable pacemakers and breast implants. 10% of medical devices fall under this category.

The FD&C Act (Section 520 (f))authorises the FDA to "promulgate regulations requiring the methods used in, and the facilities and controls used for, the manufacturing, packing, storage, and installation of a device to conform to current good manufacturing practices (GMPs)".

Under the 1976 Medical Device Amendments to the Food, Drug and Cosmetic Act, the FDA regulates devices to ensure their safety and effectiveness by means of "General Controls". These controls include provisions relating to:

- Adulteration of the product/device
- Misbranding
- Device registration and listing
- Premarket notification
- Banned devices
- Notification and repair, replacement and refund
- Records and reports
- Restricted devices and
- Good Manufacturing Practices

The 21 Code of Federal Regulations (CFR) Part 820 – Quality System Regulation (QSR) describes the Quality requirements on medical device manufacturers. This comprises 15 subparts as per Table 3.

Table 3. Quality System Regulation (QSR)

21 Code of Federal Regulations (U.S.) Part 820 – Quality System Regulation	
Subpart	Title
A	General Provisions

B*	Quality System Requirements
C	Design Controls
D	Document Controls
E	Purchasing Controls
F	Identification and Traceability
G	Production and Process Controls
H	Acceptance Activities
I	Nonconforming Product
J**	Corrective and Preventive Action
K	Labelling and Packaging Control
L	Handling, Storage, Distribution, and Installation
M	Records
N	Servicing
O	Statistical Techniques

*Subpart B of this Code (revised April 2004) deals specifically with the requirements for the Quality System and specifically addresses management's responsibility with respect to quality policy, quality planning, the quality system, and the organisational structure in place.

**Subpart J of the Code deals with Corrective and Preventive Action.

The requirements of the Quality System (under Subpart B Part 820.20) are as follows:

- **Policy** – Management must establish its policy and objectives for, and commitment to, quality and ensure that the quality policy is understood, implemented, and maintained at all levels of the organisation.
- **Organisation** - Each manufacturer must establish and maintain an adequate organisational structure to ensure that devices are designed and produced in accordance with Quality System Requirements (QSR).

- **Responsibility** – Responsibility and authority must be given to all personnel who manage, perform, and assess work affecting quality.

- **Resources** - Adequate resources must be provided including the assignment of trained personnel for management, performance of work, and assessment activities, including internal quality audits.

- **Management Representation** – Management must appoint a representative who will have established authority over and responsibility for:
    - Ensuring that quality system requirements are effectively established and effectively maintained and
    - Reporting on the performance of the quality system to management with responsibility for review.

- **Management Review** - Management must review the suitability and effectiveness of the quality system at defined intervals and frequency.

- **Quality Planning** - Each manufacturer must establish a quality plan defining quality practices, resources, and activities relevant to the devices being manufactured.

- **Quality Procedures** – Quality system procedures and instructions must be established.

Part 820.22 deals with Quality Auditing and requires that manufacturers must establish procedures for quality audits and must conduct such audits to assure that the quality system is in compliance with the established quality system requirements and to determine the effectiveness of the quality system. Quality audits must be conducted by individuals other than those who have direct responsibility for the matters being audited. Corrective actions, including re-audits, must be taken where necessary and the reports of these results must be documented and reviewed by the management responsible for the matters audited.

**Subpart J of the Code deals with Corrective and Preventive Action. Section 820.100 outlines the procedures the manufacturer must have in place for corrective and preventive action. These include requirements for

(1) Analysing processes, work operations, quality audit reports, complaints etc. to identify existing and potential causes of nonconforming product or other quality problems.

(2) Investigating the cause of nonconformities relating to the product, the process, and the quality system.

(3) Identifying the actions needed to correct and prevent recurrence of nonconforming product and other quality problems.

(4) Verifying or validating the corrective and preventive action to ensure it does not adversely affect the finished device.

(5) Implementing and recording changes in methods and procedures needed to correct and prevent identified quality problems.

(6) Ensuring that information related to quality problems or nonconforming product is disseminated to those directly responsible for assuring the quality of such product or the prevention of such problems.

(7) Submitting relevant information on identified quality problems, as well as corrective and preventive actions, for management review.

The means by which the FDA guides its staff in field inspections to ensure compliance with QSR is via its Quality System Inspection Technique (QSIT). This document was developed under the FDA's Office of Regulatory Affairs (ORA) and the Center *(sic)* for Devices and Radiological Health (CDRH) (August, 1999). The idea behind the document is to focus inspections on key elements of a firm's quality system. Within QSIT the FDA identifies seven subsystems within overall management control. These are design controls; production and process controls; equipment and facility controls; records, documents and change controls; material control; management control and corrective and preventive actions. These are reflected in Figure 7.

Figure Removed for Copyright Reasons

Figure 7. QSIT Seven Sub-Systems of Management Control.

(Source: Guide to Inspections of Quality Systems. Published by Office of Regulatory Affairs (ORA) and Center for Devices and Radiological Health (CDRH). Food and Drug Administration, 1999)

With collaboration from the medical device industry, four major subsystems were chosen by the FDA, that would represent/comprise the basic foundation of a firm's quality system. These four major subsystems are;

- Management Control
- Corrective and Preventive Actions (CAPA)
- Design Controls
- Production and Process Controls

Rather than checking every aspect of the firm's quality system, the subsystem approach focuses on those elements that are most important in meeting the requirements of the quality system regulation and which are key quality indicators.

This sub-system approach is similar to the approach adopted in the pharmaceutical sector which moves away from the investigation of a specific product towards generalising the results of an inspection to an overall evaluation of the firm. Table 4 provides a comparison of the sub-systems identified for audit during an FDA inspection within both manufacturing sectors.

Table 4. FDA Audit Approach

Pharmaceutical Audit Six System Inspection Approach	Medical Device Audit Quality System Inspection Technique
*Quality System	**Management *(Quality)* Controls
Production System	**Production and Process Controls
Facilities and Equipment System	Equipment and Facilities Controls
Laboratory Controls System	
Materials System	Material Controls
Packaging and Labelling System	
	**Design Controls
	Records, Document and Change Controls
	**Corrective and Preventive Actions

 * Mandatory inspection of the Quality System plus two others (FDA, 2006)

**Four major sub-systems identified as key quality indicators (FDA (QSIT), 1999)

QSIT applies three inspection levels. *Level 3* inspections are considered 'Compliance Follow-up Inspections' where non-compliance(s) resulted from a previous QSR/GMP inspection (reference FDA compliance program Part v). *Level 2* inspections are 'Baseline (Comprehensive) Inspections' and include inspection of all four major subsystems. This is considered a complete review of the firm's entire quality system. *Level 1* inspections are considered 'Abbreviated inspections' and always include inspection of the CAPA subsystem plus one other subsystem.

Interestingly from a firm's perspective, the QSIT guidance document suggests that using this subsystem approach offers fewer opportunities for citing minor

deviations from the QSR while those cited will be more serious (systemic) deviations. Without an effective quality audit function the quality system is incomplete and there is no assurance the manufacturer is consistently in a state-of-control.

2.8.3   International Standardisation

ISO 13485:2003 is an International Standard which specifies requirements for medical device manufacturers' quality management systems. Its intent is to facilitate the harmonisation of regulatory quality management system requirements around the world. Although aligned with ISO 9001:2000, due to some deletions and additions, those companies claiming adherence to ISO13485:2003 cannot claim adherence to ISO 9001:2000. In relation to risk management, ISO13485:2003 directs the reader to ISO 14971:2001. This standard specifies a procedure by which a manufacturer can identify the hazards associated with medical devices and their accessories; can estimate and evaluate the risks; control these risks; and monitor the effectiveness of the control. Figure 8 provides an overview of risk management activities as applied by ISO13485:2003 to medical devices.

Figure Removed for Copyright Reasons

Figure 8. A Schematic Representation of the Risk Management Process.
(Source: ISO 14971:2009 Medical Device Risk Management)

2.8.4   International Trade in the Medical Device Sector

Increasing numbers of businesses that manufacture, distribute and evaluate medical devices are becoming multi-national corporations. The need for efficiency in the application of regulatory controls has prompted national control

authorities to search for harmonised approaches to regulation and to enter into bilateral mutual recognition agreements and other international arrangements. In recognition of the growing need for international harmonisation of medical device regulatory controls, the Global Harmonisation Task Force (GHTF) was set up.

The GHTF is a consortium of world-wide national medical device regulatory officials working in conjunction with representatives of the regulated industry and other international organisations, to reach consensus on harmonised guidance relating to medical devices (e.g. pre-market evaluation, manufacturing practices, auditing and post-market vigilance aspects of medical device regulatory programmes). Since its inception, the GHTF has been comprised of representatives from five founding members grouped into three geographical areas: Europe (European Union), Asia-Pacific (Australia and Japan) and North America (United States and Canada). The purpose of the GHTF is to encourage convergence in regulatory practices related to ensuring the safety, effectiveness/performance and quality of medical devices, promoting technological innovation and facilitating international trade, and the primary way in which this is accomplished is via the publication and dissemination of harmonised guidance documents on basic regulatory practices. These documents are developed by four different GHTF study groups and can be adopted by member national regulatory authorities.

The primary goal of GHTF is the development of congruent requirements among the major medical device-producing and trading nations. By defining common regulatory approaches on a national level not only will this ensure greater human protection but will aid in reducing trade barriers and facilitate market availability of innovative, clinically useful technologies. This can be accomplished by reaching agreements on basic principles and regulatory practices that can be implemented by national competent authorities without interfering with

sovereign laws and directives. (GHTF Guiding Principles & Operating Procedures GHTF WD:99-3)

2.9 Key Findings: Quality in the Medical Devices Sector

Medical devices cover a large range of products, extending from low risk to high risk, encompassing sticking plasters through to devices used to sustain life. Manufacturers of medical devices are governed by strict quality requirements and must comply with good manufacturing practices. The complexity of these requirements has prompted the FDA to develop a quality system inspection technique to ensure compliance. With collaboration from the medical devices industry, the FDA has chosen four subsystems to reflect a firm's quality system. These include management control; corrective and preventive actions (CAPA); design controls; and production and process controls. In a similar approach to that adopted by the pharmaceutical sector, the subsystem approach focuses an inspection on those elements that are most important in meeting the requirements of the quality system, rather than checking every aspect of the firm's quality system. Internationally, there is an attempt to harmonise regulatory approaches in an attempt to reduce barriers to trade and encourage market availability of products.

2.10 Summary

This chapter has considered how new discoveries, new manufacturing technologies and new management techniques within the pharmaceutical and medical devices industries are presenting greater challenges, not only to the manufacturer, but also to the regulator. National governments implement regulatory controls to protect public safety and as part of their product approval process, firms must undergo stringent auditing of their quality management systems. It has been suggested however, that regulatory policies and practices contribute to low manufacturing efficiency. Furthermore a general lack of a systems perspective contributes to this inefficiency.

The systems perspective however is currently being addressed. Standards such as the Quality standard ISO9001, and the medical device standard ISO13485, have recognised the benefits of adopting a systems-based, process approach to managing quality systems. Regulatory quality system inspection techniques proposed by the FDA in both the pharmaceutical and medical devices sectors are moving away from a product approval approach towards a systems approval approach. Within these quality systems models, the concept of risk management and risk assessment is becoming a major focus and this is highlighted by ISO (ISO 14971:2009) and by recent FDA and ICH guidance documents outlined in this chapter. By adopting the proposed risk-based strategies proposed in these documents, it is suggested that firms will not only achieve compliance with regulatory requirements but will also benefit from technological advancement and advances in patient care.

Chapter 3: Literature Review - Focus on Safety

3.1   Introduction

Whilst chapter two outlined the requirements on companies for managing their quality systems, this chapter reviews the requirements on firms with respect to managing safety.   Whilst there are no specific requirements relating to pharmaceutical and medical device manufacturers *per se*, companies within these sectors are governed by the same national and European legal framework which governs all workplaces in Ireland. A broad outline of these legislative requirements is outlined for the reader. Literature on the management of safety is also required.

3.2   Introduction to Safety Concepts

Safety is commonly defined as "a measure of the degree of freedom from risk in any environment". An accident can be defined as "any unplanned event that results in injury or ill health to people, or damage or loss to property, plant, materials or the environment or a loss of a business opportunity" (Health and Safety Executive, 1993). Whereas engineering failure and human error have traditionally been cited as the causes of accidents, it is increasingly recognised that the fundamental cause of the majority of accidents can be traced back to poor management. (EPSC, 1994). European legislation, in particular the Seveso II Directive [96/082/EEC] (Control of Major Accident Hazards Involving Dangerous Substances) recognises that the "analysis of the major accidents reported in the *(European)* community indicates that the majority of them are the result of managerial and/or organisational shortcomings". Major public disasters have also called attention to the relevance of organisational structures and procedures in avoiding and eliminating accidents e.g. the investigation into the Clapham Junction Railway Accident outlined the co-existence of good intentions with dangerous working practices (Hidden, 1989). The investigation into the King's Cross Underground Fire showed that London Underground's approach to passenger safety was reactive rather than proactive (Fennell, 1988). The capsize

of the Herald of Free Enterprise happened because "from the top to the bottom the body corporate was infected with the disease of sloppiness" (U.K. Dept. Transport, 1987). Enhanced safety therefore requires increased attention to safety management and safety management systems.

3.3 Safety Management Systems

The statutory body responsible for the implementation of Health & Safety legislation in Ireland is the Health and Safety Authority (HSA). The HSA define a Health and Safety Management System as "the part of the overall management system that includes the organisational structure, planning activities, responsibilities, practices, procedures and resources for developing, implementing, achieving, reviewing and maintaining the occupational health and safety policy". This health and safety policy is an organisation's statement of "intentions and approach in relation to its overall health and safety performance that provides a framework for action, and for setting its health and safety objectives and targets". (Health and Safety Authority, 2010)

Many companies, particularly pharmaceutical companies using bulk chemicals, come under the auspices of the SEVESO 11 directive. This European Directive [96/82/EC] is aimed at the prevention of major accidents which involve dangerous substances, and the limitation of their consequences for man and the environment. A Safety Management System (SMS) is defined in the Seveso 11 Directive as "the organisational structure, responsibilities, practices, procedures, processes and resources for determining and implementing the major-accident prevention policy" (Council Directive 96/82/EC). It is increasingly recognised that the management of safety plays an important part in achieving and maintaining a high level of safety. Appropriate safety management starts with the safety policy which defines the overall safety intentions and direction of an organisation, as formally expressed by senior management. The requirement for a written safety policy has been emphasised in Ireland through the Safety Health

and Welfare at Work Act 2005 – the Irish legislation which implements the European Framework Directive No. 89/391/EEC. Safety management is that aspect of the overall management function that determines and implements the safety policy and will involve a range of activities, initiatives, programmes, etc., focused on the technical, human and organisational aspects of the workplace. It will include planning, organising, implementing and evaluating the work with respect to safety, as well as checking safety outcomes against the plan, and taking corrective action where necessary. In order to assist managers with these tasks, Safety Management Systems have been developed, thereby converting the management of safety into a formal system (Mitchison, N & Papadakis, G., 1999).

The SEVESO 11 (COMAH) Directive highlights the following issues that should be addressed by the safety management system:

- Organisation and personnel – this includes defining the roles and responsibilities of personnel involved in the management of major hazards at all levels in the organisation. Training requirements must be identified and provided for employees and others (e.g. sub contractors) where necessary.

- Identification and evaluation of major hazards – this involves the adoption and implementation of procedures for systematically identifying major hazards arising from normal and abnormal operation, and the assessment of their likelihood and severity.

- Operational control – this involves the adoption and implementation of procedures and instructions for safe operation, including maintenance of plant, processes, equipment and temporary stoppages.

- Management of change – this includes the adoption and implementation of procedures for planning modifications to existing installations, processes or storage facilities or the design of new installations, processes or storage facilities.

- Planning for emergencies – this involves the adoption and implementation of procedures to identify foreseeable emergencies by systematic analysis and to thereby prepare, test and review emergency plans to respond to such emergencies.

- Monitoring performance – this concerns the adoption and implementation of procedures for the ongoing assessment of compliance with the objectives set by the organisation's major-accident prevention policy and safety management system. It also considers the mechanisms for investigating and taking corrective action in the case of non-compliance. The procedures should cover the organisation's system for reporting major accidents or near misses, particularly those involving failure of protective measures. The procedures should also cover their investigation and follow-up on the basis of lessons learnt.

- Audit and Review – this includes the adoption and implementation of procedures for periodic systematic assessment of the major-accident prevention policy and the effectiveness and suitability of the safety management system. It also includes the documented review of the performance of the safety policy and the safety management system. Based on the audit and review findings, the safety policy and safety management system must be updated by senior management.

The Health and Safety Authority (HSA) in Ireland also outlines key elements of Health and Safety Management, namely;

- Policy and Commitment. This relates to how an occupational health and safety policy programme is developed and in what manner a commitment is made towards continuous improvement.

- Planning. This concerns the formulation of a plan to fulfil the health and safety policy.

- Implementation and Operation of this plan. This requires the development of capabilities and support mechanisms necessary to achieve health and safety policy, objectives and targets.

- Measuring Performance. This includes the measurement, monitoring and evaluation of health and safety performance, both reactive and active.

- Auditing and Reviewing Performance. The audit and review component of the management system is seen as critical in promoting a strong commitment to continuous improvement.

The Health and Safety Commission in the United Kingdom commissioned a report titled Organising for Safety (Health and Safety Commission, 1993) which reported on the role played by organisational factors in enhancing safety in the nuclear industry. Components of a Health & Safety management system, similar to those outlined above, were identified. These components were Policy and planning; Organisation and communication; Hazard management; and Monitoring and Review of safety performance. This management system demands explicit steps to audit the implementation of programmes and to measure the outcomes and the effectiveness of programmes.

It can be seen then, that broadly speaking, the functions of a safety management system include the functions of all generic management systems i.e. planning, organising, implementing and controlling. The common thread running through the requirements for safety management systems as outlined above, is the acknowledgement that measures to guard health and safety must be initiated at the highest level of management within a company. The organisation of safety, as Pasman (2000) suggests, has become at least as important as the technical safety of equipment and adherence to standards. Hale et al. (1994) see safety management systems as "a very complex structure, reflecting the fact that the management of safety in a continually changing environment, with a complex technology, and with an ever-changing insight into hazards is a highly demanding

and complex task". However, it is a commonly held view that the importance of safety management systems and their associated safety policies and plans lies not so much in their adequacy as in the perceptions and beliefs that people hold about them, in other words – safety culture.

3.4   Safety Culture

The term 'safety culture' arose from the Chernobyl nuclear disaster in 1986. The cause of this disaster was attributed to a breakdown in the organisation's safety culture (International Atomic Energy Agency, 1986).   Since then poor safety culture has been implicated in many of the reports of official inquiries into major disasters. The U.K. Health and Safety Commission report, Organising for Safety, referred to previously (HSC, 1993) suggests that the safety culture of an organisation is defined as "the product of individual and group values, attitudes, perceptions, competencies, and patterns of behaviour that determine the commitment to, and the style and proficiency of, an organisation's health and safety management". An organisation is regulated by government but it should go beyond just complying with externally imposed criteria. It should instead concentrate on the internal climate and organisation of the system. There must be an emphasis on the need for every individual to 'own' the actions being taken to improve safety, rather than seeing this as imposed from outside.

The study group purports that organisations with a positive safety culture are characterised by communications founded on mutual trust, by shared perceptions of the importance of safety and by confidence in the efficacy of preventive measures. Cox and Cox (1991), suggest that safety culture reflects the attitudes, beliefs, perceptions, and values that employees share in relation to safety. This means all the basic and commonly accepted moral concepts and standards as well as patterns of thinking, of solving problems, and of behaviour (with regard to safety) determine the decision making actions, and activities of the members of an organisation. Pidgeon and O'Leary (1994), (quoted in Pidgeon

and O'Leary, 2000) define safety culture in a similar manner, stating that it is "the set of beliefs, norms, attitudes, roles, and social and technical practices within an organisation which are concerned with minimising the exposure of individuals both within and outside an organisation to conditions which are considered to be dangerous". They propose the characteristics of a good safety culture to be;

- location of responsibility for safety at strategic management level
- distributed attitudes of care and concern throughout an organisation
- appropriate norms and rules for handling hazards and
- on-going reflection on safety practice.

However organisational culture is defined, it is widely acknowledged to be critical to an organisation's success or failure (Glendon and Stanton, 2000).

Dalling (1997) outlines a model of safety performance (Figure 9) which attempts to demonstrate the organisational components that are critical to safety.

Figure Removed for Copyright Reasons

Figure 9. Model of Safety Performance

(Dalling, I., 1997)

The model defines the components which affect the business process. These are explained as follows: The business **process** exists to provide products and services that provide added value to customers but unfortunately the process has potential hazards and risks which threaten people, assets, and business performance. The most critical element of the business is people. The **performance** of the process is the measure of the satisfaction of stake-holders' aspirations and needs, which are continually becoming more sophisticated and demanding. **Culture** comprises shared attitudes, perceptions, beliefs, values, social behaviour and accepted work practices (norms). Culture is particularly

shaped by corporate leadership but also by all of the other organisational components in the model. The **management system** comprises policy, responsibilities, structures, procedures and rules, and should define all the required critical actions for the effective operation of the organisation. 'Critical actions' implies that the management system is 'risk based' i.e. the defined controls are based on a systematic programme of risk assessments. A typical modern management system is highly integrated with strong feedback mechanisms to ensure continual improvement. Compliance with the management system and the efforts made to improve it are dependent on the strength of the culture. The **knowledge base** that an organisation has access to (either internal or external) is of critical importance, because it is not possible to conduct an effective risk assessment or apply effective controls if the relevant laws of nature are not fully understood. The knowledge base should also include corporate knowledge to allow the organisation to continually learn and not repeat past mistakes. The management system should take account of the knowledge base and have a component specifically designed to manage the knowledge base. **Corporate leadership** takes place at the most senior level within an organisation, typically by the directors of a company. The general style of management leadership within an organisation falls within the organisation's culture. It is corporate leadership that expresses the vision of the organisation's future, initiates plans, and which resources the overall operations of the organisation. The organisation's **stake-holders** are all of the people and organisations that have an interest in the performance of the organisation, and reside both within and outside of the organisation. They typically include an organisation's staff, society, government and regulators, customers, shareholders as well as contractors and partners. Stake-holders may have conflicting needs and requirements that have to be balanced by the organisation to ideally achieve what Dalling calls 'goal congruence'. Finally, a person's level of **consciousness** is important. Ideally, a person should be alert, responsible and creative. Factors such as stress, fatigue, ill health etc. will impact an individual's

performance and hence group performance. All these elements significantly influence health, safety, environmental, security, and any other aspect of organisational performance.

Krause (1993), addressing the issue of safety culture, proposes that culture (purpose, mission, values, goals, assumptions), the management system (accountability, attitude, training, education, resources,) and exposure (behaviour, conditions, plant, equipment) result in incidents downstream. He maintains that employee behaviour is a direct result of the management system and is the final common pathway of most incidents. The view that decisions taken at management level will result in accidents downstream, is also expressed in widely accepted theories such as Heinrich's Domino Theory of Loss Causation (Heinrich, 1931) and Reason's Theory of Active and Latent Failures (Reason, 1990). These theories support the view that managerial oversights, ill-defined policies, inadequate budgets, blurred responsibilities etc, will combine with errors, violations and component failures in the workplace to cause an accident. High profile accident investigations have supported this contention e.g. the investigation into the Challenger space disaster in the United States (Rogers, W., 1986), the capsize of the Herald of Free Enterprise in the United Kingdom (Sheen, 1987), the Piper Alpha Disaster (Cullen, 1990), and more recently the Concorde aviation accident investigation (BEA, 2000).

While a comprehensive safety management system is important in developing a culture of safety, knowledge of the workforce's risk perceptions and attitudes to safety is also required. The report into the U.K. nuclear industry (HSC, 1993) referred to previously, stresses the importance of assessing workforce perceptions of risk to achieve a proper safety culture. Many inconsistencies exist in the literature however, on the accuracy of workers' risk perceptions e.g. Fleming et al (1998) found that risk perceptions appear to be driven by organisational factors, such as safety attitudes, satisfaction with safety and job

situation. Flin et al. (2000) found that while the role of management was clearly important and appeared frequently in the literature, an understanding of the processes relating to management behaviours and their perception by the workforce, and any resulting impact on workforce behaviours are less well established. An overview of the literature by Shannon et al. (1999) found a number of organisational variables significantly related to injury rate. Among those variables were the training and empowerment of workers – variables which workers believe demonstrate a positive attitude by management towards its workforce.

In 1999, the Health and Safety Executive (HSE) in the United Kingdom produced a report which attempted to develop a Business Excellence Model of Safety Culture (Wright et al., 1999). The HSE felt that many earlier models of safety culture which had been reported in the literature were now outdated, because they were developed whilst organisations were still hierarchical and did not reflect the more common 'flatter' organisations. Another important omission in earlier literature was that of contractor working. Although the authors of that report recognise that with a trend towards outsourcing, sub-contracting, high turnover, short-term contracts and flexible periphery workforces the notion of a single culture may very well be redundant, they nevertheless present an overview of a composite safety culture model. This model is presented in Figure 10.

Figure Removed for Copyright Reasons

Figure 10. Overview of Composite Safety Culture Model

(Wright, M., et al. 1999)

According to the authors, such a composite safety model should comprise a means of defining health and safety cultural ideology, norms and goals which

takes account of the opinions, perceptions and expectations of internal and external stakeholders (A). It should have a means of communicating and demonstrating the organisation's commitment to these goals and norms, and maintaining this sense of commitment over time (C). It requires processes to facilitate the achievement of stated goals and norms, such as participation, empowerment, staff/management/contractor communications, training, proper resource management etc (B). A checking mechanism is required which will determine if the organisation's cultural goals and norms have been effectively achieved or at least that the behaviour of people is consistent with theses norms and/or within the boundaries of agreed acceptable behaviour (D). It will require a means of tracking the opinions, perceptions and expectations of stakeholders and assessing whether the organisation's norms need to be adjusted to reflect significant changes in these (E).

This model aims to show the stages of development of a safety culture and therefore does not include an auditing element. To fully align the model with other approaches to safety performance the authors suggest that auditing of the process is required. This could form part of the 'management control' process.

It is proposed by Greenstreet Berman (1999) that risk assessments and audits are useful in providing opportunities for staff involvement as well as demonstrating management commitment to a well managed safety programme. Where audits are seen as 'reality checks' rather than strictly policing efforts, they offer the benefits of raising awareness and stimulating reporting of hazards etc. With regard to developing a safety culture within the workplace, the authors further suggest that cultures can be characterised into three types: A safety culture can be **compliance driven**. In this type of culture regulatory frameworks are translated into internal procedures and compliance is assured by close supervision. **'Managed safety'** is another type of culture. In this environment a formal safety management system is implemented which sets its own targets and standards and these are achieved through management processes. The third type of safety culture identified is **'constructive intolerance'**. Responsibility is

devolved to the team level with greater emphasis on ownership of health and safety, and developing risk awareness. The aim is to encourage "constructive intolerance" of unsafe or potentially unsafe conditions, together with a commitment to taking responsibility for dealing with a hazard. This is often tied in with a commitment to continuous improvement.

