Medical Device Regulations, Industrial Capabilities, and Affordable Healthcare Technology Development: Case Studies from the United Kingdom and South Africa

Thesis

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Medical Device Regulations, Industrial Capabilities and Affordable Healthcare Technology Development:

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ABSTRACT

This thesis concerns the influence of healthcare systems regulation on firm-level capabilities and affordable healthcare technologies. Regulatory change is highly contentious, critics arguing that regulatory changes interfere with the efficiency of the market, and advocates arguing that well designed regulatory changes make markets more efficient and ensure market outcomes are more equitable. To date, very few studies analyze the influence of regulatory change on the medical device industry, and its ability to manufacture and supply affordable healthcare technologies.

To respond to this gap, this research employs the Sectoral Systems of Innovation (SSI) approach as a theoretical framework to analyze the influence of regulatory changes on industrial capabilities in medical device industries and affordable healthcare technologies in South Africa and the United Kingdom. A mixed method approach, focusing on three cases of regulatory change, emphasised documentary analysis and questionnaire-guided interview to collect primary and secondary data from different sources in the healthcare systems of the two study countries.

Regulatory changes facilitated some firms to create new strategies and innovative capabilities. Regulatory changes enabled some firms to develop close collaborative linkages with external providers in search of competitive advantage and improved market positioning. One reactive regulatory change in particular illustrated negative influence on innovative capabilities. Smaller firms were at a particular disadvantage in adapting to regulatory change. In the South Africa case, the more stringent regulatory requirements made it hard for domestic suppliers to enter the supply chain and led to joint ventures mainly with multinational corporations. The thesis argues, with empirical evidence, that a more enabling and discriminating regulation that takes into consideration of firms' technological capabilities can achieve intended goals more efficiently and effectively, than constraining and indiscriminate regulation.

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ACRONYMS AND ABBREVIATIONS

AIMDD	Active Implantable Medical Devices
AU	African Union
CT	Computed tomography
BBBEE	Broad-Based Black Economic Empowerment
BMI	Business Monitor International
BSI	British Standards Institution
CAGR	Compound Annual Growth Rate
CEASA	Clinical Engineering Association of South Africa
DRC	Directorate: Radiation Control
EC	European Commission
EEA	European Economic Area
ESRC	Economic and Social Research Council
EU	European Union
EUDAMED	European Databank for Medical Devices
FDA	United States Food and Drug Administration
GLP	Good Laboratory Practice
HPCSA	Health Professions Council of South Africa
IBs	Inspection Bodies
IEC	International Electro-technical Commission
IMDRF	International Medical Device Regulators Forum
ISO	International Organization for Standardization
IVD	In-vitro diagnostic
MCC	Medicines Control Council
MDD	Medical Device Directive
MEDDEV	Medical Device Guidance Documents
MHRA	Medicines and Healthcare products Regulatory Agency
MNC	Multinational Corporation
MRC	Medical Research Council
MRI	Magnetic Resonance Imaging
NB	Notified Body
NEPAD	New Partnership for Africa's Development
NGOs	Non-Governmental Organizations
NIS	National Innovation Systems
NHS	National Health Service
NMRA	National Medicines Regulatory Authorities
OECD	Organization for Economic Cooperation and Development
OEM	Original Equipment Manufacturer
PAHO	Pan American Health Organisation
PIP	Poly Implant Prostheses

PMA	Pre-market Approval
QC	Quality Control
QMS	Quality Management Standards
QMS	Quality Management System
RED	Radiation Emitting Devices
ROI	Return-On-Investment
SA	South Africa
SADC	Southern African Development Community
SAHPRA	South African Health Products Regulatory Agency
SALDA	Southern African Laboratory Diagnostics Association
SaMD	Software as a Medical Device
SAMED	South African Medical Device Industry Association
SANAS	South African National Accreditation System
SAQA	South African Qualifications Authority
SARPA	Southern African Radiation Protection Association
SMEs	Small to Medium sized Enterprises
SSA	Sub-Saharan Africa
SSI	Sectoral Systems of Innovation
STI	Science, Technology and Innovation
UK	United Kingdom
USA	United States of America
WHO	World Health Organization

CHAPTER ONE
INTRODUCTION

Medical device manufacturing firms operate in a regulatory-intensive environment. These firms need to understand how to adapt to and take advantage of exogenous changes such as regulations. As early as 1988, Mayo and Flynn (1988) noted that regulations can create significant new business opportunities since they often infuse radical effects on industries and firms. However, the changes in regulatory requirements represent huge challenges for many firms and are often viewed primarily as new restrictions on conducting business (Chowdhury, 2014). They can limit how firms design, develop and market their products. For some firms, regulations might be seen as a hurdle, since compliance requirements might hamper ambitions for business growth and innovation (Ashford et al., 1985). Regulations can force firms to make investments in projects that they must do, often in stark conflict to what the firm wants to do (e.g. innovation or product development) (Blind, 2012). The way in which the actors of change such as manufacturers in the industry are able to deal with the market environment is influenced by the internal capabilities of these actors.

Regardless of how regulatory changes are perceived, they will influence the structure of industries and thereby also the position and fortune of firms (Altenstetter, 2008). Firms are obliged to understand that regulations will generate new requirements and consider how best to manage implementation. By understanding regulations as a key influencing factor, firms can identify new opportunities offered by the processes of regulatory change (Curfman and Redberg, 2011). Therefore, better insight into what firms do to manage regulatory change can result in new insight into the destiny of firms.

This thesis contains two central themes. One is the evaluation of the effects of regulatory changes on overall industry capabilities. That is, how does the Sectoral System of Innovation (SSI) operate and how is it affected by regulatory change? The second theme is the evaluation of firms in two different regulatory environments with different characteristics. In this research the key characteristic is the experience firms have gained of the regulatory review process. To study the influence of regulatory

change on firm level capabilities, it is critical to first understand the concepts of a healthcare system.

1.1 Healthcare System

Healthcare systems or health systems play a central role in helping people maintain and improve their health. A number of frameworks and models have been developed and published to illustrate what a health system looks like. Some of those frameworks that have been proposed at the national level include: the widely used World Health Organization (WHO) models (WHO, 2007; 2009), the reform focused model (Cassels, 1995) and the essential public health functions model (PAHO, 2008). In this research, the WHO (2009) health system framework (as shown in figure 1.1) is used to illustrate the six operational building blocks and the overall health system goals.

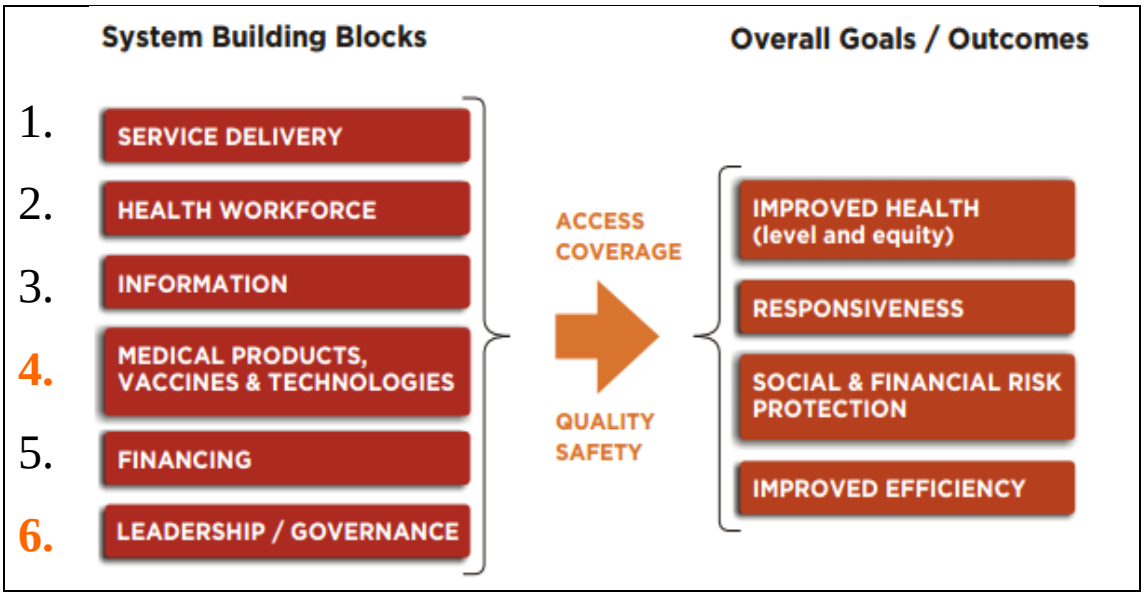


Figure 1.1: The WHO Health System Framework. Source: (WHO, 2009)

A strong health system is built on six building blocks: service delivery, health workforce, information, medical products, vaccines, and technologies, financing and governance (WHO, 2009). The various interactions among these components convert these building blocks into a system and if any of these components are missing, the health system cannot function at the level necessary to improve the health of the population. Each building block has its own unique challenges in terms of policy and organizational systems (WHO, 2011a). The areas of focus within the WHO health system framework to be examined in this study are the health technologies (medical devices) and governance (regulation), which are emanating from the fourth and sixth

building blocks of the framework.

1.2 Health Technologies

Based on functions defined by WHO, (2007), a well-functioning health system ensures equitable access to essential medical products, vaccines and technologies of assured quality, safety, efficacy and effectiveness. Healthcare technologies work towards the reduction of healthcare costs by conducting timely diagnosis, provision of effective treatment and reduction of pressure on hospital resources and staff (Matsoso and Fryatt, 2013). Liaropoulos (1997) drew a schematic representation (as shown in Figure 1.2) of the alternative definitions of biomedical, medical, healthcare and health technology:

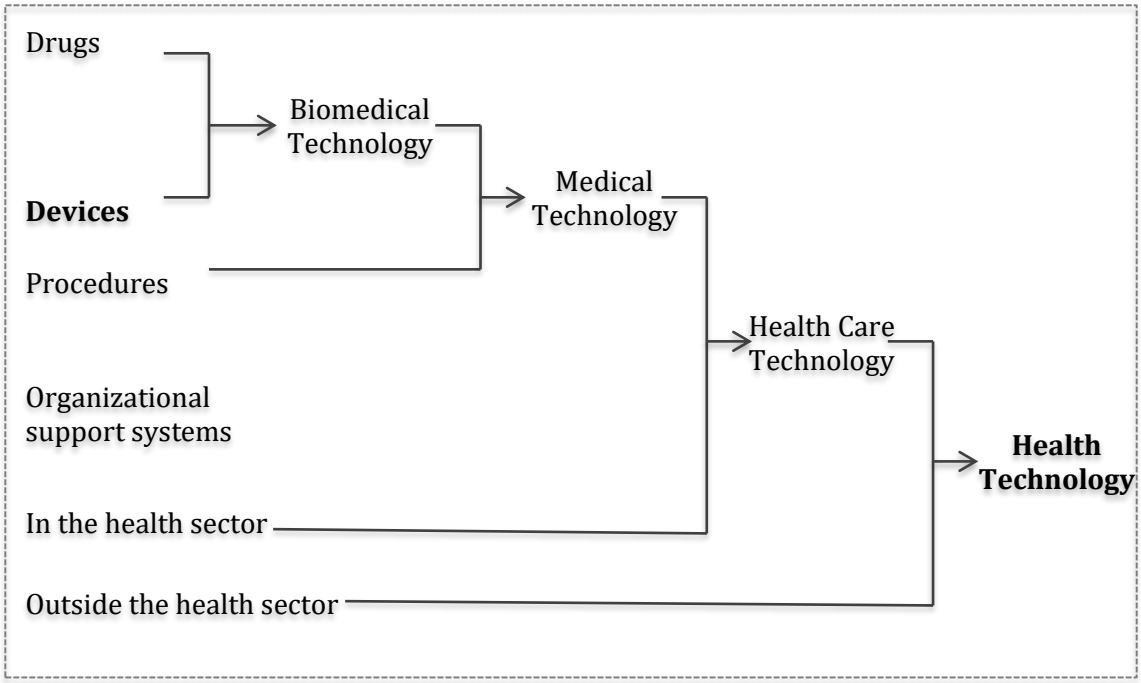


Figure 1.2: Outline of the categories in health technology. Source: (Liaropoulos, 1997, p.126)

As shown in figure 1.2 and starting from the top left of the list, drugs and devices are considered as technologies dealing primarily with the biological characteristics of the processes under which healthcare is provided therefore assigned to the category of biomedical technologies. The addition of procedures to the list refers us to the main domain of the clinical practice, thus drugs, devices, and procedures constitute medical technology. When organizational and support systems originating and operating within the broader health care system are added to the list, the category is considered

as health care technology. Health technology, on the other hand, includes all of the above as well as the societal organizational and system parameters that determine the final health outcome (Liaropoulos, 1997).

Medical devices are a subset of health technologies as can be seen from figure 1.2. They play an important role in clinical practice and improving patients' health (Altenstetter, 2008, Beksinska et al., 2011). Medical professionals make critical decisions associated with healthcare after using the devices to identify the patient's problem (Zuckerman et al., 2011). Medical devices include syringes, catheters, and face masks. There are also devices for wound management, ultrasound, artificial joints and prosthetics, invasive surgery, clinical and laboratory operations, and inhalation and infusion therapies. Others are audiometry and hearing aids, disposables, hospital supplies, kits and in-vitro diagnostics (Kramer et al., 2012a).

However, the use of medical devices entails some considerable risks to human health (Altenstetter, 2008). Regulation is one mechanism to help balance the benefits and risks of new devices (Sorenson and Drummond, 2014). Therefore all health technologies must fulfil the regulatory requirements of their targeted markets and prove that they are developed in a way fitting with their purpose (Chowdhury, 2013).

1.3 The Role of Regulation and the Need for Change

The sixth building block of the WHO health system framework is leadership and governance. This component involves ensuring strategic policy frameworks exist and are combined with effective oversight and regulation of health technologies (WHO, 2007). Regulatory institutions, policies, and processes have been developed by governments to authorize healthcare technologies for use on the market and to determine the terms of their coverage, reimbursement, and pricing. The Organisation for Economic Co-operation and Development (OECD) defines regulation as the implementation of rules by public authorities and governmental bodies to influence market activity and the behaviour of private actors in the economy (OECD, 1997).

Scope of regulations in medical devices can be divided into several phases in the product life-cycle: pre-market, placing on-market, and post-market surveillance (WHO, 2003). Thus, regulation becomes crucial already in the development phase

(pre-market) as it is required to develop and document the product according to national regulations. During placing on-market phase regulation is needed for advertising and sales of products. After placed on-market, post-market surveillance must be in place meaning that products are monitored while on the use.

Regulation is an important defining factor in the medical device industry because it influences the way in which technologies are innovated, tested and commercialized, it also influences how producers and consumers interact, and ultimately contributes heavily to the institutional structure and the innovation dynamics of the medical device sector (Beer et al., 2011). The need for regulation comes from information asymmetry between the producers on one side and patients and clinicians on the other side. Patients cannot assess safety or observe quality and efficacy of medical devices on their own, and neither can the medical practitioners who decide on their behalf (Harper, 2007). This is where regulatory bodies come in, by seeking evidence of compliance with guidelines, rules and regulations to give credibility and legitimacy to organizations inspected.

Furthermore, regulation seeks to ensure that the health technologies are improved and offer reforms to healthcare services (Wood, 2010). The forces behind changes in regulations are diverse, emanating from firms, policymakers and regulators (Jacobides et al., 2006). Firms can turn to regulatory bodies for guidance on how to adjust to regulations (Brusoni et al., 2009). The objectives of regulation are the same in most countries, however the characteristics of different regulatory regimes can be quite different.

1.3.1 Types of Regulations

The regulatory requirements and other documentation for medical device safety come in different forms and compliance with some of them is mandatory and voluntary with others. There are also some differences in terms between issuing bodies. Figure 1.3 outlines the different types of regulations, which will be discussed in this thesis in more detail.

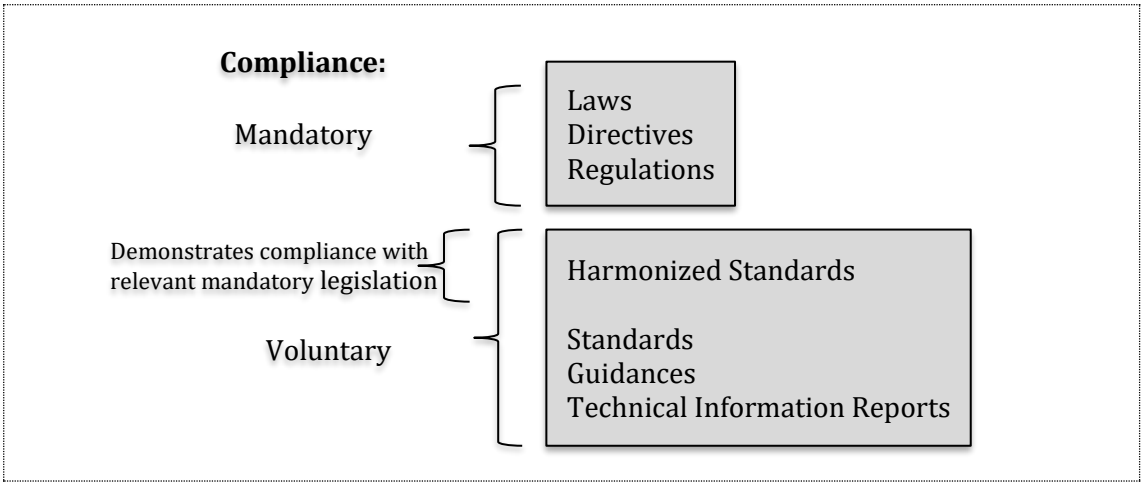


Figure 1.3: Compliance requirements

The EU law is divided into 'primary' and 'secondary' legislation. The treaties (primary legislation) are the basis or ground rules for all EU action. Secondary legislation, including directives, regulations and recommendations, are derived from the treaties (EU Law, 2018). Regulations are binding legislative acts that must be applied in their entirety. For example, when the EU wanted to make sure that there are common safeguards on goods imported from outside the EU, the Council adopted a regulation. Directives are legislative acts that set out goals that all EU countries must achieve. However, unlike regulations, it is the individual member countries who devise their own laws on how to reach these goals (EU Law, 2018).

Standards are technical specifications defining requirements for products, production processes, services or test-methods. These specifications are voluntary and are developed by industry and market actors following some basic principles such as consensus, openness, transparency and non-discrimination. Standards ensure interoperability and safety, reduce costs and facilitate companies' integration in the value chain and trade (European Commission, 2016).

In Europe, harmonised standards are developed and agreed by the three officially recognized European Standardization Organizations: the European Committee for Standardization (CEN), the European Committee for Electro technical Standardization (CENELEC) and the European Telecommunications Standards Institute (ETSI). They are created following a request from the European Commission to one of these organisations. Medical device manufacturers, other economic

operators, or conformity assessment bodies can use harmonised standards to demonstrate that products, services, or processes comply with relevant EU legislation (EU Law, 2018).

The European Commission, standards development organizations also publish guidance documents on the application of standards and regulations. Such guidance offers more insight into the application of the standards or regulations, and thus helps achieve conformance with them. Technical information reports offer information much like standards, but are not subject to a formal process of committee approval, public review, and resolution of comments (European Commission, 2016).

1.4 Medical Device Regulatory Challenges

Over the past three decades the medical device sector in advanced countries has seen increased regulation and oversight (Altenstetter, 2008). Key areas relate to the ways in which new devices are trialled, approved, and ultimately marketed. In practice, regulation of medical devices has also seen inherent limitations and challenges (Curfman and Redberg, 2011). Some challenges of regulating medical device manufacturing sufficiently have been revealed by uncovering medical devices at the market that do not fulfill safety criteria to ensure patient protection and has led to patient harm and deaths (Kramer et al., 2012b). These challenges will be explored further in the literature review chapter.

The medical device industry often maintains that the regulatory process is unpredictable and prolonged, thereby becoming a barrier to innovation and timely market entry of their products (Faulkner, 2012, Kramer et al., 2012b); regulators frequently face governmental pressures and stakeholder resistance (Peck et al., 2014), while health consumers (patients) often complain about not able to access new technologies (Matsoso and Fryatt, 2013). In most developing countries, however, regulation of medical devices is weak (Rugera et al., 2014). The majority of developing countries, and in particular those in the Africa, have a legal mandate to regulate but there is limited capacity to do so (Rugera et al., 2014). Furthermore, in these countries, most research has focused more on regulation and development of pharmaceuticals even though medical devices constitute a key component in the healthcare technologies (Kale and Mkwashi, 2015, Sorenson and Drummond, 2014,

Doherty, 2015). As a result, research on evolution of medical devices regulation, the new developments and in particular market authorisation in different countries and specifically, the global south remains a highly under-researched topic.

In order to bridge this knowledge gap and provide a useful cross-country analysis of regulation of medical devices, this study investigate the evolution of regulatory changes in the medical device sector in the UK and SA and examine its influence on industrial capabilities and development of affordable healthcare technologies. The UK and SA have recently introduced or are currently debating reforms of medical device regulation, thus it is an opportune time to examine regulatory policies and practices in both countries and identify areas for additional improvement.

1.5 Research Questions

The overall research question guiding this study is: **"How and to what extent has the evolution of medical device regulations in the UK and SA impacted industrial capabilities and contribution towards affordable health care technology development?"**

The main objective of this overall research question is to add to the existing knowledge on the effects of regulatory changes on industrial efforts to make affordable healthcare technologies in general and medical devices in particular, available in both developed and developing countries. To be able to adequately answer the overall research question, three sub questions were formulated, namely:

Sub-Question 1: What changes have been made to regulation of medical devices and what approaches were utilised by regulators to implement the changes in the UK and SA?

Sub-Question 2: What conditions, processes and events facilitated the changes to regulation of medical devices in the UK and SA?

Sub-Question 3: How have regulatory changes affected firm level investment, production and linkage capabilities of medical device firms in the UK and SA?

It is worth noting at this juncture that there is another key underlying principle besides the literature that has guided the formulation of these research questions. This

approach is adopted particularly to ensure that they will correspond with the overall motive of this research. It is indeed acknowledged that the key principal nature of regulatory requirements would typically highlight what needs to be achieved and therefore defines the expectations on the various deliverables required. In this regard, deliverables have been defined as all forms of outcomes that are expected to be achieved by medical devices manufacturing firms arising from the adherence to regulatory requirements.

Therefore, the research questions have been designed to explore three key research issues i.e. the content, drivers and impact of regulatory changes. The research questions were developed after recognizing the importance of them being clearly focused, as well as in ensuring that they are related with one another and further to "form a coherent set of issues" (Bryman, 2008: p. 73). For ease of comprehension, a table outlining the sub research questions, their relevant research application as well as the associated chapters where they will be explained in detail, is presented in Table 1.1 below:

Table 1.1 Application of Research Questions and Associated Chapters

Research Question (RQ)	Application of Research Question	Chapter
RQ1. What changes have been made to regulation of medical devices and what approaches were utilised by regulators to implement the changes in the UK and SA?	To assess and understand the **"content"** of regulatory changes and the regulatory **"approaches"** utilised by regulators to implement the changes in the UK and SA	2 6
RQ2. What conditions, processes and events facilitated the changes to regulation of medical devices in the UK and SA?	To explore and determine the **"drivers"** that facilitated of regulatory changes in the UK and SA.	2 6
RQ3. How have regulatory changes affected firm level investment, production and linkage capabilities of medical device firms in the UK and SA?	To investigate the **"effects"** of medical device regulatory changes on industry capabilities and development of affordable medical devices in the UK and SA.	7 8 9

Answering the above research questions is envisaged to generate evidence, which is generalizable in an analytical rather than statistical sense on the influence of regulatory changes on industrial capabilities and development of affordable healthcare technologies in developed and developing countries.

1.6 Key Findings

This study has shown that the interaction between medical device regulations, industrial capabilities and affordable healthcare technology development is complex and multi-faceted, such that assessing the impact of a given piece of regulation on innovation is often an empirical, case-by-case exercise. That said, our analysis has shed light, with the help of pre-existing literature, on the way in which different types of regulatory changes can affect firm level capabilities. More specifically, our main findings include the following:

- Regulatory change can, under certain circumstances, be a powerful stimulus to innovation. Regulatory changes facilitated some firms to create new strategies and innovative capabilities.
- Regulatory changes enabled some firms to develop close collaborative linkages with external providers in search of competitive advantage and improved market positioning.
- Different types of regulatory approach can have different impacts on firms' technological capabilities. Typically, we found that a more prescriptive, rigid regulatory change can hamper innovative activity by reducing the attractiveness of engaging in R&D, constraining modes of commercialization, and creating lock-in effects that force the economy into suboptimal standards. The more regulatory change is flexible and enabling, the more innovation can be stimulated. One reactive regulatory change in particular illustrated negative influence on innovative capabilities. Smaller firms who lack the resources to come up to strict legal requirements were at a particular disadvantage in adapting to regulatory change. In the South Africa case, the more stringent regulatory requirements made it hard for domestic suppliers to enter the supply chain and led to joint ventures mainly with multinational corporations (MNCs).
- During the enforcement phase of regulatory change, we found that the lower the costs of compliance and the administrative burdens, the more positive were the

influence on firms' technological capabilities.

- In addition, after the regulatory change, firms tend to replicate extant technology combinations instead of introducing new ones. This result thus indicates that innovators become more risk averse toward novelty.

The thesis argues, with empirical evidence, that a more enabling and discriminating regulation that takes into consideration of firms' technological capabilities can achieve intended goals more efficiently and effectively, than constraining and indiscriminate regulation.

1.7 The Structure of the Thesis

This thesis contains ten chapters, each of which plays a particular role in defining, formulating, and addressing the research question to deliver the assumed contribution of this research. Following this introduction, Chapter 2 provides background details for the research relevant in answering sub questions one and two. It sets the scene for all the empirical chapters in this thesis (i.e. Chapter 7 to 9). It starts by presenting the current state of the global medical device market, followed by a discussion on the UK and SA medical device industry profiles such as the market size, distribution of medical technology companies and the major segments in medical technology. In addition, it discusses evolution of medical device regulations in the two study countries and associated requirements that are specifically affecting the medical device industries are presented. Finally, it also explains the key components of the current state of medical device regulatory frameworks in the UK and SA.

Chapter 3 presents a critical evaluation of literature on health technology regulation in general and medical device regulation in particular to situate this research in the context of this literature. Particular emphasis is placed on literature on medical device regulation in both advanced and developing countries. In addition, literature on the effects of regulation on the industry is also examined. A summary of the key issues raised in each part of the literature review is provided such that knowledge gaps is identified and presented.

Chapter 4 presents the theoretical framework of this study. This chapter first presents a graphical overview of conceptual framework for the research, used as a guide to flow through the study on medical device regulation and industrial capabilities,

through the Sectoral Systems of Innovation (SSI) lens, anchored in evolutionary theory. The main factors that influence the dynamics of the system are the actors and networks, knowledge and technologies, the extent of innovation and institutions in particular regulation. These elements are the centre of this study's analytical focus. The chapter further describes other supporting theories, concepts and approaches used to unpack the effects of medical device regulatory changes on investment, production and linkage capabilities and development of affordable health technologies

Chapter 5 presents the scope of the research, and details how the research was conducted. It will first present the philosophical position of this study and methodological issues leading to the choice of methodology. The research strategy then explains the reasons for using the case study approach and discusses key characteristics of case study quality. Case study design is explained, consisting of the importance of context, the unit of analysis, and a sample selection of the firms, as well as the criteria and process. Data collection methods and data analysis strategy employed are also presented.

Chapter 6 presents three case studies of regulatory changes that have been selected for this study. The aim of this chapter is to, first, analyze and explore the two regulatory change cases in the UK that were highly significant for the medical device industry. Each regulatory change was different: one was a major extension of regulatory reach into software; the other introduced unannounced audit visits therefore toughening regulatory compliance processes. Second, the chapter will also analyze and explore the regulatory change case of radiation emitting devices in SA that promoted safety in the workplace and prevented unnecessary exposure to radiation.

Chapter 7 is the first of three empirically based chapters that present and analyze the data collected. This chapter addresses research sub-question number three identified in chapter one using empirical data from a group of sixteen medical devices firms in the UK. This chapter is focused on firm level effects in a tightly regulated national environment. The empirical evidence that comprises of two kinds of data is then analysed. The analysis begins with a generic narrative contextualising the effects of regulatory changes on industrial capability based on the sixteen UK-based firms. Thereafter, a more comprehensive narrative of three purposefully selected firms is

then presented. At the end of the chapter, the results of each regulation and each type of capability will be summarized and general characteristics of the firms' responses to the new regulation will be further described so as to provide an informative overall perspective.

Chapter 8 delves further in addressing research sub-question number three but using empirical data from a group of sixteen SA-based medical devices firms. The chapter draws its attention to the description of radiation emitting devices regulation and the subsequent changes. The analysis follows the same approach as used in chapter 7.

Chapter 9 presents the final detailed cross-case analysis of firm cases in two countries. The chapter starts by setting out the analytical approach undertaken during the analysis of regulatory change effects. In addition, the three regulatory changes that have been identified is briefly described, before the cross-case analysis is summarized and presented. The chapter then proceeds to present data relating to investment, production and linkage capabilities. Within these capabilities, the chapter analyzes in some depth each regulatory change case looking for generalizable conclusions from the study's various empirical firm data. At the end of the chapter, the results are summarized so as to provide an overall empirical and conceptual perspective.

Finally, Chapter 10 presents a summary of the findings, discusses various policy implications and addresses the limitations of the study. It commences by outlining the summary of key findings, in relation to the research questions outlined in Chapter 1. Subsequently, the chapter provides the overall discussions based on the outcomes of the research. Furthermore, arising from the understanding and insights obtained throughout the analysis, regulatory recommendations, are presented. The recommendations, in this regard, are better suited to discover enabling regulatory and policy approaches that enables industrial capabilities. In addition, this chapter also articulates the policy implications of the research and highlights the limitations of the study; as well as identifying the opportunities for further research.

CHAPTER TWO
RESEARCH BACKGROUND

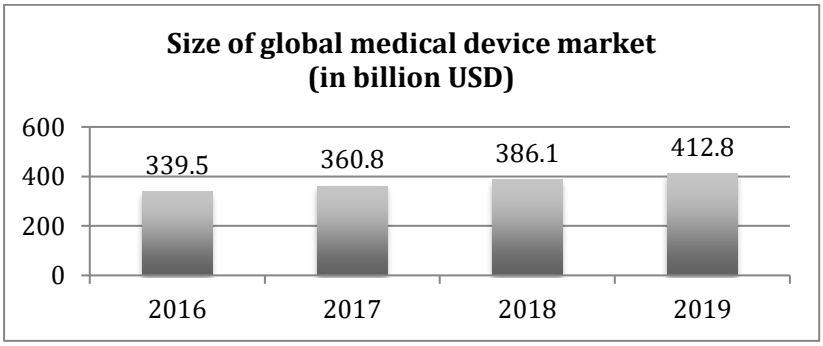
2.0 Introduction

This chapter outlines the contextual and background details of the research. It begins by presenting the current state of the global medical device market, followed by a discussion on the UK and SA medical device industry profiles. The chapter also discusses evolution of medical device regulations in the two study countries and associated requirements that are specifically affecting the medical device industries. Importantly, the discussion on the evolution of medical device regulations in this chapter contributes to answering the research sub-questions one and two aimed at assessing the drivers and contents of the regulatory changes in the UK and SA.