It is often argued that you cannot and should not separate out health and safety management or culture from the general management of the organisation as such a division can reduce the effectiveness of health and safety management. Based on this argument, it is reasonable to assess an organisation's management and culture as a single entity, reading across from one area of responsibility to another, as they form part of a single management culture. If this is the case, then a single measure of management or culture suffices for business, health, safety, quality and environmental management/culture. Wright et al. (1999) suggest that many organisations overlook health and safety when introducing participation into business management. Even organisations which have been rewarded for their proactive outward looking approach to Quality management are shown to pursue a reactive minimalist style of management for health and safety. This would indicate that it is unsafe to assume consistency and congruence of management style and attitudes across all areas of management responsibility. This issue will be dealt with in more detail in chapter five.

3.5 Legislative Requirements

A comprehensive legal framework for governing health and safety exists in Europe, predominately in the form of the European Framework Directive 89/391/EEC. This Directive outlines general guidance and duties for ensuring health and safety, along with its subsidiary or daughter Directives which deal with specific areas such as Manual Materials Handling and safety standards for Work Equipment. These Directives are binding on the Member States of the Union and are transposed into the Law of the member states. Ireland's chief

piece of health and safety legislation is the Safety Health and Welfare at Work Act 2005 but Acts dating back to 1882 (Boiler Explosions Act) and the Factories Act 1955 are still relevant. The approach required under Statute Law in Ireland is that an assessment of exposure to hazard and risk in individual workplaces/workstations must be undertaken. Based on the results of this assessment the appropriate action must be taken to eliminate or reduce the exposure. Specific requirements dictate that employers must prepare a Safety Statement which must include a written record of the hazard analysis/risk assessment carried out. In conducting this risk assessment, the employer must obtain competent advice (external if necessary) on health and safety matters. The employer also needs to take cognisance of specific regulations applying to certain issues, such as noise, electricity, Personal Protective Equipment etc. Appropriate knowledge and training must be provided to all workers. When performing a risk assessment, the employer is guided by the General Principles of Prevention outlined in Schedule 3 of the Act. These are presented in Table 5.

Table 5. Nine Principles of Prevention

(Source Safety, Health and Welfare at Work Act, 2005)

	Principles of Prevention
1.	The avoidance of risks
2.	The evaluation of unavoidable risks
3.	The combating of risks at source
4.	The adaptation of work to the individual, especially as regards the design of places of work, the choice of work equipment and the choice of systems of work.
5.	The adaptation of the place of work to technical progress.
6.	The replacement of dangerous articles, substances or systems of work by safe or less dangerous articles, substances or systems of work.
7.	The giving of priority to collective protective measures over

	individual protective measures.
8.	The development of an adequate prevention policy in relation to safety, health and welfare at work, which takes account of technology, organization of work, working conditions, social factors and the influence of factors related to the working environment.
9.	The giving of appropriate training and instructions to employees.

The Safety Statement must be updated regularly; if significant changes have occurred in work practices, equipment etc., or at the direction of an inspector from the Health and Safety Authority (HSA) - the national authority with responsibility for enforcing health and safety legislation in Ireland. In addition to the Safety Health and Welfare at Work Act, many other Acts and Statutory Instruments exist. These cover areas such as chemicals (Chemicals Act 2008), carcinogens (S.I. No 78 of 2001), asbestos (S.I. No. 589 of 2010) among others.

Whereas Statute Law allows for prosecution for a breach of Statue, a Common Law system also exists under which a civil action for compensation may be taken. Under Common Law an employer is obliged to provide: A *safe place* of work; *Safe systems* of work: *Safe plant and machinery*; and *Competent fellow employees.* Where some vagueness exists in the execution of the legislation, standards, guidelines and codes of practice etc are often used.

3.6 Safety Guidelines, Codes of Practice and Standards

In the absence of specific information companies often turn to standards, guidelines and approved codes of practice for help in complying with legislation. Many of the guidelines and Approved Codes of Practice (ACoP's) are developed by concerned parties within particular industry groupings whilst some are developed to give effect to European legislation. ACoP's are Technical Specifications or Standards intended to provide practical information as to how

an organisation can comply with a statutory provision. Under the provisions of the 2005 SHWWA such Codes of Practice are admissible as evidence in criminal proceedings.

Many proprietary safety standards exist for managing safety in the workplace such as those produced by the British Standards Institute and the International Labour Organisation. However, the Occupational Health and Safety Assessment Series (OHSAS) 18001 is gaining in popularity as this was developed on the basis of the British Standard BS8800: Guide to Occupational Health and Safety Management Systems and were designed to be compatible with ISO 900! (Quality) and ISO 14001 (Environment), as well as the International Labour Office guidelines - ILO-OSH:2001 - Guidelines on Occupational Safety and Health Management Systems. The basis of the OHSAS 18001 series is that the hazard identification, risk assessment and risk control process and their outputs should be the basis of the organisation's whole occupational health & safety system.

All these standards have in common the same elements of successful management namely policy; planning; implementation and operation; checking and corrective action; and management review. It is suggested that the compatibility of these management systems enables organisations to facilitate the integration of the management of quality, environment and health and safety.

3.7   Summary

A comprehensive national and European legal framework governs health and safety activity in the Irish workplaces. This framework supports the use of a safety management system, either formal or informal, for managing risks to health and safety and requires a thorough and documented hazard analysis, risk assessment and risk control procedure. The literature suggests that a safety management system generally incorporates the components of all generic

management systems; namely, planning, organisation, implementation and control. This is reflected in proprietary Safety Standards. The literature also suggests that a culture of safety driven from the top down is critical to an organisation's success or failure. However, a culture of safety and the management of health and safety should be pervasive across the general management of an organisation and should not be separated out from the management of other activities, for example the management of quality.

Chapter 4:   Literature Review - Focus on the Environment

4.1 Introduction

There is an increasing emphasis on the environmental implications of economic activity. To this end, European and Irish legislation exists to minimise pollution and encourage good environmental practice. The legislation aims to prevent and control pollution and its impacts arising from industrial activities so as to achieve a high level of protection for human health and the environment. Many companies use Environmental Management System Standards to indicate compliance with legislative licensing requirements. Best practice in environmental management is based on an integrated approach of risk assessment and risk control.

4.2   European Environmental Governance

The European Union has a common set of rules relating to the minimisation of pollution from industrial installations. These rules were first set out in the Council Directive 96/61/EC concerning Integrated Pollution Prevention and Control (IPPC). This directive has seen four major amendments since its inception. The first amendment was introduced to reinforce public participation in line with the Aarhus Convention in 1999 (which established rights for the public to access environmental information and to allow for public participation in environmental decision making). The second amendment was introduced to clarify the relationship between the permit conditions established in accordance with the IPPC Directive and the European Union greenhouse gas emission trading scheme (ETS). Launched in 2005, the EU ETS works on the "cap and trade" principle. This means there is a "cap", or limit, on the total amount of certain greenhouse gases that can be emitted by factories, power plants and other installations. Within this cap, companies receive emission allowances which they can sell to or buy from one another as needed. At the end of each year each company must surrender enough allowances to cover all its emissions, otherwise heavy fines are imposed. If a company reduces its emissions, it can keep the

spare allowances to cover its future needs or else sell them to another company that is short of allowances (European Commission, 2010).

The third amendment relates to changes regarding Comitology, which describes a process in which the Commission, when implementing EU law, has to consult special advisory committees made up of experts from EU countries. Finally, the last major amendment concerns the European Pollutant Emissions Register (EPER) which requires Member States to produce a triennial report on the emissions of industrial facilities to air and water. The IPPC Directive is now codified as 'Directive 2008/1/EC of the European Parliament and of the Council of 15th January 2008 concerning integrated pollution prevention and control'.

The Directive defines pollution as "the direct or indirect introduction as a result of human activity, of substances, vibrations, heat or noise into the air, water or land which may be harmful to human health or the quality of the environment, result in damage to material property, or impair or interfere with amenities and other legitimate uses of the environment". Through the prevention and control of pollution from industrial plants, European legislation aims to move towards a more sustainable balance between human activity and socio-economic development on the one hand, and the resources and regenerative capacity of nature on the other. (Council Directive 2008/1/EC).

Predating the Council Directive, legislation existed to combat air pollution and minimise the discharge of dangerous substances into water. Emissions into soil however, had not been specifically targeted. It was felt that controlling air, water and soil separately might encourage the shifting of pollution between the various environmental media rather than protecting the environment as a whole. The objective of an integrated approach to pollution control was to prevent and minimise emissions into air, water or soil in order to achieve a high level of protection for the environment as a whole.

The EU Directive lists the types of installations that are obliged to hold a licence to operate. These include industrial and agricultural activities with a high pollution potential and include some agricultural installations, pulp and paper producers and firms operating within the chemical industry, among others. The Directive specifically targets installations using a chemical or biological process for the production of basic pharmaceutical products. (Schedule 1 to the Directive Section 5.16)

An Integrated Pollution and Prevention Control licence is issued only if operators meet baseline requirements for the protection of air, water and soil, waste minimisation, accident prevention and site clean-up where appropriate. There are general principles governing the awarding of licences. These include:

- taking appropriate preventive measure against pollution
- not causing significant pollution
- avoiding waste production; recovering waste where it is produced and where this is neither technically nor economically feasible, disposing of it, while avoiding or minimising any impact on the environment
- using energy efficiently
- preventing accidents and limiting their consequences
- on cessation of activities, returning the site to a satisfactory state.

An operator, in all of their undertakings, must utilise so-called "best available techniques" (BAT). BAT is a key principle in the Council Directive 2008/1/EC or the IPPC Directive, as it is more commonly called. BAT places its emphasis on pollution prevention techniques rather than end-of-pipe treatments. Low-waste technology must be used. Hazardous substances should be substituted by less hazardous substances. Substances generated and used in the process should be recovered and recycled, and any overall impact of emissions on the environment must be prevented or reduced. Recent EU Directives on Waste Electrical and Electronic Equipment (WEEE) and on the Restriction on Hazardous

Substances (RoHS) in electrical and electronic equipment (EEE) have been transposed into Irish law. These newer Regulations require producers to be responsible for the financing of the collection, treatment, recovery and environmentally sound disposal of WEEE from 13 August 2005. It means that final users of such household WEEE will be entitled to leave that waste back free of charge, either to retail outlets in instances where a replacement item is purchased, or other authorised collection points, including local authority civic amenity sites, from that date onwards (Department of the Environment, Community and Local Government, 2011).

REACH is the European Regulation for Registration, Evaluation, Authorisation and Restriction of Chemicals and it entered into force on 1 June 2007 (European Parliament and Council, 2006). The REACH Regulation places greater responsibility on industry to manage risks that chemicals may pose to human health and the environment and at the same time enhance the competitiveness of European industry by fostering innovation. It also aims to promote alternative methods for the assessment of hazards of substances and eliminate unnecessary testing (Environmental Protection Agency, 2008).

The Sixth Environment Action Programme, which was adopted in July 2002, sets out the EU's priorities for the period to 2012. Four areas are singled out for priority action: climate change, nature and biodiversity, the environment and health, and the management of natural resources and waste. EU environment policy is guided by the precautionary principle and the "polluter pays" principle. Various institutional, financial and management instruments are available to ensure that it is implemented effectively. The involvement of the general public is also a key part of environment policy (European Commission, 2008).

4.3   Environmental Management in Ireland

Over the past decade, the profile of manufacturing industry in Ireland has changed dramatically. An increase in industrial production has created demands and pressures on the environment in terms of energy and raw material consumption, increased waste generation and the enhanced threat of pollution incidents from emissions. The highest growth rates in Ireland have been in high-technology sectors such as electronics, medical devices and the chemical and pharmaceutical sectors. The chemical and pharmaceutical sector has been the largest generator of hazardous waste. (Environmental Protection Agency, 2006).

The EPA has identified its main environmental challenges for the future. These include the following:

- **Mainstreaming environmental considerations**
  - Incorporating environmental considerations into policies and plans
  - Ensuring environmentally responsible businesses
  - Changing behaviours
- **Limiting and adapting to climate change**
  - Mitigating the causes and effects of climate change
  - Adapting to climate change impacts
  - Improving our understanding of climate change
- **Reversing environmental degradation**
  - Preventing eutrophication and other water pollution
  - Protecting natural habitats and species populations
  - Remediation of contaminated land
- **Complying with environmental legislation and agreements**
  - Building a culture of environmental compliance
  - Enforcement of legislation at national and local level
  - Meeting EU and other international obligations (EPA 2008)

4.4   Irish Legislative Requirements

The level of economic growth in Ireland from the mid 1990's (until recession in 2008), focused attention on the implications (actual or potential) for the environment (www.environ.ie). Ireland had anticipated European legislation with the Environmental Protection Agency Act of 1992. The IPPC Directive was transposed into Irish law in 2003 with the enactment of the Protection of the Environment (PoE) Act 2003. In July 2004 Integrated Pollution Prevention and Control (IPPC) licensing replaced the existing Integrated Pollution Control (IPC). This legislation placed a greater emphasis on prevention. The Environmental Protection Agency (EPA) is charged with the responsibility of implementing and enforcing environmental legislation in Ireland. This independent body was established under the Environmental Protection Agency Act, 1992. The other main instruments from which the EPA derives their mandate are the Waste Management Act, 1996, and the Protection of the Environment Act, 2003. The primary responsibilities of the EPA are:

- Environmental licensing
- Enforcement of environmental law
- Environmental planning, education and guidance
- Monitoring, analysing and reporting on the environment
- Regulating Ireland's greenhouse gas emissions
- Environmental research development
- Strategic environmental assessment
- Waste management

The EPA licensing scheme covers specific listed industrial activities deemed to have significant polluting potential. All aspects of the licensed activity's potential impact on the environment are covered, including emissions to air and water, energy and resource use efficiency, environmental management systems, and waste and residuals management. The Office of Environmental Enforcement, within the EPA, is responsible for enforcement. This office encourages businesses

to integrate good environmental practices into normal working methods. Their emphasis is on preventing environmental pollution before it has a chance to occur. The Office of Environmental Enforcement also embraces the "polluter pays" principle, ensuring that activities or persons that cause environmental damage are held financially accountable for their actions. The ultimate sanction available is prosecution.

A requirement for a mandatory environmental management system is stipulated in the conditions for licensing issued by the EPA. Through this management system the licensee must assess all operations and review options for use of cleaner technology, cleaner production and the reduction and minimisation of waste. Procedures for corrective action must also be established. These procedures will ensure that corrective action is taken where a non-compliance is raised. Many companies use accreditation to International Standard ISO 14001 to indicate compliance with these requirements.

4.5   Environmental Management System Standards

First published in 1996 and written to reflect the structure of ISO 9001, the ISO 14001 Environmental Standard is based on a cycle of continuous improvement – See Figure 11.

Figure Removed for Copyright Reasons

Figure 11. Environmental Management System

(Source: ISO 14001:2003)

The ISO views an environmental management system as an organising framework that should be continually monitored and periodically reviewed in response to changing internal and external factors. All levels in the organisation should accept responsibility for working to achieve environmental improvements (ISO 14004:2004). The Quality Standard ISO 9001:2000 requires organisations to manage their operations via the "process approach". Since the PDCA methodology can be applied to all processes, the two methodologies (i.e. the process approach and the PDCA approach) are considered compatible (ISO 14001:2003). In a similar vein to ISO 9001, the environmental standard also includes a section on nonconformity, corrective action and preventive action. Section 4.5.3 states that the organisation shall establish and maintain a procedure(s) for dealing with actual and potential nonconformities and for taking corrective action and preventive action. This should include:

- identifying and correcting nonconformities and taking actions to mitigate their environmental impacts

- investigating nonconformities, determining their causes and taking actions in order to avoid their recurrence,

- evaluating the need for actions to prevent nonconformities and implementing appropriate actions designed to avoid their occurrence,

- recording the results of corrective actions and preventive actions taken, and

- reviewing the effectiveness of corrective actions and preventive actions taken.

The guidance on the use of the Standard suggests that organisations, depending on the nature of the non-conformity, may be able to address nonconformities, and corrective and preventive actions with a minimum of formal planning, or it may be a more complex and long-term activity. Accompanying documentation should be appropriate to the level of action. In evaluating compliance, guidance

document ISO 14001:2004 outlines a number of methods to assess compliance including:

- audits,
- document and /or records review,
- facility inspections,
- interviews,
- project or work reviews,
- routine sample analysis or test results
- facility tour and/or direct observation

The guidance document goes on to suggest that a compliance evaluation programme can be integrated with other assessment activities, such as health and safety assessments, or inspections or quality assurance checks. In developing a plan for addressing a nonconformity, an organisation should consider what actions need to be taken to address (mitigate) the problem, what changes need to be made to correct the situation (to restore normal operations), and what should be done to prevent the problem from recurring (to eliminate the cause). Management should ensure that corrective and preventive actions have been implemented and that there is systematic follow-up to ensure their effectiveness.

ISO 14001, like ISO 9000, emphasises that audits are an essential part of conformity assessment activities. The Guidelines for quality and/or environmental management systems auditing, BS EN ISO 19011:2002, addresses how such audits should be conducted and also addresses the competency of auditors. These competencies include generic knowledge and skills as well as domain specific knowledge and skills as outlined in Figure 12.

Figure Removed for Copyright Reasons

Figure 12. Concept of Competence

(Source: BS EN ISO 19011:2002)

The numbers in parentheses refer to the sections within the standard which describe each component. For example, section 7.3.3. requires the auditor to have knowledge and skills in the area of quality terminology and quality tools and their application. Section 7.3.4 requires auditors to be familiar with environmental terminology and environmental tools. The generic knowledge and skills required (section 7.3.1 and 7.3.2) would include skills in preventing and resolving conflicts, the ability to plan the audit and to organise and direct audit teams.

In Ireland ISO certification shows an increasing trend year on year (with the exception of ISO9001 in 2007). The most recent data available is from 2008 and this is outlined in Table 6.

Table 6. ISO Certification in Ireland

(Compiled from ISO, 2008)

	2001	**2006**	**2007**	**2008**
ISO9001:2000/2008	248	2225	1999	2237
ISO14001:2004	247	251	370	515
ISO13485:2003	Pre-dates Standard	84	95	116

The Eco-Management and Audit Scheme (EMAS) is a voluntary European initiative designed to improve companies' environmental performance. Strongly backed by Governments and environmental regulators, its aim is to recognise and reward those organisations that go beyond minimum legal compliance and continuously improve their environmental performance. Requirements for EMAS recognition are specified in European Council Regulation (EC) No 761/2001 and the associated Commission Recommendation document. EMAS requires

participating organisations to implement an environmental management system which must meet the requirements of ISO 14001. Many organisations progress from ISO 14001 to EMAS and maintain certification/registration to both. EMAS places special significance on legal compliance, improvement of environmental performance, external communication (e.g. to local communities and customers) and employee involvement. (e.g. project-based group works or environmental committees).

Section 1-A.5.2 of Annex 1 to the Regulation stipulates that an organisation must have procedures in place for handling non-conformance and for corrective and preventive action. Any corrective or preventive action taken to eliminate the causes of actual or potential non-conformances should be appropriate to the magnitude of problems and commensurate with the environmental impact encountered.

4.6   Summary

In this chapter, it can be seen that Environmental management must be based on an integrated approach to protecting the environment. This integrated approach acknowledges that controlling air, water and soil separately might encourage the shifting of pollution between the various environmental media rather than protecting the environment as a whole, and so it assesses risks to the environment in an integrated manner based on principles of elimination, substitution and control. At European level, those responsible for protecting the environment have made it clear that meeting the challenges of today's environmental problems means looking beyond a strictly legislative approach and taking a strategic approach. This approach requires the use of a range of instruments and measures to influence decisions made by business, consumers, policy planners and citizens and proposes five main avenues for strategic action: improving the implementation of existing legislation, integrating environmental concerns into other policies, working in partnership with business, empowering

citizens and changing their behaviour, and taking account of the environment in land-use planning and management.

Environmental management aims to protect the environment utilising best available techniques based on elimination, substitution and control. The objective of Management Systems generally speaking, is to minimise losses by improving the process to deliver a product or service in the most efficient and profitable way. It can be said that this objective is the same for Quality, for Environmental and for Safety Management Systems. All three management systems are based on the same core elements of identifying the problems (hazards, poor production methods, etc.), and eliminating or controlling these problems, to ensure a continuous improvement cycle. The previous chapter highlighted how authorative opinion on the management of safety has advocated a risk assessment approach based on principles of prevention and a hierarchy of controls. Chapter 2 focussed on Quality management, and showed how, particularly among regulators, the management of quality is moving towards a risk-based paradigm. This Chapter identifies how environmental management aims to protect the environment by assessing risks to the environment in an integrated manner. The common theme emerging from all of these chapters is the focus on a risk-based systems approach. The next chapter will explore the literature on 'systems' and a 'systems approach' and further investigate the implications of this for the integration of management systems.

Chapter 5:   Literature Review – Integrated Management Systems

5.1   Introduction

Previous chapters have demonstrated that broadly speaking the functions of quality, safety and environmental systems include the generic functions of all management systems; namely planning, organising, implementing and controlling. However, as outlined in Chapter 2, a view exists that a lack of an overall 'systems perspective' contributes to low business efficiency in manufacturing organisations. To explore this idea further, it is necessary to define and explain how the idea of a system is dealt with in the literature and the relevance this has for integrated management systems.

5.2   Systems

According to Bailey, as quoted in Saunders M. and McCormick, E. (1992), a system is an entity that exists to carry out some purpose. Bailey states that the concept of a system implies that we recognise a purpose; we carefully analyse the purpose; we understand what is required to achieve the purpose; we design the system's parts to accomplish the requirements; and we fashion a well-coordinated system that effectively meets our purpose. This could, in effect, be described as a management system. Likewise, Dennis (1997) proposes that a *management* system may be defined as an orderly set of components that serve to accomplish one or more goals of the organisation. A system's specific goal, for instance, may be to facilitate the flow of information, improve quality, minimise losses due to accidents and injuries, or reduce environmental impacts.

Dennis suggests that in the absence of a systems approach, companies may be overwhelmed by the increasing complexity of the technological, organisational, and marketing components of the business environment. If quality, safety and environmental components are included in this business environment, then this adds greatly to the complexity. Managing a system to ensure its effectiveness therefore, requires coordinating system work across the organisation i.e. system

administration, as well as measurement and control of system costs i.e. system economics. System measurement covers both system outcomes (such as customer satisfaction) and the process by which the results are obtained.

The previous chapters have outlined for the reader the main issues facing organisations in relation to managing quality, safety and environmental systems. The traditional approach has been to deal with each of these systems as individual, discrete systems. However, with the increasing complexity of organisations, the validity of this approach must be questioned. According to Oakland (1993), developing systems thinking and a process focus within an organisation enables seemingly discrete parts to work together, breaking down barriers between functions and departments, and hence improving communications and information flow, process flow, quality and productivity. Having already considered the detailed and complex requirements governing the management of quality, environmental, and health & safety as discrete systems - will integrating the management of discrete systems achieve the benefits that Oakland has described?

5.3   Integrated Management Systems

Previous chapters have shown the arguments in favour of a well-established management system. For example, an effective quality management system can promote continuous improvement; an effective safety system can promote business efficiency by eliminating or reducing work-related accidents, injuries and ill-health - thereby reducing the number of lost days and lost production; similarly, an environmental management system will protect the environment and yield cost benefits to the establishment. So far, each of these systems has been treated as a distinctively discrete system. However, extensive literature exists which expounds the benefits of integrating environmental, safety and quality management systems. The main benefits are to be found in avoiding duplication of effort, and finding optimal solutions to problems (Wilkinson and

Dale, 1999; Honkasalo, 2000); reducing documentation and avoiding duplication of effort (Bamber et al, 2000); improved cooperation and communication (Karapetrovic, 2003); improved system effectiveness and efficiency (Beckmerhagen et al., 2003); competitive advantages and progress towards corporate responsibility (Jorgensen et al., 2006); as well as improvement of image and social impact (Karapetrovic et al., 2010).

Although there has been a general move towards the alignment of many quality, environmental and safety management standards, it is important to differentiate between alignment and integration of system standards. McGregor Associates (1996) suggest that whereas alignment refers to parallel management system standards, each specific to an individual discipline with a high degree of commonality of structure and content, integration is achieved by having a simple top level management core standard with optional modular supporting standards. These two approaches can be seen in figures 13 and 14 respectively.

Figure Removed for Copyright Reasons

Figure 13. Aligned Standards Approach

(Source: McGregor Associates, 1996)

Figure Removed for Copyright Reasons

Figure 14. Integrated Standards Approach

(Source: McGregor Associates, 1996)

Beckerhagen et al. (2003) propose three elements of management systems integration, namely, harmonisation; cooperation; and amalgamation. These

elements can exist in varying degrees. For instance, partial harmonisation and coordination of documentation is the least stringent degree of integration. In order to take integration one step further, integrated audits would be conducted and resources would be shared. Finally, in full integration, management systems are amalgamated into a new and comprehensive Integrated Management System (IMS). Karapetrovic (2003) considers the need for a methodology for the integration of internal management systems, rather than an integrated standard. He proposes that what is needed is not "one standard, one system" but "many standards, one system". A generic methodology is required that can "meld function-specific requirements of the current and future standards while fostering a meaningful integrated system that can be tailored to meet the needs of a specific organisation". For instance, some organisations require full integration across all hierarchical levels, whereas others may require a partial approach, focusing at top and bottom levels only. Jorgensen et al. (2006) distinguish between the following three levels of integration:

a. **Corresponding:** increase *compatibility* with cross-references between *parallel systems*

b. **Coordinated and coherent:** *generic processes* with focus on tasks in the *management cycle*

c. **Strategic and inherent:** an organisational *culture of learning, continuous improvements* of performance and *stakeholder involvement* related to internal and external challenges.

As described previously, the ISO standards ISO 9001 and ISO14001; and OHSAS 18001 are based on Deming's Plan-Do-Check-Act continuous improvement cycle. Zeng et al. (2007) have presented the shared structure of these three management systems as follows – Figure 15:

Figure Removed for Copyright Reasons

Figure 15. Structure of the PDCA Cycle

(Source: Zeng et al. 2007)

Jorgensen et al. (2004; 2007) have considered that a basic condition for an integrated management system is a common understanding of organisations and how they operate. Whereas the older versions of ISO Standards had been criticised for being static, resulting in too much paperwork, the more recent ISO standards reflect a more dynamic management system with a focus on the iterative process of activities like policy, planning, implementation, as well as on innovation and continuous improvements. The authors suggest that this more dynamic understanding of organisations seems to present an opportune time for formulating an integrated management system.

5.4   The Role of System Audits

A common element arising from the previous chapters is the requirement for compliance audits. Karapetrovic and Willborn (2000; 2002) suggest that the audit is an irreplaceable tool when compliance with standards is sought, but one which often fails in improving process performance and enabling continuous improvement. In relation to the quality system, the authors suggest that the "independence" principle of the audit be removed in favour of self-audits by the process owner. These audits are cross-functional and less formal than a traditional quality audit. The authors suggest that this type of self-assessment outperforms a quality system audit in terms of identifying strengths and opportunities for continuous improvement, prevention of problems, and incorporation of assessment results into strategic and operational business planning. Their results should be used as an input into the management review process, making self-audits a highly useful vehicle for continuous improvement. Beckmerhagen et al (2003) recognise the contribution of audits in assessing the effectiveness of a management system and offer a practical example whereby audits were used to assist in the integration of safety requirements into the quality manual of a nuclear waste disposal facility. According to Karapetrovic

(2003), when integrating management systems, requirements common to all standards should be identified and integrated first.

Conti (2010) considers systems thinking (that which considers the system's global behaviour and performance as the combined effect of all its variables) to be a critical component of quality management in order for an organisation to generate value. He introduces the concept of the 'value generation cluster', which he describes as individuals or groups of individuals (sub-clusters) co-operating to generate an expected value. Because of the synergetic effect typical of social systems, the value that is generated is more than the sum of the values that each individual could generate in isolation. A person (or group of persons) can be (and normally is) part of different clusters. Clusters can become the building blocks of the organisational architecture. Conti believes these clusters represent a systemic solution to the problem of an organisational architecture aiming to create continuous improvement and innovation propitious environments. Central to this philosophy of a holistic systems approach is the focus on a flexible and easily reconfigurable aggregation criteria – not on permanent functional divisions with rigid boundaries. This is a theme visited by Hannukainen et al. (2006); as quoted in Tervonen et al. (2009), in a survey carried out by the American Society for Quality, the results of which influenced the authors to make the observation that the application of quality thinking must become more innovative, flexible and faster to implement.

5.5   Summary

The common thread that has recently been emerging across all management systems, is a risk-based approach to protecting and continuously improving quality, safety and environmental systems. Chapter two has shown how quality management systems, particularly among regulators, are moving towards a risk-based, systems approach. Chapter three has outlined how the traditional focus of safety management systems has been on risk management, adopting

principles of prevention and a hierarchy of control. Chapter four has presented how environmental management systems are moving towards an integrated, holistic approach based on elimination, substitution and control. This chapter has identified the advantages to be accrued from integrating management systems. However, as Karpetrovic (2003) has suggested, there is a need for a generic methodology for the integration of management systems. He has suggested that when integrating management systems, requirements common to all standards should be identified and integrated first. The quality, environmental and safety systems described previously have included quality audits as a common element. Recent literature, including that of regulatory authorities, has shown a trend towards adopting a risk-based approach to auditing. Could applying a common risk-based approach to the auditing of all three systems be the first step in developing a methodology for the integration of QEH&S systems; an approach which will not only assure compliance with regulatory and statutory requirements, but will achieve our ultimate aim of continuous improvement whilst protecting the product, the process and the environment? The following chapters will present the development of an integrated risk management framework which can be adopted by the medical devices and pharmaceutical sectors in pursuit of this aim.

Chapter 6:   Methodology

6.1   Introduction

This chapter provides a general outline of the methodology used in developing a framework for integrating Quality, Environment and Health & Safety (QEH&S) management systems in highly regulated environments. The fieldwork employed uses both case study and survey methods and is based predominately on what Creswell (2003) calls a mixed methods framework, using both a qualitative and quantitative approach. The exploratory phase of this work begins with a case study which identifies the research problem domain, i.e. the rationale for FDA regulated companies not integrating their QEH&S systems. A questionnaire is then distributed nationally to determine the state-of-play with respect to integrated QEH&S Management Systems within the Irish medical devices and pharmaceutical sectors generally. Results from the literature review, case study and the survey are then used in the development of two subsequent case studies, which provide a more detailed and in-depth analysis of both sectors. A cross-case analysis is then conducted to search for common patterns within the industries. Based on the findings from the literature reviews and the results of the field work, an integrated risk management framework is proposed. The validation of this framework and the methodological approach adopted for this validation is discussed separately in Chapter 9.

6.2   Case Study Research

Creswell (2003) describes case studies as those in which the researcher explores, in depth, a programme, an event, an activity, a process, or one or more individuals. The case(s) are bounded by time and activity, and researchers collect detailed information using a variety of data collection procedures over a sustained period of time (Stake, 1994). Yin (2003) has provided a technical definition of a case study stating that it is an empirical inquiry that investigates a contemporary phenomenon within its real-life context. Lubbe (2003) suggests that from a research strategy point of view, the case study methodology is a way of establishing valid and reliable information which add to the accumulated

knowledge of the processes by which business and other organisations function. Lubbe refutes the idea that case study methodology is an informal approach and instead proposes that it requires a distinctly formal structured approach in the form of a case study protocol. In other words, a detailed master plan for the research must exist in which full details of the case study research design, including details of the questions to be asked, field procedures for the researcher, details of all types of evidence required, as well as the structure of the final research must be specified. He suggests that such a protocol is a primary tactic in increasing the reliability of the case study procedure and should include the following:

- Defining who should be interviewed

- Gaining access to the right people

- Having adequate resources available such as time, paper, tapes etc.

- Making a schedule of the required data collection activities.

- The research objectives should be outlined and an interview schedule drawn up.

All the above procedures were followed for this research. The field procedure employed can be referenced in Appendix 1.

6.3   Business Process Modelling

Business modelling is used to create an abstraction of an otherwise complex business. This will enable business stakeholders to gain a better understanding of the business functions and also promote business improvements and/or innovation. Business process modelling encourages uniform documentation of who generates what information, products, services; for whom; how; and why; and with what authorization (Lambert et al., 2006). Whilst many systems modelling tools exist, such as Unified Modeling Language (UML) and Object Management Group's (OMG) Systems Modeling Language (SysML), IDEFØ was the chosen methodology. Having its roots in a manufacturing /information environment rather than software development, IDEFØ has traditionally been

perceived as being a user-friendly methodology. This modelling tool was developed during the 1970's, by the United States Air Force, through its program for Integrated Computer Aided Manufacturing (ICAM) which sought to increase manufacturing productivity through the systematic application of computer technology. The ICAM programme identified the need for better analysis and communication techniques for people involved in improving manufacturing productivity. As a result, the ICAM programme developed a series of techniques known as the IDEF (ICAM Definition) suite. This set of techniques includes the IDEFØ component which is used to produce a "function model". A function model is a structured representation of the functions, activities or processes within the modelled system or subject area. The model is developed for understanding, analysis, improvement or replacement of the system. System parts can be any combination of things, including people, information, software, processes, equipment, products or raw materials. The model describes what a system does, what controls it, what things it works on, what means it uses to perform its functions, and what it produces. Diagrams are the major component of an IDEFØ model, and are formed based on Inputs-Controls-Outputs-Mechanisms (ICOMs) (National Institute of Standards and Technology, 1993). The diagrams contain boxes, arrows, and box/arrow interconnections which reflect associated relationships. Boxes represent each major function of the subject being modelled. These functions are broken down or decomposed into more detailed diagrams, until the subject is described at a level necessary to support the goals of a particular project. The top-level diagram (A-0) in the model provides the most general or abstract description of the subject represented by the model. Figure 16 is a graphic representation of the A-0 context diagram for an activity.

Unlike many other modelling tools, an important concept in the IDEFØ method is the abstraction from time. The IDEFØ diagrams show activation of activities, rather than flow sequences. This was appropriate and relevant for the case studies in this research. Furthermore the IDEFØ diagrams may be decomposed

into lower level ('child') diagrams. These provide more detail while maintaining the simplicity of the diagrams. The hierarchy among the levels is maintained using a numbering system which organises the parent and child diagrams.
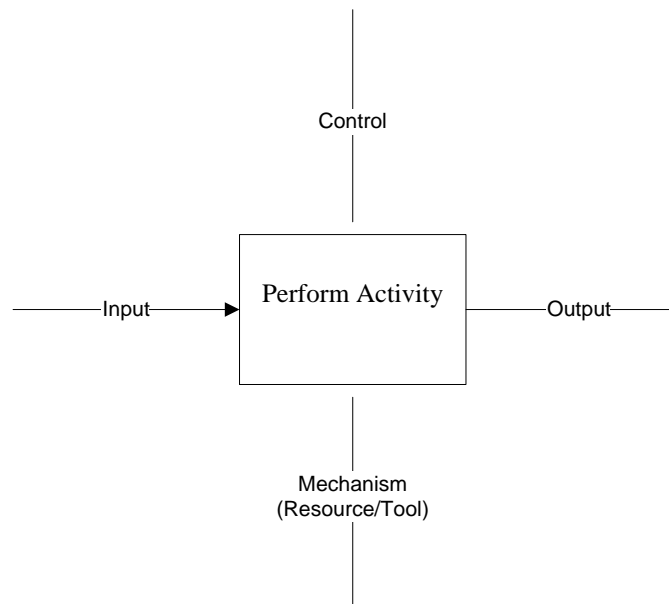
Figure 16. A-0 Context Diagram for an Activity

In the course of the author's fieldwork, a number of diagnostic techniques were used to gather information to populate the IDEFØ diagrams. These included interviews, factory tours and an examination of documentation such as company organisation charts, performance metrics, quality manuals, Standard Operating Procedures, corporate audit results etc. The outcomes of this fieldwork will become clearer as the case studies etc. are discussed in later sections/chapters.

6.4   Formulating Case Study 1

As a first step in generating activity diagrams, IDEFØ recommends compiling a preliminary activity list in which the data related to the function being composed are listed. An example of the preliminary activity list generated for the safety function can be referenced in Appendix 2. In order to enable a more detailed analysis of the inputs, outputs, controls and mechanism, following the

generation of the activity list, a series of questions were asked. IDEFØ does not provide any guidance in this regard, so a series of questions, based on the GRAI architecture (Graphs with Results and Actions Inter-Related), were used as a basis for interviewing key personnel. GRAI was developed by the University of Bordeaux in France (1993) and utilises IDEFØ as a component of its modeling tool. It uses the following questions to elicit the required information for the determination of the ICOMs:

- Who are your customers (receivers of what you send)?
- Who are your suppliers (senders of what you receive)?
- What is the form of your results?
- Who decides the form of your results?
- What are the used resources, tools, systems and machines?
- Where do you look for information?
- Can you characterise the results in terms of Cost, Quality, Time?
- Does the activity have performance indicators attached?

(Doumeingts et. al, 1993)

Together with information gathered from the diagnostic techniques mentioned in the previous section, all the information gathered was then translated into inputs, outputs, constraints and mechanisms and modelled using the IDEFØ template contained in the software program Microsoft Office Visio 2007. The validity of the model was then checked by adopting an iterative 'reader-author' cycle as recommended in the IDEFØ Standard. This work is presented in chapter 7.

6.5   Integrated Management Systems: The 'Questionnaire'

Having identified the quality function as a constraint to integrating quality, environmental, and health & safety systems within a particular FDA regulated company in the exploratory case study (Case Study 1), a broad questionnaire based survey was conducted to determine if this was universally the case in

regulated manufacturing environments. All medical device and pharmaceutical companies listed by the Industrial Development Agency (an Irish Government agency with responsibility for securing new investment from overseas in manufacturing) were surveyed. This involved eighty-two (82) medical device companies and seventy-one (71) pharmaceutical companies. The questionnaire was developed, issued and analysed in conjunction with a Final Year Industrial Engineering student from the University of Vigo, Portugal. Whilst the literature advice on questionnaire development will not be presented here, suffice it to say that the questions posed were predominately 'closed' questions with the intention of increasing the response rate. However, respondents were also given the opportunity to complete some 'open-ended' questions. The questionnaires were distributed by post and those outstanding by the return date were followed up by telephone calls. The questionnaire sought to determine the management systems currently in place and the level of integration, both existing and desired, within the companies surveyed. Information on barriers to integration was also sought. As the Quality Department appeared from the initial case study to be the main constraint to integrating management systems, and because it was known that all medical devices and pharmaceutical companies were obliged to have a quality system in place (and hence a Quality Manager), the questionnaires were addressed to the 'The Quality Manager' in each instance. A 33% response rate was achieved. More detailed results are presented in Appendix 6.

6.6   Formulating Case Studies 2 and 3.

The companies involved in this research were selected through personal contacts and based on their willingness to participate and agreement to provide access to the required individuals and support documentation. The relevant personnel were contacted and informed of the objectives of the research. Dates and times for interviews and site visits were arranged. IDEF∅ was again used to model the data from Case Studies 2 and 3. Based on the findings of Case Study 1 and the questionnaire results, a more detailed semi-structured interview schedule was

compiled to take account of the new information gathered. An example of this schedule is presented in Appendix 7. In each instance, the Quality Manager, the Environmental Manager and the Health & Safety Manager were interviewed. The interviews each lasted between thirty minutes and an hour. When permitted and where appropriate, the interviews were taped and transcribed as soon as possible post the interview session. As in Case Study 1, factory tours were undertaken and documentation was also examined. Again, to validate the data gathered, an author/reader cycle was used. Once Case Studies 2 and 3 were modelled they were examined in detail to search for common patterns and themes.

6.7   Framework Development

Once emergent patterns were captured from the case studies, a generic IDEFØ diagram was compiled to reflect these patterns. Together with the findings from the literature review, and the results of the survey, an integrated risk management framework, based on the corrective and preventive action (CAPA) process was developed. Embedded in this approach, are the required elements of the risk management process, namely, identification of hazard/non-conformity; assessment of the risk associated with these hazards/non-conformities; control of the risk; and the monitor and review of controls. The framework is then validated. This includes a validation of the data collection methods adopted in its development but also, in the absence of comprehensive methods and approaches for the validation of frameworks/models, a validation methodology is developed and applied.

6.8   Summary

This chapter has outlined the roll-out of the study and the methodology employed in carrying out the fieldwork. Integrating the results of the fieldwork with the findings from the literature review, a new integrated risk management framework is proposed. This framework reflects an integrated approach to the

management of risk to quality, the environment, and health and safety. The results of the fieldwork are presented in Chapter 7. The development of the proposed framework is dealt with in detail in chapter 8. Chapter 9 considers the validation of the proposed framework.

Chapter 7: Results and Analysis

7.1 Introduction

This chapter presents the findings from the fieldwork carried out in this study. It will describe in chronological order, the findings of the fieldwork. The chapter begins by presenting the findings from Case Study 1 which was an exploratory case study. This case study identified unique constraints faced by a highly regulated medical device manufacturer in integrating Quality, Environmental and Health & Safety management systems. To determine if these constraints were applicable to highly regulated manufacturers generally, a national survey of all Irish medical device and pharmaceutical manufacturers was undertaken. The survey considered the level of integration within these sectors as well as perceived barriers to integration. To investigate these issues in greater depth, two further case studies were carried out, one in the medical device sector and one in the pharmaceutical sector. The results of the case studies and survey are presented along with an analysis of the findings.

7.2   Detailing Case Study 1 – Exploratory Case Study

The objective of this case study was to investigate human and safety issues in advanced manufacturing systems with a view to determining if health & safety is given equal status to other key business elements. Modelling the safety management system of a medical device manufacturer, it became apparent that due to FDA (Food and Drug Administration) regulatory requirements, this company faced unique constraints, which allowed other business elements to constrain health and safety activity.

The company on which this case study is based, is located in the West of Ireland and is part of a multinational corporation manufacturing medical devices for a world market. The parent company is based in the U.S. Of the 13,000 employees world-wide, 265 are employed in this plant. The West of Ireland facility was established in January 1990 and its core technologies are in electronics, software, electromechanical assembly and pressure vessel fabrication, and medical devices

manufacture. The plant has a successful Food and Drug Administration (FDA) audit history and has been successfully audited to the international quality standard ISO 9001 and to ISO 13485 which specifically relates to medical devices. The National Standards Authority of Ireland (NSAI) carries out quality surveillance audits twice a year. Although the company is not accredited to a proprietary Environmental Standard, it requires an Integrated Pollution and Prevention Control (IPPC) license to operate. The company does not have an accredited safety management system. However, a corporate Environmental Health & Safety (EHS) policy is in place.

7.3   IDEFØ Mapping of Case Study 1

The safety management system was modelled using IDEFØ as the chosen methodology for analysis. To determine how the safety function operated a number of diagnostic techniques were used.   As stated in Chapter 6, these included interviews, questionnaires and observations; examination of the company's organisation chart, corporate audits, statistics recorded e.g. accident/injury rates, and the company's safety statement. A series of interviews were conducted with top-level management to ascertain the company's objectives with respect to safety and to determine who the main decision makers were and with whom the responsibility for safety rests. The IDEFØ Standard recommends talking to "one or more experts who possess the desired knowledge", therefore those interviewed included the Managing Director, the Manufacturing Engineering Director, the Health & Safety Engineer and the Human Resource Manager who has overall responsibility for Health & Safety. A sample of the field reports are given in Appendix 3. A tour of the factory was conducted which involved all areas including material stores, the various production lines, testing areas and shipping. Finally, the company's safety documentation was examined, including the plant's safety statement, the corporate audit etc. These investigations established how the safety function currently operated. The first step in the application of IDEFØ is to describe the activity being modelled using an imperative. This precise activity for this case

was determined to be 'Operate Safe Company'. The information gathered was then translated into inputs, outputs, constraints and mechanisms and modelled using the IDEFØ framework. The validity of the model was then checked by adopting a 'reader-author' cycle.   Figure 17 shows the initial A-0 context diagram for the company's 'as-is' situation.
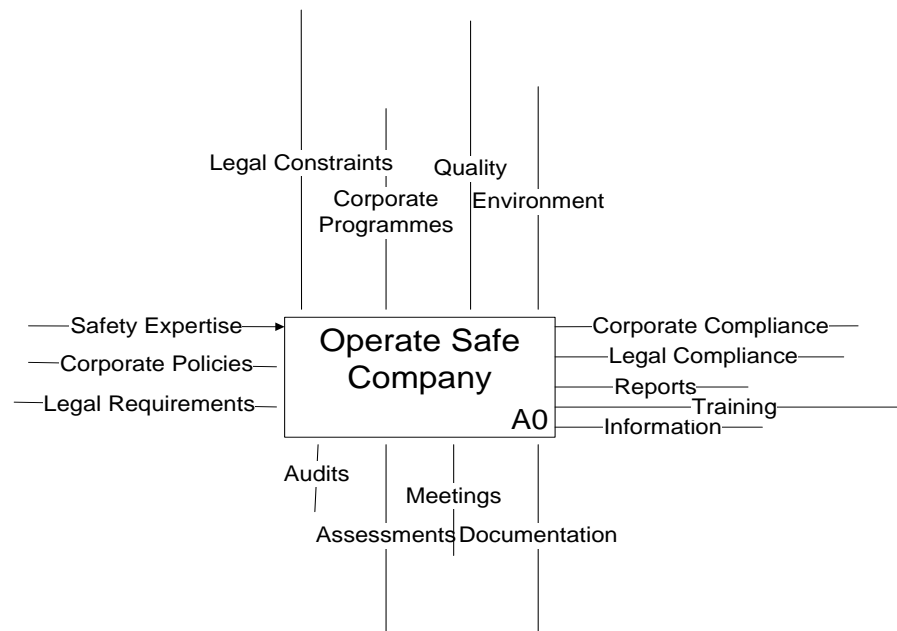
Figure 17. Operate Safe Company A-0: 'As – Is'

7.4   Outcomes of Case Study 1

Constraints:

Legislation is a major constraint in guiding the safety function of the company. The company must comply with European legislation and Irish legislation. Environmental Regulations governing the issuance of the company's Integrated Pollution and Prevention Control License (IPPC) is also a constraint on operations and safety activities. The company's in-house quality system is also identified as a

constraint. Interestingly, the Quality Department controls any changes to processes and hence to standard operating procedures as deemed necessary by the safety Engineer and so in effect constrains safety activities. The Quality Manager was unavailable to take part in the case study.

Inputs:

The A-0 parent diagram identifies safety expertise as one of the main inputs into the safety function. This safety expertise lies predominately with the Health & Safety Engineer. The Health and Safety Engineer reports directly to the Human Resource Manager but it is the responsibility of the Health and Safety Engineer to ensure the day-to-day safety of production and office personnel. She is also responsible for implementing corporate programmes relating to Health and Safety, training of personnel in safe practices, and conducting safety and ergonomic audits and assessments. It is also the responsibility of the Health and Safety Engineer to keep abreast of relevant and up-to-date legislation and bring it to the attention of management. In essence, the Health and Safety Engineer is responsible for driving safety throughout the plant.

Outputs:

One of the main outputs of the safety function is the generation of reports. These include performance reports to local management and corporate health and safety, regulatory reports to the Health and Safety Authority, and verbal reports from plant workers and the safety committee to supervisors and the Health and Safety Engineer. The Health and Safety Engineer incorporates a safety related article in the monthly newsletter. Safety training of both production and office personnel is also an output. All new production hires undergo induction training and the safety component of this training is carried out by the Health and Safety Engineer. Compliance with corporate programmes and policies and compliance with European and Irish legislation are also outputs.

Tools and Mechanisms:

The tools and mechanisms used to operate the company in a safe manner are predominantly ergonomic and safety audits and assessments. Safety meetings are held with the company's safety committee every three months to discuss safety matters, and the Health and Safety Engineer meets informally with the Human Resource manager on a regular basis. Documentation such as the Safety Statement, Material Safety Data Sheets etc. is also used as reference material.

Once the top level A-0 context diagram was defined the next step was to determine the next level A0. This time the questions asked were what activities make up the main activity and what are their associated ICOM's. It was obvious that the operation of safety was to a large extent concerned with compliance with corporate policies and programmes and legal compliance. To this end the safety activities carried out were predominately:

- conducting inspections and assessments,
- the development of safe operating procedures,
- the provision of safety training – predominately to operators,
- keeping records,
- conducting and attending meetings

Figure 18 shows the A0 diagram for 'Operate Safe Company'
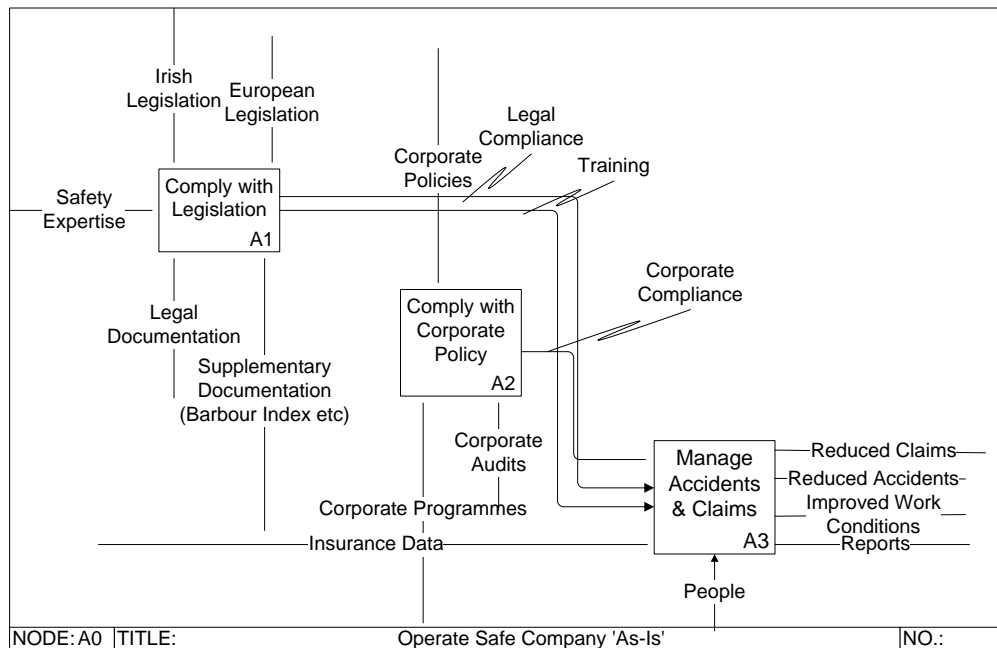
Figure 18. Operate Safe Company A0 'As – Is'

7.5   Key Findings – Case Study 1

Once the as-is situation was modelled the next stage was to analyse each component of the model. The answers to the questions outlined in the interview schedule and the IDEFØ formulation document as well as comprehensive interviews suggested that within the company the role of the safety function was narrowly defined being chiefly concerned with training, conducting inspections   and assessments, keeping records, conducting meetings and developing safe operating procedures. These activities were driven by the Health and Safety Engineer.

Although the management of safety encompasses all areas within the company there is little integration between the quality, environmental and health & safety management systems. As already stated, the quality department controls any changes to processes suggested by the Safety Engineer. The Facilities department

has overall responsibility for environmental issues and is mainly driven by requirements for maintaining the company's Integrated Pollution Prevention and Control (IPPC) license. The Human Resource department is responsible for safety. The Environmental system and the Health & Safety system appeared at first glance to be an integrated system but really are also two separate systems. The Health and Safety Engineer, reporting to the Human Resource manager, is responsible for all health and safety matters while the Facilities Engineer, reporting to the Facilities Manager, is responsible for environmental issues. An Environmental coordinator in the maintenance dept also reports to the Facilities Engineer. Two separate policies exist; a Health & Safety Policy and an Environmental Policy but they are in effect mission statements rather than any detailed statement of policy.

The main driving source of health and safety in the company is the Health and Safety Engineer. The Health and Safety Engineer is also the main source of information with chief reliance on the Health and Safety Engineers' own knowledge base and expertise. A safety Intranet exists which is maintained by corporate head office in the United States but it is accessible only to those having access to a Personal Computer and so is not directly available to production operatives. Safety activities are usually initiated from corporate policy and these policies are communicated via the company Intranet and through the hierarchical chain of command, i.e. the General Manager, the European Health & Safety manager and the Human Resource manager to the Health and Safety Engineer. A corporate Health & Safety programme exists and the company has an up-to-date specialist information service in the form of the Barbour Index. The Health and Safety Engineer is a member of the Institution of Occupational Safety and Health and the Irish Ergonomics Society and subscribes to relevant health and safety publications. Although a safety representative and a safety committee exist within the company, they tend to focus more on highlighting problems rather than offering solutions.

With regard to top management, although they must include safety in their reports, apart from the managing director and the Human Resource manager, the interviews revealed that management do not feel they 'own' safety. In other words a safety culture is not pervasive among top management.

With regard to the initial objective of Case Study 1 i.e. investigating the standing of health and safety activity in relation to other key business elements, it became apparent that in this company, due to FDA regulation, the quality department exercised control over all processes and procedures including any changes to those which may be required from a health and safety perspective. This means that in effect, quality constrains the safety function within this company. This posed an interesting question; within all highly regulated manufacturing companies, will quality take precedence over safety and does this mean that such companies will not and cannot integrate their management systems?

7.6 Survey of Medical Device and Pharmaceutical Sectors

Having highlighted the quality function as a constraint to integrating quality, environmental, and health & safety management systems within a particular FDA regulated company, it was decided to conduct a broad survey to determine if this was universally the case in regulated manufacturing environments. To this end, a survey was conducted on all medical device and pharmaceutical companies in Ireland, as listed on the Industrial Development Authority's (IDA) website. As already stated, this involved eighty-two (82) medical device companies and seventy-one (71) pharmaceutical companies.

7.6.1 Survey Aims and Objectives

The primary aim of the survey was to determine if integration of Quality, Environmental and Health & Safety Management Systems existed within highly regulated environments and, furthermore, if companies felt such integration was desirable, and feasible.

This would be achieved by means of the following objectives:

- Assess the level of integration of the Quality, Environmental and Health & Safety management systems within the medical device and pharmaceutical sectors in Ireland.

- Determine if companies in these sectors are interested in integration, and if so, determine at what level integration is desired.

- Determine if barriers to integration exist and if so what these barriers are.

7.6.2 Questionnaire Structure

The questionnaire sought to determine the management systems currently in place and the level of integration, both existing and desired, within the companies surveyed, from the perspective of the Quality Manager. The questions were formulated from the literature and from the results of Case Study 1. In determining the level of integration within the companies, the questionnaire focussed on three main areas where integration can exist; documentation, personnel and procedures. Companies were also asked the level of integration they desired, and what they perceived as the barriers to integration.

7.6.3 Survey Findings

The main findings from the survey are outlined here. However, a detailed breakdown of all responses from returned questionnaires is provided in Appendix 6.