2.1 The Global Medical Device Market

Size of market

The medical devices market is one of the fastest growing and most complex in the world (Sorenson and Kanavos, 2011). The sector in 2017 was made up of approximately 2 million devices that can be categorized into more than 22 000 generic devices groups [1] on the global market (WHO, 2017). According to the statistics from the U.S. Department of Commerce, the global market sale of medical devices in 2016 reached $339.5 billion (see Figure 2.1). The global medical market is expected to grow at a compound annual rate (CAGR) of 4.1%, and reach $522 billion by 2022 (MedTech, 2017). Figure 2.1 illustrates the global market sale of medical devices for the period 2016-19.



[1] The Global Medical Device Nomenclature Agency listed more than 22 000 generic device groups for medical devices (Source: GMDN Agency).

Figure 2.1: Values of the global medical device market. Source; (U.S. Department of Commerce, 2016).

Since innovation fuels the global medical device market's on-going quest for better ways to treat and diagnose medical conditions, when coupled with patient life expectancy increasing and aging populations globally, the medical device market should continue growing at a positive rate in the future (U.S. Department of Commerce, 2016). Figure 2.2 illustrates the global medical device market size by region based upon manufacturer prices[2] in 2016.

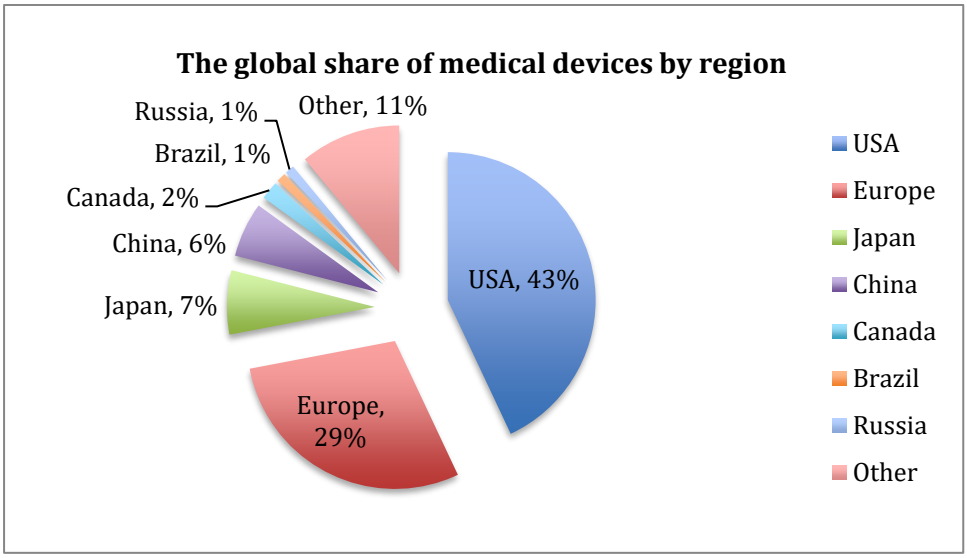


Figure 2.2: The global share of medical devices by region based upon manufacturer prices in 2016. Source: (MedTech Europe, 2018)

The United States currently has the largest medical device market in the world, with a market size of around $156 billion, and it represented about 40-43% of the global medical device market in 2016 (U.S. Department of Commerce, 2019, MedTech Europe, 2018). In the US, there are approximately 7,000 companies in the medical device market, which directly employ about 500,000 people and indirectly employ more than 2 million people (U.S. Department of Commerce, 2019).

As Figure 2.2 shows, Europe currently holds nearly 30% of the global market with market value of about $110 billion. It is the second largest medical device market after the US. In Europe, in 2018, there were approximately 27,000 small and medium-sized companies manufacturing medical devices, employing 675,000 people (European Commission, 2017). The U.S. and Europe control about 70% of global

[2] Market size estimated in manufacturers' prices, not including margins, such as value added in the wholesaling and retailing, transportation costs, some taxes included in the final price, etc.

medical device market. The market size of the top 10 European countries based upon the manufacturer prices is presented in Figure 2.3.

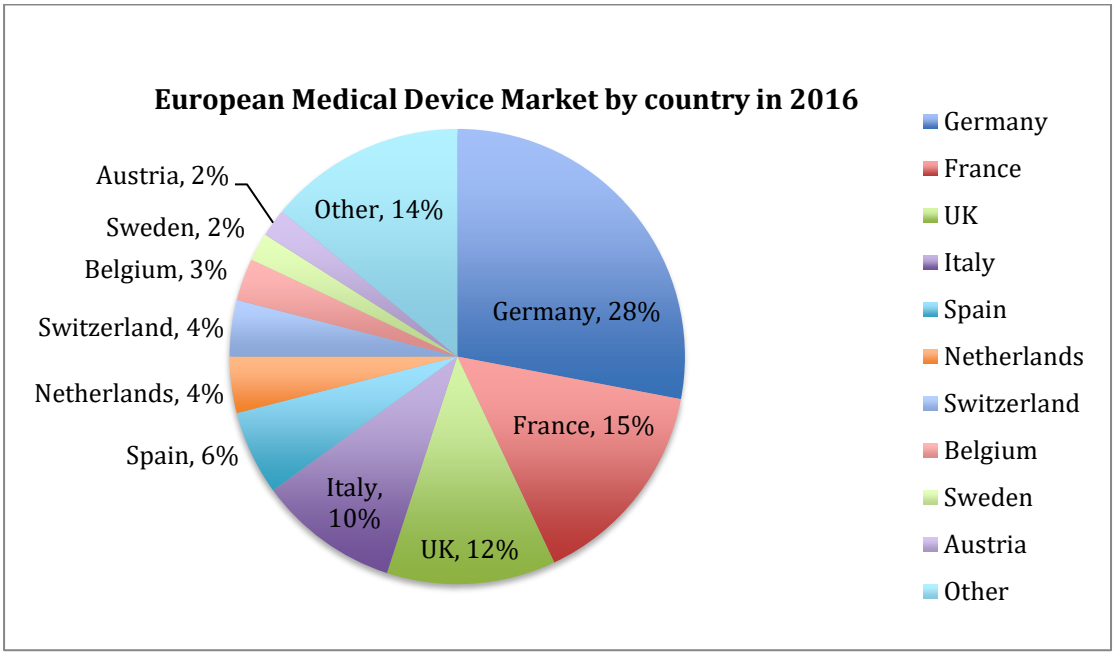


Figure 2.3: European Medical Device Market by country in 2016. Source; (MedTech Europe, 2018)

As Figure 2.3 shows, the biggest medical device markets in Europe are Germany, France, the United Kingdom, Italy and Spain.

Global medical devices industry structure

The global medical devices industry is highly fragmented. It is characterised by the presence of a few large companies with a dominant position and a large number of small and medium enterprises (SMEs), which are responsible for the development of the technological breakthroughs of todays' healthcare market (Amann and Cantwell, 2012, Chowdhury, 2014). The SMEs, however have limited resources to demonstrate the evidence on safety and efficacy of medical device to meet the regulatory requirements, and in the face of a failure on the marketplace it is difficult for them to survive (Kaplan et al., 2004). The research and development (R&D spending in the global medical device industry, as a percentage of sales, was about 12%, in 2017 (US Department of Commerce, 2018). However, most SMEs research focuses on factors that contribute to their survival such as financing, rather than a greater understanding of the medical device innovation development process (O'Regan et al., 2006).

The global medical device industry is divided into several device segments. Table 2.1 presents ten biggest medical device market segments and related market value in 2017.

Table 2.1: Global TOP 10 device areas in medical devices industry. Source: (Evaluate MedTech, 2018).

Rank	Device segment	Global sales value in 2017 (in billion US dollars)
1	In Vitro Diagnostics (IVD)	52.6
2	Cardiology	46.9
3	Diagnostic Imaging	39.5
4	Orthopedics	36.5
5	Ophthalmic	27.7
6	General & Plastic Surgery	22.1
7	Endoscopy	18.5
8	Drug Delivery	18.5
9	Dental	13.9
10	Wound Management	13.0

Table 2.1 shows that the In Vitro Diagnostics (IVD) segment is the biggest device area and an overall picture gives some hints about the volumes of investments in the global industry. Almost all high-tech medical devices have been designed and manufactured in advanced countries for use in industrialised countries, and subsequently the rest of the world. The global top 10 medical device companies are presented in Table 2.2.

Table 2.2: Global TOP 10 medical device companies in 2017. Source: (Evaluate MedTech, 2018).

Rank	Company	Country	Company sales value in 2017 (in billion US dollars)
1	Medtronic	USA	30.0
2	Johnson & Johnson	USA	26.6
3	Abbott Laboratories	USA	16.0
4	Siemens Healthineers	Germany	15.5
5	Philips Healthcare	The Netherlands	13.6

6	Stryker	USA	12.4
7	Roche	Switzerland	12.3
8	Becton Dickinson	USA	11.0
9	GE Healthcare	USA	10.2
10	Boston Scientific	USA	9.0

Table 2.2 shows that out of the top ten medical device companies, seven firms have headquarters in the USA. Medtronic achieved medical device sales of $30 billion, leading the top ten and giving the company a 7.4% market share (Evaluate MedTech, 2018).

The medical device industry in developing countries

The medical device industries based in developing countries are few and focused on the low-tech part of the sector. The diversity and scale of health challenges in developing countries make the role of medical devices even more significant but according to WHO (2012) only 13% of manufacturers are located in developing countries.

In developing countries, over 95% of the medical devices in public hospitals are imported, with very limited local production (Malkin, 2007). Moreover, most of the medical devices are inappropriate for local needs and unable to be sustained with the lack of local infrastructure (Lustick and Zaman, 2011). For example, WHO (2016) conducted a detailed analysis of medical devices policies from four selected countries in Africa (Ethiopia, Nigeria, South Africa and Tanzania) to identify opportunities for the development of local medical devices. The study found that there was a limited local manufacturing capacity and design mechanism to incentivize manufacturers to engage in the production of priority medical devices. The same study revealed that there was lack of funds for research and development (R&D) and support to bring products into the market and to final users that could be of high public health value.

2.1.1 Medical Device Development Process

Medical devices are regulated in different ways throughout their life cycle, because any phase during their life span can affect the safety and performance of the medical device. According to Blair & Goldenberg (2014), medical device development process generally includes steps such as recognizing an unmet medical need, doing

fundraising or budget, concept and feasibility studies, design and its validation, clinical studies, regulatory approval, manufacturing, reimbursement, product distribution, and post-market activities. Figure 2.4 below illustrates the major phases in the life span of a medical device from conception and development to disposal.

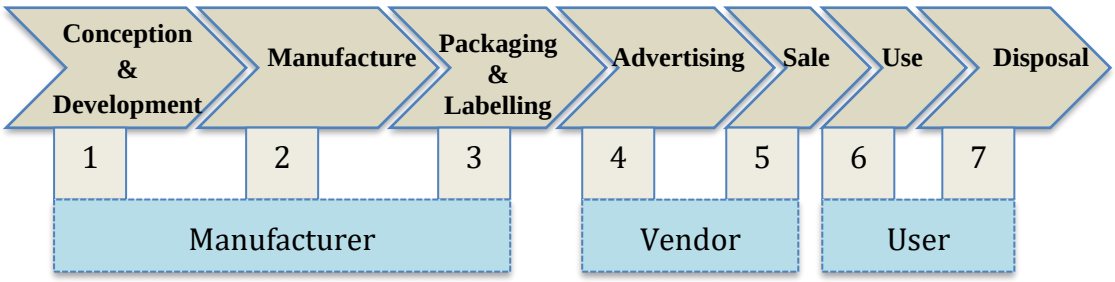


Figure 2.4: Seven major phases in the life span of a medical device. Source: (WHO, 2003, p.5)

The activity phases are simplified to make it easier to understand the regulatory system. For example, the development phase includes development planning, design verification/validation, prototype testing and clinical trials. In practice, the phases outlined below may overlap and interact (WHO, 2003, p.5). Following initial concept tests, the device is then registered for regulatory approval in the desired market(s). This step alone can take up to six years, depending on the risk category of the device and clinical trials required, and the total time for a new device to come to market can be as long as eight years (Fargen et al., 2013). It is vital in the new product introduction process in the medical device industry to get good clinical data because many times it is the main differentiator between competitors (Blair & Golden-berg, 2014).

The manufacturer, vendor, user, public and government are the stakeholders. All five play critical roles in ensuring the safety and efficacy of medical devices. The most important factor that ensures the cooperation of all these stakeholders is an informed and common understanding of the issues. Shared understanding and responsibility are achieved through communication and mutual education, which can be effectively achieved by having all stakeholders participate in establishing the process that ensures safety and performance of medical devices (WHO, 2003, p.5). The next section introduces the UK medical device industry.

2.2 The United Kingdom Medical Device Sector

Size of market

The UK medical device market is the third largest in Europe, behind Germany and France, and the sixth largest in the world (MedTech Europe, 2018). Domestic device manufacturing is characterized by a large number of small-scale medical device companies alongside a few global manufacturers with a significant presence in the market. Many large US companies operate subsidiaries in the UK. The market was estimated to have generated $26,444 billion turnover in 2015 and is forecast to grow at a USD billion 2015-2019 Compound Annual Growth Rate (CAGR) of 5.1%, making the UK the best performing market in the Western Europe region (BIS UKTI DH, 2015). The breakdown of the UK medical device firms is presented in Table 2.3.

Table 2.3: Breakdown of Medical Device Companies in the UK in 2015. Compiled by author. Source: (BIS UKTI DH, 2015)

Category	Employment	Turnover (in billion US dollars)	Number of Companies
Core companies	89,870	*21,505	2,683
Service & Supply companies	24,605	4.939	1,002
Total	114,475	26,444	3,685

*GBP/USD currency conversion was done using OANDA currency calculator tool at a rate of 1:1.25830

Data in Table 2.3 show that, in 2015 the medical device sector and service and supply chain in the UK was comprised of an estimated 3,685 companies, which employed approximately 114,475 individuals (BIS UKTI DH, 2015). Such high numbers of employees prove that the UK medical device industry is a significant player in Europe and in its economy. The core companies include all firms whose primary business involves developing and producing medical devices (ranging from single-use consumables to complex hospital equipment, including digital health products). The service and supply companies are those that have significant activity in supplying services to the core companies such as specialist consultancy and regulatory expertise to the medical technology sector (BIS UKTI DH, 2015). The rest of the composition and distribution of the medical device companies in terms of the size of their annual turnover is shown in Table 2.4 below.

Table 2.4: Distribution of Medical Device Companies – broken down by company turnover. Compiled by author. Source: (BIS UKTI DH, 2015)

2015 Annual Turnover size band	Number of medical device core companies	% of core companies	Number of Service & Supply companies	% of Service & Supply companies
$0 – $62,000	352	13%	159	16%
$63,000 - $125,000	195	7%	97	10%
$126,000 - $313,000	386	15%	199	20%
$314,000 – $628,000	385	14%	135	13%
$629,000 – $1,2m	318	12%	97	10%
$1,3m - $6,2m	534	20%	180	18%
$6,3m+	513	19%	135	13%
Total	**2683**	**100%**	**1002**	**100%**

*GBP/USD currency conversion was done using OANDA currency calculator tool at a rate of 1:1.25830

Table 2.4 shows that, in 2015, out of the 3685 medical device companies in the UK, 81% of the core companies had an annual turnover of less than $6.3 million while 77% of the service and supply companies had a turnover of less than $6.3 million (BIS UKTI DH, 2015).

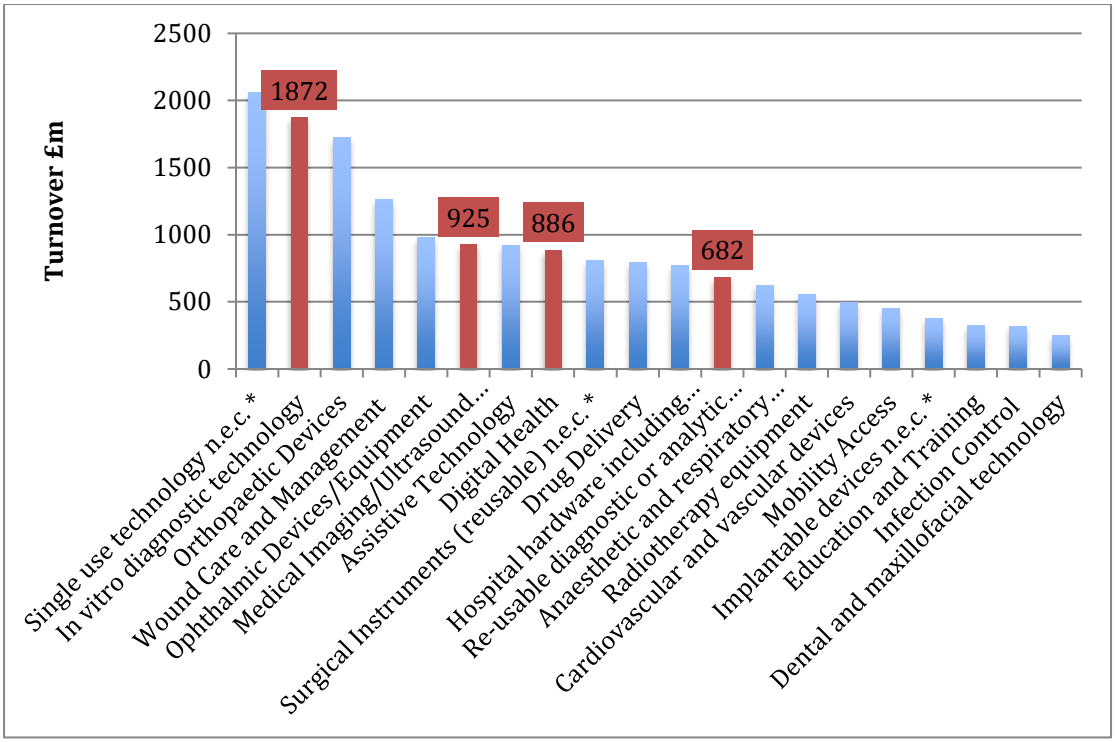
The UK medical device industry structure

The vast majority of medical device companies (98%) are small to medium-sized enterprises (SMEs). The SME status is based on the European definition that refers to businesses with fewer than 250 employees (BIS UKTI DH, 2015). Within the sector, 68% are micro-companies employing less than ten people. The overall picture is that of a sector made up of small but well-established companies as indicated in Table 2.5 below.

Table 2.5: Distribution of Medical Device Companies – broken down by employment numbers. Compiled by author. Source: (BIS UKTI DH, 2015)

2015 Employee size band	Number of medical device core companies	% of core companies	Number of Service & Supply companies	% of Service & Supply companies
0 – 4	1129	42%	532	53%
5 – 9	438	16%	135	14%
10 – 19	335	12%	119	12%
20 – 49	390	15%	114	11%
50 – 99	199	7%	54	5%
100 - 249	122	5%	31	3%
250+	70	3%	17	2%
Total	**2683**	**100%**	**1002**	**100%**

According to the Department for Business, Innovation and Skills report, the largest segment by turnover in 2015 was single use technology (i.e. disposables) followed by in-vitro diagnostics, orthopaedic devices and wound-care (the top four segments accounted for 40% of the sector's turnover (BIS UKTI DH, 2015). Figure 2.5 illustrates the turnover of major segments in the medical device sector excluding service and supply in the UK.



* n.e.c - not elsewhere classified

Figure 2.5: Turnover for the Major Segments in the Medical Device Sector in the UK. Source; (BIS UKTI DH, 2015)

As illustrated in Figure 2.5, the products highlighted in red are some of the medical technology segments that develop and market stand-alone or embedded software devices. One of the three regulatory changes analysed in this study targeted the production of software products and the influence of these changes will be discussed in more detail in Chapter eight.

Figure 2.6 and 2.7 present the composition and distribution of the medical device sector in terms of the number of companies by segment registered in the UK. Figure 2.6 shows the number of medical device core companies whilst Figure 2.7 shows the number of medical device Service & Supply companies

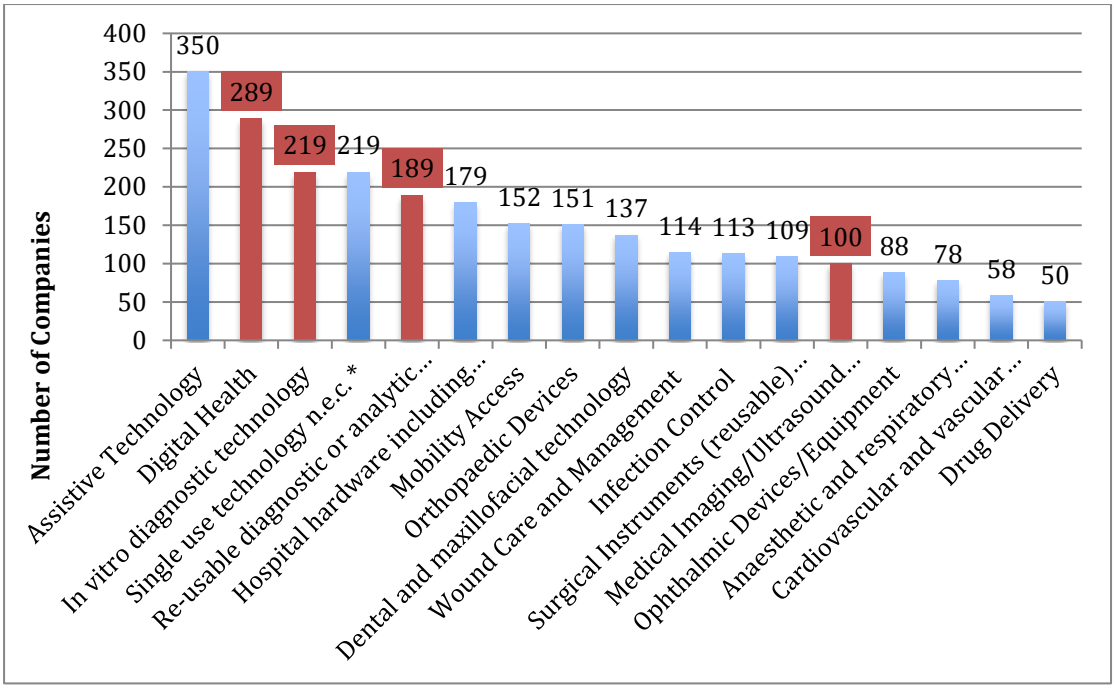


Figure 2.6: Number of Medical Device Core Companies by Segment. Source: (BIS UKTI DH, 2015)

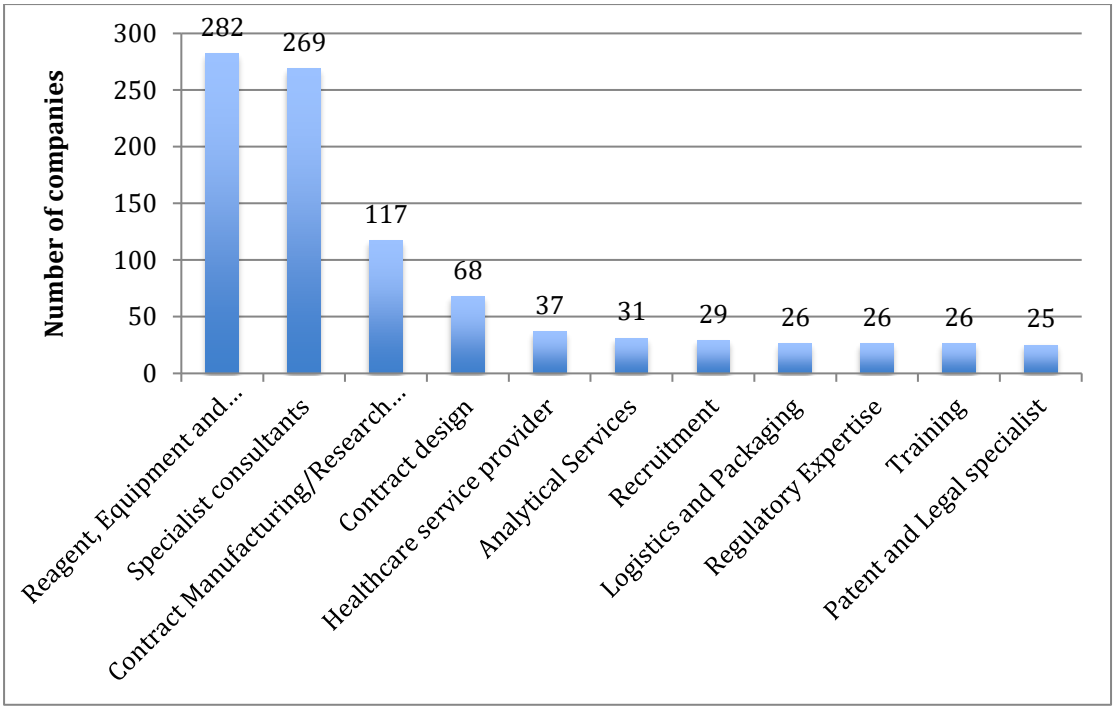


Figure 2.7: Number of Medical Device Service & Supply Companies by Segment (only segments with more than 20 companies shown). Source: (BIS UKTI DH, 2015)

Figure 2.6 shows that the digital health segment in 2015 was the second highest of all segments in the life science industry and had a total of 289 core companies. The

segment covers companies that develop and market software and/or devices that rely on software for their key functionality. As the main focus of digital health devices is on software that has high medical information content, the 2007 regulatory changes required them to be validated. The effects of such requirement will be analysed in Chapter eight.

2.2.1 Evolution of Medical Device Regulations in the UK (EU)

The Treaty Establishing the European Community, signed by six countries in 1957, marks the beginning of the EU (Altenstetter, 2003). Since then more countries have joined and the treaty has been amended several times. Member countries agree to follow the rules and regulations of the EU (Altenstetter, 2003). The evolution of medical device regulations in the UK, therefore, has to be seen in the light of the European Union's development over the past decades (Chapman et al., 2014). The formal regulation of medical devices in the EU actually began in the 1990s, following the adoption of "the New Approach" principles of 1987. Prior to that, a consolidated legislation adopted in 1965 after the thalidomide crisis regarding medicinal products covered only pharmaceuticals, thus, there was great diversity amongst EU countries in how medical devices were regulated (Altenstetter, 2012).

Harmonizing to create a 'single market'

To harmonize the technical requirements across the EU region, the core legal framework that consisted of three directives was established, dated 1990, 1993 and 1998 (see Table 2.6). The EU governments needed to put in place policies that would address all elements related to medical devices, ranging from access to high quality, affordable products, through to their safe and appropriate use, performance and disposal (European Commission, 1993, 2007). In order for the requirements in the directives to be mandatory, the directives were transposed to each member state's legislation resulting in a vast and elaborate legislative framework (Bastawrous and Armstrong, 2013). The intention of these Directives was clearly to create a single market for medical devices based on Article 100a or Article 95 of the respective EU Treaties (Casteels and Rohde, 2013).

Responsibility for the regulatory cycle

The responsibility for the regulatory cycle was assigned to three types of organizations: competent authorities, manufacturers, and third-party certification

organizations (notified bodies) (Altenstetter, 1996). A competent authority ensures that the requirements of the directives are applied. In the UK it is the Medicines and Healthcare Products Regulatory Agency (MHRA) and the legislation is the Medical Devices Regulation 2001/618 (as amended) (Heneghan et al., 2011). In addition to the transposition of the medical device directives into National Law, the MHRA is also responsible for the surveillance of medical devices on sale in the UK and the evaluation of adverse incidents (MHRA, 2008b). Many medical devices and accessories require an objective third party inspection by a Notified Body (NB) as part of the required conformance assessment procedure.

Notified bodies exist solely under New Approach Directives. Their function is to provide independent verification that particular aspects of the design, manufacture or quality system conformity have been carried out by manufacturers (European Commission, 2013b). Notified bodies are for-profit and funded by review fees from manufacturers (Kramer et al., 2012). Because of this, some have argued that there is an inherent risk of collusion between notified bodies and manufacturers (Cohen, 2012).

The New Approach Directives [3] imposed the sole and ultimate regulatory responsibility for a product and the satisfactoriness of its safety on the person who qualifies as its legal "manufacturer", who is the person who places it on the market under his own name (Casteels and Rohde, 2013). The legal manufacturer may, however, in practice subcontract some or all of the activities of design, production, labelling, packaging and distribution, although he retains full regulatory responsibility for designing and manufacturing the product in accordance with the essential requirements that apply to it, and for the carrying out of conformity assessment in accordance with a relevant applicable procedure (Chowdhury, 2014).

Medical devices regulatory framework revisions in 2000-2017

The three medical devices directives of the 1990s were a great success (Yaneva-Deliverska, 2012). The CE mark became a recognized seal of quality and safety for medical devices and a single market had basically been created (Casteels and Rohde, 2013). Together these European directives constituted a medical device legal system

[3] New Approach Directives do not contain a definition of "manufacturer" other than in Directives 90/385/EEC (active implantable medical devices), 93/42/EEC (medical devices) and 1998/79/EC (in-vitro-diagnostic medical devices)

(ibid). The medical sector, however, developed and evolved especially with the introduction of new innovative devices and thus made a revision of the directives over time necessary. Table 2.6 shows the ever-evolving amendments of Directives:

Table 2.6: List of the Three Core European Directives and their Subsequent Amendments. Compiled by author. Source: (European Commission, 1998)

	New/Amended Directive	Old/Original Directive	Description
1990		90/385/EEC (AIMDD)	Concerns active implantable medical devices (AIMDD
1993		93/42/EEC (MDD)	Concerns medical devices (MDD) and their accessories
1998		98/79/EC (IVDMD)	Concerns in vitro diagnostic medical devices (IVDMD)
2000	2000/70/EC	93/42/EEC	Concerns, among others, medical devices manufactured using tissues of animal origin, the classification of certain medical devices and Common Technical Specifications for In vitro diagnostics (IVDs)
2001	2001/104/EC	93/42/EEC	Included medical devices which incorporate, as an integral part, substances derived from human blood
2003	2003/12/EC	90/385/EEC and 93/42/EEC	Reclassifies breast implants into Class III
2003	2003/32/EC	90/385/EEC and 93/42/EEC	Introduces specifications concerning medical devices manufactured utilizing tissues of animal origin
2005	2005/50/EC	93/42/EEC	Reclassifies total hip, knee and shoulder joints into Class III
2007	2007/47/EC	90/385/EEC, 93/42/EEC, and 98/8/EC	On approximation of the laws of the member state, technical revisions and concerning the placing of biocidal products on the market and medical device software.
2011	2011/100/EU	98/79/EC	Added 'Variant Creutzfeldt-Jakob disease' (vCJD) assays for blood screening, diagnosis and confirmation as requested by the UK
2012	Two new regulations, once adopted, will replace the existing three directives.	90/385/EEC, 93/42/EEC, and 98/8/EC	The European Commission adopted a Proposal for a Regulation of the European Parliament and of the Council on: i) Medical devices and ii) In vitro diagnostic (IVD) medical devices.
2013	2013/172/EU (Recommendation)	2001/83/EC	Provisions on traceability of medical devices and in vitro diagnostic medical devices, in order to improve patient health and safety.
2013	2013/473/EU (Recommendation)	90/385/EEC, 93/42/EEC, and 98/8/EC	Recommendation aim at ensuring that the notified body carries out a proper verification of the fulfilment of the legal requirements by the manufacturer.
2017	Regulation (EU) 2017/745	90/385/EEC and 93/42/EEC	A proposal for a regulation on medical devices ("MDR"), to replace the AMDD and MDD directives

	NB. will only apply after a three-year transitional period		
2017	Regulation (EU) 2017/746 NB. will only apply after a five-year transitional period	98/8/EC	A proposal for a regulation on in vitro diagnostic medical devices ("IVDR"), to replace the IVDD directive.

Table 2.6 indicates that there have been significant changes in the regulation of medical devices in the UK. The significant aspect of the table is the introduction of major changes in 2007 and the 2012 adoption of a proposal to replace the existing core directives. In 2007, the European Medical Device Directive (MDD 2007/47/EC) made fourteen amendments to the original directive (93/42/EEC) that came into force on March 21st, 2010. A number of these changes directly affect the development of software for use in healthcare. There are four areas within the amendment of the MDD (2007/47/EC) with important significance to medical device software development, which are:

(1) Standalone Software as an active medical device,
(2) Validation of software as an active medical device,
(3) Software localization and,
(4) Safety Classification.

The most significant change in relation to medical device software development is that standalone software was now seen as an active medical device (McCaffery et al., 2011). For the first time, software is specifically included in the definition of medical devices. Prior to the release of the MDD (2007/47/EC) provision had been made within the MDD (93/42/EEC) for software to be used as a medical device. However, MDD (2007/47/EC) Article 1 Section 2 made explicit reference to software being a medical device (European Commission, 2007). The 2007 regulatory changes in relation to medical device software will be discussed in detail as a case study in chapter 6.

However, other amendments state that manufacturers are required to appoint Authorized Representatives to act on their behalf if they are not located in the EU. The amendments also require that information about the technical factors and characteristics identified as hazards that can cause risks upon reuse of the medical

device should be clearly indicated and accompany single-use devices and that manufacturers must ensure that the Declaration of Conformity and Instructions for Use are controlled documents in the quality management system of the manufacturer (European Commission, 2007).

Accordingly, the 2007 changes addressed the information exchange deficiency throughout the EU, by demanding the all-European information database to begin working by 2012. These revisions introduced were also some means to help establish the common vigilance system in Europe (European Commission, 2007). However, these amendments provoked discussions within the industry as some changes introduced make the approval process more complicated. Several weaknesses that undermine the main objectives of the three medical devices directives were identified in the Commission's 2008 public consultation[4]. In 2009, the MHRA received 9099 reports of adverse events involving medical devices (MHRA, 2009) including 1885 cases of serious injury and 202 deaths (Thompson et al., 2011).

In 2011, the regulatory framework also came under harsh criticism, in particular after high-profile cases where too many unsafe medical devices were recalled. In 2010 a French company producing silicone breast implants (Poly Implant Prothèse (PIP)) was found to be using low-grade silicone not conforming to the type specified in the design and manufacturing files after an increasing number of implant ruptures. The certification of the implants was suspended and a global backlash of patients and national authorities followed (Donawa and Gray, 2012). In 2010, the UK's MHRA released an alert for patients with metal-on-metal (MoM)[5] hip implants as the revision rate was considerably higher than in conventional metal-on-polyethylene implants. Healthcare vigilance authorities in other countries soon followed (Drummond et al., 2015). The wear or the joint surfaces against each other would cause metal debris to chip off over time, which created adverse reactions in the soft tissues and in some

[4] In mid-2008, the Commission held a public consultation on the recast of the general regulatory framework for medical devices. The consultation was published on the Commission's website. During 2009, 2010 and 2011, the issues to be tackled in the context of the revision of the regulatory framework for medical devices were regularly discussed at meetings of the Medical Devices Expert Group (MDEG), the Competent Authorities for Medical Devices (CAMD) and specific working groups in the medical device sector.

[5] Metal-on-metal hip implants manufactured by DePuy were recalled worldwide because data from the National Joint Registry (NJR) of England and Wales showed that more people than anticipated had experienced problems and required a second hip replacement surgery

cases, a systemic contamination of blood with metal ions (ibid). In July 2011 U.S. FDA gave a warning regarding serious complications associated with surgical mesh for transvaginal repair.

In light of these adverse events, in 2012 the European Parliament adopted a Resolution of the Parliament[6], calling on the Commission to take "immediate action" and amend the medical device directives in order to make sure that the legislation would not allow events such as the steps leading to the PIP scandal or controversy surrounding the MoM hip implants to occur in the future. This was followed by a swift reaction approach from the EC, who proposed for new medical device regulation. In 2012, the European Commission (EC) published a proposal to introduce a new regulatory framework replacing existing medical device directives. In fall of 2013, the European Parliament (EP) amended the proposal to be more rigorous and in June 2015 the European Council (ECO) presented its amendments based on the two formers (European Parliament, 2015). After four years of discussions on the expert level, and after an agreement with the ministers of the member states of the EU, in June 2016 the consolidated version of the new Medical Device Regulation was published.

In the EU dialogue about a regulatory agreement, an entirely new approach to previous regulation of NBs and conformity assessment processes (CAP) was included. The focus was to tighten standards to the obligations of NBs when conformity assessing high-risk devices, for instance in the requirement of qualified employees. This tightening resulted in, among others, parts of the proposal being implemented to regulation "(EU) No. 920/2013", as well as the "Commission Recommendation (of 24 September 2014) 2013/473/EU" on the unannounced audits and assessments performed by NBs in the field of medical devices. They comprise regulations pertaining to designation and supervision of NBs by competent authorities and recommendations to audits and assessments of manufacturers (European Commission, 2013a).

[6] Resolution of 14 June 2012 (2012/2621(RSP)); P7_TA-PROV(2012)0262, http://www.europarl.europa.eu/plenary/en/texts-adopted.html.

The publicized proposals met with controversy (Cohen, 2013) and raised the discussions in this study regarding their effect on involved stakeholders. Negotiations to the content of the regulation have been particularly complicated (Sorenson and Drummond, 2014). Several changes to NBs legislation directly affected manufacturers of medical devices. Some significant changes in the proposals were introduced in the structure and supervision of NBs where previous experiences have determined deficiencies. These deficiencies include a lack of transparency in NBs' daily work, concerns about NBs' competence and their independence against manufacturers that may affect decisions to CE marking (Galland, 2013). These challenges have amongst others, resulted in that all NBs will need to apply for re-designation and be audited for compliance by joint competent authorities from several Member States (ibid). The requirements of technical, clinical and scientific competence have so far resulted in suspension or closedown of several NBs.

On April 5, 2017, two new regulations were adopted replacing previous directives. Regulation (EU) 2017/745 on medical devices replacing Council Directives 90/385/EEC on medical devices and 93/42/EEC on active implantable medical devices and Regulation (EU) 2017/746 on in vitro diagnostic medical devices replacing Council Directive 98/79/EC on in vitro diagnostic medical devices. By shifting from directives to regulations, a wider scope of protection and more effective implementation of the rules can be ensured. The new regulations will only apply after a transitional period. Namely, 3 years after entry into force for the Regulation on medical devices (spring 2020) and 5 years after entry into force (spring 2022) for the Regulation on In Vitro Diagnostic medical devices (European Commission, 2017).

As the transitional period for the 2017 new regulations has yet to come, this thesis does not take them into account. However, it is worth mentioning that, while waiting for the transition period to come to pass, a recent article on faulty medical implants revealed that, in the UK alone, regulators received 62,000 "adverse incident" reports linked to medical devices between 2015 and 2018. A third of the incidents had serious repercussions for the patient, and 1,004 resulted in death (The Guardian, 2018). Adverse events such as these are the ones that call for the need for a better and enabling regulatory framework in the medical device industry.

Medical device regulation has been evolving as a distinct legal framework separate from the drug structures in the EU since the early 1990s (Altenstetter, 2012). The regulatory changes have been effective in improving patient safety and enhancing the provision of satisfactory health care. The changes allowed the notified bodies to be responsible for their activities (Amoore, 2014), enhanced the conduct of fair and free trade of the medical devices in these markets and ensured that industries meet the clinical requirements and manufacture high-quality medical technologies (Cooter et al., 2015).

2.2.2 The Current State of Medical Device Regulatory Framework in the UK

The current regulatory framework in the UK is characterized by critical market authority needs; whereby specific requirements are followed by the medical device manufacturers, sellers, buyers, and the medical professionals using the devices in hospitals (MHRA, 2016). As stated in the previous section, three overarching legal directives guide the development of medical devices including classification, CE marking, quality system requirements, and data requirements in the UK (Chapman et al., 2014):

- Medical Device Directive (MDD 93/42/EEC),
- Active Implantable Medical Device Directive (AIMDD 90/385/EE), and
- In Vitro Diagnostic Medical Device Directive (IVDMDD 98/79/EC).

Table 2.7 summarizes the three European Council Directives.

Table 2.7: List of the Core European Directives Regulating Medical Devices. Source: (European Commission, 1990, 1993, 1998)

Year	EU Council directive	Description
1990	90/385/EEC	The Active Implantable Medical Devices (AIMDD). Covers all medical devices that are implanted into the human body and need to use a source of energy that is neither gravity nor energy from the body.
1993	93/42/EEC	The Medical Devices (MDD). Covers the majority of medical devices.
1998	98/79/EC	The In Vitro Diagnostic Medical Devices (IVDMD). Covers all those products used in vitro for examination of specimens from the human body and those used as diagnostics to provide information.

The aim of these core directives is to ensure a high level of protection for human health and safety and a good functioning of the Single Market (European

Commission, 2015). In addition, there are also multiple EU guidance documents and articles governing the processes that contribute to regulatory adherence (European Commission, 2015; European Commission, 2012). The regulatory framework and hierarchy for medical devices is illustrated in Figure 2.8

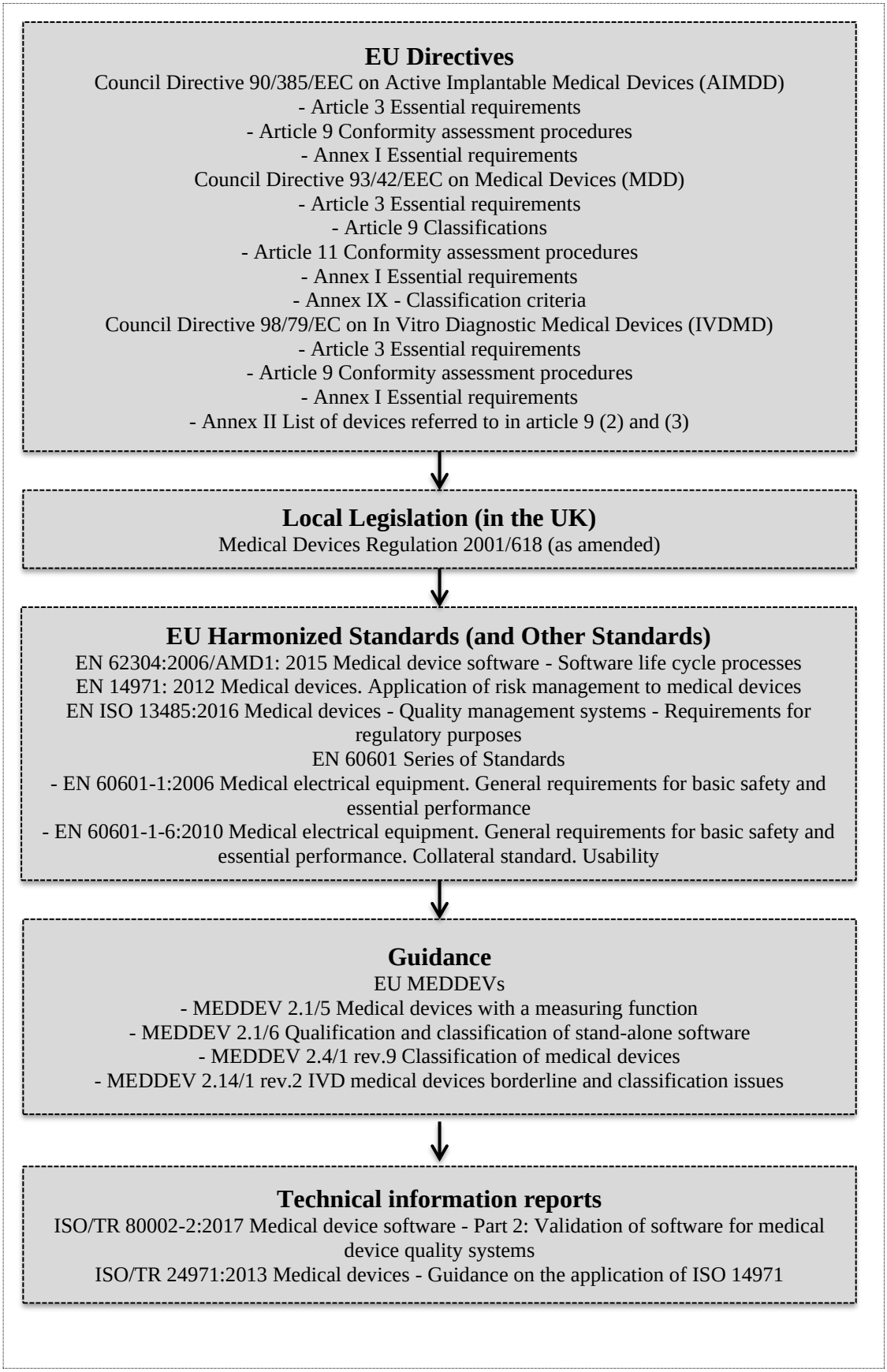


Figure 2.8: Regulatory Framework and Hierarchy for Medical Devices in the EU with the most relevant parts identified.

Figure 2.8 points out that the directives encourage the use of harmonized standards. According to Deloitte (2016), the implementation of ISO 13485, ISO 14791 and ISO 62304 can lead to CE-mark approval.

- ISO 13485 provides the comprehensive quality management system framework for the design and manufacture of medical devices.
- ISO 14791 provides fundamental guidance on a product's intended use, determination of potential hazards, risk mitigation, and post-marketing surveillance methods.
- ISO 62304 lays out a software lifecycle process for medical devices and refers to ISO 14971 in matters of risk management (IEC, 2017).

Another facet that merits close attention is the guidance documents. The Medical Device Guidance Documents (MEDDEV) published by the European Commission are the most used guidelines by the manufacturers of medical devices and they promote a common approach to the implementation of the procedures. The current MEDDEV is part of a set guidelines relating to questions of application of EU Directives on medical devices. They are not legally binding, but they have been written in co-operation with EU officials, notified bodies, industry representatives and many other expert organizations. Many standards need to be taken into account when developing a medical device especially when software is included and each of them has a certain viewpoint. Annex C of EN 62304/AMD1: 2015 shows the relationships between key medical device standards as illustrated in Figure 2.9.

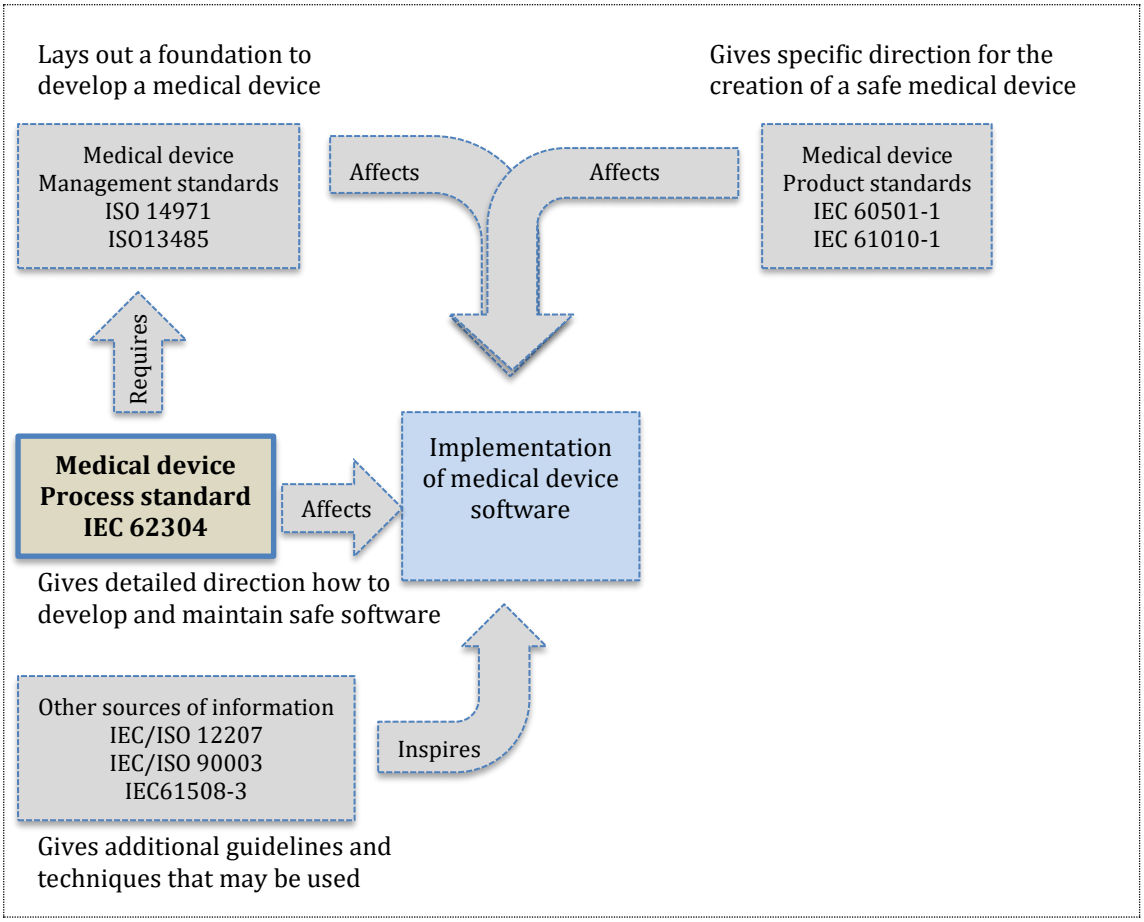


Figure 2.9: Relationships of key medical device standards. Source (IEC, 2017)

Figure 2.9 shows that medical device management standards such as ISO 13485 and ISO 14971 provide a management environment that lays a foundation for firms to develop products. The ISO 14971 international standard provides a process to address risk management related to medical devices, which is included in the harmonized legal requirements in most countries (International Medical Device Regulators Forum, 2015). Standards such as IEC 60601-1 and IEC 61010-1 give specific direction for creating safe medical devices. When software is a part of these medical devices, IEC 62304 provides more detailed direction on what is required to develop and maintain safe medical device software (IEC, 2017).

Medical Device classification process

According to the Medicines and Healthcare products Regulatory Agency (MHRA), manufacturers must demonstrate compliance of their medical devices to the essential requirements described in the applicable directive (MHRA, 2016). The level of controls needed for conformity depends on the risk that the use of the device may pose. But first, it must be determined which of the three medical device directives

apply.

Following the device type and thus the directive under which the device falls has been determined, the device classification needs to be determined. The class of the device determines the rigor of the conformity assessment procedures. The devices are classified according to criteria such as the degree of invasiveness, mode of action, impact on the body. Table 2.8 summarizes the medical device classes.

Table 2.8: Medical Device Classification by Directive. Source: (Bastawrous and Armstrong, 2013).

EU Council directive	Device classification
90/385/EEC Active Implantable Medical Device directive (AIMDD)	No classes
93/42/EEC Medical Devices Directive (MDD).	Class III Class IIa Class IIb Class I (Class Is with sterile components, Class Im with measuring function)
98/79/EC In Vitro Diagnostic Medical Devices (IVDMD)	Annex II list A devices Annex II list B devices Self-testing devices Other devices

Table 2.8 show that the Medical Device Directive defines four classes, and each group has different criteria that must be met in order to receive a CE mark of conformity. Low-risk device (class I) manufacturers may register with the MHRA and make a declaration that the product meets the statutory requirements to receive the CE mark. Class I has the loosest requirements. Medium-risk (classes IIa and IIb) and high-risk (class III) devices must meet a more stringent criterion (see (European Commission, 2010) for full classification rules).

Obtaining a CE mark for medium-risk devices involves a declaration by the manufacturer that the product conforms to the provisions of the medical device regulations and the relevant essential requirements. Once products bear this mark, they can be marketed in all member states of the European Economic Area (EEA) and other countries that recognise the above-mentioned directives for medical devices. High-risk devices generally require clinical trials to demonstrate their safety. In order to conduct a trial in the UK, the MHRA has to agree to such trials (MHRA, 2016).

Post market surveillance

Once a device is on the market, "manufacturers are required to implement a vigilance program according to National requirements, which includes reporting serious incidents to the relevant Competent Authority" (Sorenson and Drummond, 2014, p. 121). In the UK, this information is collated into a central database, the European Databank on Medical Devices (Eudamed). In addition to vigilance information, Eudamed contains data on manufacturers, certificates issued, modified, suspended, withdrawn or refused, and clinical investigations (Kramer et al., 2012). The use of Eudamed has been mandatory since 2011. The SA medical device industry profile is discussed in the next section.

2.3 South Africa Medical Device Sector

Size of the market

SA's medical devices market was estimated at USD1.2 billion in 2014 and is forecast to grow at a USD billion 2014-2019 Compound Annual Growth Rate (CAGR) of 2.2%, which will see the market reach USD1.3 billion in 2019 (BMI, 2016a). South Africa's trade of medical devices experienced strong growth from 2004 to 2013. Over the ten-year period both exports and imports were at their highest level in 2013. South Africa's exports increased by 41% in 2013, while imports increased by 13% (BMI, 2016a). This is a clear indication of the high global demand for South Africa's medical devices. The South African medical device market is well established in terms of the number of companies registered to sell medical devices, revenue generation and technology uptake, especially in the private sector (Friderichs, 2012). However, the wide diversity of product availability does not match local manufacturing and R&D capacity (Knijn and Patel, 2012). A study conducted by KPMG, (2014) indicated that the average revenue for MNCs was USD 20 million per annum, per company and USD5 million per annum for local medical device companies. The KPMG study also highlighted a company revenue split between multinationals and local companies as demonstrated in the Figure 2.10:

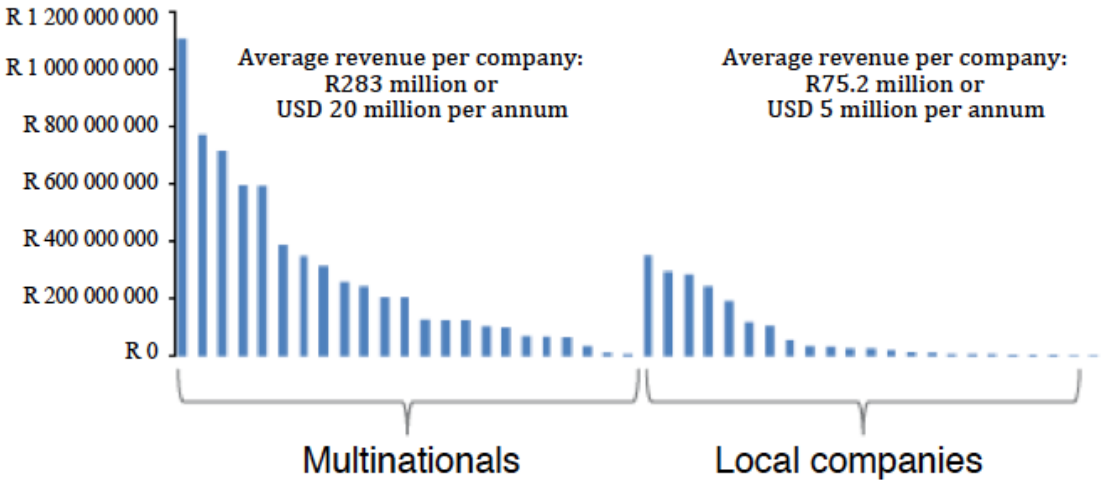


Figure 2.10: Revenue per Company split between Multinationals and Local Companies. Source: (KPMG, 2014)

The difference of revenues between MNCs and SA local companies is commonly attributed to the high entry barriers for the high-end medical imaging market: producing more technologically advanced devices is capital-intensive, require lots of technical knowledge and generally has a long time to market (KPMG, 2014). The medical device market derives most of its revenues from clients in the private sector (70%) when compared with clients in the public sector (30%) and the industry employs over 3 600 people (KPMG, 2014). SA imports 90% of medical devices used in the local market. An analysis of international trade flows of medical devices shows that the gap between imports and exports widened between 2004 and 2013 (SAMED, 2016). An estimated sales value of selected SA medical devices in 2015 is presented in Figure 2.11 below.

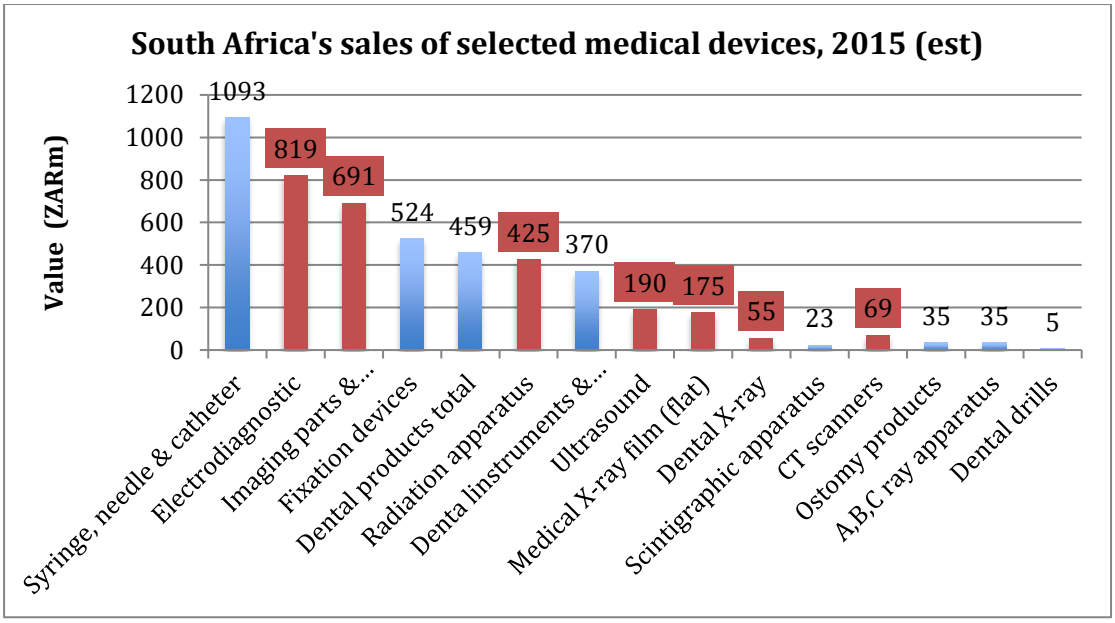


Figure 2.11: SA's 2015 estimated sales value of selected medical devices. Source: (BMI, 2016a)

As Figure 2.11 shows, the products highlighted in red comprises electromagnetic medical devices or radiation emitting devices, the only categories of devices that are currently regulated and have high technical barriers in SA. The effects of the regulatory changes of these devices will be analysed in-depth in Chapter eight. In 2015, Syringe, Needle and Catheter, Electro-Diagnostic and Imaging Parts and Accessories were the top three segments that together hold more than half of the total South Africa medical device market share (BMI, 2016a).

Leading SA medical device industry players

Currently a significant proportion of firms that occupy the SA medical device industry are MNCs such as Johnson and Johnson, Medtronic, GE healthcare, Siemens Healthcare and Philips Healthcare. Typically, these MNCs depend on their parent company to develop new products using R&D resources close to headquarters. Few MNCs have in-country control of their product development activities and spending on research and development (R&D) is inadequate (SAMED, 2016).

Other key players within the medical device industry in SA include the National Department of Health (NDoH), Medicines Control Council (MCC), the Department of Trade and Industry (DTI), the Technology Innovation Agency (TIA), SABS, PATH, Medical device companies, Industry Associations, Global Health Innovation Accelerator (GHIA), Medical Research Council (MRC).

SA's innovation ecosystem

The medical industry in SA has not been very strong for a variety of reasons. It lacks a continuing pipeline of local production, scientific and technical status, and has had difficulty in attracting qualified employees. South Africa benefits from a legacy of health technology innovation, such as that by Nobel Prize winner (1979) Allan MacLeod Cormack for the theoretical work enabling the development of X-ray computerised tomography (CT) and by Dr. Christiaan Barnard's first human to human heart transplant in 1967. Regrettably, the benefits of all these historical advances have not been equally spread. The country has instead, developed a distribution infrastructure based primarily on imported medical devices. The local device and diagnostics sector has not yet reached critical mass as a supplier to either South Africa's public health system or as a contributor to the international market. This is in contrast with the local pharmaceutical industry, which with multinational engagement, local manufacturing and distribution, accounts for more than 70 percent of Sub-Saharan Africa's annual pharmaceutical production (SAMED, 2016).

2.3.1 Evolution of Medical Device Regulations in SA

In the 1990s, South Africa undertook radical changes in the political and economic framing conditions of its innovation systems (OECD, 2007). The evolutionary national innovation system review of SA by OECD pointed out that the dynamics of the country's system involved not only steady expansion and incremental evolution of structures and institutions but also a radical transformation under a unique set of constraints and opportunities (OECD, 2007).