A 33% response rate was achieved. This included 31 responses from medical devices companies; 17 responses from pharmaceutical companies; and 3 responses from companies who described themselves as both medical devices and pharmaceutical.

As a quality management system is mandatory for regulated companies it was not surprising to find that all companies had a quality management system in place. In addition, 66% of respondents claim to have at least 2 management systems in place and just over 40% claim to have 3 systems in place. This would suggest that where those systems are not integrated, an opportunity for integration exists. Regarding commonality in written procedures, within the medical device sector 35% of respondents (n=11) utilise separate written procedures with the remainder utilising some combination of either Quality, Environment and Health & Safety (Q,E,H&S), Quality and Environment (Q,E), Environment and Health & Safety (E,H&S), or Quality and Health & Safety (Q,H&S). Within the pharmaceutical sector, almost 30% of respondents (n=5) use separate written procedures for managing their systems, another 30% (n=5) integrate their Environmental and Health & Safety procedures and 13% of those who responded (n=4) use some combination of Q,E,H&S or Q,E. Two companies failed to respond to this question and one company (n=1) claims to use written procedures for quality only. This would imply that where there is commonality in procedures/documentation, there is scope for their integration within both sectors.

Integration can exist at the level of personnel in charge of managing the systems. The respondents were asked if;

      i)   different people were in charge of each system, but this was overseen or coordinated by a third person (1 person per system/team coordinated)

ii) different people or different teams were in charge in each system without any further coordination (different people/teams un-coordinated).

iii) one person or one team was in charge of all systems (1 person/team only)

From the feedback received (Table 7), it is evident that the pharmaceutical sector has less integration of its management systems, at personnel level, than the medical devices sector. For example, the area shaded in blue shows that a total of 10 medical devices companies operate three management systems (quality, environmental and health & safety). Of these 10, 3 companies have different people in charge of each system, which is coordinated by 1 person; 3 companies have different people in charge of each system, but without any further coordination; and 4 companies have one person or one team in charge of all systems.

Table 7. Structure of Personnel Teams

| Sector | Type of integration Structure | Number of Systems | | | |
		1	2	3	Total
Medical Devices	i) Coordinated Teams	4	4	3	11
	ii) Uncoordinated Teams	4	3	3	10
	iii) One Person/Team	6	3	4	13
	Total	14	10	10	34
Pharma	i) Coordinated Teams	2	2	3	7
	ii) Uncoordinated Teams	1	0	6	7
	iii) One Person/Team	1	1	2	4
	Total	4	3	11	18

The six core management activities which are generally common to all management systems and which are reflected in the ISO standards are; management review, corrective action, documentation, process control, training and auditing. The questionnaire sought to investigate if the same procedures exist where the same activity is carried out for different systems. In other words, the questionnaire sought to determine if commonality existed among procedures regardless of how personnel are assigned or how documentation is managed. Of those companies who responded, it was evident that many companies have similar procedures for management review, corrective action, documentation, process control, training and auditing for managing quality, environment and health & safety systems, whilst some companies (n=6) share all six core elements within all three management systems.

The questionnaire sought to determine if companies are interested in integration and if so, to what level. Just over half (n=16) of all medical device companies responding expressed an interest in integrating their systems. Of those sixteen, eight would consider integrating Q,E,H&S and a further four companies would consider integrating quality and environmental systems. Thirteen medical device companies would not consider integrating their management systems. Six of these companies were happy with the level of integration already achieved. Of these, three claimed to already have full integration of quality, environmental, and health & safety systems. The remainder of the companies highlighted barriers to integration which will be dealt with later.

Within the pharmaceutical sector 8 companies were already happy with the level of integration they had. However, 1 respondent intimated that Good Manufacturing Practice (GMP) could not be integrated with health and safety or environmental systems, and 1 respondent identified lack of resources as the reason. Only 3 out of 17 pharmaceutical companies said they would consider integration, one of which

was already in progress. 1 respondent was interested in integrating all three management systems (Q,E,H&S) with 1 respondent considering either quality and health & safety *or* environment and health & safety. 1 respondent stated although they were not considering integrating their management systems they were trying to "unify" procedures between quality and EHS. Another company working towards OHSAS 18001 said they might consider it in the future. 2 companies did not respond to this question.

7.6.4   Barriers to Integration

To determine what barriers existed to integration two approaches were used; one question was a closed question offering the respondents a list of barriers as identified in the literature and the exploratory case study; the other question was an open-ended question in which the respondents had the freedom to list barriers they felt were of particular relevance to their own company and their industry sector. The predominant issues identified as barriers in the literature and the initial case study, and presented in the questionnaire, were:

- Differences between Food and Drug Administration (FDA) requirements and the requirements of International Standards Organisation (ISO).
- Lack of a single standard for integrating the systems.
- Lack of a methodology for integrating the systems.
- Stakeholders see integration as a waste of time.
- Companies lack the time and human resources to integrate the systems.
- The fear exists that integration will lead to a loss of flexibility.
- It is difficult to train internal auditors.

The majority of respondents in both sectors believed the lack of a single standard to be the most important barrier to integration with 63% of all respondents identifying this was an important barrier.

Respondents were asked if the lack of a methodology was a barrier to integrating their management systems. 57% of all respondents felt this was an important barrier while 31% felt it was unimportant.

Because most medical device and pharmaceutical companies are regulated by FDA and many conform to an ISO standard, respondents were asked if differences between FDA and ISO were a barrier to integration. Just under half (47%) identified this as an important barrier, whilst a third (33%) identified it as unimportant. 20% failed to respond to this question.

Many companies are constrained by lack of time and human resources and so respondents were asked if these issues were of relevance for integrating their systems. Almost half (49%) believed this to be an important barrier.

Interestingly, fear of losing flexibility was seen as more important within the medical device sector but less important for the pharmaceutical sector.

With respect to the training of internal auditors, a slight majority of companies (55%) did not feel that this was a barrier to integration.

The final question in the questionnaire was an open-ended question used to elicit respondents own belief as to what presented barriers to integration. Nine pharmaceutical companies identified lack of resources, both financial and manpower, as the main barrier to integration. Some other interesting comments were:

"Quality requirements relating to the actual product are considered critical and thus require more focussed management with the exception of areas where the

environment has a direct effect on product quality. Also product quality has a higher customer and regulatory risk and profit." (Pharmaceutical)

"Functional responsibility is divided via department managers." (Medical Devices)

"Systems are owned by different departments". This response was interesting as it is the antithesis of the process approach requirement of ISO 9001. This company has both ISO quality and environmental certification. (Medical Devices)

"Biggest problem is that there are no guidelines on how to do it" (Medical Devices)

"Need to provide equal resources and focus on safety as well as quality systems. Quality system is the key to business but safety needs are being driven by people not necessarily familiar or disciplined in running a management system." (Medical Devices)

"People who have worked a certain way for a number of years do not like change so barriers are management buy-in, poor direction/leadership, fear of the unknown, motivation (tangible results to improving business)." (Pharmaceutical)

"The different requirements associated with FDA and environmental/safety standards is the main barrier. Also, separate corporate groups are involved and have very different approaches to the management system associated." (Pharmaceutical)

"Integration can lead to a dilution of each individual system if you are not careful." (Pharmaceutical)

"GMP not integratable with Health & Safety or environmental." (Pharmaceutical)

"Not seen as a business priority." (Pharmaceutical)

"Resistance to change. Strong ownership of one process and slow to let go. Benefits not marketed strongly enough." (Pharmaceutical)

"Quality and EH&S systems are segregated by departmental barriers. The expertise within each department is localised and it is difficult to see the benefit in having a high level of expertise across both functions relative to the payback that could be achieved." (Pharmaceutical)

"We don't have a certified health and safety and/or environmental management system. We meet legal requirements with safety statement and associated procedures. We haven't attempted to integrate systems beyond management review primarily due to limited resources (funding and people)." (Medical Devices)

One company manufacturing both medical devices and pharmaceuticals said it is difficult to integrate certain activities such as auditing and management review where there is a different focus – "would make the activity e.g. auditing too complex."

One response suggested that "although FDA requirements are different to ISO, they must be combined, and the FDA QSR goes a long way towards integration. Once the Quality System complies with FDA and ISO9001, it is then a much easier matter to include ISO 14001 and OHSAS 18001." (Medical Devices)

7.6.5   Key Findings from Sectoral Survey

The questionnaire survey produced some interesting results. Although core management elements such as management review, corrective action, documentation, training and auditing exist across quality, environmental and health & safety systems, companies feel they lack a single standard and a methodology for integrating these systems. Although many core management elements exist, many companies use separate written procedures. This is interesting as one of the benefits of integration discussed in the literature is reduced documentation. Whilst a lack of a methodology and a single standard was found to be an important barrier, it is interesting to note that most respondents did not perceive training of auditors as a potential problem. It was clear from the responses received from the Quality Managers that quality requirements are critical, and the Quality System is perceived as being the key to business. It was also clear that management systems are segregated by departmental barriers and the approach to managing each system appears to be different. This is particularly interesting in light of Wright's suggestion (1999) expressed in Chapter 3, that it is unsafe to assume consistency and congruence of management style and attitudes across all areas of management responsibility.

7.7   Detailing Case Study 2 – Medical Devices Company

One of the main findings of the Survey was that although core management elements exist across QEH&S management systems, companies feel they lack a single standard and a methodology for integrating these systems. Following on from this, further case studies are conducted in the two sectors of interest. These are undertaken to yield more in-depth information as to how the management systems work in practice in a regulated environment and can provide an opportunity to identify common approaches to management within and across the sectors. They can also show if systems are managed along functional and departmental lines, and

if differing management approaches exist. The objective of the following two case studies therefore is to model the Quality, Safety and Environmental Management Systems of both a medical devices company and a pharmaceutical company to identify commonalities within the management systems across both sectors, as well as identifying where and why segregation of the systems might exist. The information required for the creation of the models is gathered using semi-structured interviews with top-level personnel responsible for the management of environmental, quality and health & safety systems. Once gathered, the main findings are mapped and then the common elements assembled into IDEFØ format as in the previous case study. The remainder of this section is devoted to case study 1 with case study 3 being discussed in Section 7.8.

7.7.1 Background to the Company

The company used in case study 2 is a medical devices company, is based in the West of Ireland and which is part of a multinational organisation with its headquarters in the United Kingdom. This organisation has four plants in Ireland and thirteen other plants worldwide. The plant studied employs over 2,500 workers and manufactures over 2000 different medical device products for a world market.

The company has three certified management systems; an Environmental Management System with certification to ISO 14001; and a certified Quality Management System ISO 9001; as well as ISO 13485 specific to Medical Devices. The company does not have a certified Health & Safety Management System and does not see itself pursuing certification to OHSAS 18001 in the near future as the corporate policy is to get all subsidiary companies certified to ISO 14001 first.

7.7.2   The Quality Management System

As a medical devices manufacturer, the company has a detailed and stringent quality management system. The quality management system is focused on the product and is driven primarily by compliance to FDA regulations but also to Quality standards ISO 9001:2000 and ISO 13485. The various production lines operate within cleanroom environments and production activities are procedure-based. Any changes to these procedures require Quality approval. The Quality System is audit based with the main emphasis on the Corrective and Preventive Action (CAPA) component of the audit process. The company's CAPAs are generated at two levels. Lower level CAPAs are dealt with in the 'value stream' (product line/cell). These are normally generated internally through, for example, 'exception reports' detailing issues that arise which do not conform to accepted procedures. Higher level CAPAs are dealt with at company level. These are issues more often generated externally e.g. product recalls. To deal with these higher level issues, a team is formed, the scope of the required action is determined and a close-out date for the CAPA is determined. This part of the process has a six week lead-time. The CAPA is revisited every 3 months until close-out but forms part of a monthly report generated within the Quality department. If the close-out period will not be achieved, then the team leader must inform the CAPA department and look for an extended deadline. If a deadline is not sought and the CAPA is not closed out by the due date, then the company is 'red-carded' by corporate head office. The company's CAPA system is guided by SMART criteria i.e. Specific, Measurable, Achievable, Relevant, and Time-bound objectives. CAPAs generated are dealt with using the following approach:

(i)   Containment actions – short-term actions adopted using a 'temporary change request'.

(ii)   Corrective actions – long-term action e.g. updating procedures

(iii)   Permanent corrective actions

(iv)   Preventative recurrence.

The FDA requirements on the company are to show evidence of corrective action and to show the root cause analysis. Corporate head office is currently proposing a risk assessment approach to root cause analysis. This proposed approach has not yet been clearly defined. To conduct a root cause analysis, the company currently utilises process Failure Mode and Effects Analysis (FMEA) and a Six Sigma problem-solving approach DMAIC: Define opportunities, Measure performance, Analyse opportunities, Improve performance, Control performance. When implementing corrective and preventive actions, the company uses master validation plans to ensure the product is not affected.

The company's Quality Management System is audited externally by TÜV Rheinland, a German auditing company, and by the FDA.

7.7.3   The Health & Safety Management System

The company employs a health & safety manager who is also responsible for environmental management. These systems are managed separately however. The company complies with ISO 14001 Environmental Management Standard but does not comply with any proprietary health and safety standard. The management of safety centres on the review and update of the company's safety statement; risk assessment and training. Under Irish legislation, all employers are required to have a Safety Statement. (Section 20 Safety, Health and Welfare at Work Act 2005). The safety statement is management's programme (in writing) for managing the safety, health and welfare of employees. The legislation stipulates that the employer has ultimate responsibility for health and safety and therefore the Statement should begin with a declaration, signed at senior level indicating commitment to a workplace that is as safe and as healthy as is reasonably practicable, and that all relevant statutory requirements will be complied with. The declaration should spell out management's policy in relation to overall health and safety performance, and provide a framework for the management of health and safety as well as indicating

relevant objectives. It should also indicate that statement will be revised as changes occur and periodically evaluated at set intervals. The Statement should indicate how the contents are to be brought to the attention of employees and to others who might be affected (e.g. contractors). The company's Safety Statement complies with all of these requirements.

The Safety Statement, where necessary, also refers to specific procedures contained in other documents, for example;

- Quality manuals

- Operating instructions

- Company rules

- Manufacturers instructions

- Health and safety procedures

The Safety Statement is based on the identification of hazards, an assessment of the risks associated with these hazards, and the elimination or control of these risks. It is a 'live' document as clearly stated in the legislation. Therefore it must be relevant at all times and must be updated if any of the following changes occur;

- Changes in work processes, organisational structure, equipment, substances, technical knowledge, legislation, standards etc.

- Changes in the workforce.

- If existing control measures fail.

The company maintains an accident log. In the event of an accident, a comprehensive accident investigation procedure is implemented.

The Company is aware that the regulator's guidelines (Health & Safety Authority) on compiling safety statements suggest that management undertake a review of the Safety Statement to see how effective Health & Safety management has been and to determine if;

- Health & Safety aims were relevant and appropriate

- Significant hazards were identified and their risks assessed and the necessary preventive and protective safety measures set out

- Control measures were identified implemented in practice

- New measures were applied following any accidents or incidents

- Resources were adequate

The guidelines also suggest looking forward to ensure an organisation has considered any improvements in health and safety measures that need to be made for the future.

7.7.4 The Environmental Management System

As stated previously, this company's Health & Safety Manager is responsible for the Environmental Management System (EMS). The EMS centres around six significant aspects. These are (in order of priority):

(i)   hazardous waste

(ii)   non-hazardous waste

(iii)   energy consumption

(iv)   noise

(v)   emissions to atmosphere

(vi)   emissions to drain.

The main goals are to ensure compliance with legislation and to ensure compliance with license conditions. The other goals centre on the reduction of hazardous waste, increasing recycling, and decreasing waste being sent to landfill. Targets are based on either production i.e. number of products produced or on head-count. Achieving these goals allows the company to fulfil its social responsibility and publicise what it does, as well as to show evidence that it is continually improving the EMS – one of the stipulations of the ISO 14001 standard and one which becomes more difficult the longer the system is in place.

The objectives of the Environmental Management System (EMS) are SMART objectives i.e. Specific, Measurable, Achievable, Relevant, and Time-bound and these objectives form part of the company's annual review. If its objectives are not achieved, then a non-compliance report must be written-up. The customers of the EMS are considered to be the company employees, local environment and the global environment. There is a formal reporting structure in place for suggestions and complaints.

Management of the EMS falls under the remit of the Health & Safety Manger. There is no specific EMS team although the company does have a team of internal auditors. There is a documentation system in place which controls all documents on site. This is not a standalone database system but runs on the same platform as the quality system. The systems are aligned, however, but only to the extent of document control.

There is a corporate EMS policy currently in place. Although there is no formal SMS in place, the corporation is currently performing compliance audits of the EMS and SMS, as a means of benchmarking across all the manufacturing and distribution sites. In terms of waste management, the company has, in the last year, streamlined its process by consolidating its contractors to a single waste management company which is responsible for all waste management. Furthermore, the company operates 'green' purchasing criteria for raw material. They choose their suppliers based on questionnaires and operate a scoring approval system for vendors. The company has recently made significant progress on packaging by using special 'green' dyes on packaging, using recyclable packaging, reducing the amount of packaging on finished products and using more generic packaging. If the company's stated goals and objectives are not achieved then a non-compliance report must be written-up.

7.7.5 IDEFØ Mapping of the Management Systems

From the data gathered, the key elements of the Quality, Environmental and Health & Safety management systems were determined and are represented individually in the A-0 Context Diagrams, i.e. Figures 19, 20 and 21 respectively. The main elements common to the management of all three systems are then presented in Figure 22.
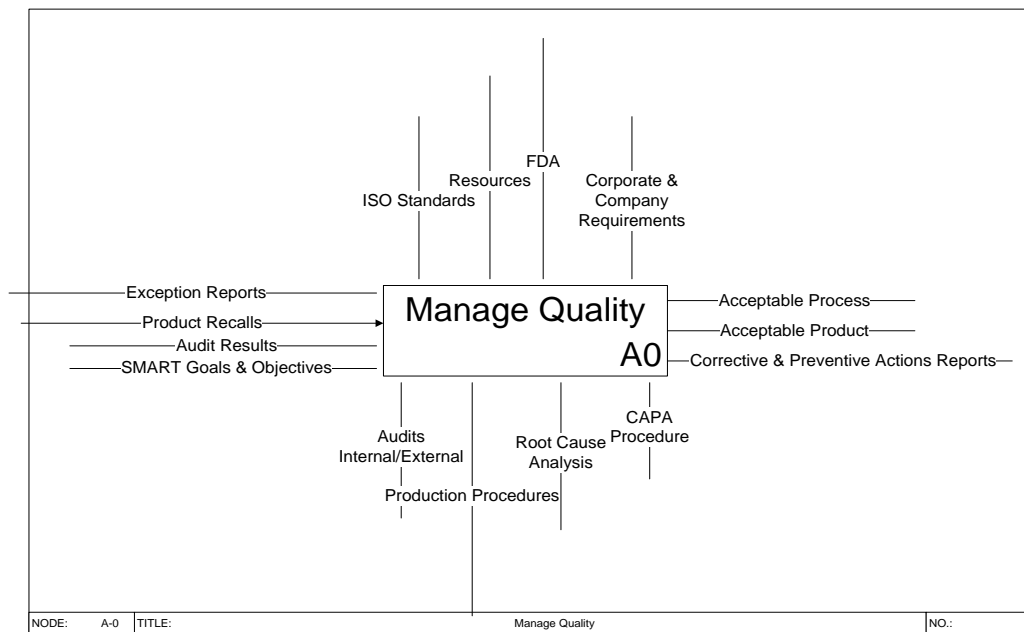
Figure 19. Manage Quality – Medical Devices Company

The A0 activity that appears in the context diagram identifies the scope of the analysis. These individual activities are; Manage Quality, Manage Environment and Manage Health & Safety, and are outlined in the following subsections.

7.7.6 ICOMs for 'Manage Quality'

Inputs:

Exception Reports: These are reports on issues which do not conform to accepted norms as generated by the CAPA audit process. This information is generated internally in the company and forms a key input to the management of the Quality System.

Product Recalls: Generated externally, product recalls provide vital information for identifying serious faults in the management of quality.

Audit Results: The results of audits, both internal and external feed into the quality programme.

SMART Goals and Objectives: The Company sets quality objectives which are Specific, Measurable, Achievable, Relevant and Timely (SMART). These would include targets for reduced rework, recalls etc.

Outputs:

Acceptable Process: One of the required outputs with respect to managing Quality is to conform to a quality process that is compliant with regulation, as well as company and corporate procedures and policies.

Acceptable Product: The Company must produce products of a quality acceptable to the market.

Corrective and Preventive Actions Reports: When the required output is not achieved (failed audits, product failures etc.), corrective and preventive action reports are generated.

Constraints:

FDA Requirements: As a medical device manufacturer the company must comply with stringent regulations as laid down by the Food and Drug Administration. These have been covered in detail in Chapter2.

Irish Medicine Board Regulations: The Company must also comply to Irish Medicines Board regulations to retain their manufacturing license.

ISO Standards: Certification to ISO 9001, ISO 13485 and ISO14001 requires the company to operate within the constraints/requirements of these Standards.

Corporate and Company Policies & Programmes: As part of a multinational corporation, the company must conform to corporate policies and programmes. For example, corporate head office requires that all Visual Display Unit (VDU) workers undergo an ergonomic training programme.

Resources: The company has finite resources for managing the Quality System.

Mechanisms:

Audits: Extensive auditing, both internal and external is used to inform the Quality System of conformance and non-conformance to stated objectives.

Production Procedures: These are Standard Operating Procedures (SOPs) to ensure that product is manufactured to specification.

Root Cause Analysis: The Company has stated its commitment to identifying the root cause of all non-conformities.

CAPA Procedure: The CAPA procedure is critical to achieving a product and a process of the required standard as specified by the regulatory authorities.

7.7.7 ICOMs for 'Manage Environment'
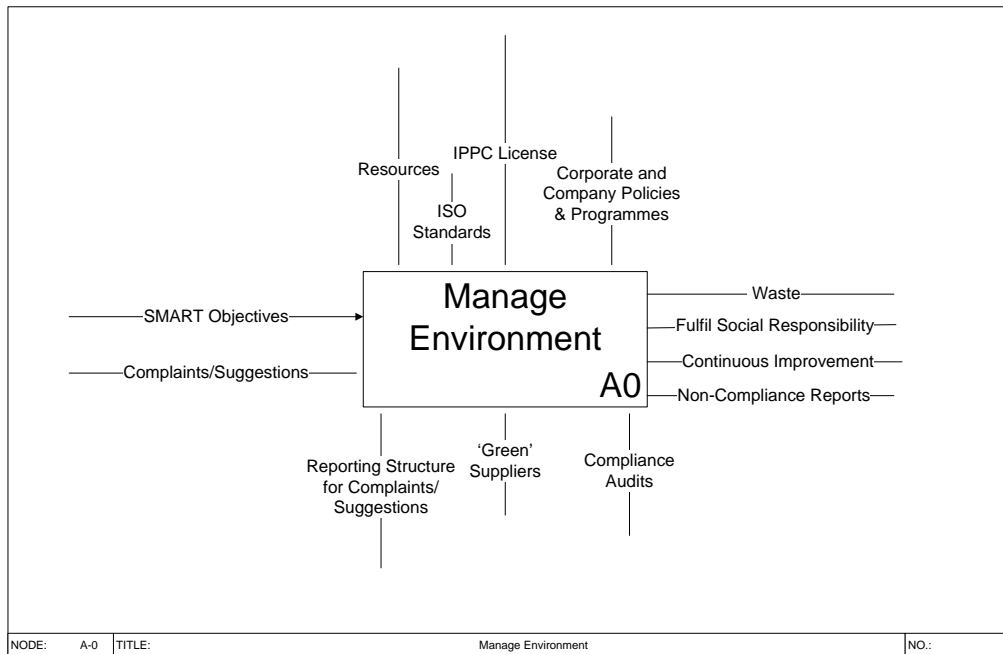
Figure 20. Manage Environment – Medical Devices Company

Inputs:

SMART Objectives: As already stated, the goals of the environmental system include reduction of waste, energy consumption, noise and emissions. Like the Quality System these are based on SMART criteria.

Complaints/Suggestions: Complaints and suggestions from regulatory authorities as well as from the general public, feed into the management of the EMS.

Outputs:

Continuous Improvement: ISO 14001 stipulates a requirement for continuous improvement and so the company is required to provide evidence of this as part of its accreditation.

Fulfil Social Responsibility: The Company wishes to fulfil its social responsibility by not harming the environment and wants to provide public evidence of meeting this responsibility.

Waste: As a by-product of its operations, waste is produced. This takes the form of emissions to air, emissions to drain, packaging etc.

Non-Compliance Reports: Non-compliance reports are generated when the stated objectives are not achieved.

Constraints:

Integrated Pollution and Prevention Control license: The Company requires an Integrated Pollution and Prevention Control license to operate. It is therefore obliged to follow pre-prescribed procedures in relation to the control of emissions to air and to water etc.

ISO Standards: The Company must operate within the constraints imposed on it by certification to ISO14001.

Corporate and Company Policies & Programmes: Internal company policies as well as corporate policies and procedures exist. An example of this would be the 'green' purchasing criteria mentioned previously.

Resources: The Company has finite resources for managing the Environmental System.

Mechanisms:

Compliance Audits: Internal and external audits are conducted to ensure compliance with programmes and policies.

'Green' Suppliers: To achieve its environmental objectives the Company extends its requirements back through the supply chain. It operates a 'scored' approval system for its suppliers.

Reporting Structure for Complaints/Suggestions: To ensure all feedback is received, the Company has a complaints/suggestion reporting structure in place.

7.7.8 ICOMs for 'Manage Safety'
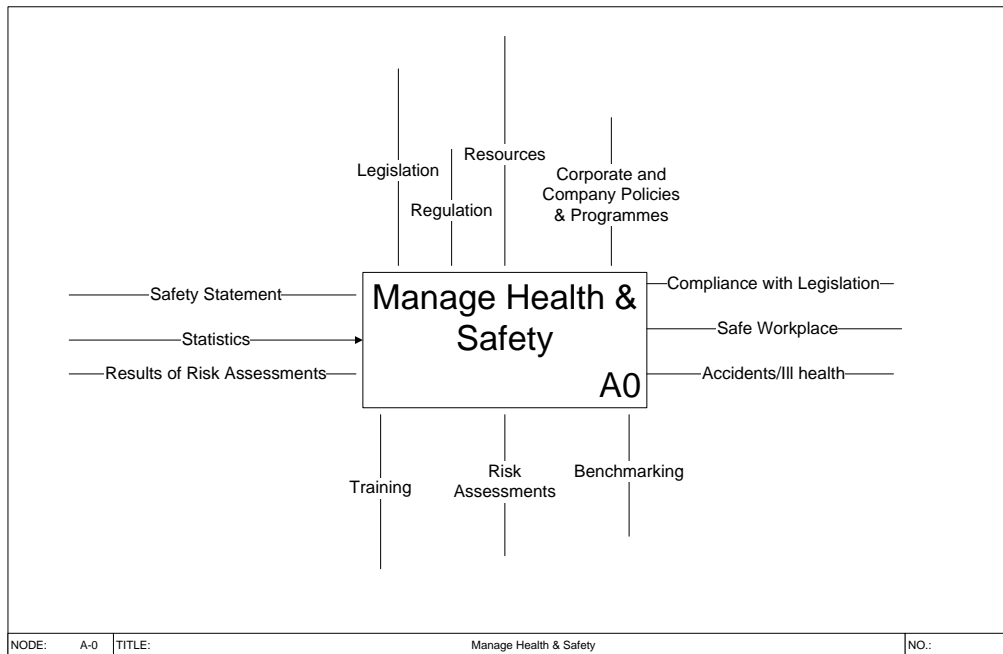
Figure 21. Manage Health & Safety – Medical Devices Company

Inputs:

Safety Statement: As outlined previously, the company uses the Safety Statement as its main input into the management of safety.

Statistics: Statistics recorded for accidents and sick leave e.g. lost time injuries give an indication as to how well the safety management system is working and this information is used to inform new policies and procedures.

Results of Risk Assessments: The results of Risk Assessments identify where failures exist or could potentially exist within the system and the severity of these.

Outputs:

Compliance with Legislation: In managing Health & Safety, the company must comply with Health & Safety legislation.

Safe Workplace: The company is committed to achieving a workplace that is as safe and healthy as is reasonably practicable.

Accidents/Ill Health: If the Health & Safety System fails, this results in accidents and/or ill-health.

Constraints:

Legislation: The Company must comply with extensive Irish Health & Safety legislation. The main pieces of legislation include the Safety, Health and Welfare at Work Act 2005 and the General Applications Regulations. Whilst these are quite broad, many specific pieces of legislation exist and are applicable depending on the tasks the company undertakes at any given time e.g. The Construction Regulation 2006. The company is also obliged to take cognisance of any Approved Codes of Practice (ACoPs) produced by the Health & Safety Authority e.g. Code of practice on the Prevention of Workplace Bullying. In the event of criminal proceedings, these ACoPs are admissible in court.

Corporate and Company Policies and Programmes: Corporate head office requires all sites to implement particular policies and programmes e.g. an ergonomic intervention training programme.

Mechanisms:

Training: The Company undertakes extensive training of personnel to ensure their health & safety e.g. manual handling training, ergonomics training.

Risk Assessments: Legislation dictates that risk assessments must be conducted based on an identification of hazards, an assessment of risk and the control of this risk. These risk assessments provide the basis for the company's Safety Statement.

Benchmarking: The Company subscribes to the 'Good Neighbour' scheme whereby they have opportunities to benchmark their safety performance and strategy against other willing participating companies.

7.7.9 ICOMs for Manage 'Q,E,H&S'

Once the key elements of the individual Quality, Environmental and Health & Safety management systems were mapped, the main elements common to the management of all three management systems were identified. These elements are presented in the following IDEFØ diagram and subsequently described in more detail – see Figure 22.
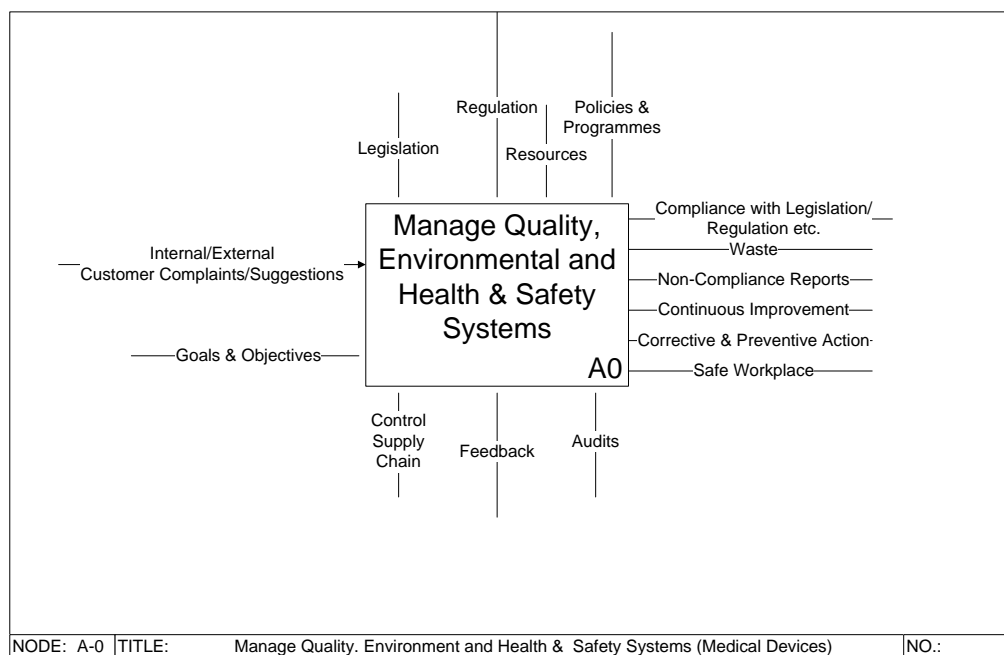
Figure 22. Manage Quality, Environment and Health & Safety Systems –Medical Devices Company

The ICOMs are described as follows:

<u>Inputs:</u>

Goals & Objectives: The management of Quality, Environment and Health & Safety centres on the goals and objectives which provide the chief inputs into the system. For all three systems, the main goal is that of compliance either to legislation, regulation or company and corporate policies and procedures.

Internal and External Complaints and Suggestions: Complaints and suggestions offered by the customer, regulator, legislator or general public will be used as an input to managing the systems.

Outputs:

Compliance: The system is performing according to its objectives when it achieves compliance with legislation, regulation, customer requirements etc.

Non-Compliance: When the system fails to achieve its objectives it is in a state of non-compliance.

Waste: A by-product of production is waste. Good management will minimise the extent of waste produced and its potential harm.

Continuous Improvement: Managing the QEH&S systems according to the principles of proprietary standards, regulation and legislation will lead to a cycle of continuous improvement.

Constraints:

Legislation: Companies operating in a country or state are governed by its laws. Irish legislation and European legislation is extensive and must be complied with.

Regulation: Medical Devices manufacturers operating within the medical devices sector are regulated both in the country of manufacture and in the country where the products are being used. In the case of this manufacturer, this will include regulation by the Irish Medicines Board and the FDA in the U.S.

Policies and Procedures: Whether an independent company of part of a multinational corporation, policies and procedures exist to direct the day-to-day running of the company. These reflect strategic, tactical and operational plans.

Resources: Resources must be managed to maximise profits and hence satisfy shareholders.

<u>Mechanisms:</u>

Audits: All management systems must be measured and monitored to ensure they are meeting stated objectives. There must be some form of performance measurement to determine to what extent these objectives are being achieved or not achieved. The main tool used in all three systems is auditing. The results of these audits provide feedback to the system so that it can be corrected.

Feedback: Feedback is received from a number of sources; customer feedback, public feedback, and internal and external audit feedback.

Control Supply Chain: A means of managing a system is to control the supply chain feeding into the system. This can include purchasing policies, vendor assessments etc.

7.7.10 Key Findings - Case Study 2

Case Study 2 was undertaken in a medical devices company to gain a deeper understanding of how QEH&S is managed and to identify commonalities within the Quality, Environmental and Health & Safety management systems. Mapping the ICOMs of all three management systems using IDEFØ, common ICOMs were identified. The inputs to the system are the company's stated goals and objectives as well as feedback from customers, regulators etc. Ultimately the required outputs of all three systems are compliance - compliance with regulatory requirements, with legislation, with the requirements of corporate or local policies or programmes, compliance with standards such as ISO, and compliance with customer requirements. However, the systems may produce unwanted goals such as non-compliance with stated objectives and waste.

In order to achieve the system goals, the management systems utilise a number of tools. The chief mechanisms or tools used in managing the systems are audits – quality audits, environmental audits and health & safety audits. Based on the results of these audits some form of corrective and preventive action is taken to find the root cause of the non-compliance. The tools used to conduct the root cause analysis range from simple problem-solving techniques such as Cause and Effect Diagrams to methodologies such as Six Sigma within the Quality Management System; monitoring of emissions within the Environmental System; and risk assessments within the Safety Management System. Discussions with those responsible for managing the systems indicate that there is a definite trend towards adopting a risk-based approach to root cause analysis.

The next case study (Case Study 3) will examine the pharmaceutical sector and map how a company in this sector manages its environmental, quality and health & safety systems. Again, each system will be mapped individually and then commonalities across the management systems will be identified and mapped. The results from case studies 1 and case study 2 will then be examined to identify common elements across both medical devices and pharmaceutical companies.

7.8 Detailing Case Study 3 – Pharmaceutical Company

The objective of Case Study 3 is to identify and map the activities governing the management of Quality, Environment and Health & Safety management systems within a pharmaceutical manufacturing environment. As in the previous case studies, the data gathered is presented using IDEF∅ as a modelling tool. The information required for the creation of the models is gathered using semi-structured interviews with top-level personnel responsible for the management of environmental, quality and health & safety systems. The interview schedule is that used in Case Study 2 (Appendix 7). Once gathered, the individual findings for Quality, Environment and Health & Safety management systems are mapped. The common elements among all three systems are then assembled and modelled using the IDEF∅ format.

7.8.1 Background to Company

The company is based in the south of Ireland, where much of Ireland's pharmaceutical activity is centred. It is a manufacturer of Active Pharmaceutical Ingredients (API's), producing eleven different products by chemical synthesis. The company employs one hundred thousand people worldwide with five hundred of these employees based in its Irish plant. Alongside its manufacturing facility, the company has a large research and development department. Because it stores bulk chemicals on site, the company is a top-tier Seveso 11 facility. It is therefore obliged to operate a Major Accident Prevention Policy (MAPP). Quality requirements are FDA driven. The company's Safety policy is driven by compliance to Irish safety legislation, particularly the Safety Health and Welfare at Work Act 2005. Environmental policy is driven by the requirements for an Integrated Pollution Prevention and Control (IPPC) license and the Seveso 11 Directive. Q,E,H&S requirements particular to this company are outlined in the following sections.

Where similar requirements exist to Case Study 2 (e.g. health & Safety legislative requirements) these will not be treated in detail.

7.8.2 The Quality Management System

As outlined earlier, Quality compliance is driven by FDA regulations. ICH Q7A Good Manufacturing Practices (GMP's) for Active Pharmaceuticals is the chief guidance document currently being used to ensure FDA approval for products. This places requirements on the manufacturer to have an effective Quality Management System, to establish Quality Units which are independent of production, to devise written procedures for production of the product(s), to conduct regular internal audits to verify compliance with the principles of GMP for Active Pharmaceutical Ingredients (APIs), and to conduct regular quality reviews of the manufactured product(s). The company also holds an Irish Medicines Board (non-product specific) GMP license. The company is not registered to any proprietary standard such as those operated by the ISO. The Quality Management System is integrated with the Environmental and Health & Safety System at a corporate level. Integration occurs via the level of the engineering change control process associated with Standard Operating Procedures (SOP's) and workflow diagrams. This requires safety, quality, and environmental approval for most, but not all, engineering changes. Traditionally, compliance to quality requirements has been achieved through the use of SOP's but these are gradually being replaced by workflow diagrams which give a diagrammatical representation of the procedures to be carried out. These workflow diagrams are more generic than the SOP's and the company feels this will decrease the need for revisions and control of documentation. The Quality System aims to achieve an acceptable product via an effective and acceptable process. If the required product or process is not achieved the company instigates a corrective and preventive action procedure. The company's Quality System is audited internally by in-house auditors and externally by the IMB and the FDA.

7.8.3   The Environmental Health & Safety Management System

The company has a combined Environmental, Health & Safety Team, comprising one EHS manager and twenty five others, responsible for managing EHS activities. Ensuring compliance with IPPC licensing requirements and the requirements of the Seveso 11 Directive dictates that a large number of the team members have responsibility for environmental issues. The company is not registered to any proprietary standard for any of its management systems, such as ISO, but must comply with detailed and stringent internal corporate standards. For example, there are currently sixty-four corporate Environmental, Health & Safety standards with which the company must comply, as well as extensive Health & Safety legislation as outlined in Case Study 2. Whilst the EHS manager has responsibility for both environmental and health & safety matters, because of the demands of the IPPC license and the Seveso 11 Directive, environmental concerns dominate.

7.8.4   IDEFØ Mapping of the Management Systems

The key elements of the Quality System (Figure 23), as well as the Environment, Health & Safety management systems (Figure 24) were determined and are represented next. Because the Company operates one EHS System as two separate systems, this is presented on one diagram. Figure 25 then presents the main elements common to the management of all three management systems. The individual elements/activities for Manage Quality and for Manage Environment, Health & Safety are described as follows:

7.8.5   ICOMs for 'Manage Quality'
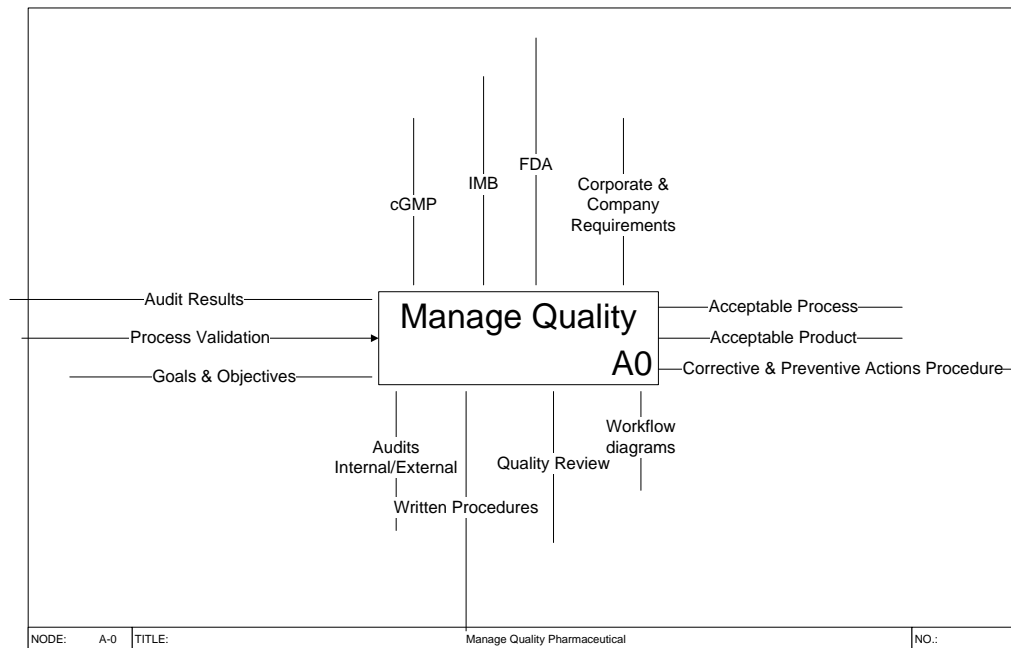
Figure 23. Manage Quality – Pharmaceutical Company

Inputs:

Goals & Objectives: The viability of the company is determined by its capacity to produce an approved product for the pharmaceutical market. It aims to achieve this via a validated production process.

Manufacturing Process Validation: As a continuous process industry, validation of the manufacturing process is critical. Each production batch is rigorously controlled to ensure it conforms to predetermined specifications.

Audit Results: Results from quality audits provide feedback to improve the management of the Quality System.

Outputs:

Acceptable Process: The Company must comply with the requirements of its IMB license, with the requirements of FDA and with cGMPs as outlined in Q7A.

Acceptable Product: As well as satisfying the IMB and FDA requirements, the product must be acceptable to its target market.

Corrective and Preventive Actions Reports: When the required outputs are not achieved, corrective and preventive action reports are generated. These must be dealt with urgently.

Constraints:

cGMPs: ICH document Q7A outlines current Good Manufacturing Practices for Active Pharmaceuticals and is the chief guidance document used to ensure FDA approval for products.

IMB: The Irish Medicines Board places constraints on the manufacturing facility.

FDA: The FDA requires evidence of stringent quality management.

Corporate and Company Requirements: Company and corporate requirements must be met e.g. the inclusion of workflow diagrams in the quality manual.

Mechanisms:

Written Procedures: All quality procedures are documented in the form of Standard Operating Procedures.

Workflow Diagrams: These are being phased-in as a replacement to SOPs in an attempt to decrease the revision and control of documentation.

Audits - Internal/External: The Company has an internal audit team to verify compliance with the principles of GMP for APIs. It is audited externally by the FDA and IMB.

Quality Review: Product quality reviews of the manufactured products are undertaken. HOW??

7.8.6   ICOMs for 'Manage Environmental, Health & Safety'
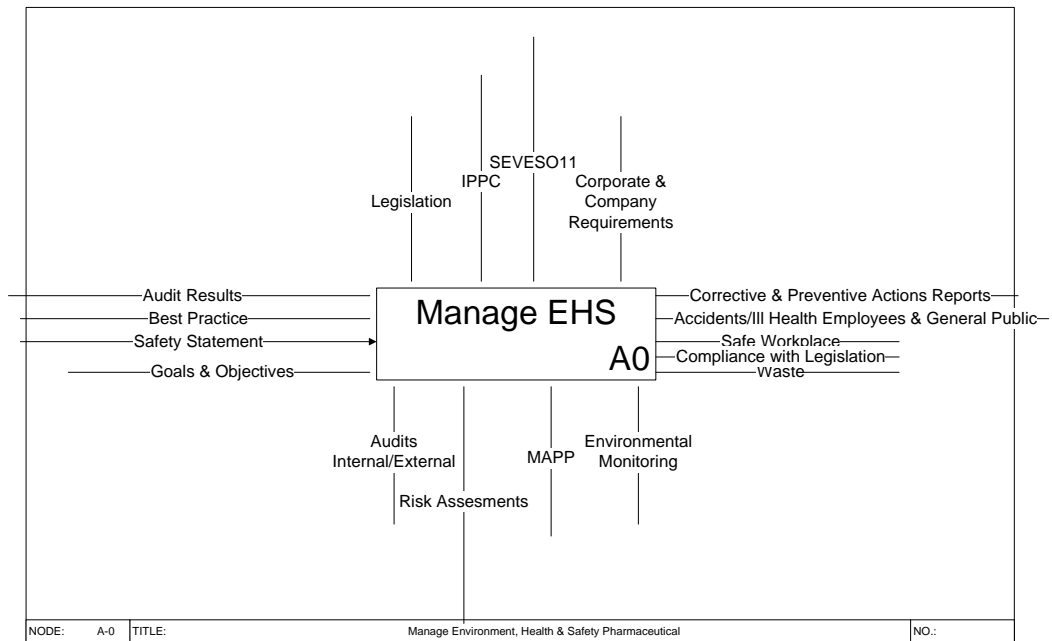
Figure 24. Manage Environment and Health & Safety – Pharmaceutical Company

Inputs:

Audit Results: The company uses the results of environmental audits to feed into its management policy.

Best Practice: The company identifies best practice (predominately, but not exclusively, in environmental management) in the manufacture of APIs and uses this to continuously improve their facility.

Safety Statement: The Safety Statement provides the principle input to the management of safety.

Goals & Objectives: The EHS management policy is centred on company and corporate goals and objectives.

Outputs:

Corrective & Preventive Actions Reports: A corrective and preventive action report is generated when the system fails. This could be a failure of the environmental

system or the health & Safety system. The proposed preventive or correction action is always signed off by the quality department.

Compliance with Legislation: The Company must comply with Irish Health & Safety Legislation and has been routinely inspected by the Health & Safety Authority.

Waste: The company's IPPC license dictates that all waste generated must be strictly controlled.

Accidents and Ill health to Employees and the General Public: All accidents or incidents which have environmental repercussions, whether internal or external to the plant, are reported to the general public. In the event of an accident or incident, the company will meet formally with local residents and residents associations to answer queries.

Safe Workplace: The company is committed to achieving a workplace that is as safe and healthy as is reasonably practicable.

Constraints:

Legislation: The Company is obliged to comply with all Irish legislation pertaining to its activities.

IPPC: The conditions of the IPPC license constrain the activities of the EHS System.

SEVESO11: The conditions of the SEVESO11 Directive dictate certain protocols and procedures the Company must adopt.

Corporate and Company Requirements: Corporate head office in the United Kingdom requires all sites to implement particular policies and procedures.

Mechanisms:

Audits Internal/External: The EHS system is audited to ensure it is meeting stated objectives, regulatory requirements and legislative requirements. These audits are both internal to the company and external e.g. IMB and FDA.

Risk Assessments: Risk Assessments are conducted on identified risks so that they can be eliminated or controlled.

MAPP: As a holder of bulk chemicals, the Company implements a Major Accident Prevention Policy under the SEVESO 11 Directive.

Environmental Monitoring: Emissions are monitored to ensure they are within specified limits.

7.8.7 ICOMs for 'Manage Q,E,H&S'

The main activities common to both the Manage Quality and Manage EHS functions are modelled in Figure 25 and described below:
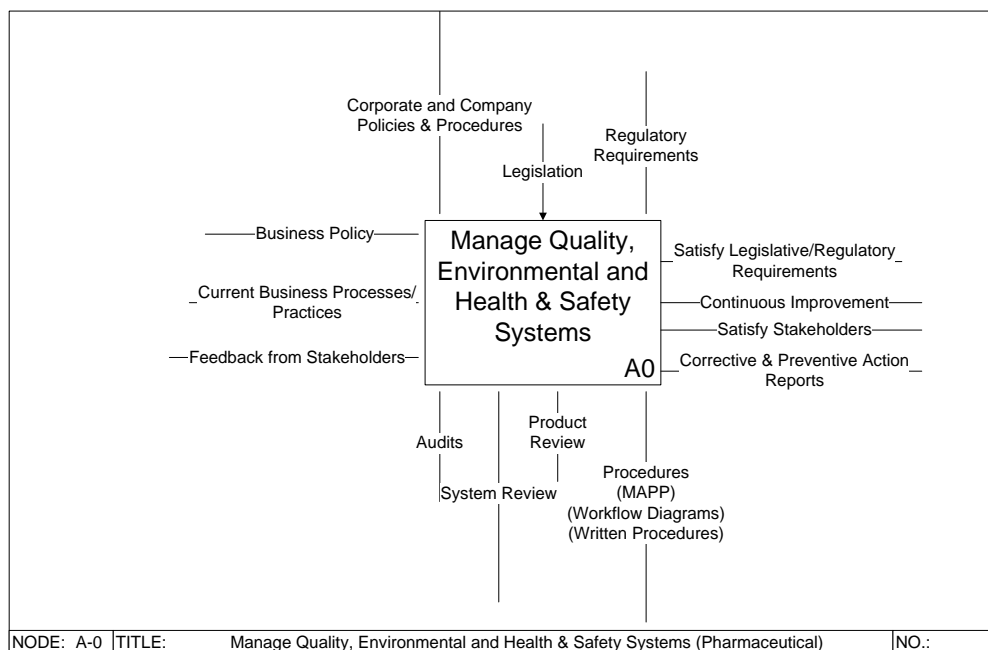
Figure 25. Manage Quality, Environment and Health & Safety Systems – Pharmaceutical Company

Inputs:

Business Policy: The business policy, as dictated by head office provides an input into all management systems. This policy outlines the goals and objectives of the Company.

Current Business Processes/Practice: Business processes and procedures are agreed upon and feed into the management system.

Feedback from Stakeholders: Feedback from stakeholders (employees, customers, general public) will influence how the systems are managed.

Outputs:

Satisfy Legislative/Regulatory Requirements: All three systems must comply with legislative and regulatory requirements. This can be conditions for IPPC license, IMB license, ICH document Q7A, Safety, Health & Welfare at Work Act, 2005 etc.

Continuous Improvement: The Company is committed to continuously improving the output of its management systems in terms of acceptable product, minimising effects on the environment and reducing accidents and ill health among its workforce etc.

Satisfy Stakeholders: The stakeholders the Company must satisfy are diverse, and include the general public, the regulatory authorities, employees and shareholders among others.

Corrective and Preventive Action Reports: In the event of a non-compliance, a CAPA report is generated. This requires immediate action to rectify the problem.

Constraints:

Corporate and Company Policies & Procedures: Corporate head office requires that particular policies and procedures are implemented. The company will often generate internal policies and procedures to ensure that corporate goals are achieved.

Legislation: The company must comply with Irish and European legislation.

Regulatory Requirements: As a manufacturer of APIs and utilising large amounts of chemicals, the company must comply with extensive regulation.

Mechanisms:

Audits: Regular internal quality audits are required to verify compliance with the principles of cGMP. Internal EHS audits are also conducted to ensure compliance with stated objectives. External audits are performed by IMB, FDA, HSA and Corporate head office.

System Review: All systems, but particularly the quality system, are reviewed on a broad 'systems' level. The Quality Team, for example, comprises approximately twelve percent of the total workforce and is made up of the Quality Assurance and Validation Group; the Laboratory Control Group; the Analytical Development Laboratory, and a Specialist Group. A systems level review is necessary to ensure cohesion within the function.

Product Review: Regular quality reviews of the manufactured products are required.

Procedures: Management of the systems entails adherence to documented procedures in the form of SOPs, workflow diagrams and emergency procedures.

7.8.8   Key Findings - Case Study 3

Case Study 3 was undertaken in the pharmaceutical sector to clarify the activities governing the management of Quality, Environmental and Health & Safety systems in that sector. In conjunction with top-level management, the ICOMs of these management systems were modelled using IDEFØ. ICOMs common to all systems were then identified and modelled in Figure 25 (Section 7.8.7). This diagram demonstrates that the manner in which the systems are managed is determined by business policy and practice, and feedback from stakeholders. Stakeholder feedback is generated internally and externally and is both local and international. The company's objectives are to satisfy its legislative and regulatory requirements and satisfy its stakeholders, while demonstrating continuous improvement. Where the objectives are not met, corrective and preventive action reports are generated. Company activities are constrained by agreed policies and procedures generated internally, and by those generated by head office. Activities are also constrained by

extensive legislative and regulatory requirements. The tools at the company's disposal are chiefly procedures, audits and review. Again, some of these tools are dictated by legislative and regulatory requirements (e.g. written procedures, MAPP) and some are driven by company or corporate policy (e.g. Workflow Diagrams to replace SOPs).