At present, only electromagnetic medical devices or radiation emitting devices are regulated through the Hazardous Substances Act, No. 15 of 1973 (RSA DoH, 1973). Early studies on X-rays such as one done by Mole (1990) recognised that chronic exposure to lower levels of radiation may result in cancer. However, the use of X-rays plays an indispensable role in the clinical management of patients. Concerns about the possible effects of exposure to radiation on the human body were raised to a high level during the 1980s and 1990s, therefore driving the need to propose basic safety standards to control and limit exposure to such radiation (Herbst and Fick, 2012). The Department of Health (DoH) in South Africa then, through its Directorate: Radiation Control (DRC), adopted the radiation safety standards. In addition, the Ministry of

Health is mandated to administer the Hazardous Substances Act of 1973 by granting, suspending or revoking licenses to importers, manufacturers and users of electro medical products (X-rays). The license is issued if the product and usage comply with legislative and international requirements for safety and performance (Herbst and Fick, 2012).

In 2014, South Africa published for public comment draft regulations designed to regulate all health products, devices and pharmaceuticals (SA Government Communications, 2014). The draft regulations include a provision for a four-tiered, risk-based classification system of medical devices and in vitro diagnostic medical devices (IVDs); the Medicines Control Council (MCC)[7] would determine the classification of devices. The regulations would require the registration of all devices with the MCC before they can be sold or used in South Africa.

While the draft regulations did not appear to impose a specific time frame for the completion of a regular registration process, they would permit expedited registration of devices if for example; the medical devices in question are in short supply or are unavailable. In these instances, the MCC is required to inform the applicant of its decision within nine months of the receipt of the application (Deloitte, 2014).

The proposed new regulatory framework was leaning towards European Community guidelines. Products would need to carry the CE mark in addition to FDA approval. The exception is electro-medical devices (radiation emitting devices), which are regulated by the South African Health Ministry: Directorate Radiation Control. FDA approved only devices will no longer be acceptable.

In order to rectify some of the inefficiencies of the MCC, a Medicines and Related Substances Bill was considered by parliament to transform MCC into a new entity called the South African Health Products Regulatory Agency (SAHPRA) and extend the mandate to include medical devices, including in-vitro diagnostics. Some of the proposed medical device legislations for SAHPRA include regulation for licensing, device classification and labelling regulations (SAMED, 2016).

[7] The Medicines Control Council (MCC) is a "statutory body that regulates the performance of clinical trials and registration of medicines and medical devices for use in specific diseases."

2017/18 was a landmark year in which medical technology devices and their products became subject to statutory regulation for the first time in South Africa's democratic era. The Medicines and Related Substances Act of 2015, promulgated in June 2017, along with regulations on medical devices that preceded it, paved the way for medical technology and IVD manufacturing and distributing companies to be licensed by August 2017, while wholesalers were given until February 2018 to lodge applications for licensing. Compliance with these developments and implementation of licensing requirements created a fair degree of uncertainty among our members. The regulations still require some adjustment to align with the amended Medicines and Related Substances Act of 2015, which was promulgated in June 2017. The evolving amendment of South Africa's public Act is presented in Table 2.9 below.

Table 2.9: List of the SA's Core Public Health Acts and their Subsequent Amendments. Source: (SAMED, 2016)

	New/Amended Act	Old/Original Act	Description
1919		Public Health Act of 1919	South Africa's first national public health measure.
1971	Public Health Amendment Act of 1971	Public Health Act of 1919	The legislative control of electronic products the first time introduced. Added section 133A to the Public Health Act of 1919, allowing the Minister of Health to make regulations mandating the Secretary of Health to grant, suspend and revoke licenses in respect of electronic products and prescribe conditions and requirements for the categories of electronic products, premises and persons in control of the equipment.
1973	The Hazardous Substances Act, 1973	Public Health Amendment Act of 1971	Comprehensive regulations concerning the use of X-ray equipment in terms of the 1971 Amendment Act. These regulations pertaining to hazardous substances are still in force
1992	Hazardous Substances Amendment Act, No. 53 of 1992	Repeal of section 133A of Act 36 of 1919, and Act 42 of 1971	Control and division of substances or products into groups in relation to the degree of danger. Substances included those which may cause injury or ill-health to or death of human beings by reason of their toxic, corrosive, irritant, strongly sensitizing or flammable nature.
2008	Medicines and Related Substances Amendment Act of 2008		• The main aim of the act was to register medicines, products, medical devices, certain foodstuffs and cosmetics • Although the Act has yet to come into operation, the new regulator (the South African Health Products Regulatory Authority (SAHPRA)) was expected to have started functioning in April 2012 and is destined to replace the Medicines Control Council (MCC)
2014	Proposed draft for public comment Medicines and	Medicines and Related Substances Act, 1965	Concerns the applications to import, export, manufacture and supply medical devices and IVDs. The key elements of the regulatory control of medical devices and IVDs include:

	Related Substances Act, 1965 (Act 101 of 1965 as amended)	(Act 101 of 1965)	• Requirements for a person or entity to hold a license to manufacture, import, export, wholesale and or distribute a medical device and or IVD in South Africa. • Product requirements for quality, safety, and performance. • Options as to how compliance with the Essential Principles can be demonstrated. • Ongoing monitoring of medical devices & IVDs that are available on the market. • Regulatory controls for the manufacturing processes of medical devices& IVDs. • A range of corrective actions that may be taken if there is a problem with a medical device or IVD.
2017	The Medicines and Related Substances Act 72 of 2008 and Act 14 of 2015, promulgated in June 2017	Amended Medicines and Related Substances Act of 2015	• Landmark year in which medical technology devices and their products became subject to statutory regulation for the first time in South Africa's democratic era. • Provides for the establishment of a new regulatory authority (SAHPRA) • Provides for the transition of MCC to SAHPRA • Provides for expansion on the regulatory oversight of Medical Devices • Provides for the licensing of Scheduled substance Manufacturers and Wholesalers • Promulgation: June 2017 •

As Table 2.9 shows, there has been a steady evolution and implementation of the country's regulatory system. From 1973 to 2017, SA was relying only on the regulations concerning the use of X-ray equipment in terms of the 1973 Act. The South African medical device sector is now in a transition phase. The first phased implementation of the new regulatory changes was clinical trials. As of 1 June 2017, all protocols for clinical trials with medical devices must be approved by SAHPRA prior to initiation of the trial (SAMED, 2018).

Importantly, the end of the transition period will not mark a point when the regulatory environment for medical devices is complete, for managing such a large and vast field as medical devices will always be work in progress, but it will nevertheless introduce a considerably higher level of quality to the management of medical devices in SA than ever before. The next section briefly compares the UK and SA regulatory frameworks.

2.3.2 The Current State of Medical Device Regulatory Framework in SA

South Africa does not have a comprehensive regulatory framework governing medical devices. As mentioned before, at present, only listed electronic products (also

known as electromagnetic medical devices or radiation emitting devices) are regulated through the Hazardous Substances Act, No. 15 of 1973[8] and must be registered (CE certification) before they can be sold, leased, used, operated, or applied in South Africa (DoH South Africa, 2014).

The interpretation of the Hazardous Substances Act and Regulations by the Directorate Radiation Control DRC are described in the Code of Practice, Requirements for quality control tests and guideline documents from the DRC. The Code of Practice document (DRC 2011) provides references and refers readers to guideline documents and also provides a link to the DRC website[9]. The regulatory framework and hierarchy for radiation-emitting medical devices in SA is illustrated in Figure 2.12.

[8] Hazardous Substances Act, No.15 of 1973, available on the University of Pretoria website, *at* http://www.lawsofsouthafrica.up.ac.za/index.php/browse/medical-and-health/hazardous-substances-act-15-of- 1973/act/15-of-1973-hazardous-substances-act-24-feb-2000-to-date-pdf/download.
[9] The SA DRC website: https://sites.google.com/site/radiationcontroldoh/.

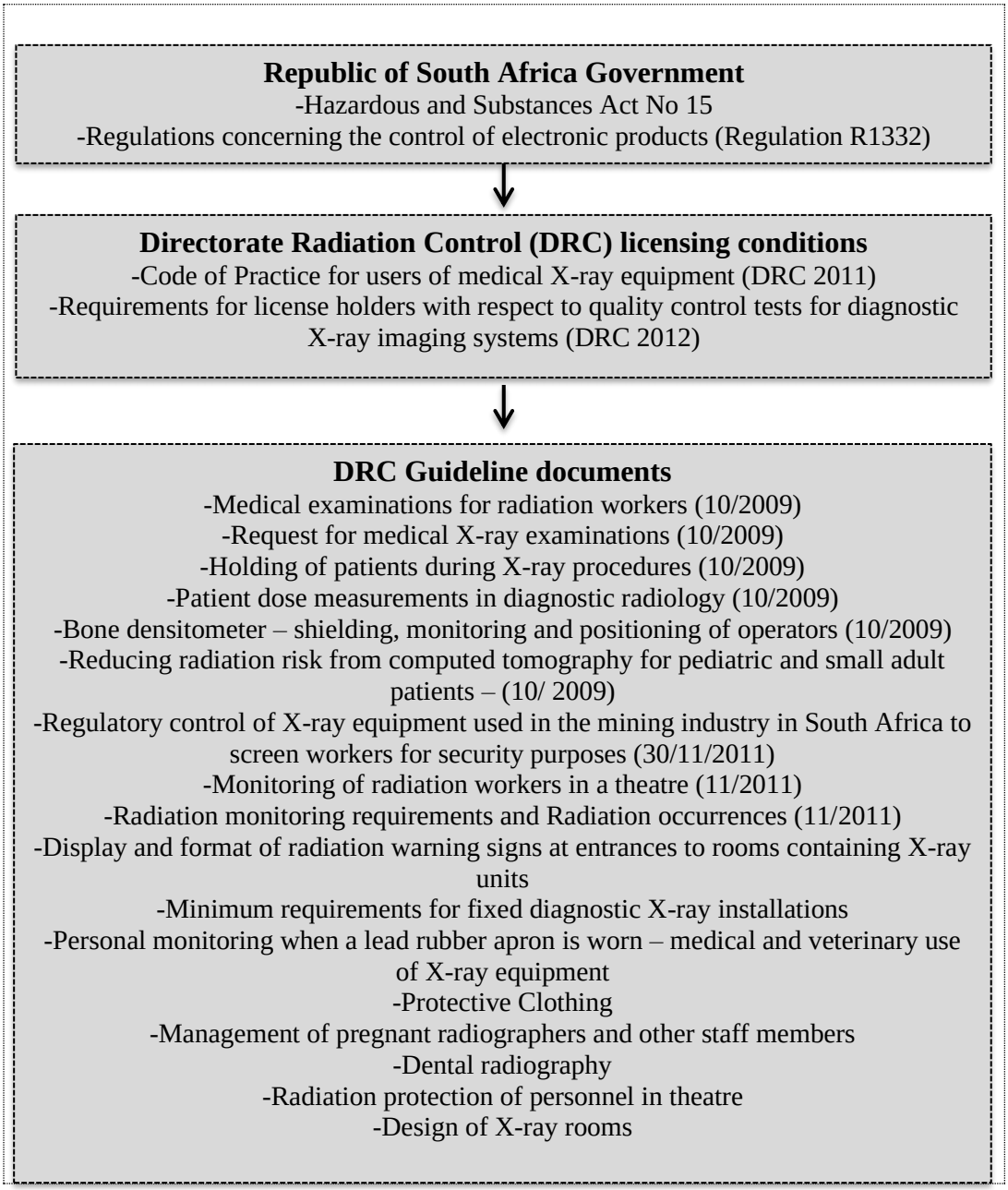


Figure 2.12: Regulatory Framework and Hierarchy for Radiation-Emitting Medical Devices in SA with the most relevant parts identified.

The contents of regulations (Regulation 1332) pertinently indicate that a holder of a license shall be accountable for the all-inclusive scope of radiation protection. The requirements contained in the mentioned document include:

1. “Effective protection organization and continual conscientious regard for optimum methods of working with particular reference to routine operations;

2. Technical investigations to ensure reliability and overall technical excellence of equipment, buildings and interlocks;

3. The display of appropriate warning signs or notices which are easily intelligible to all persons, at the entrances to or at appropriate places in all areas where persons may enter and may be exposed to ionizing radiation; and

4. Ensuring that radiation workers and members of the public are subjected to minimal risks from radiation exposure and that the maximum permissible doses and dose limits are not exceeded" (RSA DoH, 1973).

The licensing of medical equipment is subject to the prescribed conditions, the Director-General may in each case, issue to any person a license to sell, let, use, operate, install or apply any Group III hazardous substance. The refusal or granting of a license will be notified in writing. Non-compliance with prescribed conditions will result in the suspension or cancellation of licenses (Doh South Africa, 2012). Inspectors are appointed and certified to indicate for which groups of hazardous substances they have been thus appointed. The powers of inspectors are prescribed with clear reference to inspection, entrance to premises, demanding information and placement of a restriction.

The applicant for the license must be knowledgeable and experienced regarding the basic principles of radiation protection in general, as well as radiation protection as applicable to the installation. Although the licensee may appoint a medical physicist as the "responsible person", not all practices have the luxury of having the benefit of this essential service. An inspector must be allowed to confirm evidence of compliance, therefore manufacturers and suppliers as license holders must be equipped with the knowledge and skills to be able to meet the stipulated requirements (BMI, 2016a).

The researcher includes the Code of Practice for users of medical x-ray equipment (DRC 2011) document as part of this thesis for information purposes in order for the reader to be acquainted with the current interpretation of DRC regarding the Hazardous and Substances Act as well as Regulation 1332. The content of the Code of Practice, Act and regulations will be further presented in detail in chapter seven in order to ascertain their impact on medical devices manufactures involved in radiation safety in SA.

Another guidance document significant and very relevant to this study is requirements

for license holders with respect to quality control tests for diagnostic X-ray imaging systems (DRC 2012). The DRC published a second document that is provided as part of the diagnostic license conditions with respect to quality control (QC) tests in order to outline the requirements for the acceptance- and quality control tests of diagnostic X-ray equipment. As from 31 March 2009 an Inspection Body (IB), approved by the Department of Health (DoH) or an appropriately trained professional registered with the HPCSA as a medical physicist, must be used to perform all the acceptance tests as well as the routine tests. The significant aspects of these requirements for Quality Control Tests Document include the requirement of the license holder to acquire the relevant quality control manuals or compile in-house written protocols, which describe each test step by step to ensure that QC tests listed in the Requirements for Quality Control Tests Document are correctly performed. The quality control tests are influenced by the age, stability, make, model, etc., of the equipment, but must be performed at the prescribed frequencies as specified in the Requirements for Quality Control Tests document. The image display monitors and reporting monitors must comply with the requirements in of the said document (Doh South Africa, 2012).

South Africa currently has no mandatory quality standard for medical devices other than those of a radiation emitting nature. Currently, all such regulation is left to the discretion of individual procurers. In order to rectify this, the introduction of an internationally graded and compulsory Quality Management Standards (QMS) needs to be introduced as like the standard for most of the developed countries. This, in turn, will prevent substandard products from entering the healthcare market and equalize opportunities for local manufacturers whilst ensuring patient safety (Deloitte, 2014).

There is little enforcement, verification or validation of compliance of all other medical devices with the exception of those of a radiation emitting nature. This has a negative effect of allowing products of a sub-standard quality to enter the market impacting patient safety and undercutting the local manufacturing industry and thus inhibiting upgrading and development of local industry (SAMED, 2016).

2.4 Comparative Summary of the UK and SA Medical Devices Markets and Regulatory Frameworks

This chapter has provided some historical background and structural information of the UK and SA medical device markets and regulatory frameworks. The UK medical device industry is one of the most competitive in the world, recognized for its ability to continually design, develop, and place innovative medical devices in the UK and foreign markets (BMI, 2016b). This can be attributed in part to a higher level of R&D investment and greater availability of venture capital, compared with the SA industry, which lacks government support and funding in the areas of R&D and technological development (Deloitte, 2014).

Compared to the UK, which has a robust local product development capability and strict regulation (BMI, 2016b), the SA medical device market is supplied primarily by imports and has limited regulation requirements, providing excellent opportunities for foreign device manufacturers. Despite the milestones in healthcare provision, the UK and SA healthcare technologies are not easily affordable because of their increased costs associated with R&D, approval, compliance, and quality control. To that end, this study aims to further examine the impact of regulatory changes on industrial capabilities and development of affordable medical devices for the local population in the UK and SA. A summary of the key factors associated with the two countries' medical device sectors is presented in Table 2.10 below.

Table 2.10: Comparative summary of the UK and SA Medical devices markets and regulatory frameworks

Area of comparison	UK	SA
Medical device market growth	Estimated at USD11, 3 billion in 2014 and is forecast to grow at a US$ billion 2014-2019 CAGR of 5.1%, which will see market reach USD14.5 billion in 2019.	Estimated at USD1.2 billion in 2014 and is forecast to grow at a US$ billion 2014-2019 CAGR of 2.2%, which will see market reach USD1.3 billion in 2019[10].
Export trade status	UK exported medical devices to the SA worth approximately US$ 228 million between the period 2004 and 2013.	SA exported medical devices to the UK worth approximately US$32.1 million between the period 2004 and 2013[11].
Regulatory framework	• Operates under the three core EU directives of the 1990s. • The framework has often been viewed as superior to many countries, given its somewhat faster regulatory process for devices and earlier access to some high-risk technologies	• At present, only electromagnetic medical devices or radiation emitting devices are regulated through the Hazardous Substances Act, No. 15 of 1973. • Considered to have had a relatively 'good' system of electro-medical device regulation in place, which started in 1971 compared to the rest of the African countries
Regulatory changes	• The 1990s three main directives have been supplemented over time by several modifying and implementing directives, including the last technical revision brought about by the MDD 2007/47/EC • Since September 2012 the UK through the European Commission adopted and have been debating a new proposal to reform current regulation of medical devices, and, once adopted, will replace the existing three device directives • On April 5, 2017, two new regulations were adopted replacing previous directives.	• The Public Health Act of 1919 which is country's first national public health measure has also been supplemented over time by amendments such as Public Health Amendment Act of 1971[12] and the last technical revision concerning the use of X-ray equipment brought about by The Hazardous Substances Act, No. 15 of 1973[13] • Since 22 April 2014[14], South Africa published for public comment draft regulatory changes designed to regulate all health products, devices and pharmaceuticals • Act 14 of 2015, promulgated in June 2017

[10] Medical device market growth figures source: (BMI, 2016a: 2016b) reports.
[11] Export trade figures source: (Deloitte, 2016).
[12] SA Government. Act no 42: Public Health Amendment Act. (GN 888 in Government Gazette 3119 of 26/5/1971).
[13] SA Government. Regulation R1332: Regulations concerning the control of electronic products. (GN R1332 in Government Gazette 3991 of 3 August 1973).
[14] Government Gazette No 37579 of 22 April 2014 – Notice R 315 "Medicines and Related Substances Act (101/1965).

What stands out in this table is the dominance of the regulatory frameworks and the constant changes associated with them. The constant regulatory changes have been influenced by the need to improve societal safety (Sorenson and Drummond, 2014). The scandals witnessed in the UK related to the usage of the medical devices, such as hip replacement and breast implants were key drivers of regulatory change (Cohen, 2012). In contrast, SA regulatory changes came about as a result of concerns about the possible effects of exposure to radiation on humans (Herbst and Fick, 2012). The processes that also drove regulatory changes included; the process of ensuring consistency amongst EU member states in the recognition of notified bodies, process of better coordination in the supervision of notified bodies; use of unannounced checks of manufacturer premises by notified bodies, improving vigilance systems and leveraging tools for traceability of medical device (European Commission, 2012)[15].

The increased demand for the health technologies led to changes in how the devices are manufactured and the rules followed in the supply of those devices in the market (Seedat and Rayner, 2012). The changing law associated with medical care provision and the complaints raised by health consumers following poor health care services remains other drivers to change. As such, there is a gap in our understanding of the processes of market entry and how regulatory changes impact efforts to make affordable healthcare technologies in general and medical devices in particular, available in both advanced and developing countries. For this reason, this study aims to help bridge the gap left by the previous studies. The next chapter provides a critical evaluation of existing literature focusing on healthcare technology and medical device regulation.

[15] (For specific regulatory changes see ec.europa.eu/health/medical-devices/documents/revision/)

CHAPTER THREE
LITERATURE REVIEW

3.0 Introduction

This current chapter will present a critical evaluation of literature on health technology regulation in general and medical device regulation in particular to situate this research in the context of this literature. Particular emphasis is placed on literature on medical device regulation in both advanced and developing countries. In addition, literature on the effects of regulation on the industry is also examined. A summary of the key issues raised in each part of the literature review will be provided such that knowledge gaps will be identified and presented.

3.1 Regulation and Technological Capabilities: Health Technology Regulation in Advanced Countries

As described in chapter one, health technologies include medicines, medical devices, assistive technologies, techniques and procedures developed to solve health problems and improve the quality of life (Liaropoulos, 1997, WHO, 2011a). Such technologies play a major role in contemporary health care systems and contribute directly to the quality of patient care (Cohen, 2012). However, the use of health technologies entails some considerable risks to human health (Altenstetter, 2008). Regulation is therefore, one mechanism to help balance the benefits and risks of new devices (Sorenson and Drummond, 2014). Regulation influences the way in which healthcare technologies are tested, commercialized and innovated, how producers and consumers interact, and ultimately contribute heavily to the institutional structure and the innovation dynamics of the medical device sector (Bloom et al., 2014).

3.1.1 Regulation and Technological Capabilities: Insights from the Pharmaceutical Industry

Health technology regulation has a long and significant history in national and global health policies (WHO, 2011a). Since the beginning of the 21st century, academic and policy research interest in health technology regulation has elevated and become more visible. However a majority of studies in advanced countries have concentrated mainly on effects of regulation on pharmaceutical markets with regards to product safety, drug development costs, patent life, and other issues including (Abraham and Davis, 2005, Grabowski and Wang, 2006, Katz, 2007, Chowdhury, 2013, Cullmann et

al., 2012, Eisenberg, 2012, Griffin et al., 2013, Tobin and Walsh, 2008, Smith, 2005, Wood, 2010). These studies discuss various negative and positive influence of regulation on the pharmaceutical industry.

The negative influence of regulation includes the contention by Griffin et al. (2013) that the tightening of regulation for pharmaceuticals in advanced countries such the US and the UK has at least doubled the cost of new product development in the last two decades. In a study exploring European regulation and the effect on regulatory uncertainty in the marketing authorization of medical products, Chowdhury (2013) argues that the health technology industry exhibits high level of regulatory uncertainty that undermine the effectiveness of the regulatory framework. The study found that although the sources of uncertainty varied across sectors, firms developed complex compliance strategies that allowed them to tolerate and in certain circumstances even circumvent regulatory uncertainty. Equally, Grabowski and Wang (2006) found that the direct effect of regulation on some (typically smaller) firms ultimately causes some of them to exit the industry. However, Eisenberg (2012) argues that the indirect effect on the industry is that the remaining incumbent firms benefit from reduced competition and increased revenues. Eisenberg further argue that the patent system works in tandem with drug regulation to defer market entry by competitors, thereby preserving profitable exclusivity in the market for a new product more effectively than patents could do without the regulatory assist.

On the positive side of the impact of regulation, Abraham and Davis (2005) found that firms in the US pharmaceutical industry had fewer product safety withdrawals because the regulatory agency applied more stringent pre-market review, which took longer than UK regulatory checks, but prevented unsafe products marketed in the UK from entering the US market. Katz (2007) argued that the regulatory review of new drugs is an efficient mechanism for assuring the quality of medicines. Similarly, this points to the argument by Tobin and Walsh (2008) that drug regulation can provide the quality assurance necessary to persuade consumers to purchase drugs and increase the expected returns from innovation. In this sense, the regulatory framework is not solely a burden imposed on the industry but it also provides a valuable service to the industry (Katz, 2007).

3.1.2 Regulation and Innovation: Insights from Emerging Health Technologies

Some studies have looked at emerging health technologies regulation, such as nanotechnologies, that are posing significant challenges to regulatory governance due to the uncertainties of development trajectories, product properties, and potential risk problems (Paradise et al., 2008, Dorbeck‐Jung et al., 2010, Bannister and Wilson, 2011). Due to the complexity, ambiguity, and uncertainty of risk problems, Dorbeck‐Jung et al. (2010) noted that governments and regulators appear to have the unenviable task of balancing innovation and benefits against scientific uncertainty and the need for risk management.

Paradise et al. (2008) argued that medical innovations using advances in nanotechnology are confusing the existing product classification scheme. This is because many products containing nanomaterials fall into the so called "combination products" or products in "borderline cases" involving medicinal products, human tissues and cells, or biocidal products, that are classified according to their "primary mode of action". In the European Union, the study of the Working Group on New and Emerging Technologies in Medical Devices (2007) concluded that existing legislation is adequate to deal with nanotechnology-based medical devices. However, devices presenting risks associated with nanomaterials have to be subjected to a systematic pre-market review (European Commission, 2008). Bannister and Wilson (2011) explore the relationship between emerging technologies, citizen autonomy and the regulatory state. They argue that technology already enables a significant increase in the level of governmental interference in and control of the lives of citizens. They outline two frameworks: the activating state, and the regulatory state to analyse possible developments and their implications. Many researchers have agreed that there are inherent limitations and challenges to regulation in practice, given the multiplicity of available health technologies (Faulkner, 2012, Chowdhury, 2013).

3.1.3 Health Technology Regulation and Innovation in Production

The influence of regulation on health technology production, innovation entrepreneurship and small businesses in general has attracted some attention (Herzlinger, 2006, Blind, 2012, Tait et al., 2017). Firms see regulation as one of the core factors influencing the innovation process (Herzlinger, 2006). Most studies have looked at the impact of regulation on innovation in quantitative terms, for example,

examining the number of patent applications (Golec et al., 2010, Mayfield, 2016) or the number of new products introduced (Nemet, 2009). Golec et al. (2010) found that policy uncertainty related to price controls can reduce R&D spending well before the regulation is in effect, but also change the nature of innovation from developing expensive breakthrough drugs to cheaper patentable innovations that do not require heavy R&D investment.

Tait et al. (2017) conducted a study on the role regulations, guidelines and standards on innovation. The study argues for deregulation and support for the short-term interests of businesses by making *"governance systems more proportionate and adaptive to the needs of innovative technologies"* (Tait et al., 2017, p5). The study proposes a responsible innovation framework tailored to companies, which presumes that companies can be certain about the risks and benefits of their products, and certain about public concerns. Blind (2012) embarked on the study to find out what types of institutions affect innovation. The author identified six types of institutions, including competition legislation, price controls, product legislation, environmental laws, intellectual property rights and legal and regulatory frameworks; and adopted the endogenous growth approach as a conceptual analysis to examine the impact of the different types of institutional settings on innovation. Blind (2012) argued that, although regulation, innovation, and competitiveness in global health technology markets have been discussed for several decades, little progress has been made to understand the effect of regulation on the ability of industries to innovate. To fill this gap, the current study examines how regulatory changes enables or, in contrast, constraints innovation in production of affordable healthcare technologies in the UK and SA industries.

3.1.4 Health Technology Regulation and Market Entry

Previous regulatory studies have shown that the majority of health technologies require regulatory approvals before entering the market (Abraham and Davis, 2005, Cullmann et al., 2012). However, some researchers have argued that there have been high regulatory barriers to market entry, such as the number of procedures, extended approval timeframes and the compliance costs (Chataway et al., 2007, Faulkner, 2012, Kramer et al., 2012a). Previous studies have also noted that high health technology regulatory entry barriers have a strong influence on the industry capability, reducing

productivity, employment and increasing labour costs (Tobin and Walsh, 2008), decreasing research and development (R&D) efficiency and hindering innovation (Cullmann et al., 2012). Griffin et al. (2013) postulate that new cost-effective health technologies have a substantial impact on patient quality of life, the health budget, and the wider economy; therefore, slow uptake means these important benefits are delayed. Some researchers suggest that governments seeking to promote new health technologies should focus on the longer-term effects of the regulations on the industry (Wood, 2010, Smith, 2005). Furthermore, as new health technologies are largely driven by competition, the governments should seek to lower the barriers to entry for new companies (Preissl, 2000).

The pharmaceuticals are not the only sector in which research on health technology regulation would be of interest. However, the pharmaceutical industry is closely related to the medical device industry. It is also the industry for which a comparatively rich literature is available. While the pharmaceutical and medical device industries are related, the industrial dynamics are not necessarily similar (Wood, 2010, Chowdhury, 2013). A detailed assessment of the medical device industry, and particularly the high-risk sector, will thus provide additional insights.

3.2 Medical Device Regulation in Advanced Countries

The regulation of medical devices is a vast and rapidly evolving field that is often complicated by legal technicalities (WHO, 2011b). Over the past twenty years, there has been an effort to study medical device regulation in advanced countries, however the studies are very few compared to those that have focused on pharmaceutical regulation.

3.2.1 Medical Device Regulation and Innovation in Production

Some studies have appeared examining the effects of regulation and regulatory change *on innovation* in the medical device sector (Crafts, 2006, Curfman and Redberg, 2011, Faulkner, 2009, Bergsland et al., 2014, Bloom et al., 2014, Guerra-Bretaña and Flórez-Rendón, 2018, Davey et al., 2011). The literature about the impact of medical device regulation on innovation discusses and focuses upon concepts such as resource scarcity, allocation, and exchange. Crafts (2006) notes that, regulatory constraints influence innovation in two different ways. First, regulatory changes are

associated with different costs. Second, regulation may potentially enable innovation by providing larger expected profits (Crafts, 2006). However, Craft argues that the larger expected profits could either be associated with a higher level of production output or come from the regulatory effect on the potential entry of the products. According to Faulkner (2009) the most obvious cost of regulation is that productive resources are used for compliance rather than for product output.

Faulkner (2009) addresses the role that regulation plays in processes of technological innovation. The study provides a view that regulation 'lags behind' innovation. Conversely, Bergsland et al. (2014) found that the introduction of innovative medical devices to the health service is slower than for other consumer products due to the regulatory barriers to innovation.

Davey et al. (2011) argues that open innovation models can allow medical devices firms to manage the ideas of multiple stakeholders and lower existing barriers for reaching the market more quickly. Successful case studies exist of collaboration between academia, health institutions, industry and regulatory agencies for developing innovative medical devices (Bonutti et al., 2008, Courvoisier, 2016, Markiewicz et al., 2017), overcoming the barriers to innovation in medical products by coordinated efforts among critical stakeholders.

In a recent study on innovation under regulatory uncertainty: evidence from medical technology, Stern (2017) considers that the regulatory process strongly affects market entry patterns of the small firms and that they are less likely to be pioneers in new devices because of the relatively higher costs of doing so for more financially constrained firms. In this study we will contribute to the existing literature by considering how regulation influence of the entire cycle of innovation, which includes resource allocation for the innovation process, the innovation process itself, production, firm linkages and the sales/use of final products

3.2.2 Medical Device Regulation and Patient Safety Concerns

Some studies gave attention to patient safety concerns, product recall and regulation (Heneghan et al., 2011, Thompson et al., 2011, Cohen, 2012, Zuckerman et al., 2011). Heneghan et al. (2011) noted that the number of medical devices subject to recalls or warnings in the UK has risen dramatically. A substantial number of these devices may have caused serious adverse effects in patients and contributed to healthcare costs. To

that end, significant problems exist in the UK with a lack of access to transparent data and a registry of the highest-risk devices (ibid). Similarly, Thompson et al., (2011) contend that the UK regulatory system for medical devices fails to show sufficient transparency and especially in the context of device recalls. A study done by Cohen (2012) examines the evidence of risk from metal-on-metal hips, the manufacturers' inadequate response, and how the regulatory bodies failed to give doctors and patients the information they need to make informed decisions. This study concluded that after a series of failures, device regulation is in need of radical change as there is some doubt that the current regulatory system is fit for purpose.

The most important conclusion of these studies on patient safety concerns is that, despite the fact that strong regulations exist, the risk of putting into the market insufficiently tested devices still remains, and that the effective review process is still an issue of academicians, industry, government and social concern (Zuckerman et al., 2011).

3.2.3 Medical Devices Regulation and Industrial Conformity and Compliance

Due to the fact that medical device regulation is not static, conformity and compliance to regulatory changes have been major challenges to the industry. A few studies have examined industrial conformity and compliance to regulation (Jefferys, 2001, Lee et al., 2006, Sorenson and Drummond, 2014). Conformity assessment is the key mechanism for assuring that a medical device is safe and performs as intended through meeting the essential principles. The requirements for conformity assessment become more stringent as the risks associated with the medical device increases (Sorenson and Drummond, 2014).

Lee et al. (2006) criticized the second core directive for medical devices (MDD 93/42/EEC) for burdening the medical device manufacturers with high approval costs. A conformity assessment study by Jefferys (2001) described the role of medical device regulation and argued that long and complicated authorization procedures hinder development of new devices and increase complexities needed to meet local requirements. Therefore, timeliness of regulatory decisions during the compliance and approval procedures and access to technology is a major concern for the stakeholders in the medical device industry (Sorenson and Drummond, 2014).

Blanchard and Giavazzi (2001) conducted a study on the effects of regulation on labour markets and argued that there are high entry costs challenges faced by the manufacturers. This argument has also been supported by Djankov et al. (2002) whose study on regulation of market entry in 85 different countries noted that official costs of entry are extremely high in most countries.

By reviewing evidence of regulation effects in various OECD countries, Craft (2006) concluded that whether the regulation influence is negative or positive, depends on the extent of the compliance cost and the incentive. Regulatory compliance and conformity is indeed a requirement in the medical device sector. However as shown in literature more studies are needed that not look at regulatory compliance but also on the overall effects of regulation on industrial technological capabilities and thus what this study is trying to achieve.

3.2.4 EU and US Medical Device Regulatory Frameworks

A field of comparison studies of EU and US medical device regulatory frameworks reflecting on development commonalities, differences and challenges have also been published (Abraham and Davis, 2005, Altenstetter, 2012, Kramer et al., 2012a, Kramer et al., 2012b, Sorenson and Drummond, 2014, Sorenson and Kanavos, 2011). From these previous studies, they found that the two systems differ in a few aspects: for example, the U.S. system is highly centralized, i.e., the Food and Drug administration (FDA) has control of all procedures for the admission of a product to the market. On the contrary, European law on medical devices has "outsourced" the certification of safety criteria to external entities, called notified bodies.

Moreover, U.S. regulation has been seen as more stringent, and sometimes this has been seen to have a negative effect on the speed of innovation. On the other side, European patients have faster access to certain devices, but these products are marketed with less rigorous proof of effectiveness and may have a greater chance of later-identified adverse events (Kramer et al., 2012a, Sorenson and Drummond, 2014).

The comparative studies have shown that the US regulatory authority is a governmental entity, and as such it is equipped with considerable powers. Yet in the European system the privately organised product certification partner, the Notified Body, is often a much smaller player than the firm seeking approval (CE certification)

for its product. It can happen that a product is certified for the EU market earlier than it is approved for the US market, simply because firms are able to pass through the necessary steps more easily in Europe. The Notified Body certification appears to be a lower hurdle than the government agency-owned process in the US. The comparative studies found that device classification decision in both regulatory systems is initially performed by the manufacturer who decides according to available guidelines into which class a specific product should fall and applies for approval accordingly (Altenstetter, 2012).

3.2.5 Harmonization of Medical Devices Safety Regulation

Some studies have examined *harmonization* of medical device safety regulation in advanced countries (Kaplan et al., 2004, Altenstetter, 2008, Marchant and Allenby, 2017, Pombo et al., 2016). Kaplan et al. (2004) found that important differences have evolved in the clinical-regulatory environment between the United States and Europe that have impacted the location of clinical testing and the relative timing of commercial availability. This has led to substantial differences in the speed of introduction and the extent of testing of these devices in the United States and Europe. Pombo et al. (2016) pointed out that harmonization reduces regulatory load and promotes industry compliance. However, Altenstetter (2008, p. 230) argued that "countries instituting medical device programs should be cognizant of ongoing international harmonization effects so as to preclude regulatory controls that conflict with actual harmonized rules and guidelines or with the spirit and goals of on international hamonization."

Marchant and Allenby (2017) explored the role of soft law in governing emerging technologies, arguing that there are at least ten different reasons why nations may seek to harmonize their oversight of a specific technology. A new generation of more informal international governance tools are being explored, often grouped under the term "soft law." They include private standards, guidelines, codes of conduct, and forums for transnational dialogue. However, Pombo et al. (2016) pointed out that the implementation of harmonized regulations depends on the national regulatory capabilities. Therefore, these capacities have to be strengthened to allow the incorporation and deployment of common standards in all countries.

3.2.6 International Collaboration on Medical Device Regulation

A study on international collaboration done by Altenstetter (2005) argued that, regulation raises complex issues which require highly specialized scientific and technological knowledge and skills that often surpass the capability of national regulators. The pooling of resources, knowledge and expertise at the global and regional levels is seen as producing the most appropriate regulatory solutions based on the latest state-of-the-art medical technology in a host of different disciplines. While the pooling of resources has benefits, it also carries a heavy price. That price is dependence on the knowledge and expertise of a small number of industry scientists, clinical innovators, and regulatory affairs specialists of multinational companies with little accountability. In this study we want to investigate these complex issues further but not only restricted to the capability of national regulators' point of view but also from the firm level capabilty's point of view.

3.2.7 Evolution of the EU Regulatory Framework

A recent study that is in line with this research has been done by (Casteels and Rohde, 2013) who looked at the evolution of the EU regulatory framework. The study found that the strength of the decentralized European regulatory framework for medical devices has been to provide timely access to life-saving and life-enhancing technologies to patients and doctors in the EU (and beyond) while guaranteeing a high level of safety. Conversely, the study argues that the EU framework needs now to be reformed to respond to increased expectations and technological advances and to avoid incidents such as the fraudulent PIP breast implant case. The study however makes no attempt to consider the impact of the evolutionary changes on the industry dynamics and also fails to compare the evolution with other frameworks outside the EU. This is what this study sets out to examine further.

3.3 Health Technology Regulation in Developing Countries

A considerable amount of literature has been published on health technology regulation in developing countries. These studies include: (Kale, 2013, Rugera et al., 2014, Sheikh et al., 2015, Ensor and Weinzierl, 2007, Chataway et al., 2007, Mori et al., 2013, Harmon and Kale, 2015). A major challenge some researchers have pointed out is that the absence of regulation has an impact on the development of health technologies and development of health sectors (Kale, 2013, Rugera et al., 2014). This augment is supported by Pigou's (1938) public interest theory of regulation that

suggested that unregulated markets would be destined to frequent failures (Djankov et al., 2002).

Sheikh et al. (2015) adopted a stepped research methodology to map health technology regulatory institutions and argued that ineffectiveness of health technology regulation in developing countries is widely observed, but there is little empirical research exploring the reasons for these failures. This argument is in line with Ensor and Weinzierl (2007) who had also looked at health technology regulation in low and middle-income countries and argued that there is need to invest in structures and institutions especially in Africa to encourage a more coherent regulatory approach. Chataway et al. (2007) states that health technology developments are evolving faster than relevant policy and regulatory systems and many of the new emerging products cross the boundaries of existing regulatory systems.

Mori et al. (2013) conducted a study in Tanzania to identify whether reforms of pharmaceutical policy were undertaken to improve efficiency or whether they just presented an opportunity for vested interests. Findings from the study highlighted the influence of politics on decision making at many levels of the reform process, with regulation remaining a challenge. There is a call on governments to limit the political influence on policy, in the interests of appropriate public health outcomes for the populations of developing countries. A study on multiple roles for medical research and products regulation in Argentina and India by Harmon and Kale (2015, p. 21) argues that "both sound healthcare interventions and socially useful innovation may be best encouraged through regulatory innovation, and emerging jurisdictions are in a strong position to 'leapfrog' developed jurisdictions reliant on more entrenched regulatory instruments and pathways".

A number of studies reviewed in this literature on health technology regulation in developing countries highlighted the challenges and shortfalls of current regulatory systems. However, very little is known about the effects of regulation on firm level capabilities and affordable healthcare technology development, the concern of the current study.

3.4 Medical Device Regulation in Developing Countries

Most developing countries do not have their own regulations on medical devices, but many refer to the EU or US normative system, including the International Medical Device Regulators Forum (IMDRF) to facilitate the manufacturing and selling of their products in Europe, US and to the rest of the world (Shah and Goyal, 2008). For instance, WHO (2005) reported that only 7% of the 46 sub-Saharan African countries had National Medicines Regulatory Authorities (NMRA) in place. Of the remaining countries, 63% had minimal regulation and 30% had no regulation. As a result, studies on medical device regulation in developing countries have recently started to receive some attention (Deloitte, 2014, Herbst and Fick, 2012, Kale, 2013, Lamph, 2012, Sheikh et al., 2015, Rugera et al., 2014, Saidi, 2016, De Maria et al., 2018, Saidi and Douglas, 2018). The need for such research is notable to ensure safe and effective healthcare in developing countries.

One of the few studies conducted on regulation of medical devices in developing countries has strongly indicated that streamlining and harmonizing regulatory processes is needed in order to reduce delays, unnecessary expense and improve access to new medical devices (Rugera et al., 2014). In their study of six countries (Burundi, Kenya, Rwanda, Tanzania and Uganda), Rugera et al. (2014) indicated that some countries are taking steps towards strengthening medical device regulation and these countries are receiving support through a project with the WHO.

De Maria et al. (2018) conducted a study aimed at comparing the certification route that manufactures must respect for marketing a medical device in some African Countries and in European Union. The study found that in developing countries, poor regulatory control results in the use of substandard devices, and often it becomes a constraint for those wanting to produce, sell, or even donate these devices. Similarly, Saidi (2016) explores the importance of medical device regulation in promoting access to high quality, safe and effective medical devices. The study emphasizes that medical device regulation in developing countries helps to prevent the importation and use of substandard devices thereby protecting the users from falling prey to unscrupulous market influences that put patients' lives at risk. To that end, governments have the responsibility of putting in place regulations aimed at

addressing all elements related to medical devices, ranging from access to high quality, affordable products through to their safe and appropriate use and disposal.

Kale (2013) conducted a study focusing on regulatory policies and their impact on innovation and technology capability development in the Indian medical device industry and argued that regulation can have many beneficial effects, therefore neglecting to regulate, or deregulating where frameworks already exist, is not necessarily the way forward. Herbst and Fick (2012), whose study focused on SA regulation, radiation protection and the safe use of X-ray equipment indicated that poor management of regulatory system, lack of financial resources and deficient human regulatory capacity put the health and safety of the local population at risk. Accordingly, Saidi and Douglas's (2018) study found that the absence of specific and comprehensive regulations that guided the manufacturing and sale of medical devices had far reaching repercussions on the health delivery system in SA. This is because good and functional medical devices are produced when the manufacturing process is adequately regulated.

In a case study of SA medical device regulatory framework, Poluta (2006) argued that regulation of medical devices is well established in industrialised countries with increasing standardization and harmonization. In developing and poor resourced countries, however, there is a much greater degree of variability and implementation. The scope of Poluta (2006)'s research, however, was relatively narrow, being primarily concerned with proposing a compact framework model. The study makes no attempt to consider the historical background of the current framework and the broader implications of regulation on industry capability.

3.5 Medical Device Regulation Effects on Industry

The medical device industry includes both large global firms and a large number of small entrepreneurial companies and start-ups (Chowdhury, 2013). Previous studies on the effects of regulation on research and product development (R&D) have argued that regulation can cause new innovations to concentrate in larger, multinational firms that are better able to deal with the compliance costs (Bloom et al., 2014), therefore reducing competition in the industry, resulting in less market innovation and thus a decline in the supply of affordable medical devices (Curfman and Redberg, 2011,

Bergsland et al., 2014). However, Kale (2009) argues that innovation capabilities in the case of firms in developing countries differ in complexity in comparison with firms in advanced countries. In some cases, regulation in developing countries may not directly influence innovative R & D of multinational companies as this might be influenced by their corporate strategy rather than be subjected to the policies of the developing country. But governments may dictate that multinational companies develop local firms in order to gain entry into those markets. These local firms usually result in local innovations on products as the demands of the market are easier to understand. Healthcare policy researchers have argued that a strong local capability for both technological and social innovation in developing countries represents the only truly sustainable means of improving the effectiveness of health systems (Hsieh and Tsai, 2007).

Using the concept of co-production of science and society in his comparative study Faulkner (2012) argued that bringing together empirical and theoretically informed research to analyze industrial regulatory trends in a range of health technologies have implications for human health. This study wants to examine this further and understand whether medical device regulatory implications are bringing positive outcomes in particular access and affordability outcomes and if not then how can the system be improved.

3.6 Concluding Remarks and Knowledge Gap

Kale (2013) pointed out three major reasons why regulation is criticised: the first criticism is that it increases cost of innovation therefore reducing possibilities of affordable healthcare technologies; the second is that the presence of regulation may effectively prevent disruptive technological improvements from occurring. This argument is based on the theory of disruptive innovation (Hwang and Christensen, 2008). The author lastly, points out that regulation can constrain growth of a sector by creating rigid entry barriers that slow evolution of the sector.

Malerba and Mani (2009, p.21) claimed that the separation of research from development and production capabilities could be very harmful for innovation and development. Smith (2005) argued that the capabilities of the industry cannot be understood in isolation from the system of regulation and, increasingly, the international regulatory structures, and from what is happening elsewhere in the

regulation of science. Intarakumnerd and Fujita (2009) argued that in developing countries, production capability is as important as innovation capability. How technological change affects market structures have been investigated thoroughly by many researchers including (Cohen and Levinthal, 1989, Suarez and Utterback, 1993, Von Tunzelmann, 2003). However, the effects of regulation and regulatory change on the industry capabilities have attracted much less attention. Few studies reported on specific firms and their implementation activities. Also, no studies differentiate the performance of individual firms' capabilities in responding to new regulations. Indeed, we can gain new insight into firms' behavior by investigating the implementation actions that they take in response to a specific regulatory change.

Some studies have surveyed the dynamics of industries, e.g. the pharmaceutical industry, from patenting to productivity (Pammolli and Riccaboni, 2004, Scherer, 2000, Syverson, 2004). However, the medical device industry has not been investigated much in this regard. This argument is further supported by a legislative and policy framework study done by Rugera et al. (2014) that also argued that studies on pharmaceutical products regulation and development have received more attention and that less attention has been placed on the regulation and development of medical devices.

Some efforts have been made to study the regulation of medical devices but only by a few researchers as shown in this literature. Despite the ever-expanding knowledge base, more research is needed, especially to assess new regulatory developments and evolutions in practice (Sorenson and Drummond, 2014). Kramer et al. (2012a) used a systematic review process to compare US and EU medical devices regulatory systems. The authors argued that changes are necessary for the evolution of regulatory systems, however this systematic review did not provide some insights for policymakers or regulators seeking to reform device regulation. To avoid this limitation, this study will deploy the sectoral systems of innovation approach as it provides valuable recommendations to policy-makers designing national, sectoral or regional-level innovation policies (Malerba and Mani, 2009).

While studies have shown that there is medical device manufacturing capacity in both the UK and SA (BMI, 2016), though at different levels, there are no systematic

studies that identify from an evolutionary perspective, the impact of medical device regulation on industrial capabilities to develop healthcare technologies as well as the barriers to commercializing them at an affordable cost. In this regard, a study enhancing our understanding in this respect would indeed be an interesting area that is worth further exploration.

This study chose to do a comparison of regulatory change cases using empirical data from the UK and SA based firms because: first, both countries have oriented their regulatory processes for medical devices on the EU system. Second, SA is one of the African Biomedical Engineering Consortium (ABEC) [16] countries that has implemented or harmonized with European directives in its legislation, despite the fact that the legislation is particularly strict (De Maria et al., 2018). Third, the legislative frameworks of the UK and SA both adopt the International Medical Device Regulators Forum (IMDRF) philosophy of accelerating international medical device regulatory harmonization and convergence (IMDRF, 2020). For this reason both study countries adopted the Risk Classification System formulated by the Global Harmonization Task Force (GHTF). Fourth, the UK was a pioneer in risk-based regulation following the Hampton Review (Hampton, 2005), and the UK's regulatory reforms have drawn the interest of policymakers and regulators in other countries (Etienne et al., 2018) including those in SA. To that extent, SA has replicated regulatory tools or frameworks that were initially developed in the UK[17].

But while there may be some convergence of regulatory objectives and substantive principles, the character of national regulatory institutions is still best understood within each jurisdiction's culture. In the words of Foster (1992, p.417) 'while the underlying economic principles and therefore the regulatory offences should be relevant in all economies, how the offences should be expressed, monitored and controlled can only be decided in the context of the constitution, laws and political habits of the individual country'

[16] The African Biomedical Engineering consortium was founded in 2012 with the mission of pursuing capacity building in Biomedical Engineering for sustaining local healthcare systems.

[17] Much of the Better Regulation drive at EU level can be traced back to UK initiatives (Etienne et al., 2018).

Another limitation of existing studies is that most of the studies were conducted after the regulation was significantly revised. Considering the interactive learning within the innovation ecosystem, the impact of regulation observed in this period could be different after the regulation has been implemented and stabilized. It is these gaps that this research aims to fill. The importance of a study of this nature can further be attributed to the anticipation that more, as well as stricter regulations are likely to be imposed in the future.

Our examination of literature in this chapter not only provided a basis for articulating the relevant research gaps on how firms manage regulation and regulatory change but also provide a starting point for the identification of suitable theories for studying the issue of firms' management of the impact of regulatory change. The next chapter, therefore, will present the theoretical framework and conceptual framework developed to answer the research questions of this study.

CHAPTER FOUR
THE STUDY THEORETICAL FRAMEWORK

4.0 Introduction

This chapter presents the theoretical framework of this study. The chapter will first present an overview of the conceptual framework of the research. We use a flow-guide that flows from medical device regulation and industrial capabilities, through the Sectoral Systems of Innovation (SSI) lens, anchored in evolutionary theory. The main factors that influence the dynamics of the system are the actors and networks, knowledge and technologies, and the institutional dynamics associated with a particular regulation. These elements are the centre of this study's analytical focus. The chapter further describes other supporting theories, concepts and approaches used to unpack the effects of medical device regulatory changes on investment, production and linkage capabilities and development of affordable health technologies. Figure 4.1 below shows the conceptual framework:

Medical Devices Industry Pre-Market Impact analysis

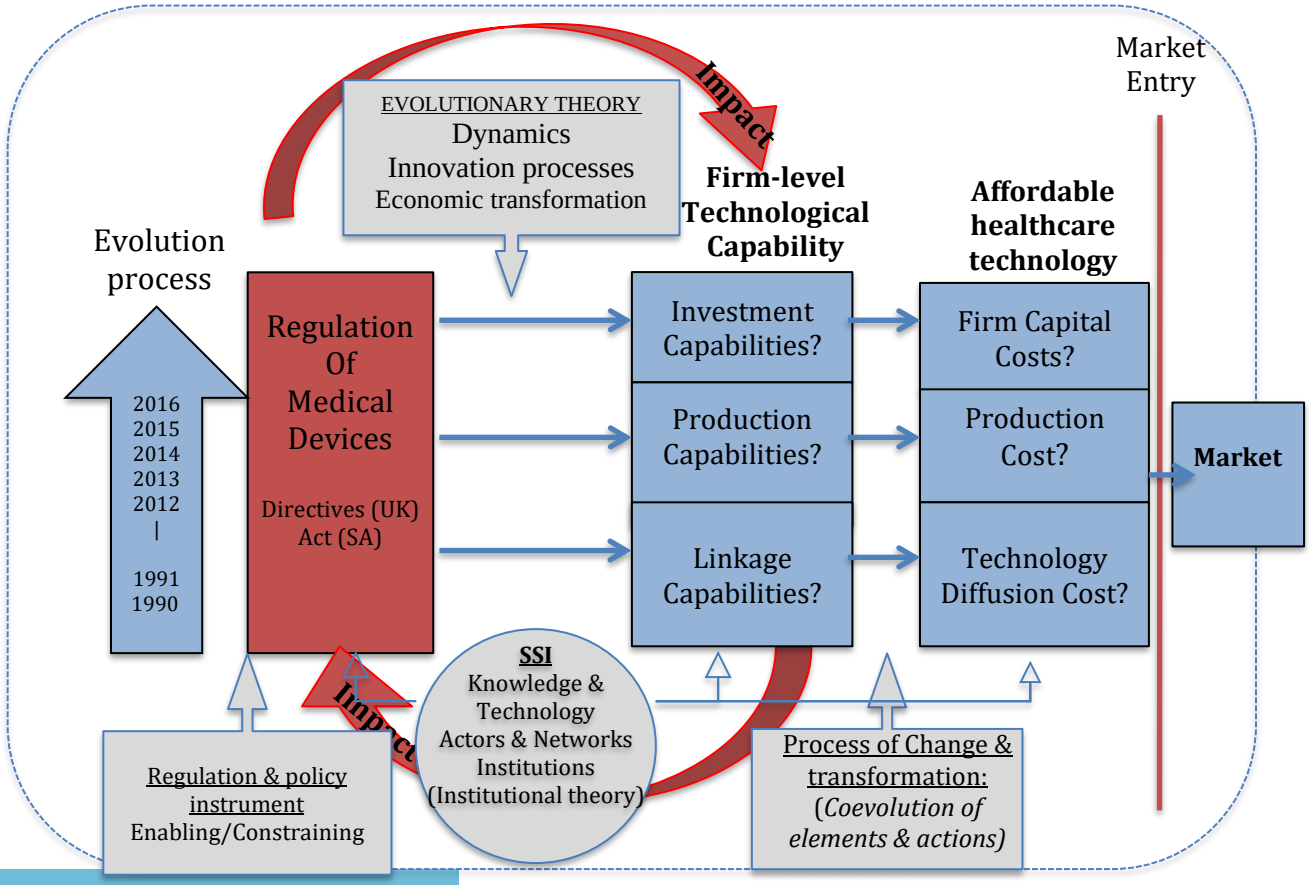


Figure 4.1: Conceptual framework bringing together theoretical and analytical components of the study. Source: (Malerba and Mani, 2009)

In the above diagram, the main object is regulation of medical devices. The main impact factors to be considered in this study are, industrial technological capabilities and the development of affordable healthcare technologies. In order to examine the dynamics within the medical device sector under consideration, the SSI approach is used to unpack the elements of medical device manufacturing processes that have been compiled from the literature which include industrial capabilities and development of affordable health technologies. The adoption of the SSI approach in the study has the potential to enhance our understanding of the process of regulatory change, drivers behind the changes, and impact of the changes on industrial capability to develop affordable healthcare technologies. The SSI concept is anchored in evolutionary theory, which will be used to analyse the changes and transformations, the links, the interdependencies and the sectoral boundaries between regulation, industrial capability and the development of affordable healthcare technologies.

4.1 Industrial Capabilities

The previous chapters provided information on medical device regulatory systems, and the literature survey showed that the UK medical device industry has witnessed radical transition during the past three decades. Medical device industry operations, however, require specific knowledge and skills in technology that may be called "capabilities" of the firm as illustrated in Figure 4.1. These firm-level technological capabilities are examined in this study from the perspective of Lall's definition as a "complex array of skills, technological knowledge, organizational structures, required to operate a technology efficiently and accomplish any process of technological change" (Lall, 1992). Castellacci (2008) suggested that in any given historical era, industrial sectors whose knowledge base and capabilities are closely related to the constellation of emerging radical innovations face a broader set of opportunities and tend therefore to follow dynamic trajectories. By contrast, industries less directly involved in the production and use of the new general-purpose technologies experience a lack of opportunities and are therefore forced to move along less dynamic paths.

Importance of technological capability

Technological capabilities play a strategic role in affecting the competitive advantage of a company, an industry, and even a country (Lall, 1992). Thus, the development of technological capabilities is critical for companies, especially those manufacturing companies in the countries that are in a catch-up phase of industrialization. The development of technological capabilities has also attracted extensive attention both from the theoretical and empirical viewpoint. In addition, extensive research on the development of technological capabilities is carried out not only in emerging countries (Kim, 1997, Lall, 2003) but also in advanced countries (Miyazaki, 1995).

Technological capabilities are therefore crucial both in order to effectively use technologies that have been developed elsewhere (i.e. other countries or other organizations) as well as to be able to adapt, improve and create new, own technologies (Lall, 1992, Bell and Pavitt, 1995). The technological capabilities approach therefore highlights the very crucial role of technological learning.

Relationship between government regulatory systems and industrial capabilities

There is a strong relation between government regulatory systems and industrial capabilities. For example and as mentioned before, "the New Approach" principles of the 1990s assigned responsibility for the regulatory cycle to three organizations: competent authorities, manufacturers, and third party certification organizations (notified bodies) (Altenstetter, 1996). Whilst competent authorities and notified bodies ensure that the requirements of the regulations are applied, the manufacturers' capacity to respond to the new regulatory environment resides in the capabilities of the firm, defined by Teece et al. (1994, p.18) as "a measure of the firm's ability to solve both technical and organizational problems". The firm-level technological capabilities therefore determine what the firm is potentially able to do in response to the new regulatory demands. Figure 4.2 illustrates the link between government regulation and industry.

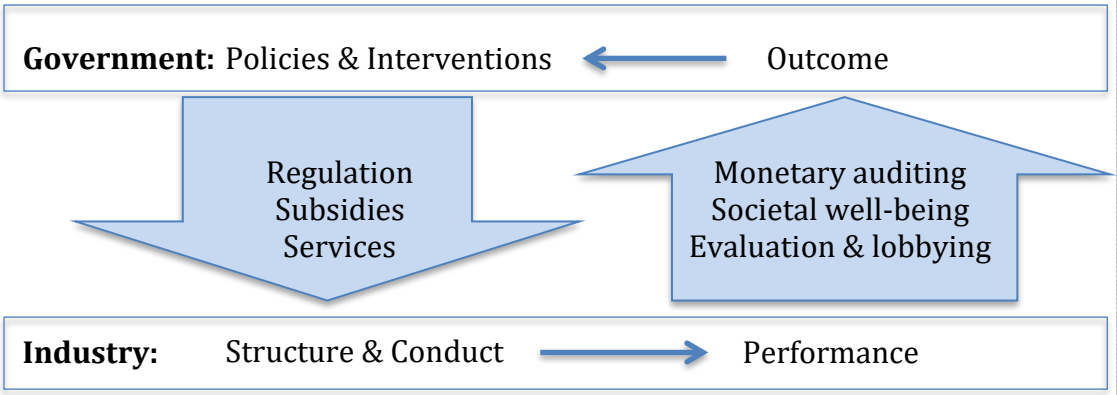


Figure 4.2: Government regulation effect on industry
Adapted from (Hermans et al., 2009)

As presented in the conceptual framework (see figure 4.1), regulation will shape industrial dynamics and in most countries, regulatory authority for medical devices resides at government level as shown in figure 4.2 above. The changed structure will have an effect on the industry conduct and capabilities i.e. on how the actors in an industry will act, respond and how will they interact, leading to different competitive strategies by the companies in the industry. Thus, industry structure and conduct will have an effect on the industry performance (Gaynor and Haas-Wilson, 1998). Ultimately, industry performance will lead to different macroeconomic outcomes for societies that include affordability of health technologies. Whether the outcomes will be positive or negative concerning social welfare, is dependent on how the industry has reacted through its structure and conduct to the changes in government regulation and whether the changes in the industry have led to a net efficiency gain or only to an increase in market power (Hermans et al., 2009).

4.1.1 Theoretical Perspectives of Industrial Capabilities

As illustrated in the conceptual framework (Figure 4.1), this study sets out to examine in some depth the influence of regulatory changes on industrial capabilities. These industrial capabilities can be studied on various theoretical perspectives. One relevant theoretical strand of thought is "evolutionary theory" developed by Nelson and Winter (1982), and explained in Nelson (1987) and Dosi (1988). They argue that firms are modeled as having, at any given time, certain capabilities and decision rules. Over time these capabilities and rules are modified as a result of both deliberate problem-solving efforts and random events (Nelson and Winter, 1982, p.4). Random

events are defined as ('the timely appearance of variation under the stimulus of adversity' (ibid, p. 11).

In the evolutionary theory of the firm, it has been argued that the firm is a repository of knowledge (Nelson and Winter, 1982) and this knowledge exists in the organizational capabilities of the firms, which then determine the performance of the firm. The capabilities addressed in the evolutionary theory of the firm are routines, routinized patterns of behavior that in turn are products of organizational learning and knowledge (Nelson and Winter, 1982). Organizational learning has been characterized as a social and collective phenomenon (Teece and Pisano, 1994) that involves joint problem solving and coordinated search. Moreover, organizational learning is cumulative and path-dependent in nature. What has been learned is stored in routines and expressed in the firms' capabilities.

Teece et al. (1997) developed a theoretical concept of "dynamic capabilities", an extension of the resource-based view of the firm. The concept refers to capabilities within the firm, which allow the firm to create new products and processes and to be in a position to respond to changing market environments. The term "dynamic" is referred to as "the capacity to renew competences so as to achieve congruence with the changing business environment" (Teece et al., 1997, p. 515). Helfat et al. (2009, p.4) define a dynamic capability as 'the capacity of an organization to purposefully create, extend, and modify its resource base'. The 'resource base' includes the 'tangible, intangible, and human assets (or resources) as well as capabilities which the organization owns, controls, or has access to on a preferential basis'. Helfat and Peteraf (2009) also state that dynamic capabilities have a direct effect on firm performance and competitive advantage, as well as an indirect effect through resource reconfiguration. Dynamic capabilities thus reflect an organization's ability to achieve new and innovative forms of competitive advantages given the path dependencies and market positions.