7.9   Commonalities in Medical Devices and Pharmaceutical Sectors

Case Study 2 identified common activities for managing QEH&S systems within a medical devices manufacturing facility and Case Study 3 identified common activities for managing QEH&S within a pharmaceutical manufacturing facility. Based on these findings, the results of the survey, and data gathered from the exploratory Case Study 1, the management of Quality, Environment and Health & Safety can be distilled as follows (Figure 26):
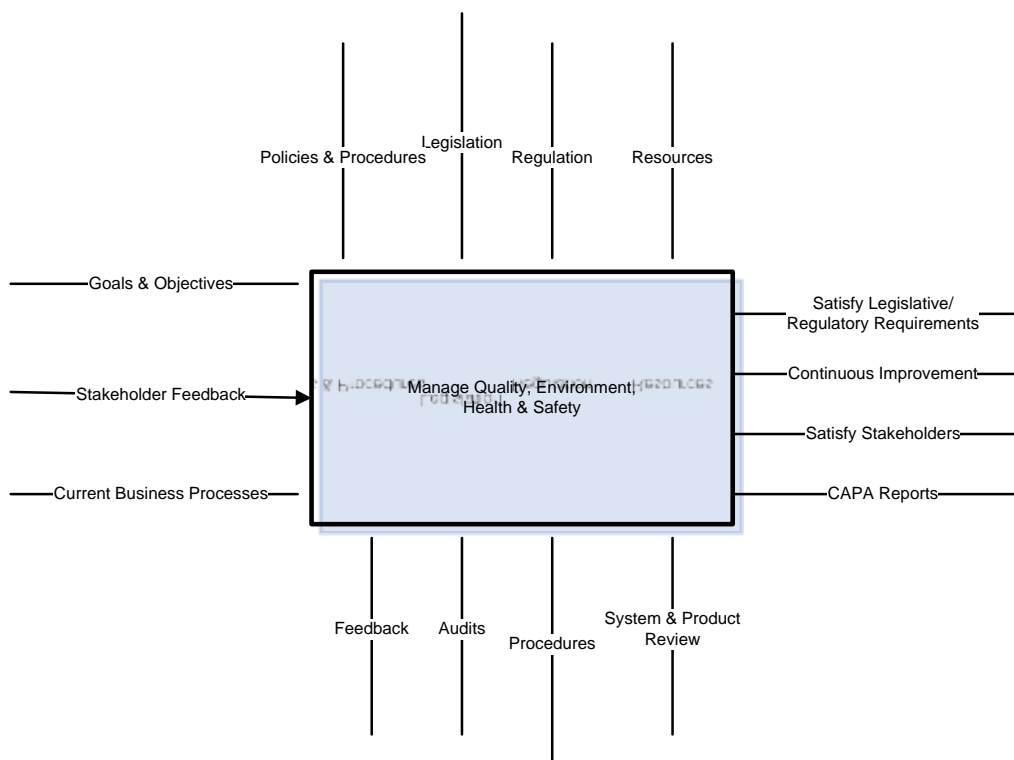
Figure 26: Common ICOMs in Managing Quality, Environment, and Health & Safety

The inputs to the activity of managing quality, environment and health & safety can be considered to be the goals and objectives of these systems, feedback from stakeholders, and the business processes in place at any given point in time. Companies utilise feedback mechanisms, audits, procedures, and system and product reviews as tools or mechanisms for managing their activities in these domains. They operate within the constraints of legislation, regulatory requirements and oversight, policies and procedures, and finite resources. Quality, environmental and health & safety management produces outcomes which include satisfying the legislative and regulatory requirements, satisfying the stakeholders, continuous improvement of the management system and corrective and preventive action (CAPA) reports.

As previously stated, when integrating management systems, it is suggested that requirements common to all standards should be identified and integrated first (Karapetrovic, 2003). A common thread emerging across all management systems, including regulatory systems, is a risk-based approach to system management. Quality management systems, are moving towards a risk-based, systems approach. This is not only in evidence in the Standards governing quality (e.g. ISO9001 and ISO 13485 etc.,) but increasingly in quality system inspection documentation devised by the regulators. Environmental management systems are also moving towards an integrated, holistic approach to the management of risk based on the recognition that the elimination, substitution and control of hazards can only be guaranteed by adopting an integrated risk-based approach. Safety management systems have traditionally taken a risk based approach and have developed and utilised risk assessment tools and methodologies for the identification of hazards, the assessment of risk and control of risk.

The first principle of quality risk management as outlined by the ICH Q9 draft guidance for Quality Risk Management (March 2005) is that the evaluation of the risk to quality should ultimately link back to the protection of the patient. In other

words, protecting the product will offer protection to the patient. The mechanism for quantifying and controlling this risk is based on a corrective and preventive action (CAPA) approach. Regulatory requirements governing medical device and pharmaceutical manufacture also specify the requirement for formal processes for managing non-conformities (CAPA) and will always include this in their inspections. Standards governing environmental management require evidence of a corrective and preventive action system. The management of safety has always included a corrective (reactive response to accident or injury) and preventive (proactive risk assessment) action components, and the standards guiding the management of safety systems explicitly require a CAPA component. Appendix 8 provides a list of the requirements for CAPA taken from ISO and OHSAS standards relating to quality management, environmental management and health & safety management, as well as FDA requirements governing medical device and pharmaceutical manufacture.

7.10 Corrective and Preventive Action (CAPA)

As outlined previously, Corrective and Preventive Actions are required for accreditation and approval by ISO and by FDA. According to the ISO and FDA the purpose of CAPA is threefold:

- To undertake remedial corrections of an identified problem
- To undertake a root cause analysis, with corrective action, to help understand the cause of the deviation and potentially prevent recurrence of a similar problem
- To undertake preventive action to avert recurrence of a similar potential problem

Rigorous regulatory requirements exist in relation to CAPA within the medical devices and pharmaceutical industries, and the criticality of CAPA to a company's operation was clearly in evidence throughout the research field work. Companies are required to investigate discrepancies or deviations from

established procedures and to document, in writing, the conclusions and follow-up to the investigation. These investigations must determine the root cause of the non-conformity. According to the FDA (Guide to Inspections of Quality Systems, 1999), one of the most important quality system elements is the corrective and preventive action subsystem. The purpose of the corrective and preventive subsystem is to collect information, analyse information, identify and investigate product and quality problems, and take appropriate and effective corrective and/or preventive action to prevent their recurrence. Verifying or validating corrective and preventive actions, communicating corrective and preventive action activities to responsible people, providing relevant information for management review, and documenting these activities are essential in dealing effectively with product and quality problems, preventing their recurrence, and preventing or minimising device failures. This approach is reiterated in other FDA documentation (Guidance For Industry: Quality Systems Approach to Pharmaceutical cGMP Regulations, 2004) where it is demonstrated how the elements of a quality system correlate closely with the requirements in the cGMP regulations. This approach includes: Analyse Data for Trends; Conduct Internal Audit; Risk Assessment; Corrective Action; Preventive Action; and Promote Improvement.

Having identified the trend towards a risk-based approach as a requirement in quality management systems, environmental management systems and in health & safety management systems and having identified the CAPA process as being a common critical requirement for each management system, the next chapter will develop a framework to support an integrated risk-based approach centred on the CAPA process which, it is proposed, will achieve the systems' objectives of customer satisfaction, compliance and continuous improvement.

Chapter 8:   Framework Development

8.1   Introduction

This chapter presents the development of an Integrated Risk Management framework for proactively managing risk to quality, the environment and health & safety. This framework has been developed to provide highly regulated organisations with one standard set of concepts which can be used to manage, quality, environmental and health & safety risks. It is intended that this framework will support existing processes and activities for managing compliance to regulatory and legislative requirements and will align with existing management standards/systems. It is proposed that the adoption of this framework will encourage a move away from functionally discrete management towards an integrated management approach which will offer protection to the product, the process and the environment in a continuous improvement cycle. It is useful here to provide an explanation of the term framework. In the context of business process reengineering (BPR), Reijers and Mansar (2005) provide a useful explanation. They suggest that a framework exists to help practitioners, and it does so by identifying topics that should be considered, and the relationship between these topics when choosing best practice in the implementation of BPR. A framework is therefore an explicit set of ideas that helps in thinking about the business process in the context of reengineering.

8.2   Rationale for an Integrated Risk Management Framework

A common theme emerging from the literature is one of transition from the management of functionally discrete units to a risk-based systems approach. The compliance system in the medical devices and pharmaceutical sectors is seen to inhibit or prevent innovation. The FDA has recognised this and has been to the forefront in proposing a new risk-based approach to quality management. This approach is built on the FDA's conclusion that modern quality systems, when coupled with manufacturing process and product knowledge, can handle many types of changes to facilities, equipment and process without the need for a regulatory submission. The International Conference on Harmonisation (ICH) has

recognised that setting a common quality standard will help companies streamline their "time/resource/quality triangle" and they propose an interdisciplinary quality risk-management process based on risk assessment, risk control and management review. Standards such as ISO9001 and ISO13485 have recognised the benefits of adopting a systems-based, process approach to managing quality systems and the concept of risk assessment and risk management is becoming a major focus. This is also reflected in ISO14971:2009 (Application of Risk Management to Medical Devices). The management of safety has always advocated a risk-based approach based on principles of prevention and a hierarchy of controls. Under Irish and European law companies are legally bound to carry out an identification of hazards, an assessment of the risk associated with these hazards and control of this risk. Current Environmental management also requires an integrated approach to risks based on principles of elimination, substitution and control.

Whilst the literature clearly recommends a risk-based approach to managing Quality, Environmental and Health & Safety systems, and the research undertaken demonstrates the commonalities that exist in the management of these systems, functionally discrete units and a functionally discrete approach to the management of these systems still dominate. The lack of a methodology compounds a company's inability to integrate its management systems. The development of a framework for proactively managing risk in quality, environmental, and health & safety management systems would ensure that quality, safety and environmental issues are given equal consideration. Such an approach would offer a synergistic solution to quality, environmental and safety risks and provide protection for the product, the process and the environment.

8.3 The Framework

Having identified the catalyst for the implementation of the framework, the next step is to determine how this will operate in practice. Processes operate independently of departmental boundaries and it is at the interface between

departments that the greatest problems arise. The cause of a 'quality' non-conformance, for example, may have its roots in an environmental or health & safety problem. If a narrow, single focus approach is taken in investigating such a non-conformity, more systemic issues may be missed. With the functional approach there is a tendency towards multiple ways of doing something rather than focusing on best practice for the organisation. What is required is a change in direction away from documenting 'what you do' to designing effective processes. The safety function conducts safety audits, the environmental function conducts environmental audits, and the quality function conducts quality audits. Each function is operating to constraints imposed on it via legislative requirements, regulatory requirements or by conformance to standards. Each function uses tools and techniques to identify hazards in the system and assess the risk posed by these hazards. Each function has some form of corrective and preventive action system in place to ensure compliance to requirements. The literature has shown that these systems are moving towards a risk-based approach and towards the utilisation of similar tools and methodologies for assessing risk. Indeed, tools such as Fault Tree Analysis, Hazard and Operability Analysis etc., which have traditionally been associated with Safety, are now being considered for use in the field of Quality (ICH, 2005).

If it is accepted that implementing QEH&S systems is the responsibility of all employees (Beckmerhagen et al 2003) and that the key to effective process development is to involve the people who contribute to measured outputs, then an integrated management approach to managing QEH&S will satisfy these requirements and achieve 'goal congruence'. However, such a system must be comprehensive yet simple, and provide a common reference framework and common technological language. Keeping in mind the *process-based* approach used in the ISO standards, the *risk-based* approach proposed by the regulatory authorities and the *systems approach* put forward in the literature, the framework

for a new integrated CAPA risk management approach is presented as follows (Figure 27):

Figure Removed for Copyright Reasons

Figure 27: Risk Management Framework (CAPA)

The elements of the framework can be described as follows:

Open CAPA: The framework opens with a Corrective Action and/or Preventive action (CAPA). A CAPA can be driven by a non-conformity arising from a quality, environmental or safety matter. This could be, for example, a product recall (quality); excessive emissions which do not comply with IPPC licensing requirements (environment); or an accident to an employee (safety). Once the CAPA is opened, a multidisciplinary team is assembled comprising experts from each of the three domains. This team will comprise domain expertise from quality, environmental and health & safety, thus ensuring that solutions and corrective and preventive actions are appropriate across all systems and the control of risk in one system does not generate risk in another. Responsibilities and authority of the team members is then clearly defined before moving onto the next stage of the process.

Perform Integrated Risk Management: The assembled team undertakes an integrated risk management process. This follows the standard procedure of identification of hazards or non-conformities, assessment of the risk associated with the hazard/non-conformity, control of this risk, and the monitoring and review of controls. Based on the field work and the literature, the required elements or the risk management process are presented in Figure 28 below.
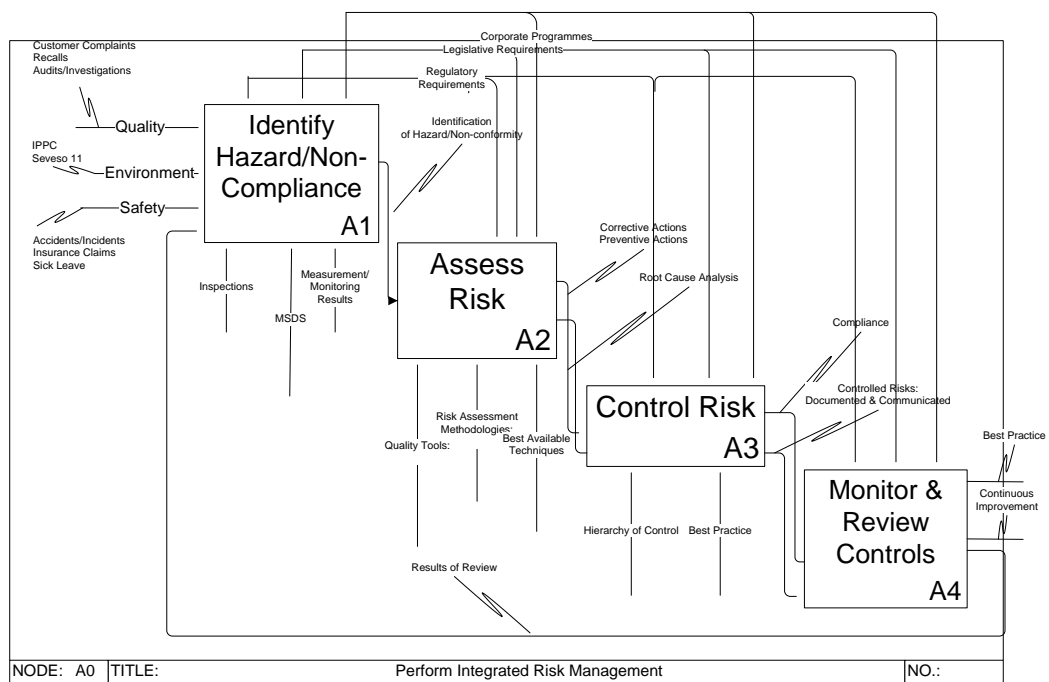
Figure 28: Context Diagram – Perform Integrated CAPA

This integrated approach to managing quality, environment and health & safety systems is based on an identification of hazards/non-compliance, assessment of risk, control of that risk and the monitoring and review of controls. The ICOMs generated on the diagram are not exhaustive. Instead they show a sample of the inputs/outputs/tools and constraints common to the industries investigated and the literature reviewed. While the inputs or drivers of each system may be different and require domain expertise, the required objectives or outputs are the same. Each system is in pursuit of compliance, continuous improvement and best practice. To ensure these outputs a 'team-based' risk assessment must be conducted. All systems operate within the same constraints and are governed and constrained by legislation, regulation and corporate policy and programmes. Again, these requirements differ depending on whether the system being managed is quality, environment or health & safety.

Approve CAPA: Approval of the CAPA will generate an action plan which should include all changes that must be made to correct the non-conformity and prevent a

recurrence. This may include changes to processes, procedures or other system modifications. It may also include employee training. These changes will include verification and/or validation which will document that the root cause of the problem has been solved; proper controls have been established and these controls will not lead to other adverse effects. All changes will be communicated to personnel, departments and suppliers etc. who will be affected.

Implement: During the implementation phase, the action plan is executed and all required changes/modifications are completed.

Monitor and Review: Monitoring and review of the CAPA is undertaken to assess the effectiveness and appropriateness of the actions taken i.e. did the actions implemented correct the problem and prevent recurrence.

Close CAPA: Finally, the CAPA is closed and completion of the process feeds into the continuous improvement cycle.

Throughout the whole process, the initial source of the CAPA is contained i.e. the non-conformity is controlled. Furthermore, all stages of the process are documented.

Conducting a CAPA compliance procedure is the same for each system individually. However, it is only by approaching the CAPA procedure in a team-based manner that a holistic solution will be found which transcends system boundaries, as well as the often too prevalent 'silo' mentality evident within organisations. It will help transform the system away from a fragmented management approach towards a more systems oriented style capable of providing synergistic solutions, optimal performance and ultimately value generation.

8.4   Summary

This chapter has presented the development of a framework for managing risk to quality, environmental and health & safety systems. The framework is based on research conducted in companies operating within the medical devices and pharmaceutical manufacturing sectors – a sector which presents unique challenges for organisations. Based on the research literature and field work, common elements across all management systems in both sectors were identified. Identified as the key component of all three management systems, a framework was developed based on the Corrective and Preventive Action process. This framework utilises an integrated 'team-based' approach to CAPA, an approach which integrates the knowledge of quality, environmental and health & safety personnel in generating corrective and preventive action solutions together. This integrated approach will remove the traditional functional boundaries which engender the silo mentality, hence limiting solutions to one's own functional division. The framework will encourage a systems view which will consider an organisation's overall behaviour and performance. Furthermore, it addresses some of the barriers to integration as identified by surveyed companies, namely 'lack of a single standard' and 'lack of a methodology for integrating the systems'. Furthermore, the framework addresses some of the barriers to integration as identified by surveyed companies, namely 'lack of a single standard' and 'lack of a methodology for integrating the systems'. The validation of the framework is presented in the next chapter.

Chapter 9:   Validation

9.1   Introduction

This thesis has presented the development of a proposed Integrated Risk Management Framework for Quality, Environmental and Health & Safety management systems in regulated environments. This chapter presents a validation of the proposed framework. The previous chapter put forward the notion of a framework as a set of ideas which exists to help practitioners, in the context of reengineering, choose the correct best practice by identifying topics, and the relationships between them. The common use of the term validation is in answering the question "are we building the right system?" (Everdij et al., 2009). Ultimately, a framework must be of some practical use. As stated by Moody (2003), "research knowledge is not intrinsically valuable: it only becomes valuable if it is used in practice - what Denning (2004) refers to as the difference between *invention* (a new idea) and *innovation* (the adoption of this new idea). While there is no guarantee that an idea or invention, no matter how clever, will become an innovation, it is proposed here that validation of the proposed framework will help ensure its credibility, thereby increasing its appropriateness and acceptance, and hence its potential impact on practice.

A certain degree of disagreement exists in the literature as to what constitutes a universal approach to validation. Rykiel (1996) reviewed validation literature from an ecological modelling perspective and concluded that validation is not a procedure for testing scientific theory but can more accurately be described as when 'a model is acceptable for its intended use'. He suggests that validation has a strong subjective element and quotes McCarl (1984) in his defence; "there is not and never will be, a totally objective and accepted approach to model validation". Much of the literature does recognise that the most accurate form of validation is an iterative process of in-field testing, feedback and redesign. However this is not always feasible or practical, and the literature is sparse in providing detailed validation protocols for such situations. The most comprehensive literature on validating conceptual and theoretical models and frameworks comes from the fields

of computer science and software engineering. This domain recognises the importance of capturing user requirements, and evaluating and improving the quality of models/frameworks early in the design cycle. This recognition has developed from the realisation that the cost of errors increases exponentially throughout the development lifecycle (Moody, D. and Shanks, G, 2003). Although Beecham et al. (2005) found very little in the literature directly relating to how process models have been validated, the authors quoted experiences in software development where organisational issues in implementing systems were found to be more prevalent than technical problems.

It seems clear that a full and complete validation of the framework developed in this work would require implementation and subsequent evaluation in numerous organisations over a prolonged time period. This is beyond the scope of this dissertation. Therefore, an alternative validation approach is therefore adopted.

9.2   Validation of the Data Collection Approach

The validation approach adopted incorporates a validation of the data collection component of the research and the validation of the modelling tool used. As outlined in the methodology chapter previously, the study, although predominately qualitative in nature, used what Creswell (2003) calls a 'mixed methods framework', based on both case study and survey methods. The initial exploratory case study identified the rationale for the unwillingness of FDA regulated manufacturing companies to integrate their QEH&S management systems. To determine if this was the case within the Irish medical device and pharmaceutical sectors generally, a questionnaire survey was undertaken. This survey was then followed by detailed case studies to collect data in each sector. Lincoln & Guba, (as quoted in Thurmond, V. 2001) suggest that mixing data-collection methods in this manner is a sensible approach. Modell (2005), suggests that surveys may improve our understanding of the incidence of a particular phenomenon observed in case studies, whereas case

study methods may add to a more holistic and richer contextual understanding of survey results.

The case studies undertaken in this work employed a number of techniques to gather detailed information for understanding the processes and procedures in place within the organisations studied. This information was then represented by IDEFØ diagrams. The techniques employed in data collection included interviews with personnel, examination of documentation (e.g. performance metrics, audit results) and comprehensive tours of the manufacturing facilities. This 'methods triangulation' (Patton, 2002), helped authenticate the interpretation of the case study findings, as the review of the documentation and observation on the factory floor corroborated the responses of the interview respondents. The interviews represented the views of top management personnel holding responsibility for each management system being studied and followed a predetermined field research strategy. The validity of the IDEFØ models was checked by adopting an iterative author-reader cycle of presenting the completed documentation to participants, reviewing the feedback obtained, and incorporating changes as necessary. This approach is a requirement of the IDEF standard (National Institute of Standards and Technology, 1993) and such systematic soliciting of feedback about one's data and conclusions from the people under study is often referred to as "member checks" or respondent validation (Maxwell, 2005).

9.3 Validation of the Proposed Framework

Validation of the framework proposed in this work proved more problematic. Refining the framework until it reaches a 'usable' model state would take many iterations of implementation-feedback-redesign over a prolonged period of time. Even before the next stage of development, it is essential to determine if the proposed framework is acceptable from an academic/research and also from a practical/practitioner point of view. Although many approaches exist for capturing specific user requirements e.g. focus groups, nominal group technique, usability

tests, etc, there is little published work available on methods and approaches for supporting a comprehensive validation of frameworks without going through a full implementation. Moody (2005) has recognised that conceptual models continue to be evaluated in an *ad hoc* way, based on common sense, subjective opinions and experience. There is no standard for evaluating conceptual models or frameworks. But, in order for conceptual modelling to progress from an art to an engineering discipline, such standards need to be defined, agreed and applied in practice. The main thrust of the application of quality principles has been the recognition that it is cheaper and faster to 'get it right first time' and identify and rectify problems and defects in the early development stages. In a paper titled "Improving the quality of data models: empirical validation of a quality management framework", Moody and Shanks (2003) presented the following Quality Framework Model (Figure 29).

Figure Removed for Copyright Reasons

Figure 29. Quality Framework Model

(Source: Moody, D. and Shanks, G., 2003)

Central to this model, the authors identify *quality factors* as those that define the characteristics of a data model and which determine its overall quality. A quality factor represents a desirable property or dimension of value of a model. The goal of the evaluation process is therefore to maximise the value of the model with respect to these qualities.

Stakeholders are identified as those people involved in building or using the data model, and who therefore have an interest in its quality. Different stakeholders will generally be interested in different quality factors.

Quality metrics define ways of evaluating particular quality factors. A metric is a way of measuring a quality factor in a consistent and objective manner. The more specific and detailed the definition of the metric, the less open it will be to

interpretation. The definition can be refined over time to increase its reliability. The identified stakeholders will rate the quality factors. As the quality of any rating will be largely dependent on the reviewer's expertise and experience, getting the best qualified people to carry out an assessment or validation exercise is essential. Also, by using multiple reviewers, bias can be minimised. *Weightings* define the relative importance of different quality factors in a problem situation. These are used in making trade-offs between quality factors. Again, it is likely that different stakeholders will assign different weightings to factors.

Improvement strategies are techniques for improving the quality of data models with respect to one or more quality factors. A particular improvement strategy may affect multiple quality factors.

For the purposes of this research, in the absence of required standards, a 'quality' perspective was adopted. In adopting this approach, quality factors applicable to the proposed framework were identified from a variety of books, peer reviewed journals and Standards. (Moody et al., 2003; Beecham et al., 2005; ISO 25021:2007; ISO 9241-210:2010; Stanton et al. 1996). These quality factors, or requirements of the framework, are described as follows:

- Usability: "the efficiency, effectiveness and satisfaction with which specified users achieve specified goals in particular environments" (ISO 9241:11)

- Flexibility: The ease with which the framework can cope with business and/or regulatory change.

- Simplicity: The framework is clear and contains the fewest possible entities and relationships.

- Completeness: All user requirements are included.

- Integration: The framework is consistent with the organisation's business processes.

- Understandability: The concepts and structures can be easily understood.

- Implementability: The ease with which the framework can be implemented within specified lead-times and budget constraints.

- Maintainability: The extent to which the framework can be maintained.

Quality factors (desirable characteristics) are measured by quality metrics. Given the vagueness associated with the quality factor descriptors, it is necessary to find measurements or metrics which can be used to quantify them. A scheme was therefore devised which would evaluate the quality factor identified with a view to defining relevant measurements/metrics. For every factor, a question, or set of questions was devised. These were also derived from the literature and Standards. The answers to these questions are then scored on a scale of 1 to 5 (where 1 = poor/unimportant and 5 = excellent/very important), hence providing a measurement of the factor. The metrics associated with each factor are described as follows:

1. Usability
    a. The framework is capable of allowing users to achieve their goals in an efficient, affective and effective manner.

2. Flexibility
    a. The framework can be modified to reflect business or regulatory changes

3. Simplicity
    a. The minimum number of elements is used to represent the process.

4. Completeness
    a. There are inconsistencies within the model i.e. does it map against the existing business processes.
    b. There are items in the framework that are not required.
    c. There are requirements that are not represented in the framework.
    d. There are items in the framework that are required but are not accurately defined.

5. Understandability
    a. I understand the terminology used and the IDEFo methodology.

      b. I can interpret the framework correctly using actual business examples.

6. Importance

      a. It is technically possible to implement the framework.

      b. It is economically feasible to implement the framework.

      c. Implementation of the framework will meet legal and regulatory requirements.

7. Integration

      a. The framework elements have been defined to match corporate/business definitions.

      b. There are elements in the framework which have the same meaning but different names in the overall business model.

      c. There are elements in the framework with the same name but which have different meaning to concepts/elements in the overall business model.

8. Maintainability

      a. The framework can be diagnosed for deficiencies or failures in an audit process.

      b. The framework can avoid unexpected effects from modifications

Appendix 9 provides the reader with the complete validation protocol.

Best practice dictates that the design of usable systems depends on the participation and satisfaction of all relevant stakeholders in the design process – a user centred design approach. At this stage of the framework development, the main stakeholders, and the reasons for their inclusion, were identified as follows (Table 8):

Table 8. Stakeholders Involved in Validation

Stakeholders	Reason for Involvement
Academic/Researcher	Framework must be theoretically sound
Business User/Practitioner 1 (Medical Device Sector)	Framework needs to be practical/usable from medical device sector perspective
Business User/Practitioner 2 (Pharmaceutical Sector)	Framework needs to be practical/usable from pharmaceutical sector perspective
Regulator (HSA)	Framework must meet regulatory requirements
Standards Expert	Framework must meet criteria for certification

Individual experts from each group of stakeholders were identified. They were approached and requested to act as expert reviewers for the risk framework. Once they agreed to participate, a face-to-face meeting was set-up. During this meeting, the framework was introduced. This included some background to the IDEF methodology used, and an explanation of the components of the framework. Reviewers' levels of expertise in the relevant areas were confirmed by asking them to complete a short questionnaire outlining their experience in the field. Table 9 provides a synopsis of the experts' profiles.

Table 9. Expert Profiles

Stakeholder	Educational Level Achieved *	Years Experience QEH&S	Current Role
Academic	4th Level	12	Associate Professor (Human Factors/Safety)
Business User 1 (Medical Device)	4th Level	20+	Senior Environment, Health & Safety Manager

Business User 2 (Pharma)	4th Level	18	Senior Executive
Regulator	3rd Level	12	Inspector and Projects Manager
Standards Expert	3rd Level	24	Accreditation Officer

* 1st Level Secondary school education only

  2nd Level Bachelors Degree

  3rd Level Masters Degree

  4th Level PhD

It was agreed that the experts would use the quality metrics to form both a summative and formative evaluation of the proposed framework. Patton (2002) states that **summative** evaluations serve the purpose of rendering an overall judgement about the effectiveness of a programme, policy or product; **formative** evaluation serves the purpose of improving it. As such, this evaluation method also addresses the 'improvement strategy' component of the Moody and Shank's Quality Framework Model presented earlier. Experts were asked to give an opinion on how well they felt each of the quality metrics was met and then to provide an overall rating on the quality factor associated with these metrics on a scale of 1 to 5 (where 1=poor and 5=excellent). The reviewers were asked to weight the relative importance of each quality factor, again on a scale of 1 to 5 (where 1 is unimportant and 5 is very important).