In constantly changing environments, the dynamic capabilities approach can give a more substantive picture than traditional views of how competitive advantage is gained and sustained (Levitas and Ndofor, 2006). The dynamic capabilities approach is an especially useful lens to examine firms in rapidly changing business

environments (Blyler and Coff, 2003, Davies and Brady, 2000). The importance of responding to a rapidly changing environment is a plausible explanation as to how young resource constrained firms can enter markets and even outperform large competitors (March, 1991).

However, dynamic capabilities are only one tool among other explanations in understanding how firms change (Winter 2003). Indeed, in addition to utilizing stable and learned change patterns (dynamic capabilities), firms constantly change themselves by learning, experimenting, and creating new solutions without relying on existing dynamic capabilities. This type of change sometimes leads to the formation of new dynamic and ordinary capabilities (Zollo and Winter, 2002), but it sometimes only happens as a single event of creative problem solving (referred as ad-hoc problem solving in Winter 2003). Either way, firms that are more flexible in terms of learning, knowledge creation, and problem solving, are also likely to be continuously successful in changing environments.

An example of a dynamic capability is strategic decision making ("in which managers pool their various business, functional and personal expertise to make the choices that shape the major strategic moves of the firm" (Eisenhardt and Martin, 2000, p.1107). Other dynamic capabilities focus on for instance "reconfiguration of resources within firms", as well as "transfer processes, including routines for replication, and brokering are used by managers to copy, transfer and recombine resources, especially knowledge-based ones, within the firm" (ibid).

At the firm level, the technological capability development is the outcome of company-level efforts to build up new organizational and technical skills, its ability to generate and tap information, the development of an appropriate specialization vis-a-vis other industry actors, and the formation of linkages with suppliers, buyers and institutions (Lall, 1992). Bell and Pavitt (1995) proposed the category of supportive capabilities to look at the interactions among actors within the system of innovation. In this regard, supportive capabilities include technology transfer that is necessary for a further diversification into new products and new industries. Viotti (2002) proposed the category of improvement capabilities to stress the importance of internal technology upgrading. This function may be encountered in other categories such as

production capabilities. Ernst et al. (2003) proposed the category of strategic marketing capabilities to emphasize behavioral patterns related with suppliers as well as the importance of building close customer links as a competitive advantage. Lall (1992) classify firm-level technological capabilities according to the different functions they perform and their degree of complexity (i.e. different levels ranging from basic via intermediate to advanced). This study adopts Lall (1992)'s firm level technological capabilities functions model, made up of "investment", "production" and "linkage" capabilities.

Investment Capabilities

Lall (1992, p. 168) defined investment capabilities as "the skills needed to identify, prepare, obtain technology for, design, construct, equip, staff and commission a new facility (or expansion)". This includes the capabilities to assess the feasibility and profitability of a project, define specifications, what technology is required, negotiations of the purchase, recruit and train skilled personnel and design the basic process and supply the equipment. Investment capabilities determine the capital costs of the project, the appropriateness of the scale, product mix, technology and equipment selected, and the understanding gained by the operating firm of the basic technologies involved (Lall, 1992). The medical device industry is a high-tech industry with high investment in R&D and the capability of firms to shape technology investments into innovation is likely to be influenced by firm-specific resources such as managerial skills, know-how, experience, the presence of technical experts, and prior technological investments (Koellinger, 2008).

Production Capabilities

Lall (1992) defined production capabilities as skills and knowledge required to carry out activities in the manufacturing or production area. Production capabilities range from basic skills such as quality control, operation, and maintenance, to more advanced ones such as adaptation, improvement or equipment "stretching," to the most demanding ones of research, design, and innovation (Lall, 1992). They also cover both process and product technologies as well as the monitoring and control functions included under industrial engineering (Viotti, 2002, Lall, 1992).

Linkage Capabilities

While investment and production capabilities have been specified as primary activities (Bell and Pavitt, 1995), linkage capabilities are supporting activities with the ability to link up with other actors in the economy. Lall suggested a broader definition of linkage capabilities as "skills needed to transmit information, skills and technology to, and receive them from, component or raw material suppliers, subcontractors, consultants, service firms, and technology institutions" Lall (1992, p. 168). Amann and Cantwell (2012) suggested that firm linkages with other firms could be in the form of local and international links that includes local universities, and public research institutes, consultants, industry associations, regulatory bodies and training institutions. The majority of such linkages are informal in character (Amann and Cantwell, 2012) and affect not only the productive efficiency of the firms but also the diffusion of technology through the industrial structure, which would have been affected by the government regulation either directly or indirectly (Hermans et al., 2009).

The discussion above shows why technological capabilities are at the center of the conceptual framework presented at the beginning of this chapter in Figure 4.1. In this regard, Lall (1992) claimed that in developing countries, the success or lack thereof for the development of technological capabilities is a function of the response of firms to the policy market and institutional framework. These capabilities are the most refined resources needed in the commercialization of innovations and can be used to build firm competitive advantages (Lall, 1992). Thus, the conceptual framework allows us to develop questions pertaining to the regulatory changes that influenced the development of firms' technological capabilities.

4.1.2 Industrial Capability and Affordability

Industrial capabilities are strongly related to the affordability of healthcare technologies (as shown in Figure 4.1). The medical device industry is highly competitive, and cost-effectiveness is one of the priorities of any organization engaged in the manufacturing of medical devices. However, there is a paradox with regard to affordability. The medical device industries have to ensure the highest standards of quality for their services and products, irrespective of affordability of the healthcare technologies. Such standards are mandatory for regulatory compliance

(Spiegelberg et al., 2003). The products and services developed should guarantee appropriate quality assurance to the clients. At the same time, medical device industries should prioritize cost-effective processes and discourage unnecessary expenditure in building industrial capabilities. As illustrated in Figure 4.1, the process of change and transformation allows questions to be developed that probe whether or not affected capabilities, ultimately influenced affordability of healthcare technologies.

4.2 Evolutionary Theory: Principal Characteristics and Applications to Medical Device Sector

According to Malerba and Mani (2009, p.5) "The notion of sectoral systems has evolutionary theory and the innovation systems approach as building blocks". Evolutionary theory places a key emphasis on dynamics, processes, and transformations at the centre of the analysis (Malerba and Mani, 2009). The purpose of using evolutionary theory is "to explain the movement of something over time, or to explain why that something is what it is at a moment in time in terms of how it got there; that is the analysis is expressly dynamic" (Dosi and Nelson, 1994, p.154).

In this study evolutionary theory is used to explain the changes of medical device regulations over time. The behavioural foundation of evolutionary theory rests on learning processes involving adaption and new discoveries (Dosi and Nelson, 1994). Knowledge produced through learning by interaction is conveyed to the key elements in the change process that takes place within economic systems (Hodgson, 1993, Metcalfe, 1998, Saviotti and Metcalfe, 1991). Evolutionary theories surfaced in reaction to the rather static neo-classical economic theories, which simplify the characterization of economic processes, firms and the way these firms use knowledge (Duysters, 1995).

Some scholars have suggested innovation can be understood as an evolutionary process, however the evolution in innovation is a relatively new economic approach that was roughly modelled on Darwinian concepts in biology with regard to variation and selection (Dosi and Nelson, 1994, Nelson and Winter, 2009). Some might not accept the correspondence to evolution in a biological sense, but the evolutionary perspective aligns well with a systemic view of an industry (Malerba and Mani,

2009). All the developments and their outcomes in medical devices sector are considered as interconnected, and the outcomes act as inputs to the ongoing evolutionary process. Within the SSI, the evolutionary theory is related to the theoretical concept of change and transformation in sectors.

4.2.1 Process of Change and Transformation Concept

A sectoral system undergoes processes of change and transformation through the coevolution of its various elements (Malerba, 2002). The concept may be used "to analyze sectors in several aspects, namely for better understanding, dynamics and transformation of sectors, for the identification of factors affecting performance and competitiveness of firms and for the development of new public policy proposals" (Intarakumnerd and Fujita, 2009, p.207). Some scholars have discussed these processes at the general level by focusing on the interaction between technology, industrial structure, institutions and demand (Metcalfe, 1998, Nelson, 2006). The direction and the pace of evolution depend very much on existing absorptive capabilities of agents, strength of their linkages and their process of collective learning to withstand the threats and exploit the opportunities (Malerba and Mani, 2009).

In this study the main elements to be interrogated using the change and transformation concept as indicated in section 4.1.2 are; industrial capabilities and affordability of healthcare technologies. Often co-evolution is related to path dependent processes, which brings changes among different components within a system (Arthur, 1989, David, 1985). It is anticipated in this study that within the medical device sector changes come about through co-evolution of the various elements in the system, and primarily as a result of regulation.

4.3 National Innovation Systems (NIS)

The concept of Sectoral Systems of Innovation (SSI) followed, to some extent, the innovation system approach that was articulated initially at the national level, namely the National Innovation Systems (NIS). In the NIS framework, the nation component is presented from different aspects by various contributing authors. Some researchers stress the importance of national public policy and the structure of national production systems as influential factors in innovation (Edquist, 2005, Lundvall, 2010). Johnson (1992) discusses the dependence of innovative capabilities on interactive learning and

communication, which are in turn dependent on geographic and cultural proximity. In taking a NIS analytical approach to the examination of the medical devices sector, this study requires an investigation of the organisations, or formal structures that are involved in innovation in this national sector.

The limitations in the NIS framework are perceived as being a failure to take into account the supply side or the demands of consumers, and the relevance of the nation state in an age where science and technology production is becoming increasingly globalised (Senker et al., 1999). Due to these limitations and also the fact that NIS literature presents less of a formal theory, but more a conceptual framework for analysing country specific factors at the macro-level. It considers in detail the concepts of innovation, learning, system and nation. This research will therefore, integrate co-existing NIS not only at the same but also across different analytical levels. However the perspective most applicable to the medical device sector is the sectoral perspective, therefore, the main approach of this study follows the conceptual framework of Malerba's Sectoral System of Innovation and Production (Malerba and Mani, 2009).

4.4 Sectoral Systems of Innovation (SSI)

The Sectoral Systems of Innovation (SSI) is a framework that "considers a wide range of factors that affect innovation and production in a sector. It places firms and the related capabilities and learning processes as the major drivers of innovation and production" (Malerba and Mani, 2009, p.3). At the same time the framework pays central attention to other relevant factors such as the variety of actors, networks, demand and institutions (Malerba and Mani, 2009). In this study, regulatory changes in the medical device sector, both intended and unintended are considered as factors that affect the ability to manufacture and supply affordable healthcare technologies, thus a suitable example for analysis in the framework of a SSI. The approach of SSI has a dynamic perspective and takes a process view in a co-evolutionary setting (Malerba and Mani, 2009). This study takes an evolutionary perspective, therefore the concept of SSI is considered an appropriate framework.

Breschi and Malerba (1997, p.131) first introduced the SSI and defined the approach as "…a system (group) of firms active in developing and making a sector's products

and in generating and utilising a sector's technologies; such a system of firms is related in two different ways: through processes of interaction and cooperation in artefact-technology development and through processes of competition and selection in innovative and market activities". Another definition was later provided by Malerba as a "…set of new and established products for specific uses and the set of agents carrying out market and non-market interactions for the creation, production and sale of those products" (Malerba, 2002, p.250).

The SSI builds on five pillars as shown in Figures 4.1 and 4.3, which are: knowledge and technologies, actors (i.e. firms and other organizations) and networks, as well as institutions (e.g. standards, laws, rules and regulations) (Malerba, 2002, Malerba and Mani, 2009, Malerba and Orsenigo, 1999). Thus, in order to understand the dynamics and the innovation processes of a given sector, due consideration to these key elements should be given. According to SSI thinking, successful new technologies emerge from a favourable combination of all of these factors.

The literature on SSI strongly emphasizes differences in the knowledge base, the heterogeneity of agents, and the variety of organizations involved in sectoral innovation systems (Castellacci, 2008). This focus on specific sectoral characteristics leads scholars to suggest that sectoral innovation systems are characterized by the interactions between agents and institutions at various geographical levels (Carlsson et al., 2002, Malerba, 2004).

4.5 Sectoral Systems of Innovation Building Blocks

Whilst the NIS fails to consider industrial factors in its conceptual framework, the SSI concept allows mapping out of actors and innovation capabilities at the industry level (Malerba and Mani, 2009). As previously mentioned, the notion of sectoral systems has the evolutionary theory and innovation systems approach as building blocks. This study seeks to examine three main elements within the medical device sector, which are the regulatory changes (content), the drivers of regulatory change and the impact of regulatory change on industrial capability to develop affordable health technologies for the local population. Using building blocks of SSI initially presented in Figure 4.1, the three complex phenomena under examination are mapped accordingly as shown in Figure 4.3 below and is followed by an explanation of each building block

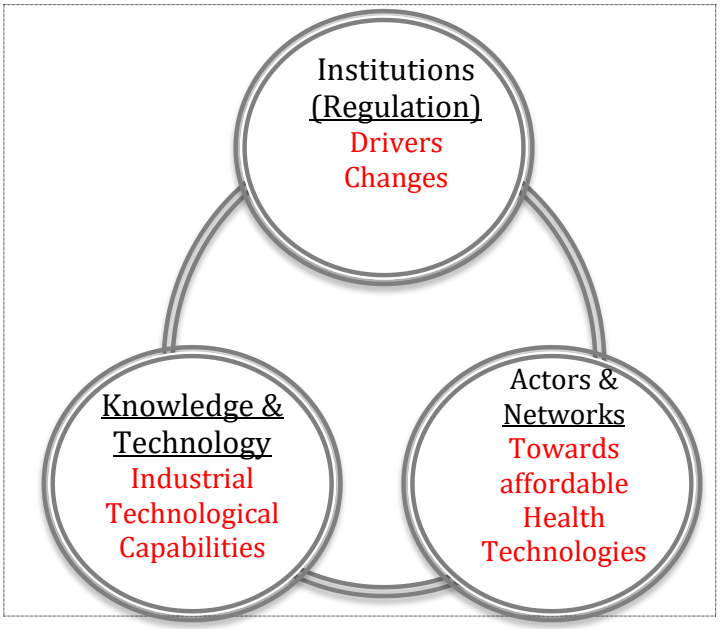


Figure 4.3: Malerba and Mani (2009)'s building blocks of sectoral systems of innovation. Author's additions in red.

4.5.1 Knowledge and Technologies in SSI

The evolutionary theory places major emphasis on dynamics, which in general means constant change. The same holds for the SSI technology building block. The history of technology is contextual to the history of industry structure associated with that technology (Dosi, 1982). Technologies change over time and affect an organization's learning and production processes (Patel and Pavitt, 1997). Technologies tend to increase (rather than decrease) specialization and complexity in the organization (Pavitt, 1998). Technologies come in different forms (Granstrand and Sjölander, 1990). Dosi (1982, p. 152) defined technology in a broader sense as "a set of pieces of knowledge, both directly "practical" (related to concrete problems and devices) and "theoretical" (but practically applicable although not necessarily already applied), know-how, methods, procedures, experience of successes and failures and also, of course, physical devices and equipment'.

The medical devices sector is a high technology multi-disciplinary sector whose key components are medicine, engineering and information technologies. It is in close relation with pharmacy and has been reported to converge with pharmacy as well. This study aims to put forward the main building blocks of the medical devices sector in the UK and SA. While doing so, pharmaceuticals are taken as a reference point at

times since medical devices and pharmaceuticals are two relevant components of a healthcare supply and pharmaceuticals are subject to more variety and number of studies than medical devices.

The mechanisms of learning are at the heart of the evolution-based SSI approach. In this regard, Lundvall (1992) suggests that the most important resource in the modern economy is knowledge and, accordingly, the most important process is learning. Malerba and Mani (2009, p.10) state that 'knowledge affects the types of learning processes and the relevant capabilities that firms have in order to be competitive and innovate'. Knowledge, especially technological knowledge, involves varying degrees of complexity, complementarity and independence, and differs in terms of its source, domains and its application (Cowan et al., 2000, Malerba and Adams, 2014). In terms of learning, firms accumulate knowledge through internal processes as well as through processes that involve interaction with external actors that have varied knowledge and capabilities (Malerba and Adams, 2014). Capabilities refer to the ability to absorb, develop, and integrate tacit and codified knowledge and to use it for specific functions, application and technological and productive transformations (Dosi et al., 2000). The analytic framework in this study is underpinned by the notion of technological capabilities as shown in Figure 4.1, thus the SSI knowledge base building block will be used to help unpack the complexities related to industry capabilities such as technology transfer and domestic independent R&D.

4.5.2 Regulation as a Defining Institutional Element of the SSI

Institutions are the rules of the game, they not only shape the interactions of actors, but they are also shaped by the interactions and activities of actors (Malerba, 2004, Fagerberg and Godinho, 2005). This view is based on evolutionary theory which emphasize that a wide range of institutions (infrastructure, regulation) are shown to be co-evolving with technology (Nelson, 1995). Regulation is viewed in this study as a dominant feature of the institutional environment. These institutions affect the actions of sector participants (Malerba, 2005).

As shown in Figure 4.1, regulatory regime is not static, but changes over time and is the product of a long-term process of regulatory decision-making (Kramer et al., 2012a). Because of regulatory change, access to the market becomes more complex

and burdensome for medical devices manufacturers (Eisenberg, 2012, Kaplan et al., 2004). However, inefficiency of regulatory change is not always a consequence of the policies design; it can arise from their inadequate implementation (Von Tunzelmann, 2003). It is with this thought in mind that this study focuses on further research by asking the question what is the impact of regulatory changes on industry's ability to manufacture and supply affordable healthcare technologies.

4.5.3 Actors and Networks in SSI

A sector is composed of heterogeneous agents ranging from individuals to organizations (Malerba 2004). Individuals include: consumers, entrepreneurs, and scientists influencing the innovation process of the sector. Organizations include firms and non-firm organizations too, such as university, financial institutions, government agencies, trade unions, local authorities and technical associations. Firms are the key actors of SSI, they play a big role in the innovation and production processes, in the sale of products, the generation, adoption and use of technologies. The evolutionary perspective considers that firms evolve over time when they attempt to adapt themselves to their regulatory environment (Malerba and Mani, 2009). It is anticipated in this study that the adaptation process has implications on activities undertaken by firms in the production of affordable new healthcare technologies as indicated in Figure 4.1. The actors specifically analysed in this study are firms operating in the medical device sector and regulators in the UK and SA.

In terms of networks, the variety of links and connections among agents greatly affects the dynamics of sectoral systems (Malerba and Adams, 2014). In manufacturing firms, it is important for R&D departments to be connected to production (Pavitt, 1994). In cases where knowledge is not produced in R&D departments but elsewhere, network connections between actors (individuals and organizations) are important connections, which can exist along supply, production and distribution channels as well (Bell and Pavitt, 1995, Sutton and Barto, 1998).

In examining the medical device sector using the help of the SSI framework, its theoretical bases and its building blocks, it is anticipated that the study will be able to identify in detail factors such as knowledge base underpinning regulation, innovative and production activities in the medical device sector.

4.6 Institutional theory

Institutional theory has traditionally been concerned with how organizations establish their positions and achieve legitimacy in order to survive and make profit. This has been done by conforming to the rules, norms and social structure of the institutional environment (Meyer et al., 1991, Schot and Geels, 2007). The institutional environment is set up of institutions, a term that refers to the regulatory, social and cultural aspects that exert pressures on organizations to adapt to the surrounding environment. These aspects define what is considered appropriate behavior and therefore exert conforming pressures on organizations not to act in an unacceptable manner (DiMaggio and Powell, 1991). Scott (2005) summarized the pressures of the institutional environment first identified decades ago into three pillars. These are regulative, normative and cognitive pillars.

The regulative pillar guides organizations behavior by governmental legislation, industry agreements and standards for example. The normative pillar guides organizations in interaction with other actors by defining what is expected and appropriate in different situations, such as social or commercial situations. Values and norms are central to the second pillar, establishing the softer rules that organizations conform. The last and third pillar is derived from social behavior at a more individual level, such as cultural differences and language. This cognitive pillar is important because it highlights the taken-for-granted and preconscious behavior present in the institutional environment that defines the right thing to do and is important for new actors to understand. These three pillars may resemble each other and often reinforce one another in a particular institutional environment (Scott, 2005). The importance of these pillars is significant because if a company fails to understand any of them the company can risk losing legitimacy (Kostova and Zaheer, 1999).

Organizational legitimacy is defined by Suchman (1995) as “a generalized perception or assumption that the actions of an entity are desirable, proper, or appropriate with some socially constructed system of norms, values, beliefs and definitions”. Therefore, in order to be successful, the firm needs to fit in with different institutions (authorities, potential business partners, customers or governments) that defines the normative, cognitive and regulative rules (Kostova and Zaheer, 1999). If the firm breaks the rules and thus do not obtain adequate legitimacy at any market, it can

hinder company survival.

Institutional theory is a dominant theory that "has been widely used to analyse and explain corporate responses to environmental and social issues" (Hahn et al., 2010, p. 221). Institutional theory not only concerns how organizations are influenced by external pressures, but also describes how organizations influence others (DiMaggio and Powell, 1983). With the guidance of this theory as presented in the conceptual framework in Figure 4.1, it is believed that this study will be able to unpack and further understand the effects of regulatory change on organizations that are seeking to establish their market positions and achieve legitimacy in order to survive.

4.7 Regulation and Policy Instrument

Enabling policies are likely to have a more rapid impact and are less expensive to monitor and enforce. The third research objective of this thesis is to investigate the "effects" of medical device regulatory changes on industry capabilities and development of affordable medical devices in the UK and SA. The intended outcomes therefore should be evidence based. To unpack this research objective, a regulation and policy instrument that reflects perspectives from company managers in responding to regulatory initiatives and emphasizing on the effectiveness and efficiency of regulatory instruments will be adopted (see Figure 4.1). Chataway et al. (2006) proposed this instrument by categorizing policies and regulations according to whether they are perceived as enabling or constraining by industry managers or whether they were seen as indiscriminate or as discriminating among products.

On the one hand, enabling or constraining regulatory policies can have a major impact on their effectiveness and on the cost of implementation. On the other hand, indiscriminate policies are usually much less effective than intended, or can even have negative, counter-intuitive effects on the regulatory target (Chataway et al., 2006). Enabling regulation serves both as the legislative mandate for the competent authorities to act, and as a starting point for these regulators' discretion and oversight. The enabling content will allow for the control and the evaluation of the performance of the regulation. The latter can only be carried out where a well-defined and focused set of objectives in the founding regulation exits (Frank, 2003). Good governance is most likely to be achieved by creating a policy and regulatory environment that is enabling in the desired direction, rather than being constraining and restrictive, and

also that discriminates among products on the basis of the most relevant criteria (Chataway et al., 2006).

4.8 Conclusion

This chapter has reviewed theories, concepts, and research studies regarding medical device regulation and industrial capabilities. The Sectoral Systems of Innovation (SSI) approach as a theoretical framework has been emphasized and will be employed to analyze the influence of regulatory changes on industrial capabilities. The study of regulatory reforms is a study of a change process. Generally, the SSI, anchored in evolutionary theory, has a dynamic perspective and takes a process view in a co-evolutionary setting (Malerba and Mani, 2009), therefore the concept of SSI is considered as an appropriate framework. Evolutionary theory is used to explain the changes of medical device regulation over time. The behavioural foundation of the evolutionary theory rest on learning processes involving adaption and new discoveries (Dosi and Nelson, 1994). In the evolutionary view, technological development and innovation play an important role in the sense that innovation brings about the changes in the system and influences the selection process.

The analytic framework in this research is underpinned by the notion of technology capabilities. As Dosi et al. (2000) point out that a firm can only successfully develop if it comprehensively utilize its present capabilities. Essentially, the effects of regulation on firm level technological capabilities will be examined in the rest of the chapters in this study using Lall (1992)'s functions model, which is made up of "investment", "production" and "linkage" capabilities.

As a methodological and empirical contribution, this study has used Chataway et al. (2006) policy and regulatory instrument empirically, in a detailed way. It was previously used only in a generic way. We have been able to show its utility in the analysis of different types of firm capabilities in a specific way. The next chapter presents the scope of the research, and details how the research was conducted.

CHAPTER FIVE
THE STUDY RESEARCH METHODOLODY

5.0 Introduction

The previous chapter presented the theoretical framework of this study. This chapter presents the scope of the research, and details how the research was conducted. It will first present the philosophical position of this study and methodological issues leading to the choice of methodology. The research strategy then explains the reasons for using the case study approach and discusses key characteristics of case study quality. Case study design is explained, consisting of the importance of context, the unit of analysis, and a sample selection of the firms, as well as the criteria and process. Data collection methods and data analysis strategy employed are also presented.

5.1 Research Philosophy

The research questions in this study focus on how medical device regulations have evolved, the impact of changes on industry capabilities and contribution to affordable healthcare technologies. Therefore the underlying approach to the research strategy and research design is based on the regulatory realities in terms of knowledge, technologies, institutions, actors, networks, process of change and transformation within the medical sector (Malerba and Mani, 2009). A research philosophy is a belief about how data about a phenomenon is gathered, analysed and used. There are two main research philosophies commonly used in western traditional studies namely the positivist and interpretivist paradigms (Galliers, 1991). There is also a philosophical position called ‘‘Critical realist’’, formulated by Bhaskar (1975) and extended by a number of authors including (Archer, 1995, Collier, 1994, Danermark et al., 2001, Lawson, 1996, Layder, 1990, Outhwaite, 1987, Sayer, 1992).

Positivism is largely concerned with the testing, confirmation and falsification, and predictive ability of generalizable theories about an objective, readily apprehended reality (Orlikowski and Baroudi, 1991). The positivist position was considered as a possible option, but not used for this study because the position adopts a hypothetic-deductive approach (Hempel, 1965), where hypothesis are tested (mainly quantitatively) in line with Popper’s principle of falsification (Grennes, 2001). This study however does not intend to formulate a hypothesis. Interpretivism on the other hand focuses on understanding the subjective meanings that participants assign to a

given phenomenon within a specific, unique context (Orlikowski and Baroudi, 1991). The interpretivist position will also not be used for this study for two reasons; firstly, the position adopts a relativist stance ‘‘such that diverse meanings are assumed to exist and to influence how people understand and respond to the objective world’’(Gephart, 2004, p.456). Secondly, interpretivists aim to ‘‘interpret the meanings and actions of actors according to their own subjective frame of reference’’ (Williams, 2000, p.210).

Critical realism is a theory-driven approach focussed on understanding the mechanism of what works for whom in what circumstances and how structures worked or did not work in their contextual setting, rather than simply measuring outcomes (Pawson and Tilley, 1997). The nature of reality of critical realism is objective, stratified reality, that is, domains of the real, actual, and empirical (Bhaskar, 1975, Sayer, 1992). Domains of “empirical” include observable experiences. Domain of “actual” includes actual events, which have been generated by mechanisms. Finally, the domain of “real” includes the mechanisms that have generated the actual events, Figure 5.1 illustrates the three categories in the realm of realism (Bhaskar, 1975).

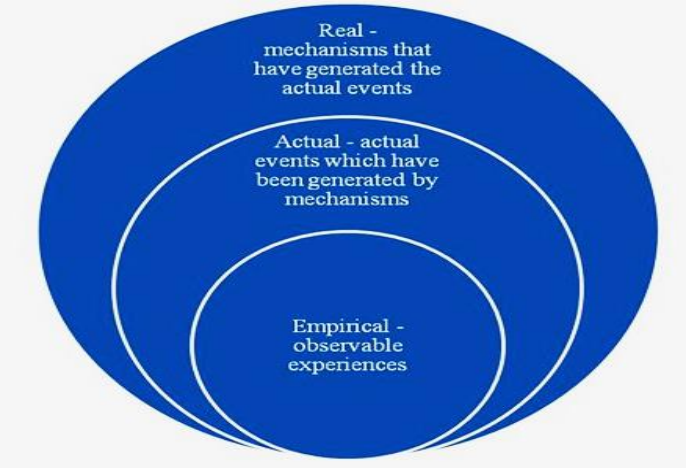


Figure 5.1: Schematic representation of three domains of critical realism
Source: (Willcocks and Mingers, 2004)

According to the critical realism perspective, knowledge can be required of that reality through abduction mechanisms (Sayer, 1992). Critical realism acknowledges the role of subjective knowledge of actors in a given situation as well as the existence of independent structures that constrain and enable these actors to pursue certain

actions in a particular setting (Wynn and Williams, 2012).

The philosophical position of this study is critical realism. The basis for the choice for this approach is that this philosophical position provides more detailed explanations of a given set of phenomena or events in terms of both the actors' interpretations and the structures and mechanisms that interact to produce the outcomes in question (Wynn and Williams, 2012). This study proposed not only to examine events (regulatory changes and impacts) in the empirical domain, but also aims to understand the generative mechanisms in the real domain leading to the event (drivers). Given the epistemological principles of critical realism, Easton (2010, p.123) states that "the research questions could be of the form 'What caused the events associated with the phenomenon to occur?'" By asking about the causes of specific events, we are targeting the how question associated with explanatory case research (Yin, 2003). A critical realist philosophy provides an appropriate framework to investigate the impact of evolving medical device regulation on industrial capability to develop affordable healthcare technologies and will guide the development of the research strategy.

5.1.1 Research Strategy

Having adopted critical realism as the philosophical position of this research, and in order to provide some valid and reliable scientific claims from the research process, a concurrent mixed-methods data collection and analysis approaches was used (Bryman, 2007). Mixed methods, in which quantitative and qualitative methods are combined, are increasingly recognized as valuable, because they can capitalize on the respective strengths of each approach (Jick, 1979, Tashakkori and Teddlie, 2010). Exposure to a broader range of perspectives and experiences can in turn assist with the formulation of explanation (McEvoy and Richards, 2006, Borkan, 2004). The combination of qualitative and quantitative methods enables research findings, to be further reinforced (McEvoy and Richards, 2006).

5.2 Case Study Research Methodology

This study consists of three case studies of regulatory changes (two of them set in the UK and one in SA) and uses a variety of methods to generate data. A case study methodology is defined as an intensive investigation of a contemporary phenomenon within its real-life context, and where the boundaries between phenomenon and the context are not clearly evident (Yin, 2009, Benbasat et al., 1987). Cases can include

studies of decisions, individuals, organisations, processes, programs, neighbourhoods, institutions and events (Yin, 2003). Case studies are also the preferred research strategy when researching a topic on which very little is known (Bengtsson et al., 1997, Schwandt, 1997). The approach is based on compiling multiple sources of evidence to examine; the relationships, complex links and working procedures that requires continuous interaction between the research questions and the data being collected (Yin, 2013). Furthermore, this study aims to trace the regulatory changes and the premarket entry activities of the medical device firms over time, and thereby understand the connection between them. Case study research is an ideal research tool for processual studies (Langley, 1999, Pettigrew, 2012) as it can open up the processes that lead to individual and organized actions (Doz, 2011), and is able to interpret the complexity of context (Birkinshaw et al., 2011).

There are some criticisms made of case study research methods due to "the problem of relevance of other cases, sometimes expressed in other traditions as generalizability" (Gerrish and Lacey, 2006, p.303). In other words, critics of case study methods believe that the findings cannot be generalized to similar populations especially when they are single case studies or if the sample sizes are considered small (Kader, 2006). However, Eisenhardt (1989) indicates that using comparison of the emergent concepts or theory with existing literature can enhance generalizability of multiple-case studies. In short, the use of theory, in conducting a multi-case study, not only supports the appropriate research design and data collection, but also becomes the main vehicle for generalizing the findings of the case study (Yin, 2003). Furthermore, when conducting multiple-case, the findings are generalized from one case to the next on the basis of a match by means of conceptual or theoretical grounds for the underlying theory or for the research setting/context not on representative grounds and not to a large universe (Miles and Huberman, 1994).

This study is an empirical inquiry of the evolution of medical device regulation and its impact on industrial capabilities and development of affordable healthcare technologies. Very little is known about this topic, especially in Africa, hence necessitating the need for a case study approach. In addition, historical, political and cultural contexts in which the cases are situated present many variables that affect the development of affordable devices and their commercialization. A number of similar

studies reviewed adopted the case study approach, for example, studies such as those; on national health biotechnology innovation systems (Chataway et al., 2007, Mugwagwa, 2010, Smith, 2005); on regulatory and industrial policy hurdles for medical device industry (Davis and Abraham, 2011, Ensor and Weinzierl, 2007, Heneghan et al., 2011, Rugera et al., 2014, Gollaher and Goodall, 2011) and on health social technologies (Chataway et al., 2010).

5.2.1 Selection of Regulatory Change Cases

It is well recognized that proper case selection is imperative for understanding the phenomenon under study (Yin, 2003). In the context of multiple case study research, the chosen cases need to be similar in some ways, be relevant, provide sufficient diversity across cases, and present good opportunities to learn about complexity and contexts (Yin, 2009). In this study, the selection criteria for the three regulatory change cases were established based on theoretical considerations, factors of the research design and the research question. Criteria included the presence of significant perceived impact, indications of differences in impact between firms, and the availability of empirical data relevant to the study. In particular, the two regulatory change cases in the UK were highly significant for the medical device industry; and, each regulatory change was different: one was a major extension of regulatory reach into medical device software; the other a major toughening of regulatory compliance and therefore a strong strengthening of regulatory processes. The selection criterion for the SA radiation emitting devices regulatory change was based on the fact that this was the only type of formal medical devices regulation in the country that had been implemented long enough to provide empirical data relevant to this study. A better understanding of the impact of the selected regulatory changes will reveal differences in the firms' responses and thereby uncover key dynamics related to firm strategy, innovation and operations. The three selected regulatory change cases were informed by a group of firms whose activities were related to the development of healthcare technologies. (In-depth case study details of the three regulatory changes are presented in chapter six).

5.2.2 Criteria for Selecting Medical Device Firms in the United Kingdom

The study adopted purposive sampling method in selecting suitable manufacturing firms. Purposive sampling, also called judgement sampling, is a non-probability

sampling technique, which involves selecting study participants deliberately because of some qualities/characteristics they possess (Tongco, 2007). The first criterion set to identify suitable UK-based firms for this study was that the firm should fall under medical device software segment. The study was interested in eliciting the most important challenges with respect to developing embedded or standalone software for medical purpose, understanding the extent to which the regulations that have been developed, recognized and have affected the industry's capabilities. Another reason for selecting firms involved in the development of medical device software was that, today, many medical devices cannot fulfill their intended use without the software embedded within them, which implements a variety of functions and features. Surveys of trends in the medical device industry indicate that software is one of the most decisive factors for producing innovative products with new capabilities, and predict that the importance of software will only further increase in the future (Denger et al., 2007).

A second criterion was set based on the longevity of the firm's operations in the medical device industry. The firm should have been registered and in operation in the UK since the publication of first major regulatory changes in 2007. Potentially, the longer these firms were in the UK medical device industry, the more changes in operations they may have encountered, which may have been made in response to the change in the external regulatory environment. The long establishment also indicates firm learning to adjust quickly to regulatory changes so that they can continue operating.

The third requirement was to pursue firms that had available public company accounts so that annual reports and other public records could be examined to make sure these UK firms have operated for more than ten years[18] and establish whether regulatory changes had influenced firm' technological capabilities such as investment and production capabilities. A sample of 16 firms selected in the UK is presented in the Table 5.1 below.

[18] Ten years is an arbitrary figure. However, based on UK Company house reports, several medical device firms that have been in operation for more than ten years are significantly more profitable than those counterparts with less than ten years' experience.

Table 5.1: United Kingdom firm selections (source: author calculations, company website and annual reports)

Firm Name	Respondent Position	Firm Background	Device Segment/ Key Product(s)
Alpha Ltd	Quality Manager	-Year established: 1975 -Size: SME -Employee size band: 20 - 49 -2017 Turnover: £1.3 million -Exports to over 28 countries -Approved supplier to a wide range of customers, including the UK NHS and private hospitals	-Embedded software devices -Oxygen-therapy products -Electrical magnetic products.
Bravo Ltd	Medical Devices Principal Consultant	Year established: 2006 Size: SME Employee size band: 0 - 4 2017 Turnover: £500 000	- Orthopaedics - Biosensors - Embedded software
Charlie Medical	Director of Regulatory Affairs	Year established: 1978 Size: SME Employee size band: 100 -249 2017 Turnover: £17.2 million	- Embedded software - Wound care products - Blood processing products
Echo Ltd	CEO	Year established: 2007 Size: SME Employee size band: 5 - 9 Turnover: Not disclosed	- Medical device software - Radiotherapy simulators - Software in radiotherapy liner accelerators - DNA specification technology
Foxtrot Ltd	Chief Operations Officer	Year established: 1992 Size: SME Employee size band: 50 - 99 2016 Turnover: £5.2 million The firm has over 3,000 CardioQ-ODM systems Exports their product to over 40 countries	-Cardiac flow monitoring devices - Fluid Management devices
Garner Ltd	Senior Quality Assurance Director	Year established: 1977 Size: SME Employee size band: 100 - 249 2016 Turnover £24.4 million	-Innovative diagnostic test kits
Hex Ltd	Technical Director	Year established: 1994 Size; SME Employee size band: 10 -19 Turnover: £825 904	Medical device software development
Indigo Ltd	Managing Director	Year established: 2007 Size: SME Employee size band: 0 - 4 2017 Turnover: <£100 000	-Embedded software -Surgical instruments decontamination products

Kilo Ltd	Chairman	Year established: 1986 Size: SME Employee size band: 50 - 99 2017 Turnover: £6 million	-Urodynamic products CT3000
Delta Ltd	Associate Director Regulatory Affairs	Year established: 1998 Size: MNC Employee size band: 250+ R&D employees – 122 Sales & marketing -113 Administration – 48 Manufacturing – 29 Total employees - 312 2016 Turnover: £1.51b	-In-Vitro Diagnostic products -Oncology products - Novel technologies for the analysis of DNA - Gene sequencing
JM Medical	Managing Director	Year established: 1971 Size: MNC Employee size band: 250+ Production employees – 701 Administration and support -110 Sales employees – 124 Total employees - 935 2016 Turnover: £206.2m Two Nobel Price-winners in the world. Ranked in the third place among the medical device manufacturers in the world.	-Cardiac conduit monitors -Diagnostic cardiology -Ultrasound -Patient monitoring - CT scanning -MRI
Lima Medical	Head of Operations	Year established: 1991 Size: MNC Employee size band: 250+ Average number of employees – 1 802 2016 Turnover: £579m	-Radiology -Radiosurgery -Proton therapy -Wound care
Med Tec Ltd	CEO	Year established: 1986 Size: MNC Employee size band: 250+ 2017 Turnover: £408 million	-Oncology products -Radiotherapy products -Software development
Neiva Medical	Director	Year established: Size: MNC Employee size band: 250+ 2016 Turnover: £3.78b	-Knee and hip implants - Arthroscopic enabling technologies - Advanced wound care devices
Optics Ltd	Director	Year established: 1954 Size: MNC Employee size band: 250+ 2016 Turnover: £58.1m	-Diagnostics systems - Integrated analytics solutions technologies - Infusion devices and software

As Table 5.1 shows, care was taken to study both MNCs and SMEs. The firms highlighted in darker shade are SMEs and the non-highlighted are MNCs. The rational for choosing UK-based firms for this study is because the UK represents the global north with sophisticated medical systems, it meets the criteria for appropriateness of the study as it has advanced local healthcare technological capability (BMI, 2016b), has a highly regulated industry structures and there has been a significant but complex regulatory evolution since the 1990s. The UK medical device industry was considered a well-developed market in a global comparison (Evaluate Medtech, 2017). Hence, the observation of this industry promises insights

that should be of relevance also for a global audience (including academic and practitioners alike).

Given the nature of the research question, this study consisted of two kinds of empirical data (Chapter 7) and it was considered valuable to focus first on data from sixteen UK-based manufacturing firms presented in Table 5.1. The sixteen firms all have distinguished histories and well-known reputations for providing advanced healthcare technologies. The sixteen firms were selected to develop a deeper understanding and provide a broad scope of the effects of the two significant but different regulatory changes on the firm level technological capabilities. Among the sixteen firms, three were found to have appropriate data to support their inclusion for detailed firm specific empirical analysis. Therefore, the second empirical data involved a more comprehensive narrative of these three purposefully selected UK-based firms.

5.2.3 Criteria for Selecting Medical Device Firms in South Africa

Some criteria were set to identify suitable SA-based firms for this study. First, the firm should have been involved in the manufacture or supply of electromagnetic medical devices or radiation emitting devices. The reason was that this is the only segment that has been regulated for a longer period through the Hazardous Substances Act, No. 15 of 1973 (DoH South Africa, 2014). Devices for use in radiology usually are not targeted at individual patients but at hospitals and doctors' practices. They include ultrasound and microwave imaging and treatment devices, and magnetic resonance imaging equipment (MRI). The second criterion was simply based on the longevity of the firm's operations in the SA medical device industry. Company selection was made with these key criteria but the chosen firms were otherwise diverse with respect to geography, core technological focus area(s), and capabilities not directly related to innovation, ownership structures, history, age, local context and so on. The approach taken to select the final firms was essentially based on the approach proposed by Yin (1994), which involves screening "candidate" firms and choosing the best among them.

To illustrate more specifically, my approach for the SA firms was to first make a database of all companies that I could find, which met the two key conditions (this

resulted in a list of over 50 firms). I then looked for and recorded any information that indicated whether a given firm undertook innovative activities. The latter was complemented by consultation with individuals who were knowledgeable with domestic medical device firms. These efforts helped me to identify an initial 12 companies, which were then instrumental in identifying more firms along with other local informants that I met as I travelled through SA. A sample of 16 firms selected in SA firms is presented in the Table 5.2 below.

Table 5.2: South Africa firm selections (source: author calculations, company website and annual reports)

Firm Name	Respondent Position	Firm Background	Device Segment/ Key Product(s)
Southmed (Pty) Ltd	Managing Director	Year established: 1987 Size: SME Employee size band: 100 - 249	-Electro-medical devices and medical consumables - Ultrasound imaging - Radiology devices
DK med Supplies	CEO	Year established: 2007 Size: SME Employee size band: 0 - 4	- X-RAY Imaging Systems
BV Medical	Projects Manager	Year established: 1994 Size; SME Employee size band: 10 -19 Turnover: £825 904	Medical imaging**:** -X-ray Machines -CR - Computed Radiography -DR - Digital Radiography -RIS - Radiology Information
SISA Manufacturing company	Regulatory Affairs and Quality Officer	Year established: 1989 Size: SME Employee size band: 20 - 49	- Diagnostic equipment: -X-ray Machines -Ultrasound medical products
AA Biomedical (Pty) Ltd	Reimbursement and Regulatory Affairs Manager	Year established: 1998 Size: SME Employee size band: 50 - 99	- Cardiac diagnosis and Cardiac Rhythm Management product range - Electrophysiology
TM AFRICA (Pty) Ltd	Director	Year established: 2001 Size: SME Employee size band: 20 - 49	- Radiology equipment - Magnetic Resonance Imaging (MRI)
UMC (Pvt) Ltd	Managing Director	Year established: 1991 Size: SME Employee size band: 20 - 49	-Radiology -Radiosurgery -Wound care
Gabler Medical	CEO	Year established: 1963 Size: MNC Employee size band: 250+	- Electric and pipeline suction equipment - Flow meters
CR Medical	CEO	Year established: 1960 Size: MNC Employee size band: 250+	- Medical imaging equipment for breast cancer diagnosis

PH Healthcare	Senior Quality & Regulatory Systems Manager	Year established: 1919 Size: MNC Employee size band: 250+	- Radiology products
SSA (Pty) Ltd	Strategic & Key account Manager	Year established: 1864 Size: MNC Employee size band: 250+	- X-RAY Imaging Systems
Northmed Healthcare	Projects Manager	Year established: late 1892 Size: MNC Employee size band: 250+	- Embedded software - Wound care products - Blood processing products
Medtech Solutions	Director	Year established: 1987 Size: MNC Employee size band: 250+	- Electronic implantable hearing aids - X-ray units - X-ray machines
BS Medical Specialists	Health Economics & Government Affairs Manager	Year established: 1979 Size: MNC Employee size band: 250+	Radiology equipment
PE Medical company	Sales Account Manager	Year established: 1975 Size: MNC Employee size band: 250+	- Screening and diagnostic equipment

The rational for choosing SA-based firms for this study was because they represent global south countries that are less often included in comparative studies but offer valuable insights to the healthcare technologies that are often overlooked. In addition to the SA medical device industry's suitability from a research design perspective, there is also a good theoretical fit. The effect of implementing new requirements in connection with regulatory change could be expected to evolve over long periods of time (Jacobides and Winter, 2010). SA has low local healthcare technological capability (BMI, 2016a), has less regulated industry structures and slow regulatory evolution over the past three decades. To isolate the effects of a regulatory change, it is to our advantage if the other dynamics of the SA medical device industry are slow, because the firms' actions will be more visible. However, SA has a relatively large economy and has the largest medical device market share in Africa. The above combination of empirical and theoretical factors offers a solid rationale for studying this industry with a historical approach over a long time period (Ferraro and Gurses, 2009).

The empirical evidence from SA presented in this study (Chapter 8) also comprised of two kinds of empirical data. The first type of empirical evidence involved comparative analysis of sixteen SA manufacturing/distribution firms that supply

medical and dental diagnostics as presented in Table 5.2. The second type of empirical evidence involved a more comprehensive narrative of three purposefully selected SA-based firms. Criteria for selection of the three firms were based on availability and accessibility of the firm's empirical data pertinent to the study.

5.2.4 Analytical Units

Yin (2009, p.29) suggests that analytical units are selected according to the research topic and can include single individuals, programs, events, decision and so on. This research employs evolutionary theory which takes the firm as its unit of analysis, with the proposition that organizational capabilities are central to an understanding of firms and industries (Malerba and Mani, 2009, Nelson and Winter, 1982). Building on that the analytical units to be used in this research are regulation and medical devices firms. Among the possible analytical units, the regulatory policies are frequently chosen as analytical units for the comparisons with each other.

5.3 Data Collection Methods

It was the aim of the research that the answers to each sub-question would inform the overarching question at the center of this study. Accordingly, four data collection methods were used some of which were used in parallel to address the sub-questions. The methods used were in-depth interviews, focus groups, document analysis, and archival research.

Interviews: The main method of collecting primary data for this study was semi-structured in-depth interviews and was conducted mainly in the respective firms. Part of the objective of using interviews was to be able to access and subsequently understand the regulation of medical devices phenomenon through descriptions of it, in the participants' own words. This format allows the respondent to identify and describe concerns or concepts that may not have been anticipated or considered by the researcher (Curry et al., 2009). The study aimed at eliciting in-depth responses, personal accounts and experiences from actors in the medical device sector which provided insights and understanding of their identities, values, perceptions, experiences and the meanings they attach to regulation of medical devices and interviews are the best way to do this (Britten, 1995, Patton, 1999).

A total of four pilot interviews guided by the broad checklist of questions were

conducted telephonically and face-to-face with some stakeholders in the UK and SA during a field study between October 2016 and May 2017. After these pilot studies, which helped identify, confirm and shape key issues around medical devices regulatory changes in the UK and SA, a total 73 defined as guided conversations or semi-structured were conducted (see **Appendix 6** for the full list of interviews conducted). The interviews were conducted with a consistent line of inquiry that was two-fold: (1) Understanding the process of regulation and regulatory changes; (11) Understandings of the impact of regulatory changes. The chosen line of inquiry was to an extent based upon the theoretical framework in order to facilitate as easy and accurate analysis (Eisenhardt and Graebner, 2007). The interviews conducted with various stakeholder categories within the medical device sector are shown in Table 5.3.

Table 5.3: Categories of stakeholders who participated in the study

Stakeholder category	Number of interviews in the UK	Number of interviews in the SA	Totals
Government/ Competent authority	1	3	4
Regulatory agency/Notified body	4	2	6
Academic and research institution	0	3	3
Health facility	0	1	1
Medical device manufacturing	19	32	51
Industry association	1	7	8
Totals	25	48	73

As Table 5.3 shows, actors such as the notified bodies (that are involved in regulatory enforcement), national competent authorities and industry associations were also included. Although the focus was on medical device firms' perceptions (identified as the primary 'regulatees'), the study also wanted to know whether these were different from the views of other stakeholders. Most of the interviews took place in natural setting of the interviewees. Visits were made to the working sites (i.e. business premises or hospitals) of the participants to conduct the research. This enabled the development a level of detail about the individual or place in actual experiences of the participants. In some cases, the participants did provide medical devices company

records such as manual books and regulatory compliance documents to support the evidence of their innovative solution and regulatory challenges.

The duration of interviews and the number of questions varied among different participants and was determined by knowledge and willingness of participants to discuss issues. On average most interviews lasted for fifty minutes. All the interviews were digitally recorded and transcribed. Each interviewee was asked to suggest a person who may provide more information on the topic (referral sampling or 'snowball' method). Interestingly, most of the respondents referred to other potential respondents who were previously or planned to be interviewed confirming our approach. When getting references for further interviews I was careful to follow guidelines suggested by Dexter (2006): get introductions from trusted sources and avoid intermediary explanation of the project to avoid bias. This continued until the point of theoretical saturation, whereby no new information was being obtained from new interviewees. The interviews assisted in constructing the narrative and building up the analysis of this study. The interviewing protocol can be found in **Appendix 1 and 2**.

Besides getting references from previous interviewees I also participated in events and seminars where high-level representatives of government and medical device industry associations spoke. For example, I facilitated a session on Regulation in the diagnostics sector at the Southern Africa Network for Biosciences (SANBio) Annual Event held in February 2017 in South Africa; virtually all medical device sector representatives participated.[19] This provided me with valuable opportunities to make contacts and arrange new interviews.

Focus Groups: Data collection in this study included a participant-focus group that was held at CSIR offices in SA. By participant-focus group, we refer to the mode in which the researcher was not merely a passive observer. The researcher participated in the SAMED/SALDA (medical device manufacturers) focus group in SA in

[19] Proceedings and summary report of the SANBio annual event the researcher participated and facilitated can be found on http://www.nepadsanbio.org/sites/default/files/2017-05/SANBio%20Annual%20Event%202017%20-%20Proceedings.pdf

November 2016 (See **Appendix 6**). The group discussion focused on the guideline on essential principles of safety and performance for medical devices and IVD's, the regulatory requirements as well as question and answer session focusing on the industry's regulatory challenges.

Another focus group was conducted with three participants from the national medicines and healthcare products regulatory authority of Zimbabwe (MCAZ) via Skype to gather data from a regional point of view (See **Appendix 6**). This guided discussions with small groups of people who share a common characteristic central to the regulation of medical devices proved useful as a method of collecting primary data (Krueger and Casey, 2000). The goal for using focus groups in this study was to understand differences in perspectives between different stakeholder groups or categories of people and uncover factors that influence regulatory changes and the ability to develop affordable healthcare technologies in the medical device sector. This approach widened the range of responses and activated forgotten details of individual experiences (Krueger and Casey, 2000).

Document review: A wide variety of legal written materials served as a valuable source of data in this study. Documents included; institutional documents and organizational records such as clinical test records, compliance test records, R&D records, public medical device regulatory historical documents, legislative documents and approval documents. The documents were searched for and collected from the UK and SA's departments of health databases (e.g. the UK MHRA and SANAS databases), UK and SA's medical device industry association databases such as the ABHI and SAMED and also from EU commission database. The bibliography contains reference to each document reviewed. The study applied content analysis as a method to review documents. A content analysis is a strategy that generates inferences through objective and systematic identification of core elements of written communication (Holsti, 1969).

Collecting archival data: Archival research was performed in this study by examining historical records of organizations. Historical archives are well recognized in the case study method in both a historical and contemporary context (Easton, 1995, Yin, 2003). They can enable longitudinal research to cover a considerably longer

period of time to observe process and change, and they can provide the generous descriptions that case studies require (Pettigrew, 2012).

Some researchers consider archival research as a type of secondary data analysis, where the researcher will probably not have been involved in the data collection, but extracts information to answer their research questions (Bryman, 2007). Archival research could be considered as a continuation of the efforts of the interviewer to provide concrete evidence for the findings through the interview (Cassell and Symon, 2004). It deserves mention that using secondary data in archival research could save time and cost during the research process (Cassell and Symon, 2004).

The archival data collected in this study includes newspapers, company archives, public records, governmental announcements, etc. The archival data for the firms includes company histories, annual reports, press releases, and presentations throughout the years, as well as past interviews given by the executive and managers. These documents were obtained mainly from the firms through their corporate websites, and in some cases were requested directly during the interviews. In addition, technical and industrial journals and newspapers were scanned to identify relevant articles about these firms. These archival materials about the activities of the firms are valuable as they are rich in detail, which allows the researcher to have a better understanding of these past events. A weakness of historical data can be the difficulties of verification (Welch, 2000). As this research also includes interview data as well as a cross-check done whenever possible, it is therefore less of a concern.

Institutional Support and Practicalities of Data Collection

NEPAD-The Southern Africa Network for Biosciences (SANBio) and the Medical Imaging and Radiation Sciences Department (MIRS), University of Johannesburg in SA hosted the fieldwork visits (see Affiliation Letter in **Appendix 7**). The researcher was attached to these research and academic institutions whilst undertaking data collection. This afforded the opportunity to present the project proposal and findings to personnel at NEPAD SANBio and experts in the field of medical devices. This methodological cross-checking is perhaps worth noting. Association with these institutions also facilitated gaining access to certain individuals and organizations.

Data collection is SA was divided into two stages. An initial visit of two and a half months from the beginning of October to mid-December 2016 and a second visit of another two and a half months from mid-February to end of April 2017. There are certain advantages of designing the data collection phase as two distinct parts. For example, the interim provided a useful breather to reflect and if required ask for any clarifications. The interim period was also used to collect data from the UK-based firms.

5.4 Ethical Considerations

Ethical considerations are vital in the conduct of this research as it involves collection of data from people and organizations. A project registration and risk checklist for the research detailing the methods, nature of information being sought and types of participants was prepared for each type of data collection activity. It also included an assessment of the types of issues that may arise. The project registration, risk checklist and participant consent form were submitted and ethics approval obtained from the Open University Ethics Committee for all phases of this research (see **Appendix 3** for the research ethics approval memorandum). The necessary steps for ensuring anonymity and confidentiality were designed into the research schedule. Prior to the interviews, informed consent to participate in the interview was obtained from each interviewee as outlined in the ethical procedure spelt out from the Open University Ethics Committee. A copy of the consent form used for this study is provided in **Appendix 4**.

5.5 Data Analysis Methods

5.5.1 Thematic Analysis

The nature of the findings was mostly qualitative in this research (regardless of the findings of archival research). There was more emphasis on opinions and perceptions, rather than the numerical differences between the responses from different respondents. The qualitative interview data was therefore analyzed thematically with relevance to the research questions (Gillham, 2005). Thematic analysis can be defined as the interpretation of qualitative data through organizing it into codes, categories and themes (Boyatzis, 1998). It is a method by which patterns (themes) within the data can be identified, analyzed and reported, allowing the researcher to both organize data and interpret the research topic (Braun and Clarke, 2006). Extracting and

analyzing emerging themes, categories and codes from the data was an ongoing process throughout the research.

Both the UK and SA study questionnaires (see **Appendix 1 and 2**) were formulated on the basis of the research questions and also on the conceptual framework. It was divided into three parts. The first part was entitled background information – this was to elicit information about the nature and scale of operations of the company, regulator, industry association, notified body, consultant, etc. The second part was entitled understandings on regulation and regulatory changes. The aim here was to document what interviewees considered to be the primary norms operating within the regulatory space, whom did they identify as the key stakeholders and to benchmark what they considered to be the most important regulatory changes. The changes could relate to both normative as well other physical changes in the industry. In the third part, the interviewees were asked about their perception of the effects of regulatory changes on industrial capabilities and development of medical devices.

5.5.2 Thematic Analysis: the process

After the audio recordings were transcribed and checked, the scripts were re-read to gain further familiarity with the text. Coding, the process whereby all data (individual sentences and/or chunks of text) are assigned a descriptive label, was then conducted. The NVivo program was used to tabulate the transcribed data. Coding is referred to as *"the transitional process between data collection and more extensive data analysis"* (Saldana, 2009, p.4). In making sense of this mass of data, at the first stage key themes were generated, guided mainly by the research questions, the theoretical framework used and also by aspects that were reiterated by the interviewees. Thereafter, the ultimate analytical categories were selected through a process of iteration. The categories when seen as a set could help envelop the entire gamut of responses in a logically related manner that would address the research questions. The linkage between the analytical categories and the research questions have been further explained and presented in chapters 7 and 8 detailing the case study results.

5.5.3 Data Matrices

A data matrix is a way to present qualitative data as well as make an analysis. Matrices are essentially tables that consist of columns and rows representing

theoretical concepts and observations from research units. Data matrices were initially introduced by Miles and Huberman (1994) as a device to present data. Yet the decisions of the columns and rows need to rest on theoretical analysis of the data. Hence, data matrices can possess both a descriptive and an explanatory function Miles and Huberman (1994). Data matrices are frequently adopted by researchers conducting analyses on multiple units of research, e.g., firms or regulation (Nadin and Cassell, 2004, Averill, 2002). In this study, cross-case data was analyzed through a matrix containing different firm capability theoretical themes and the selected regulatory changes (categorized as either enabling or constraining and their sub-categories). Levels of sub-categories are included to indicate whether the regulatory changes were discriminating or indiscriminate among products on the basis of intended target. Detailed data matrix analysis is presented in the Cross-case analysis Chapter 9.

5.6 Conclusion

This chapter has described the methodological approaches employed in obtaining and analyzing data for this study, including the practicalities and ethical issues faced by the researcher. The data collection and analysis approaches employed all reflect a desire to adopt a holistic approach in dealing with this complex relationship between firms, institutions, health technologies and regulatory changes. Following on from this presentation and discussion of methodological issues, the next chapter gives further details on the three selected regulatory change case studies.

CHAPTER SIX
CASE STUDIES ON MEDICAL DEVICES REGULATORY CHANGES IN THE UNITED KINGDOM AND SOUTH AFRICA

6.0. Introduction

This chapter presents three case studies of regulatory changes that have been selected for this study. The research question discussed in this chapter is: What changes have been made to regulation of medical devices and what approaches were utilised by regulators to implement the changes in the UK and SA? Therefore, the aim of this chapter is to, first, analyze and explore the two regulatory change cases in the UK that were highly significant for the medical device industry. Each regulatory change was different: one was a major extension of regulatory reach into software; the other introduced unannounced audit visits therefore toughening regulatory compliance processes. Second, the chapter will also analyze and explore the regulatory change case of radiation emitting devices in SA that promoted safety in the workplace and prevented unnecessary exposure to radiation.

As discussed in the research methodology chapter, selection criteria of these three regulatory changes included the presence of significant perceived impact, indications of differences in impact between firms, and the availability of empirical data relevant to the study. The dates of the regulatory changes are sufficiently far back to permit long-term analysis, but not so distant as to make data access difficult. These changes are also well suited for exploring the impact areas outlined in the theoretical chapter (i.e. investments, production, and linkage capabilities). As such, the case narratives serve as an important basis for the analyses that follows this chapter.

6.1. Regulatory Change Case: Software as Medical Device in the UK

Failures in medical device software in the past have resulted in severe or fatal consequences. Between 1985 and 1987, according to McHugh et al., (2012) four people died and two were left permanently disfigured by a software-controlled radiation therapy machine known as Therac-25. Therac-25 used software to control a beam spreader plate, which reduced a patient's exposure to radiation. However, due to software malfunctions, the plate was not in place when required and patients received massive doses of radiation. This case highlighted the need for adequate safety

measures to protect patients and third parties i.e. clinicians, using medical devices controlled by software (ibid).

A revision to the European Medical Device Directive (MDD) 2007/47/EC was motivated by the past software failures and the request of the member states to expand and cover all aspects of community regulatory framework for medical devices made amendments to the original directive (93/42/EEC). The revision included all areas relevant to medical devices including risk and quality management.

6.1.1 New Requirements for the Development of Medical Device Software

The MDD 2007/47/EC regulatory changes required manufacturers to provide proof of clinical efficacy for all devices. In addition, the amendments made it mandatory for all customized medical devices to undergo post-market surveillance. It was also required that the patient for whom the device was customized should be given particular information (European Commission, 2007).

The most significant amendment within the MDD 2007/47/EC was the provision for standalone software to be used as an active medical device. The MDD 2007/47/EC Annex IX Section 1.4 states: *"stand-alone software is considered to be an active medical device". It defines an active medical device as "any medical device operation which depends on a source of electrical energy or any source of power other than that generated by the human body or gravity"* (European Commission, 2007).

The new regulatory requirements highlighted that software was to be considered as a medical device if its intended purpose is to be used for diagnosis, monitoring, treatment or alleviation (Klümper and Vollebregt, 2009). For software that qualifies as a medical device but is not yet CE-marked or is a new version that is not covered by the previous CE mark (for example, because it is an update to remedy a flaw that caused an incident), a manufacturer is prohibited from running that software in human tests outside of an approved clinical trial setting (Klümper and Vollebregt, 2009).

Therefore, safeguards must be put in place to ensure that such software is safe and fit for purpose. To ensure this, the amendment also states: *"the software must be validated according to the state of the art taking into account the principles of*

development lifecycle, risk management, validation and verification[20] *"* (European Commission, 2007). The MDD 2007/47/EC, therefore, marks the introduction in the European Union of stricter rules for software used with medical devices (Klümper and Vollebregt, 2009).