9.4   Framework Validation Results

Firstly, the relative importance that the reviewers assigned to the quality factors is presented. Because the quality factors and associated metrics were derived solely from the literature, it was necessary to determine if the stakeholders did indeed consider these to be important. Reviewers were therefore asked to rate each quality factor on a scale of 1 to 5 (where 1 = unimportant and 5 = very important). The results are presented in Figure 30.
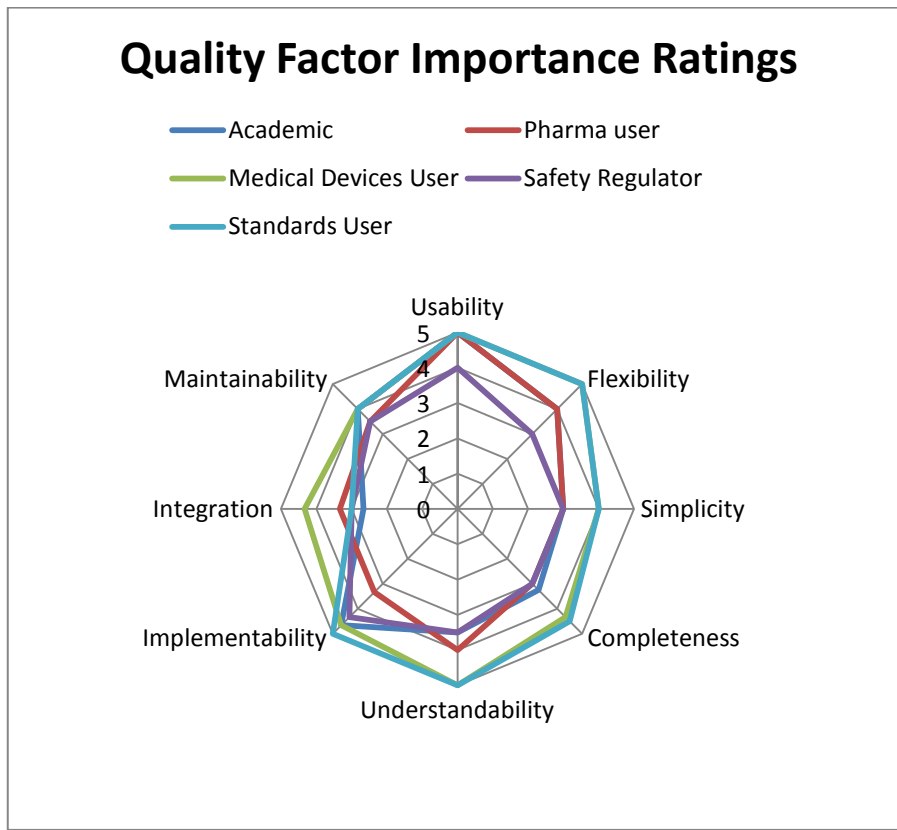
Figure 30: Reviewer Assessment of the Importance of Quality Factors
(1 is unimportant - 5 is very important)

It can be seen that all the factors identified, were considered by the reviewers, to be important considerations in the proposed framework.

Next, the reviewers were asked to rate how well they felt the framework met each of the quality factors. Generally, the feedback from the expert review was very positive. The results are presented in Figures 31 through 38 with a short commentary on each.
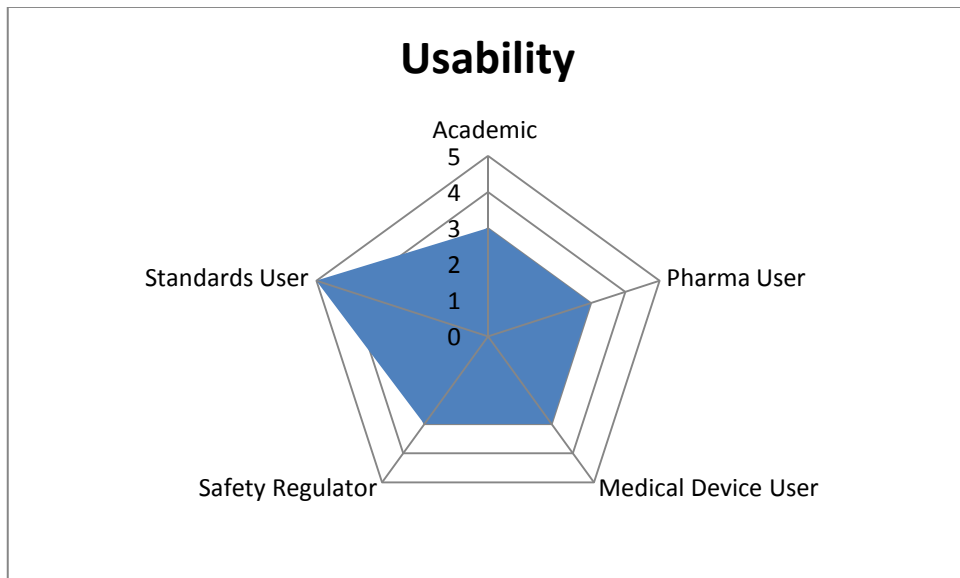
Figure 31: Reviewer Assessment of Framework Usability

With respect to the usability of the proposed framework, the reviewers offered the following comments:

- Currently presented as a guideline/draft but I feel for a real audit a lot more detail/definition would be required. (Medical Device User)
- The top level document is excellent in that all requirements are addressed. However the success of the system depends on interpretation and implementation and therefore the type of forms used and the process of implementation. (Standards User)
- Use of colour coding? (Safety Regulator)
- In order to overcome inherent resistance to change, it is critically important that new systems are user friendly. (Pharma User)
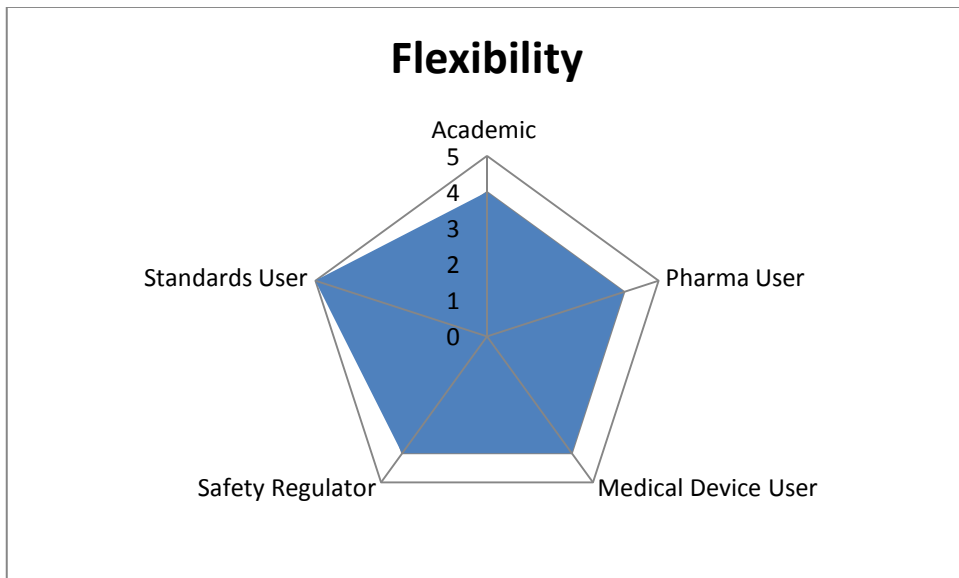
Figure 32: Reviewer Assessment of Framework Flexibility

With respect to the flexibility of the framework, the following feedback was offered:

- All possible inputs addressed. (Standards User)

- I think it is flexible, may require some element for keeping up-to-date with regulation. Need to be sure that the framework incorporates key elements e.g. management accountability. (Safety Regulator)
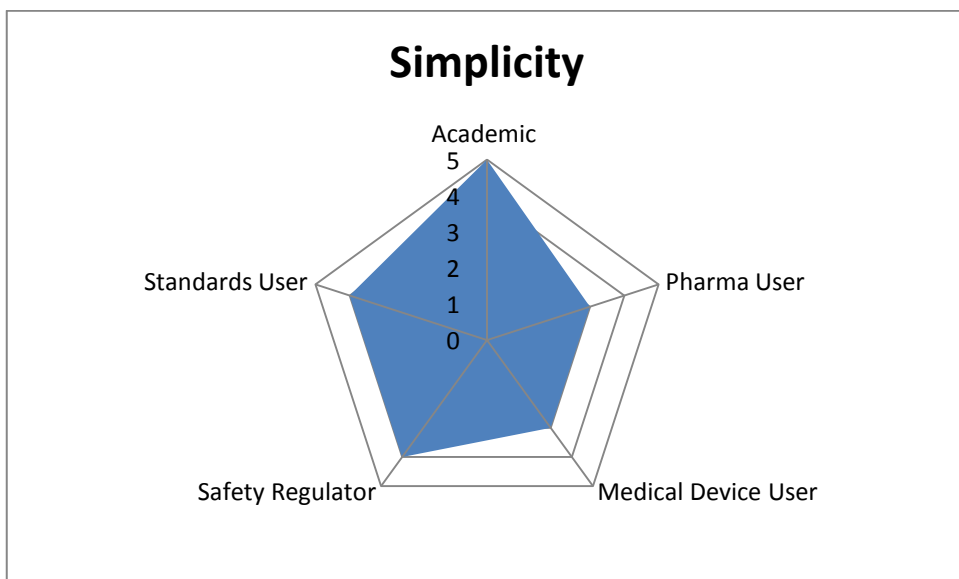
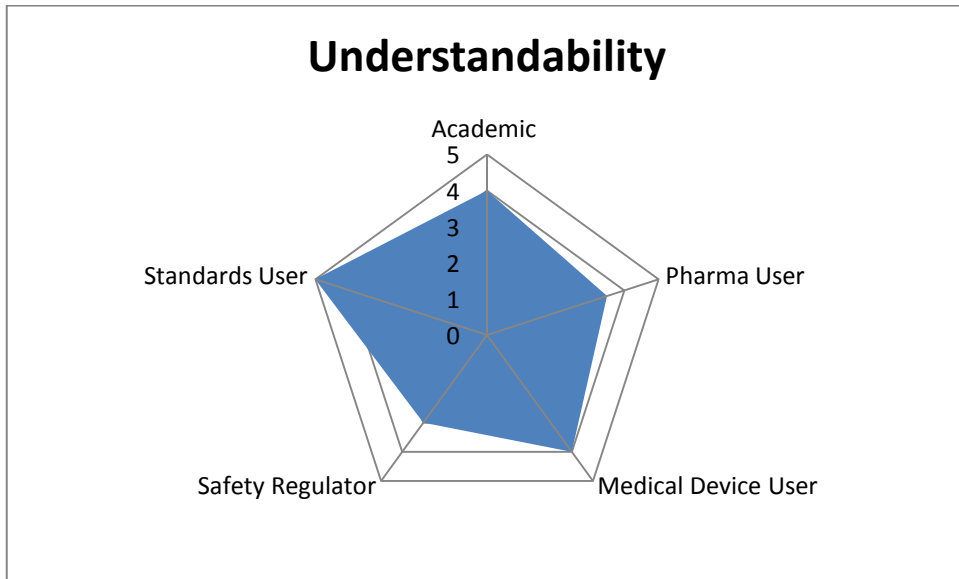**Figure 33: Reviewer Assessment of Framework Simplicity**

In terms of simplicity, the Standards user asked if there was "a need to include non-conformances and preventive actions/improvements as inputs for quality, environmental and H&S audits? (Perhaps covered by inspections?). (Standards User)
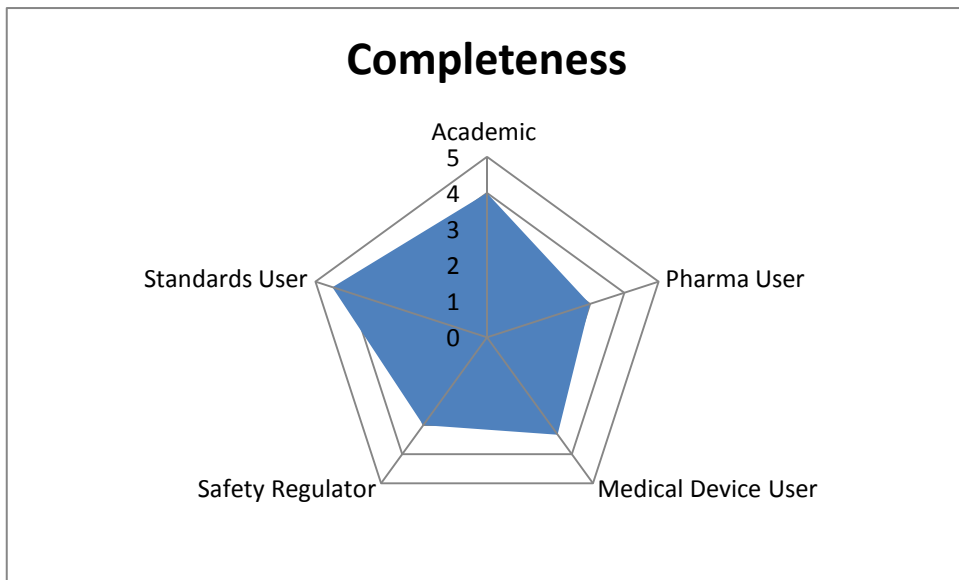
Figure 34: Reviewer Assessment of Framework Completeness

The reviewers commented on the completeness of the framework as follows:

- Suggest expanding controls to identify types of controls and communication (e.g. change in systems, training needs, new work procedures, new equipment etc.)

- Under 'Monitor and Review' incorporate trend analysis/key performance indicators.

- Under 'Hazard Identification' include something around consultation with staff or stakeholders where necessary. (Safety Regulator)

- I suggest Sick Leave (v Work-related lost time); I would not include 'Insurance claims' for an FDA audit. Maybe MSDSs? Root cause analysis (H&S of Quality FMEA or both?). (Medical Device User)

- As a general framework it is possible that some requirements are absent. (Academic)

Figure 35: Reviewer Assessment of Framework Understandability

With respect to understandability, reviewers observed the following:

- Yes. Methodology is very much based on PDCA. (Medical Device User)

- Have audited successful systems of this type. Emphasis may have been more on quality than Environment or Health & Safety. (Standards User)
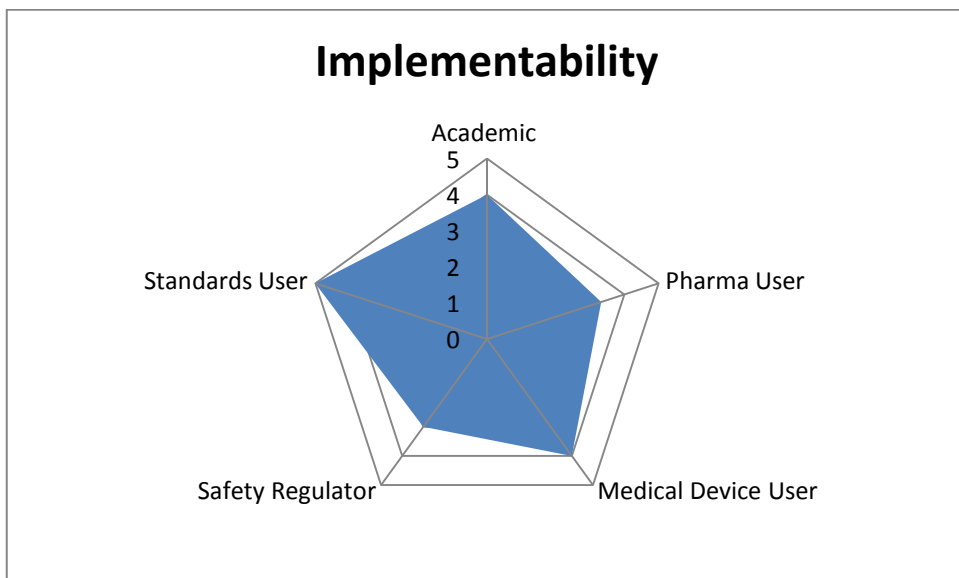
Figure 36: Reviewer Assessment of Framework Implementability

The reviewers assessed the implementability of the framework as follows:

- Yes, providing it has Senior Management support. Clear intent to meet compliance and other requirements. (Medical Device User)

- May need to compare model against relevant safety/environmental legislation to ensure it includes core elements. For example, in safety legislation there is major reference to consultation, need for continuous risk assessment, director responsibilities etc. I think there is great scope for developing this type of model. The use of some cost data if available would be useful. (Safety Regulator)

- Have audited successful systems of this type. (Standards User)

- As far as I know, it won't require additional resources. (Academic)
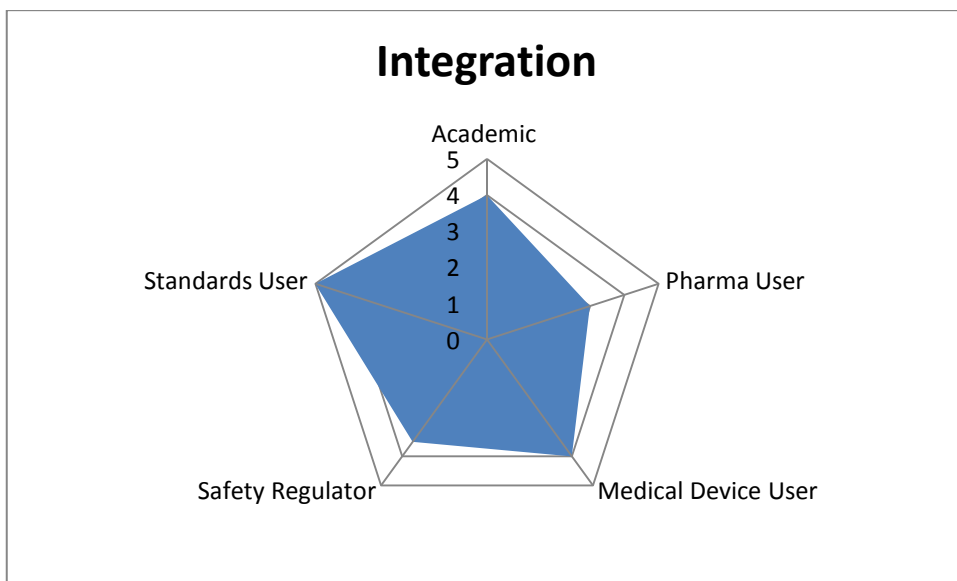
Figure 37: Reviewer Assessment of Framework Integration

With respect to integration within the proposed framework, the following comments were made:

- In my opinion, the model uses an accurate terminology which is also similar to the terms in companies. (Academic)

- Common terms are used. (Standards User)

- Generally looks fine to me. (Medical Devices User)
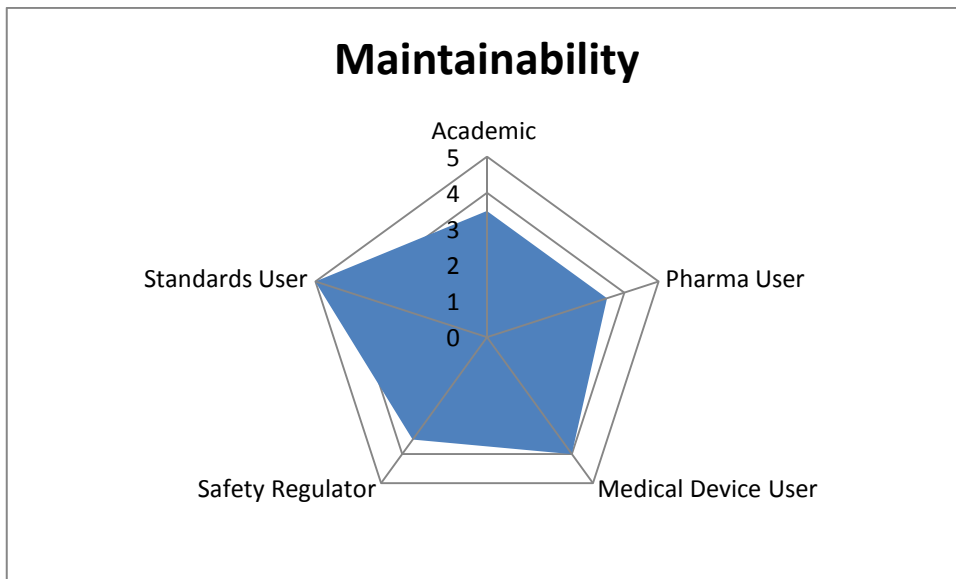
Figure 38: Reviewer Assessment of Framework Maintainability

In terms of the maintainability of the framework, reviewers commented:

- Without stress testing the framework, I couldn't say this for sure. (Pharma User)

- May be useful to have a separate part of process on auditing or expand review performance section. (Safety Regulator)

- Potential to serve this function - dependant a lot on degree of detail in framework. (Medical Devices User)

- Controls reviewed and monitored. (Standards User).

The feedback on the Framework was very positive, generally scoring well on all factors. Given the diverse backgrounds and experience of the reviewers, and considering this is a 'first past the post' attempt, this affirms the relevance and applicability of the Framework. The standards expert, who has successfully conducted integrated audits in the past, was particularly positive and gave a top score of 5 (excellent) on 7 out of 8 factors. In terms of advancing the Framework, some comments included the criticality of Management support and management

accountability in the successful implementation of the Framework. Also, the requirement for more detail and definition was suggested by the medical device expert. In terms of simplicity (Figure 33), it is interesting to note that the academic gave this a score a 5, whereas the medical device user and the pharma user scored this at 3. It is anticipated that these issues would be addressed in further iterations of the Framework.

Chapter 10:   Conclusions

10.1   Conclusions

The medical device and pharmaceutical sectors are important to the continual growth of Ireland's economy. These sectors differ from traditional manufacturing in that they are highly regulated. Not only must they comply with regulation in the country of manufacture but also in the country of export. Many companies within these sectors manufacture for the United States market and so are regulated by the U.S. Food and Drug Administration (FDA). A failure to secure FDA approval for a product means that a company may not sell that product in the U.S. resulting in a great economic cost to the company or ultimately even closure.

The focus of an FDA approval inspection is on a company's quality management system, based on the premise that a system which can guarantee the quality of the product will lead to the protection of the customer and/or patient. With an ever increasing volume and range of medical device and pharmaceutical products being manufactured, the FDA is finding it increasingly difficult to maintain the number of inspection audits and the depth of these audits. As a result of this pressure on resources, they are adopting a systems-based approach to inspections. This approach moves away from the investigation of a specific product towards generalising the results of its inspections to an overall evaluation of the firm. Rather than checking every aspect of the firm's quality system, key quality indicators are examined. Within this systems model, the concept of risk management and risk assessment is a major focus. Risk management can guide the setting of specifications and process parameters; risk assessment can determine the need for discrepancy investigations and corrective actions. A main focus for inspections is a firm's Corrective and Preventive Action (CAPA) process. This process focuses on investigating and correcting discrepancies and attempting to prevent recurrence.

Manufacturing companies have traditionally been structured as a hierarchy of functional units. The difficulty with this type of structure is that problems that

occur at the interfaces, or at function boundaries, are often given less priority than the short-term goals of the functional unit. Corrective actions are usually focused on the unit concerned, resulting in little benefit to the overall organisation. Companies are obliged to manage quality, environment and health & safety issues but if these systems operate independently of each other then the barriers between each system will not be crossed. The organisation will not only fail to achieve its goal of continuous improvement but may, as part of its risk control measures in one system, actually create risk in another. Integrating these key management systems may provide a solution.

The benefits of an integrated management system have been described in the literature. However, none of this literature refers to those companies governed by stringent regulation such as that required by the FDA. These companies differ from other manufacturing companies in that approval of their quality system is crucial for their existence. The fear exists that integrating environment and health & safety management systems with the quality system will jeopardise FDA approval. If this is the case, does this mean that these manufacturing sectors are bereft of the benefits expounded in the literature? More insidiously however, does it mean that a risk control action taken within the quality system for example, could have negative repercussions for the environment or for health and safety?

These questions were raised as a result of a detailed case study conducted in a company manufacturing a range of products, some of which were classified as medical devices. This company chose not to integrate its quality, environment and health & safety management systems because of its fear of potentially failing an FDA quality audit because of a failure in one of its other systems. To determine if this was generally the case in Ireland, a population survey was conducted on the medical device and pharmaceutical sectors within the country. The results of this survey showed that while the environmental and health & safety management systems were often managed together, the quality system was managed separately.

This was despite the fact that many of the core management elements were common across all systems. The main barriers to integration identified by the survey were the lack of a single standard and the lack of a methodology for integration. Training internal auditors was not seen as a barrier.

The proposed framework does not suggest a single standard, but goes some way towards addressing this requirement by providing a single approach to the management of risk and clearly provides for the methodological gap identified. Furthermore, based on the feedback from the validation exercise, it is evident that this approach is practical and implementable.

Follow-up case studies supported the findings of the survey. Common elements were found across all three management systems. In particular, the case studies highlighted the common use of audits and the significance of the corrective and preventive action component (CAPA) of these audits. Having identified this as one of the key drivers of the management systems and taking into account the findings in the literature, a new framework for adopting an integrated risk management approach for managing Quality, Environment and Health & Safety Systems was developed. Considering that companies often use ISO or other proprietary standards to meet their regulatory requirements; that these standards often advocate a process approach; that the framework must reflect best practice in shifting from a functionally orientated management model to a process based approach; and that the CAPA requirement is critical in gaining regulatory approval; a new risk management framework, based on an integrated CAPA approach, is proposed.

This framework was then validated via an expert review process. The experts, representative of stakeholders and end-users of the framework, were asked to rate a set of quality factors, defined by a series of quality metrics. Generally, the

feedback from the reviewers was positive, and some recommendations for further improvements to enhance usability in the field were offered.

The integrated CAPA approach requires inputs from quality, environment and health & safety personnel and achieves the following:

- It utilises a common risk language. This will enable the communication of risk awareness throughout the organisation ("model uses an accurate terminology which is also similar to the terms of companies"; "common terms are used") Ref. Section 7.6.4.

- It meets the business needs of senior management and gives equal status to safety, environment and quality considerations within the business ("all requirements are addressed"; "all possible inputs addressed") Ref. Section 7.6.4.

- It includes the involvement and participation of all parties by creating cross-functional teams thus enabling enhanced communication, information-sharing and buy-in to the process.

- It ensures corrective and preventive actions in one system will not result in non-compliance in another system.

- It provides evidence of a 'robust' CAPA process in its requirement for a comprehensive root cause analysis. This will reflect well on the company's overall quality system during an FDA inspection.

- It complies with the process approach required by ISO standards.

Further benefits an organisation can anticipate include the following:

- It can lead to an integration of tools and techniques for risk management.

- It can determine the need and/or develop the content for SOPs, guidelines etc.

- It can reduce 'audit fatigue'.

- It can lead to a culture of continuous improvement.

- It can lead to rationalised procedures utilising an input – process – output model.

- It can lead to empowered auditors who focus on opportunities for improvement rather than on non-conformities.
- It should satisfy all stakeholders by ensuring protection for the product, the process and the environment, as described in Figure 39 below.

Figure Removed for Copyright Reasons

Figure 39: Meeting Stakeholder Concerns

10.2   Aims and Objectives Revisited

The aim of this research was to develop a framework whereby highly regulated medical device and pharmaceutical companies could adopt an integrated approach to managing their quality, environmental and health & safety systems, whilst assuring compliance with regulatory requirements. Furthermore, adoption of this framework should ensure a cycle of continuous improvement for the organisation. The research aim would be achieved by meeting clearly identified objectives: Firstly, by determining the prevalence of integrated QEH&S management systems within the Irish medical device and pharmaceutical sectors; and also determining the extent to which these companies believed integration was desirable and feasible. This objective was achieved by conducting a questionnaire survey of all medical devices and pharmaceutical manufacturers in Ireland. Results from the survey indicated that companies in these sectors tend towards little or limited integration with respect to documentation, procedures and personnel. The perceived barriers to integration were identified as lack of a single standard and lack of a methodology.

Another objective was to identify the regulatory requirements on medical device and pharmaceutical companies and other requirements that may constrain the

management of their activities (e.g. legislative, corporate requirements). An extensive literature review and detailed in-company case studies addressed this objective. Informed by the results of the literature and field work, a Framework to assist companies in adopting an integrated approach to managing their QEH&S systems was developed. Following the development of the Framework, and in the absence of any existing validation tools, a validation methodology was developed. This validation methodology was then successfully applied to the Framework, with positive results.

10.3   Contribution to Knowledge

This thesis contributes to knowledge by synthesising existing knowledge and research, carrying out new empirical work and utilising a cross-disciplinary approach to develop a new framework for integrating the management of risk in quality, environmental and health & safety systems.

This research investigates a hitherto unexplored application of integrated management systems in sectors facing unique constraints on their activities, namely medical devices and pharmaceutical manufacturers (new empirical work).

It synthesises research and theory from risk, quality, environment, health & safety, regulation and legislation which had previously existed in a complex, fragmented manner (new synthesis).

It takes a cross-disciplinary approach linking a business process engineering modelling tool and a risk assessment methodology to the development of the proposed framework and embeds it in a corrective and preventive action (CAPA) approach which is cognisant of the requirements of regulatory bodies, standards bodies and legislators. It therefore combines aspects of systems engineering, risk assessment, safety engineering and quality engineering (cross-disciplinary).

It develops a new framework to assist organisations in highly regulated sectors (medical device/pharmaceutical) to manage risk in an integrated manner (adding to knowledge in developing new tools).

It proposes a novel approach to the validation of the new proposed framework (utilising knowledge from the field of computer science and usability engineering and expanding and applying it to a new area).

10.4   Limitations of the research

As with any body of work, this research faced some limitations in its execution. For instance:

- Complete validation of the framework presented would require many iterations of implementation – feedback – redesign over a prolonged period of time, and in a number of settings. This was not possible within the timeframe of this research and therefore a validation methodology was developed and employed.

- Travelling to meet with the reviewers was very time consuming. The time and expense involved in the review also limited the possibility of revisiting the reviewers or generating a review panel. This would be the preferred approach in a user-centred, iterative process.

- The implementation of the framework is contingent on the development of tools centred on the CAPA aspect of risk management. The development of such tools would necessitate a similar effort to that employed in the generation of the risk management framework presented here. For example, this might include examination of existing inspection and audit tools for all management systems – environmental, health & safety, and quality, followed by the development of an integrated audit tool suitable in

the first instance to individual companies, and which would subsequently be developed to have a sector-wide application.

- Despite protracted efforts to include a representative from the Food and Drug Administration (FDA), they were unwilling to participate in the research.

- The risk management framework addresses the CAPA process only. While this is reasonable as a 'first pass', complete integration must include all aspects of the risk management process. Implementation of this aspect must be concluded before the other common elements of the management systems are considered, as only then can the lessons learned from this implementation be used to support integration across other areas.

10.5   Recommendations for further research

- This risk management framework developed has considered the CAPA component of the compliance audit. The next step is to implement this framework within companies in the medical device and pharmaceutical sectors. The results and feedback received will help refine the model, and lead to the development of tools to support its implementation. This framework can then be applied to other elements common to quality, environment and health & safety management systems, for example the management review process.

- This framework considers highly regulated industrial sectors. If applicable to these sectors then its applicability should easily be widened to consider less well regulated sectors. Small and Medium Enterprises (SMEs) are also required to manage their quality, environment and health & safety systems. The literature on SMEs suggests a lack of expertise, intelligence and resources within these organisations for managing these systems (Pickvance,

2003). Adopting this framework could go some way to addressing these issues.

- There are opportunities for extending the Risk Management Framework to encompass the whole supply chain. This could include eliminating or mitigating risk to the environment, to health & safety and to quality in purchasing, logistics, materials management, the manufacturing process and in the disposal process.

- It is proposed to develop a web-based application of the framework. IDEFØ can be used as the reference architecture for developing this application.

References

- ACNSI (1993). ACSNI Human Factors Study Group Third report: Organising for Safety. Advisory Committee on the Safety of Nuclear Installations, Health and Safety Commission, 1993

- Baily, R. (1982). Quoted in McCormick, M. and Saunders, E. Human Factors in Engineering and Design. McGraw-Hill Inc.

- Bamber, C., Sharp, J. and Hides, M. (2000). Developing management systems towards integrated manufacturing: a case study perspective. In *Integrated Manufacturing Systems*. **11** (7), 454-461

- Beckmerhagen, I., Berg, H., Karapetrovic, S., and Willborn, W. (2003). Integration of management systems: focus on safety in the nuclear industry. In *International Journal of Quality & Reliability Management* **20** (2) pp. 210-228

- Beckmerhagen, I., Berg, H., Karapetrovic, S., and Willborn, W. (2003). Auditing in support of the integration of management systems: a case from the nuclear industry. In *Managerial Auditing Journal* **18** (6-7) pp. 560-568

- Beecham, S., Hall, T., Britton, C. and Cottee, M. and Rainer, A. (2005). Using an expert panel to validate a requirements process improvement model. In *The Journal of Systems and Software* **76** (3) pp. 251-275

- Blewett V. and Shaw, A., (1997) Best Practice in OHS Management. CCH Australia Limited

- British Standards Institute (2007). OHSAS 18001:2007: Occupational Health and Safety Management Systems

- Bureau Enquêtes-Accidents (2000). Accident on 25 July 2000 at La Patte d'Oie in Gonesse (95) to the Concorde registered F-BTSC operated by Air France. Published by Ministere de l'Équipement des Transports et du Logement. Burea D'enquêtes et d'Analyses pour la Securité de l'Aviation Civile. France

- Commission of the European Communities (2003). *A Stronger European-based Pharmaceutical Industry for the Benefit of the Patient – A Call for*

Action. Communication from the commission to the council, the European Parliament, the Economic and Social Committee and the Committee of the Regions. Published by the European Commission Brussels 1.7. 2003

- European Commission (2007) (5th Revision). The Rules governing Medicinal Products in the European Community. The Notice to Applicants. Volume 2A Procedures for marketing authorisation. Chapter 2 Mutual Recognition. Published by the European Commission, Brussels, ENTR/F2/SM (2007)

- Commission Directive 2001/83/EC of the European Parliament and of the Council of 6th November 2001 on the Community Code relating to Medicinal Products for Human Use. Official Journal L-311, 28/11/2004, pp. 67-128 as amended by Directive 2002/98/EC of the European Parliament and of the Council of 27 January 2003 setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components and amending Directive 2001/83/EC

- Commission Directive 2003/12/EC of 3 February 2003 on the reclassification of breast implants in the framework of Directive 93/42/EEC concerning medical devices

- Commission Directive 2003/32/EC of 23 April 2003 introducing detailed specifications as regards the requirements laid down in Council Directive 93/42/EEC with respect to medical devices manufactured utilising tissues of animal origin

- Confederation of British Industry (CBI) (1990)

- Conti, T., (2010). Systems Thinking in Quality Management. *The TQM Journal.* **22** (4)

- Cooper, MD., (2000). Towards a model of safety culture. In *Safety Science.* 36 pp. 111-136

- Council Directive 89/391/EEC (1989) on the introduction of measures to encourage improvements in the safety and health of workers at work

- Council Directive 90/385/EEC (1990) Active Implantable Medical Devices (AIMDD)

- Council Directive 93/42/EEC (1993) General Medical Devices (MDD)

- Council Directive 96/082/EEC Seveso II Directive (Control of Major Accident Hazards Involving Dangerous Substances)

- Council Directive 96/61/EC (1996) of 24 September 1996 concerning integrated pollution prevention and control

- Council Directive 96/82/EEC (1996) of 9 December 1996 on the control of major-accident hazards involving dangerous substances

- Council Directive 98/79/EC (1998) *In-vitro* Diagnostic Medical Devices (IVDD)

- Council Directive 2000/70/EC (2000) of the European Parliament and of the Council of 16 November 2000 amending Council Directive 93/42/EEC as regards medical devices incorporating stable derivates of human blood or human plasma

- Council Directive 2001/104/EC of the European Parliament and of the Councilof 7 December 2001 amending Council Directive 93/42/EEC concerning medical devices

- Council Directive 2003/94/EC (2003) laying down the principles and guidelines of good manufacturing practice in respect of medicinal products for human use and investigational medicinal products for human use

- Council Directive 2007/47/EC (2007) of the European Parliament and of the Council of 5 September 2007 amending Council Directive 90/385/EEC on the approximation of the laws of the Member States relating to active implantable medical devices, Council Directive 93/42/EEC concerning medical devices and Directive 98/8/EC concerning the placing of biocidal products on the market

- Council Directive 2008/1/EC of 15 January 2008 concerning integrated pollution prevention and control (Codified Version)

- Cox, S. and Cox, T. (1991). *The structure of employee attitudes to safety – a European example.* In *Work and Stress* pp. 93-106

- Creswell, JW. (2003). Research Design: Qualitative, Quantitative, and Mixed Methods Approaches (2nd Edition)

- Cullen, W., (1990). *The Public Inquiry into the Piper Alpha Disaster.* HMSO, London

- Dalling (1997). Understanding and Assessing Safety Culture. Journal of Radiological Protection. **17** (4) pp. 261 - 274

- Damelio, Robert (1996) *The Basics of Process Mapping.* Published by Productivity Press

- Denning, P.J. (2004). The Social Life of Innovation. Communications of the ACM **47** (4) April 2004

- Dennis, P. (1997) *Quality, Safety, and Environment; Synergy in the 21st Century* (ASQC Quality Press, Milwaukee, Wisconsin)

- Devine, B. (2010). In *Business and Leadership*. Available at http://www.businessandleadership.com/economy/item/26388-irish-manufacturing-on-the. (Sourced November 29th, 2010)

- Doumeingts, G., Chen, D., Vallespir, B. and Fénié, P. (1993). GIM (GRAI Integrated Methodology) and its evolutions. A methodology to design and specify Advanced Manufacturing Systems. In *Information Infrastructure Systems for Manufacturing.* Yoshikawa, H. and Goossenaerts, J. (Eds.). IFIP. Elsevier Science

- Environmental Protection Agency (2006). Environment in Focus: Environmental Indicators for Ireland. Compiled by the Environmental informatics and Reporting Unit.

- Environmental Protection Agency (2008). 2008 – State of the Environment Report

- European Commission (2007). Rules Governing Medicinal Products in the European Community. EudraLex - Volume 2 - Pharmaceutical Legislation Notice to applicants and regulatory guidelines medicinal products for human use. Volume 2A - Procedures for marketing authorisation

- European Commission (2010). Emissions Trading System (EU ETS). Last updated 15th Nov. 2010. Available at http://ec.europa.eu/clima/policies/ets/index_en.htm

- European Commission (2010). Eudralex. Volume 4. EU Guidelines to Good Manufacturing Practice. Medicinal Products for Human and Veterinary Use. Part 1. Chapter 1. Quality Management. Published by the European Commission, Enterprise and industry Directorate-General.

- European Community (2010). 'Environment 2010: Our future, Our choice' - The Sixth Environment Action Programme. COM/2001/0031 final Communication from the Commission to the Council, the European Parliament, the Economic and Social Committee and the Committee of the Regions on the sixth environment action programme of the European Community

- European Council Regulation No 761/2001 of the European Parliament and of the Council of 19 March 2001 allowing voluntary participation by organisations in a Community eco-management and audit scheme (EMAS)

- European Process Safety Centre (1994). Safety Management Systems: Sharing Experiences in Process Safety. Published by the Institution of Chemical Engineers, UK

- Everdij, M., Blom, H., Scholte, J., Nollet, J. and Kraan, B. (2009). Developing a framework for safety validation of multi-stakeholder changes in air transport operations. In Safety Science **47** pp. 405-420.

- Federal Drug and Cosmetic Act 1938

- Fennell, D. (1988). Investigation into the King's Cross Underground Fire. The Department of Transport. HMSO, London.

- Fleming, M., Flin, R., Mearns, K. and Gordon, R. (1998). Offshore workers' perceptions of risk: comparisons with quantitative data. Risk Analysis **18** pp. 103-110

- Flin, R., Mearns, K., O'Connor, P. and Bryden R. (2000). *Measuring safety climate: identifying the common features*. Safety Science **34** pp. 177-192.

- Food and Drug Administration (1996).Quality System Regulation QSR Requirements for Medical Device Manufacturers for 21 CFR Part 820 Compliance October 7, 1996 (Vol 61, Number 195)

- Food and Drug Administration (1999). *Guide to Inspections of Quality Systems QSIT*. Published by Office of Regulatory Affairs (ORA) and Center for Devices and Radiological Health (CDRH). Food and Drug Administration, 1999.

- Food and Drug Administration (2004). *Pharmaceutical CGMPs for the 21st Century.* Published by the Department of Health and Human Services. US Food and Drug Administration. Published by the PAT Team and Manufacturing Science Working Group Reprt:

- Food and Drug Administration (2006). Quality Systems Approach to Pharmaceutical CGMP Regulations. Guidance for Industry. Published by the US Department of Health and Human Services Food and Drug Administration. Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), Center for Veterinary Medicine (CVM), Office of Regulatory Affairs (ORA). September 2006.

- Food and Drug Administration (2004). Pharmaceutical cGMPs for the 21st Century – a risk-based approach. Final Report, September 2001. Department of Health and Human Services. Available at http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/Manufacturing/QuestionsandAnswersonCurrentGoodManufacturingPracticescGMPforDrugs/UCM176374.pdf

- Food and Drug Administration (2006). Guidance for Industry. Quality Systems Approach to Pharmaceutical CGMP Regulations. September 2006. U.S. Department of Health and Human Services

- Food and Drug Administration (2010). Code of Federal Regulations Title 21, Volume 8. Revised April 1, 2010. Subchapter H – Medical Devices. Part 820 Quality System Regulation

- Food and Drug Administration (2010). *Strategic Priorities 2011-2015. Responding to the Public Health Challenges of the 21st Century*. Draft 9/29/2010.

- Food and Drug Administration (2011). Quality System Regulation. Available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/QualitySystemsRegulations/default.htm

- Food and Drug Administration (No Date). About FDA. Availaibe at http://www.fda.gov/AboutFD/ReportsManualsForms/Reports/ucm227527.htm. Sourced June 2009.

- Glendon, A. and Stanton, N., (2000). Perspectives on safety culture. Safety Science **34** (1-3) pp. 193-214

- Global Harmonisation Task Force (1999). Guiding Principles and Operating Procedures. GHTF WD:99-3. Available at http://www.ghtf.org/information/proced.pdf

- Greenbaum, D. (1997) Quoted in *Framework for Environmental Health and Risk Management. Final Report. Volume 1.*

- Greenstreet Berman Ltd. (1999) In: Safety cultures: Giving Staff a Clear Role. HSE Contract Research Report.

- Hale, A.R., Heming, B.H.J., Carthey, J. and Kirwan B., (1994). Modelling of safety management systems. In *Safety Science* **26** (1-2) pp. 121–140

- Health and Safety Authority (2010). Managing Health and Safety. Available at http://www.hsa.ie/eng/Topics/Managing_Health_and_Safety/Safety_and_Health_Management_Systems/#What Downloaded Dec 2010

- Health and Safety Commisson (1993). Third Report: Organising for Safety. ACSNI Study Group on Human Factors. HMSO, London.

- Health and Safety Executive (1993). The Costs of Accidents at Work. Health and Safety Executive, HMSO, London.

- Health and Safety Executive (2001). Involving Employees in Health & Safety. HSG217. HSE Books

- Heinrich, H., (1931). Industrial Accident Prevention, A Scientific Approach. McGraw-Hill. Quoted in Hollnage, E., (2009). Safer Complex Industrial Environments: A Human Factors Approach.

- Hidden, A., (1989). Investigation into the Clapham Junction Railway Accident. Department of Transport CM820, HMSO, London.

- Honkasalo, A. (2000). Occupational health and safety and environmental management systems. In *Environmental Science & Policy* **3**, 39-45

- Hoyle, D. and Thompson, J. (2001 2nd Ed.). *Converting a Quality Management System using the Process Approach.* (Transition Support Ltd. U.K)

- Industrial Development Authority Annual Report (2002). Enriching Ireland. Available at http://www.idaireland.com/news-media/publications/annual-reports/pdfs/anrep02.pdf

- Industrial Development Authority (2002). Annual Report

- Industrial Development Authority (2003). Annual Report

- Industrial Development Authority (2004). Annual Report

- International Atomic Energy Agency, (1986). Summary Report on the Post-accident Review Meeting on the Chernobyl Accident. INSAG Series No. 1. August 1986.

- International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (2005). *ICH Harmonised Tripartite Guideline. Quality Risk Management Q9*. November 2005.

- International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human use. (2000). *ICH Harmonised Tripartite guideline. Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients.*

- International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human use. (2005). *Q10 :*

Pharmaceutical Quality Systems Final Concept Paper, dated 9 September 2005

- International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human use (2009). *ICH Harmonised Tripartite Guideline Pharmaceutical Development Q8(R2) Current Step 4* version, dated August 2009

- International Standards Organisation (No date). Available at http://iso.org/iso/en/aboutiso/introduction/index.html.

- International Standards Organisation (No date). Available at http://www.iso.org/iso.en/iso9000-14000/iso9000/faqs.html

- International Standards Organisation (2000). ISO 9001:2000: Quality management systems -- Requirements

- International Standards Organisation (2000). ISO 9000:2000 Quality management systems – Fundamentals and vocabulary

- International Standards Organisation (2001). ISO 14971:2001 Medical devices. Application of risk management to medical devices

- International Standards Organisation (2002). ISO 19011:2002 Guidelines for quality and/or environmental management systems auditing

- International Standards Organisation (2003). ISO:13485:2003 Medical devices -- Quality management systems -- Requirements for regulatory purposes

- International Standards Organisation (2003). ISO 9000 Guidance on the Concept and Use of the Process Approach for management systems. Document: ISO/TC 176/SC 2/N 544R2

- International Standards Organisation (2003). ISO 14001:2003 Environmental Management

- International Standards Organisation (2004). ISO 14004:2004 Environmental management systems - General guidelines on principles, systems and support techniques

- International Standards Organisation (2005). ISO 9000:2005 Fundamentals and vocabulary

- International Standards Organisation (2007). ISO/IEC TR 25021:2007 Software engineering. Software product quality requirements and evaluation (SQuaRE). Appendix A Selected Quality Measures.

- International Standards Organisation (2008). ISO 9241-11: Ergonomic requirements for Office Work with Visual Display Terminals (VDTs). Part 11—Guidelines for Specifying and Measuring Usability, International Standards Organisation, Geneva (1997b).

- International Standards Organisation (2008). The ISO Survey of Certifications. Available at http://www.iso.org/iso/survey2008.pdf. Published by The ISO Central Secretariat (ISO/CS), Switzerland.

- International Standards Organisation (2009). ISO 14971:2009 Medical devices. Application of risk management to medical devices

- International Standards Organisation (2010). ISO 9241-210:2010 Ergonomics of human-system interaction Part 210: Human-centred design for interactive systems

- Irish Medicines Board (2004). *IMB Guidance Note 1. About the Medical Devices Department of the IMB*. Published by the IMB, 2004. Available at http://www.imb.ie/images/uploaded/documents/GN013MedicalDevicesDepartment.pdf

- Irish Medicines Board (2010). Human Medicines. Available at http://www.imb.ie/EN/Medicines.aspx. Sourced 13/12/2010.

- Jorgensen, T.H., Remmen, A. and Mellado, M.D. (2006). Integrated Management Systems – Three different Levels of Integration. In Journal of Cleaner Production **14** (8) pp. 713 - 722

- Jørgensen, T. H. (2007). Towards more sustainable management systems: through life cycle management and integration. *Journal of Cleaner Production*. 16 (10) pp. 1071 – 1080

- Karapetrovic, S. (2002). Strategies for the integration of management systems and standards. In *The TQM Magazine* 14 (1) pp. 61-67

- Karapetrovic, S. (2003). Musings on integrated management systems. In *Measuring Business Excellence* 7 (1), 4-13.

- Karapetrovic, S., Casadesus, M. and Heras, I. (2010). Empirical Analysis of Integration Within the Standards-Based Integrated Management Systems. International Journal for Quality research **4** (1)

- Karapetrovic, S. and Wilborn, W. (2000). Quality assurance and effectiveness of audit systems. In *International Journal of Quality & Reliability Management* **17** (6) pp. 679-703.

- Karapetrovic, S. and Wilborn, W. (2000). Generic audit of management systems: fundamentals. In *Managerial Auditing Journal* **15** (6) pp. 279-294

- Karapetrovic, S. and Wilborn, W. (2002). Self-audit of process performance. In *International Journal of Quality & Reliability Management* **19** (1) pp. 24-45

- Keegan, R. and O'Kelly, E., (2004). Applied Benchmarking for Competitiveness: A Guide for SME Owner/Managers

- Krause T. (1993). Safety and Quality: Two sides of the same coin. Occupational Hazards pp. 47-50

- Lambert, J., Jennings, R. And Joshi, N. (2006). Integration of risk identification with business process models. In *Systems Engineering* **9** (3) pp. 187-198.

- Lubbe, S. (2003) The Development of a Case Study Methodology in the Information Technology (IT) Field: A Step by Step Approach. *Ubiquity* Vol. 4 Issue 27. Published by ACM Press.

- Mansar, S.L. and Reijers, H.A. (2005). Best practices in business redesign: validation of a redesign framework. In *Computers in Industry* **56** pp. 457-471

- Maurino, Daniel E., (1995). Beyond Aviation Human Factors: safety in high technology systems,

- McCarl, B.A. (1984). Model validation: an overview with some emphasis on risk models. Review of Marketing and Agricultural Economics **52** pp.153-173

- McCarthy, F.D. (2001). Social Policy and Macroeconomics: The Irish Experience (World Bank)

- McDonald et al (2000), McDonald et al (2000)

- McGregor Associates (1996) Study on Management System Standards. Published by British Standards Institution. London.

- Maxwell, J. A. (2005). *Qualitative research design: An interactive approach* (2nd ed.) Thousand Oaks, CA: Sage.

- Mitchison, N. and Papadakis, G. (1999) Safety management system under Seveso II: implementation and assessment, *Journal of Loss Prevention in the Process Industries* 12

- Modell, S. (2005). Triangulation between case study and survey methods in management accounting research: An assessment of validity implication. In *Management Accounting Research* 16 (2) pp. 231-254

- Moody, D. L., (2005). Theoretical and practical issues in evaluating the quality of conceptual models : current state and future directions. In *Data and Knowledge Engineering* **55** pp. 243-276

- Moody, D. L. and Shanks, G. G. (2003). Improving the quality of data models : empirical validation of a quality managment framework. In *Information Systems* **28** pp. 619-650

- National Institute of Standards and Technology (NIST) (1993). Draft Federal Information Processing Standards Publication 183 Integration Definition for Function Modeling (IDEFØ). December 21, 1993

- Nutely, C. (2000). The *Value and Benefits of ICH to Industry* International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)

- Oakland, J. (1993).Total Quality Management (2nd Ed.). Heinemann, London

- O'Hanlon, T. (2002). *Quality Audits for ISO 9001:2000: Making compliance Value-Added.* (American Society for Quality (ASQ) Quality Press, Milwaukee, Wisconsin).

- Patton, M. Q. (2002). *Qualitative evaluation and research methods* (3rd ed.). Thousand Oaks, CA: Sage Publications, Inc.

- Pickvance, S. (2003). Arguing the Business Case for Occupational Health. In *Occupational Health Review*, **103**, (May /June 2003).

- Pidgeon, N. & O'Leary, M., (2000). Man-made disasters: why technology and organizations (sometimes) fail. *Safety Science*, **34**, pp. 15-30

- Presidential/Congressional Commission on Risk Asessment and Risk Management (1997) Framework for Environmental Health Risk Management.

- Reason, J., (1990). Human Error. Cambridge University Press.

- Reijers, H.A. and Mansar, S.L. (2005). Best Practices in Business Process Redesign: An Overview and Qualitative Evaluation of Successful Redesign Heuristics. In *International Journal of Management Science* **33** (4) pp. 283-306

- Rogers, W. P., (1986) Report of the Presidential Commission on the Space Shuttle Challenger Accident.

- Rykiel, E.J. (1996). Testing ecological models: the meaning of validation. In *Ecological modelling* **90** pp. 229-244

- Shannon, H., Robson, L., and Guastello, S. (1999). Methodological criteria for evaluating occupational safety intervention research. In *Safety Science* **31** pp. 161-179.

- Sheen, B (1987). Mv Herald of Free Enterprise: Report of Court No. 8074. Formal Investigation (Merchant Shipping Act 1894 formal investigations). Department of Transport. HMSO. London

- Safety, Health and Welfare at Work (Exposure to Asbestos) (Amendment) Regulations 2010 (S.I. No. 589 of 2010)

- Stake, R. E. (1994) in *Handbook of Qualitative Research* Eds. Denzin N.K. and Lincoln Y.S. (1994) (Sage Publications)

- Stanton, N. and Baber, C. (1996). Factors affecting the selection of methods and techniques prior to conducting a usability evaluation. In *Usability Evaluation in Industry* by Jordan, P. W., Thomas, B., Weerdmeesster, B. A. and McClelland, I. L. (Taylor & Francis Ltd.)

- Swann, J. (1998) Adapted from Kurian, G. (Ed.)., *A Historical Guide to the U.S. Government* (New York: Oxford University Press)

- Tervonen, P., Pahkala, N. and Haapasalo, H. (2009). Development of TQM in steel Manufacturers' Production. In *IBIMA Business Review* **1**, 2009.

- Thurmond, V.A. (2001). The Point of Triangulation. In *Journal of Nursing Scholarship* **33** (3). pp. 253-258

- UK Department of Transport (1987). *MV Herald of Free Enterprise: Report of Court No. 8074 Formal Investigation.* Published by Her Majesty's Stationary Office. London

- Wilkinson, G. and Dale, B. (2001). Integrated management systems: a model based on a total quality approach. In *Managing Service Quality*. **11**(5), 318-330

- Wilson, R., and Harsin, P. (1998). *Process mastering: How to establish and document the best know way to do a job*. (Productivity Press)

- Wright, M., Brabazon, P., Tipping, A. and Talwalkar, M. (1999). *Development of a business excellence model of safety culture.* Contract Research Report by Entec UK Ltd. For the Health and Safety Executive. London: Entec.

- Yin, R. K. (2003). Applications of case study research. 2nd Ed. Applied Social Research Methods Series Volume 34

- Zeng, S. X., Shi, J. J., and Lou, G. X. (2007). A synergetic model for implementing an integrated management system: an empirical study in China. *Journal of Cleaner Production,* **15** (18), pp. 1760-1767.