Since this requirement was introduced, software development firms must validate software whether integrated or standalone, regardless of device class. The "state of the art" medical device software processes is understood within the industry as developing software in accordance with the harmonised standard "International Electro-technical Commission (IEC) 62304" and other standards that are aligned with it (McCaffery et al., 2011).

IEC 62304 contains a number of processes for medical device software development and maintenance which firms are recommended to follow in order to implement medical device software best practices and to streamline the process of achieving regulatory approval. IEC 62304 as it is a software development standard; it does not cover or provide full guidance on system level activities such as validation and release. As a result, IEC 62304 roles off the system processes to aligned standards such as ISO 13485 which provides the comprehensive quality management system framework for the design and manufacture of medical devices and ISO 14971 which provides fundamental guidance on a product's intended use, determination of potential hazards, risk mitigation, and post marketing surveillance methods (McCaffery et al., 2011).

To summarise, IEC 62304 is a medical device software development lifecycle process standard. Software developed that follows to IEC 62304 activities and tasks is established upon the principle that the software is developed in accordance with a quality management standard (e.g. ISO 13485), a risk management standard (ISO 14971) and a product level standard (EN 60601-1) (Fiedler, 2017).

[20] Software verification and validation (V&V) is performed in order to ensure the quality of the software. Verification ensures that the software or product meets the requirements for it. In other words, that the software works as specified. Validation on the other hand is concerned with whether the software meets the customer needs and requirements. In other words, does the software work in its intended use.

The relationship between these standards and the EU medical device regulation is shown in table 6.1.

Table 6.1: Applicable Directive, Standards and Technical Report for the development of medical device software and achieving regulatory approval. Source: (Fiedler, 2017)

European Regulation	Medical Device Directive 93/42/EEC (Amendment 2007/47/EC)
Applicable Standards	ISO 13485 – Quality Management Systems, IEC 62304 – Software Lifecycle Processes, IEC 60601-1 Medical Electrical Equipment, ISO 14971 – Application of Risk Management
Technical Reports	IEC TR 80002-1

As Table 6.1 shows, medical device manufacturers wishing to achieve regulatory conformance are recommended to follow the relevant applicable standards. Evidence of the applicable standards can improve the process of achieving regulatory conformance.

Furthermore as shown in the Table 6.1 above, the device manufacturers' were required to prepare the technical documentation for the medical devices to demonstrate the conformity of the device with the MDD. Technical documentation has to cover the following aspects of the medical device: device description; raw materials and component documentation; intermediate product and sub-assembly documentation; final product documentation; packaging and labeling documentation; and design verification which includes the results of qualifications tests and design calculations relevant to the intended use of the device (MHRA, 2008a). Clinical data and manufacturing testing records are also required as part of the technical documentation (MHRA, 2008a). Manufacturing and test records are required to show compliance with the defined procedures and specifications. In the case of implantable devices, and in addition to existing requirements, manufacturers were now required to retain the technical documentation for at least 15 years from the last date of manufacture and keep it available for the national authorities (European Commission, 2007).

As part of the MDD 2007/47/EC amendment, there are other major areas, which have had a huge impact on medical device manufacturers: One area is that, prior to the

release of MDD 2007/47/EC, clinical data was only required when seeking regulatory approval for Class IIa, Class IIb and Class III devices. However, this has now changed and as a result clinical data must be supplied when seeking regulatory approval regardless of device classification. Clinical data is defined as safety and/or performance information that is generated from the use of a medical device (McHugh et al., 2012).

6.1.2 Outsourced Design and Manufacturing Process Requirement

The other area within the amendment of the revised MDD 2007/47/EC with important significance to medical device software development is outsourced design and manufacturing process. As part of the MDD 2007/47/EC amendment, should a device manufacturer outsource any part of the design or manufacturing process, then the manufacturer must be able to demonstrate that adequate controls over the whole chain of development of the software concerned have been put in place (European Commission, 2007).

Firstly, the medical device manufacturer must ensure that the supplier is fully utilising a quality management system such as the ISO 13485.

Secondly, the manufacturer must ensure that the development process of the software fits the requirements imposed by the new regulation and the applicable standards, such as EN 62304 (European Commission, 2007). To achieve this, the manufacturer must ensure that they know from where all the elements of their software originate i.e. the software should not contain any software of unknown provenance.

Thirdly, the manufacturer must ensure that all of the elements of the software have been developed according to the requirements in the annexes to the MDD and the applicable standards (European Commission, 2007). This means that it is also mandatory for third parties to conform to these requirements and standards.

Fourth, the manufacturer must ensure that they have access to or preferably ownership of the third-party developer's data that must be submitted in the technical file for CE-marking (European Commission, 2007).

Finally, the manufacturer must require that its subcontractors report any design changes in their software, as design changes may necessitate notification to the notified body that audited the software before it was altered and should be included in the manufacturer's technical file (Klümper and Vollebregt, 2009).

In summary, the effects of this first regulatory change are far-reaching, determining overall company strategies, which types of company succeed, and ultimately the structure and dynamism of the sector as a whole. The firms' actions related to the implementations of new requirements had an influence on their in-house capabilities and position in the market vis-a-vis other firms. This regulatory change allows us to assess firm response to a major extension of regulatory reach. The next section describes the second regulatory change case selected for this study that introduced the unannounced audit visits to medical device manufacturers and their critical suppliers.

6.2 Regulatory Change Case: Introduction of unannounced audit visits in the UK

In May 2008, the European Commission launched a public consultation for a 'recast' of the medical devices legislations. This was met with some amount of surprise and skepticism by the industry and some national competent authorities (NCA) given that recast was close on the heels to the significant amendments that introduced the new Directive 2007/47/EC, which entered into force on 11 October 2007 (Chowdhury, 2014) (discussed in the last section). This was followed by the NCA's coming together to establish the Central Management Committee in September 2010, partially in response to the implied criticisms of the enforcement deficits within the current regulatory regime (Horton, 2012).

On 24 September 2013, the European Commission (EC) published new guidance on the designation and supervision of Notified Bodies (NBs) in the field of medical devices and on the audits and assessments performed by the NBs (recommendation 2013/473/EC). The new regulation was formed *"in response to the most frequent shortcomings of the previous practices"* (European Commission, 2013a). The need for routine unannounced audits by all NBs was stipulated specifically as part of the Commission's response to strengthen and tighten controls on medical devices and restore public confidence in the regulatory system following the Poly Implant

Prothèse (PIP) breast implants scandal (European Commission, 2013b). Although the main industry association EUCOMED sought to underline that this was a case of willful violation of the legal obligations of the manufacturer and not as such a failure of existing regulation, questions has been raised about the fundamental effectiveness of the legislations (Chowdhury, 2014).

Unannounced audits are additional audits where the auditors commissioned by the notified body will arrive on the sites to be audited and undertake the audit without giving the manufacturer prior notice. This type of audit came in addition to the initial, surveillance or renewal audits of the three-year certification cycle (European Commission, 2013a).

The EC recommendation 2013/473/EC regarding the audits performed by the NB has a distinct effect on medical device manufacturers, as three annexes address the evaluation of their products and their Quality Management System (QMS), and the structure of the unannounced audit visits. The features of the new recommendation for the evaluation of the device most relevant to the manufacturer include the following.

Firstly, the NB should verify, where relevant, the fulfillment of the essential safety and health requirements contained in Directive 2006/42/EC.

Secondly, they are instructed to facilitate the verification of the technical documentation, the manufacturer's device identification system and the declaration of conformity (European Commission, 2013a).

Within the assessment of the QMS of the manufacturer, the NB verification should ascertain that the application of the quality system assures the conformity of the devices with the legal requirements. In the case of production or product quality assurance, the verification should ascertain that the application of the quality system ensures the conformity of the devices with the device type (European Commission, 2013a).

6.2.1 Modalities for Conduct of unannounced audit visits

The most radical reformation within the NB instruction concerns their audit policy or

the modalities for conduct of assessments. First, the NB should audit not only the premises and processes of the manufacturer, but also those of its critical subcontractors or its crucial suppliers (European Commission, 2013a).

Secondly, the NB is instructed to perform unannounced audits at least once every three years. Nevertheless, the frequency of the audits may be increased if the devices present a high risk, if the types of devices are often found to be non-compliant and/or complaints were high in the previous audit reports, and if some information leads to suspicion of lack of conformity in the devices themselves, or on the manufacturer's premises (European Commission, 2013a).

Furthermore, NB should verify the manufacturer's system ensuring traceability of materials and components, from the entry into the manufacturer's, suppliers' or subcontractors' premises to the delivery of the final product. Verify that experience gained in the post-production phase, in particular user complaints and vigilance data, is systematically collected and evaluated for the devices covered by the application of the manufacturer. At each annual surveillance audit, the notified bodies should verify that the manufacturer correctly applies the approved quality management system and the post-market surveillance plan (European Commission, 2013a).

6.2.2 Enforcement of the unannounced audit visit rules

Independent assessors also known as notified bodies are the first in line enforcers of unannounced audit visit rules. Their principal role is to review the measures taken by manufacturers identified as the primary 'regulatees' to ensure that they fulfil their regulatory obligations, this procedure is formally referred to as the conformity assessment (Chowdhury, 2014). Two important aspects of conformity assessment within this regulatory change should be noted. First, the manufacturers in the UK are free to choose any notified body operating within the European Union. Thus there is no territorial linkage between manufacturing site and the location of the notified body.

In summary, the European Commission played a very important role in this regulatory change case, as it was not only the principal architect of the Directives but it also played an active role by periodically publishing interpretative documents that clarified provisions from these Directives. They also are the prime movers in undertaking

legislative amendments and revisions of the regulatory structure as is evident from this discussion. So far, this chapter presented two cases of regulatory change set in a tightly regulated medical device national environment. The next section focuses on a regulatory change case set in a different national environment.

6.3. Regulatory Change Case: Radiation emitting devices (REDs) in South Africa

The medical device industry in South Africa was conspicuous by the absence of a comprehensive system of regulation until the enactment of the Medicines and Related Substances Amendment Act of 2015 (SAMED, 2016). There were no specific regulations governing the sale and use of medical devices in SA, except for a few medical technology product categories, which emit radio frequencies and electromagnetic waves. Though there are two types of radiation (i.e. ionizing, non-ionizing), the greatest concern for patients and healthcare workers comes from ionizing radiation because of the harmful impact on human genetic structure that can result from accumulated exposure (Fiedler, 2017). In fact the Department of Health (DoH) recognized that industrial radiography devices emit sufficient ionizing radiation to constitute a significant health hazard unless adequately shielded and handled with proper care (DoH South Africa, 2011). To promote safety in the workplace and to prevent unnecessary exposure to radiation, the DoH had to put radiation control measures in place.

6.3.1 Historical Legal Framework for Radiation Control in SA

The legislative control of electronic products was for the first time introduced by the Public Health Amendment Act of 1971[21] that added section 133A to the Public Health Act of 1919, allowing the Minister of Health to make regulations mandating the Secretary of Health to grant, suspend and revoke licenses in respect of electronic products and prescribe conditions and requirements for the categories of electronic products, premises and persons in control of the equipment. The Directorate: Radiation Control (DRC) of the Department of Health was assigned to be the body responsible for enforcing the Hazardous Substances Act, which was introduced in 1973 (Act 15 of 1973)[22] applicable to Group III and Group IV hazardous substances, as well as the regulations published under this act. In 1992, new conditions for

[21] SA Government. Act no 42: Public Health Amendment Act. (GN 888 in Government Gazette 3119 of 26/5/1971).
[22] SA Government. Regulation R1332: Regulations concerning the control of electronic products. (GN R1332 in Government Gazette 3991 of 3 August 1973).

licensing of Group III hazardous substance were introduced by the Hazardous Substance Amendment Act, 1992 (Act no. 53 of 1992)[23]. The latest change is the Medicines and Related Substances Amendment Act 14 of 2015, which included Group III and IV Hazardous Substances contemplated in the Hazardous Substances Act, 1973 (Act No. 15 of 1973) in its definition of a medical device.

The Hazardous Substances Act was created because early studies on X-rays had recognized that exposure to high levels of radiation may cause tissue damage, and that chronic exposure to lower levels of radiation may result in cancer (Herbst and Fick, 2012, Fiedler, 2017). However, the use of X-rays is key part of diagnosis and plays an indispensable role in clinical management of patients (ibid). The innovative use of radiation, and specifically X-rays, imposes risks if inadequately controlled by manufacturers, suppliers, users and the government. Furthermore, because diagnostic imaging involves a multi-step process that include human and equipment factors, not controlling the imaging process properly can produce sub-quality images. This may affect accuracy of diagnosis and result in repeat exposures that increase both patient dose and costs to the medical facility (Grundlingh, 2015).

The Hazardous Substances Act (1973), therefore, prohibits and controls the importation, manufacture, sale, use, operation, application, modification, disposal or dumping of substances and (electronic) products that may hurt or kill human beings by reason of their detrimental direct or side effects (RSA DoH, 1973). The Act classifies such substances and products in groups according to the degree of danger. The Act therefore, provided protection against radiation, however the act was undermined by poor administration and uncertainty about regulations and licensing conditions (Herbst and Fick, 2012).

The Hazardous Substances Act (1973) indicated "the Minister may regulate manufacturing, modification, import, storage and transportation as well as disposal of the hazardous substance. The application for a specific purpose is regulated, including prohibiting that the grouped hazardous substance is sold, advertised or named under a

[23] SA Government. Act no. 53: Hazardous Substances Amendment Act, 1992. (GN 13955 in Government Gazette 1237 of 6 May 1992). Commencement date: 1 March 1993

name other than a name so prescribed. The procedures to be followed, the forms to be completed, the records to be kept and the other requirements to be complied with in connection with issuing licenses in respect of Group III hazardous substances and in respect of the premises on which they are installed, are described explicitly" (RSA DoH, 1973).

The regulations further prescribe the precautions to protect from injury the persons involved in manufacturing, operation, application or disposal of the substances. The appointment of committees, or the duties to be performed by inspectors, is also set out (RSA DoH, 1973)

The licensing of medical equipment (RSA DoH 1973) is subject to the prescribed conditions, the Director-General may in each case, issue to any person a license to sell, let, use, operate, install or apply any Group III hazardous substance. The license will be issued in the public interest. The refusal or granting of a license will be notified in writing. Non-compliance with prescribed conditions will result in suspension or cancellation of licenses. Inspectors are appointed and certified to indicate for which groups of hazardous substances they have been thus appointed. The powers of inspectors are prescribed with clear reference to inspection, entrance to premises, demanding information and placement of a restriction. Persons will be guilty of an offence if any restriction is removed without permission from the inspector. Penalties include a fine or imprisonment. No person, including the State, shall be liable in respect of anything done in good faith in exercising or the performance of a power or duty conferred or imposed by or under this Act" (RSA DoH, 1973).

6.3.2 Licensing Conditions for Owners of Medical and Dental Diagnostic X-ray Equipment

The regulatory practice of X-ray equipment used in industrial radiography published under the Hazardous Substances Act, 1973 as amended in terms of Article 3 (1) prescribed that when a license is issued to the license holders, (i.e. the owners of medical and dental diagnostic X-ray equipment), the Directorate: Radiation Control (DRC) should attach licensing conditions as an annexure to the license (DoH South Africa, 2011). Generally, the annexure refers to only two conditions directly but to

more conditions indirectly. The annexure does not contain the licencing conditions but refers the license holder to documents containing the licensing conditions on the Department of Health website. These web-based documents therefore possess legal authority as license requirements, but may change without further notice to the license holder (Herbst and Fick, 2012). The two specific licensing conditions are elaborated in the next section.

6.3.3 The Code of Practice for Industrial Radiography - X-ray Equipment

The first licensing condition namely the *"Code of Practice for industrial radiography - X-ray Equipment 2011"* and was drawn up in order to limit the risk of overexposure of workers and members of the public, and to keep radiation doses as low as is reasonably achievable. The holder of a license must ensure that the requirements laid down in the "code of practice" are adhered to at all times (DoH South Africa, 2011). The code of practice called for a number of administrative and medical requirements from those applying for the license. These requirements have a significant impact on the license holders, as they must show that they possess the necessary equipment, facilities and trained personnel to ensure that the radiographic work will be performed in a safe manner.

Furthermore, the license holder must nominate a person to act as Responsible Person who must either be a full-time employee or the owner. The person nominated to act as Responsible Person must pass an approved examination before he/she can assume this position. Candidates must have an approved Level II Industrial Radiography qualification with two years experience. A service contract must be compiled between the holder and the responsible person in terms of Paragraph III.3 of the Regulations Concerning the Control of Electronic Products (Regulations No R1332 of 3 August 1973) as amended. Responsibilities for the transfer of duties when resigning or when the contract expires must be included in the service contract (DoH South Africa, 2011).

In addition, the holder of the license must ensure that a document is drawn up outlining correct working procedures. The document must include details of all relevant safety procedures laid down by the Directorate (i.e. it is recommended that the code of practice form a major part of the document) and must specify what actions

are to be taken in the event of an emergency. The holder of the license must take steps to ensure that his employees adhere to the correct working procedures (DoH South Africa, 2011).

The licensing requirements further stipulate that, industrial radiation workers must be declared medically fit by a company appointed doctor before employment. A copy of this pre-employment medical evaluation must be entered into the health register of the worker concerned. A medical examination must also be performed at termination of radiation work with the employer. A copy of the post-employment medical evaluation must be kept in the health register of the relevant worker (DoH South Africa, 2011).

Lastly, the license holder must not transfer any industrial radiography X-ray units unless this is done with the prior approval of the Directorate. This requirement refers to situations where X-ray units are transferred between firms and when X-ray units are permanently transferred between different sections of a company (ibid).

6.3.4 Requirements for License Holders with respect to Quality Control tests for diagnostic X-ray imaging systems

The second licensing condition attached to a license enforces annual quality assurance according to a prescribed list (Herbst and Fick, 2012). The DRC provided this second document as part of the diagnostic license conditions with respect to quality control (QC) tests in order to outline the requirements for the acceptance and QC tests of diagnostic X-ray equipment. The tests ensures that medical and dental diagnostic X-rays and the overall technical performance of equipment are reliable and limits the dose to the patient to the lowest value compatible with successful diagnosis or therapy (DoH South Africa, 2011).

Since September 2000 it is a regulatory requirement that suppliers and license users of diagnostic x-ray equipment must ensure that a series of specific QC tests at frequencies mandated by the DoH are done on all diagnostic x-ray units and processors (Grundlingh, 2015). The regulatory program was implemented in September 2000 specifically to assist medical facilities to recognize when parameters are out of limits (ibid). The out of limit parameters could result in poor quality images

and could give rise to unnecessary radiation exposure to the patient (Fiedler, 2017). Quality control tests play an important role in diagnostic imaging to limit the population dose growth. Results of QC tests must be reported to the DoH and the DRC analyzes the results (Grundlingh, 2015).

6.3.5 The Introduction of the Accreditation System and Inspection Bodies (IBs)

The SA government recognized:

(i) the need for an internationally recognized national accreditation system as a crucial element of a well-functioning technical infrastructure that is aligned with international best practice;

(ii) the importance of ensuring that the accreditation system of SA continues to support the needs of their enterprises competing in a fast-paced global economy and

(iii) the importance of supporting public policy objectives in terms of health, safety and broad-based black economic empowerment (B-BBEE) compliance issues (DoH South Africa, 2007).

This led to the *Accreditation for Conformity Assessment, Calibration and Good Laboratory Practice Act*, 2006[24]. The purpose of this Act was to first, provide for an internationally recognized and effective accreditation and compliance monitoring system for SA. Secondly, it was to establish the South African National Accreditation System (SANAS) as a public entity and as the only accreditation body in the Republic responsible for carrying out the accreditations in respect of conformity assessment[25], calibration and monitoring of good laboratory practice (GLP)[26] compliance to the Organization for Economic Cooperation and Development (OECD) principals; and lastly to provide for matters connected therewith (DoH South Africa, 2007).

In an effort to overcome the insufficient number of inspectors in SA for more than 6 500 license holders and 16 000 X-ray machines (Herbst and Fick, 2012), SANAS

[24] SA Government. Act no 19, 2006: Accreditation for Conformity Assessment, Calibration and Good Laboratory Practice Act, 2006. (GN 29712 in Government Gazette of 16 March 2007).

[25] "Conformity assessment" means the procedure used to determine, directly or indirectly, that the relevant requirement in technical regulations, standards or any other relevant and validated documentation has been fulfilled.

[26] "GLP" (good laboratory practice) means a quality system concerned with the organizational process and the conditions under which non-clinical health and environmental safety studies are planned, performed, monitored, recorded and reported.

was mandated by the DoH to accredit companies/users to perform the prescribed acceptance and QC tests and to ensure through this process that a high standard of testing is maintained that will directly benefit the patient. These companies/users are called Inspection Bodies (IBs) once they are accredited by SANAS (Grundlingh, 2015).

In addition to being accredited, IBs are also approved by the DoH before they may start operating. This implies that "routine" tests/inspections are performed by IBs and in doing so; it increases the capacity of the DoH by allowing its own DRC inspectors more time to focus on problem areas. Inspection bodies that have been accredited against international standards also inspect diagnostic imaging machines providing services such as MRI Ultrasound and CT scans (Grundlingh, 2015). This results in the assurance of safe, high quality care with reliable outcomes that patients can trust.

As from 31 March 2009 an IB approved by the Department of Health (DoH) or an appropriately trained professional registered with the HPCSA as a medical physicist, must be used to perform all the acceptance tests as well as the routine tests listed in the requirements for Quality Control Tests Document. Acceptance tests are the initial tests performed directly after installation and before any X-ray equipment is put into clinical service or substantially upgraded (DoH, 2011).

It is the duty of SA regulators and all suppliers to monitor products available and to provide reasonable levels of protection against unscrupulous behavior of suppliers and or users (Rogers, 2015). The over-riding intention of market surveillance, including pre-market assessments and approval systems and post-market surveillance activities, is to enhance patient and user protection, in the context of limited resources (ibid). Accreditation of Conformity Assessment Bodies means that these certification bodies certifying medical device manufacturers and distributors to ISO 13485 are operating to global levels of assurance (Doh South Africa, 2012, Rogers, 2015). Accreditation certification is used to assess conformity of quality management systems and medical devices against an international and appropriate standard (Fiedler, 2017). The development of the conformity assessment capabilities in SA and accreditation thereof by SANAS to global levels of assurance are critical elements in the successful implementation of the medical device regulatory framework (Rogers, 2015). The

introduction of SANAS had distinct effects on medical device manufacturers/suppliers and users in SA, as they had to put new strategies to meet annual conformity assessments.

6.4 Conclusion

This chapter has focused on the specificities of the three selected regulatory changes, the drivers that led to the changes have been discussed, why the changes were important for the two medical device industries and how they have been strengthened over the years. Since regulatory requirements such as those contained in these three case studies are hardly ever revoked, and new ones continue to be endorsed (Eisenberg, 2012), it might be essential for firms to view compliance activities as an opportunity to directly enhance their capabilities and the value to business. However, the prospect of more stringent regulatory requirements to be implemented may inevitably place a substantial demand on the already stretched organizational resources, and further influence their associated opportunity costs. The three regulatory changes explored in this chapter, now allow us to assess firm responses to these major toughening of regulatory compliance processes and therefore, the next chapter will discuss and analyze the actions of the firms implementing the regulatory changes.

CHAPTER SEVEN
THE EFFECTS OF REGULATORY CHANGE ON TECHNOLOGICAL CAPABILITIES OF MEDICAL DEVICE FIRMS IN THE UNITED KINGDOM

7.0 Introduction:

The aim of this chapter is to collate the empirical findings of the two major regulatory change cases in the UK. This chapter addresses research sub-question number three identified in chapter one: *How have regulatory changes affected firm level investment, production and linkage capabilities of medical device firms in the UK?* using empirical data from a group of sixteen medical devices firms in the UK. This chapter is focused on firm level effects in a tightly regulated national environment.

This study includes two kinds of empirical data. The first empirical data involved sixteen UK manufacturing firms. Therefore, the general context and implications narrative of the two new regulations will first be constructed based on the sixteen firms. Then a more comprehensive analysis of three firms will be presented. The narratives are organized in accordance with patterns emerging from the empirical data. At the end of the chapter, the results of each regulation and each type of capability will be summarized and general characteristics of the firms' responses to the new regulation will be further described to provide an informative overall perspective.

To analyze the effects of regulatory changes, this chapter applies an evolutionary economic understanding of industrial capabilities, focusing particularly on technological capabilities at the firm level. This framework of industrial analysis is also used in the subsequent chapters in this research.

7.1 Effects of the first regulatory change (software) on firm level technological capabilities

This section will describe data from the sixteen UK-based firms showing the effects of the two significant regulatory changes on three aspects of technological capabilities. The two regulatory changes examined in this study are also considered to be institutional changes and refers to the process of regulations and laws being

modified (Malerba, 2006). The analysis therefore is guided by Lall (1992)'s firm level technological capabilities functions model, which is made up of "investment", "production" and "linkage" capabilities (1992). Technological capabilities refer to the dynamic and competence-building activities firms undertake to generate new products, process and services (Malerba and Mani, 2009, p.161).

Once the new requirements of the first regulatory change were presented by the European Commission, UK firms were supposed to take a range of actions in response. In fact, the country's industrial policies, regulations and market governance influence the direction and extent of technological capability, the network of the sectoral actors' dynamism and trajectory (Marques and de Oliveira, 2009, Malerba and Mani, 2009). The actions taken by firms in reaction to regulatory changes, in turn, affected their business operations. Such effects depended on how each firm tried to acquire the regulatory standards or develop the assets to deal with the change. From the interviews conducted with different stakeholders, firms responded in different ways to changes in regulations depending on their management, product offerings and position in the market.

7.1.1 Effects of the first regulatory change (software) on firm level investment capabilities

Investment capability refers to the skills for expanding and establishing new production facilities (Malerba and Mani, 2009, p.162). The investment capabilities determine the capital costs of the project, appropriateness of the scale, product mix, technology and equipment selected, and the understanding gained by the operating firm of the basic technologies involved (Lall, 1992).

Research and Development (R&D)

The approach to implementation of new regulation and firm structure significantly affect the propensity of regulated firms to engage in R&D activities (Mayo and Flynn, 1988). Firms that invest in R&D extend their technical knowledge base, which allows them to design and develop new innovative products or services (Malerba and Mani, 2009). However, the extent to which firms can extract value from their R&D efforts to develop innovative output depends on institutional quality. Associate Director of Regulatory Affairs of Delta Ltd noted:

"Our R&D expenditure increased after the new regulation. Our directors regarded investment in this area as a prerequisite for the success in the medium to long-term future" [Res O57 (MAN), Jan, 2017].

The effects of the first regulatory change on R&D elicited various responses among the medical device firms. Some firms highlighted that the impact of new regulation on R&D created substantial shifts in the distribution of inventive efforts to meet market requirements. However, the interview results also indicated that R&D expenditures were positively related to firm size, the degree of specialization in medical device sales, and the earned rate of return on investments. CEO of Med Tech and Director of Neiva Medical shared the same views on the need to increase the level of investment in R&D in spite of the stringent regulated environment:

"After the 2007 regulation, we continued to increase our level of investment in R&D commensurate with our objective of our market place and enhancing our competitive position" [Res O72 (MAN), Apr, 2017].

"The changes in regulation made us to increase our investment in R&D. In fact, we dedicated 5% of our revenue towards R&D activities and innovation [Res O73 (MAN), Apr, 2017].

The new amendment specified that a manufacturer is prohibited from running any software "that qualifies as a medical device but is not yet CE-marked", in human tests outside of an approved clinical trial setting (Klümper and Vollebregt, 2009). The Chairman of Kilo Ltd indicated that this regulatory change curtailed R&D considerably as reflected in the following remark:

"In the past, the process of R&D and placing of a medical device on the market, as long as it was safe, was fairly easy to do. Now almost any product change or new product development has to go through a whole series of regulatory hoops before you can get a CE mark" [Res O66 (MAN), Jan, 2017].

Majority of firms emphasized that the introduction of the new regulation made the

approval times much longer, therefore directly affecting the time to market, which, in turn, impacted return on investment made for product development. Director of JM Medical remarked:

"In 2008, our firm's investment on R&D activities reduced to £45.8m from (2007 £54.1m). The decrease was due to a reduction of projects in pre-clinical trials as compliance cost had rose steeply and delays in regulatory decision times" [Res O65 (MAN), Jan, 2017].

This suggests that changes in regulations can lead to undesirable impact in terms of increased barriers to entry and decreased investments in R&D, which are counterbalanced by favorable effects, such as reduced risk in investments and minimized product turnovers.

Recruitment and training of skilled personnel

The study identified "capacity and expertise" as critical determinants that support the capability of implementing new regulatory requirements. The introduction of the first regulatory changes had dual competitiveness at domestic and international levels that required adequate staff training. At the domestic level, the medical device firms had the opportunity to improve the quality and innovativeness of their software beyond the CE mark approval and ISO certification benchmarks by training their employees. Furthermore, the new regulation created competitiveness among the UK firms as the staff members received training to new rules and standards regulating software design processes, and technological scalability. Associate Director of Regulatory Affairs of Delta Ltd and the CEO of Foxtrot Ltd commented:

"The MDD 2007/47/EC made us create more jobs within our firm and increase our in-house training so that we could have a competitive local market advantage" [Res 057 (MAN), Jan, 2017].

"In response to the new regulation, in 2008, we took in-house responsibility for training of personnel while engaging the help of a local distributor for regulatory support" [Res 059 (MAN), Jan, 2017].

The quotes above reinforce the notion that, a highly skilled workforce with regulatory expertise was an important competitive factor in the medical device software segment to meet the EU 2007/47/EC requirements. This is reflected in the following two quotes from the Managing Directors of Indigo Ltd and Neiva Medical:

"We had to increase our recruitments and staff training to meet the requirements of EN/IEC/62304 such as software devices planning, requirement analysis and implementation, verification, integration and software release at different stages within our firm [Res 064 (MAN), Jan, 2017].

"Our employee numbers increased to 453 in 2010 from 439 in 2009 in order to cope with the new regulatory requirements" [Res 072 (MAN), Apr, 2017].

Evidence also suggests that the firms that had skilled and trained employees managed to comply with the MDD 2007/47/EC requirements and compete more effectively in the global market. Some respondents emphasised that the regulatory change affected the companies whose primary market was the UK but expanding their business outside Europe to other advanced countries such as the USA. Chairman of Kilo Ltd noted:

"We were now forced to employ people that we would train and nurture for them to be able to comply with the USA and the rest of the world registration requirements" [Res 056 (MAN), Jan, 2017].

Other respondents said that the level of scrutiny of all aspects of the medical devices and the level of regulatory documentation had a cost effect on: first, the sheer amount of manpower and labour to comply with the regulatory requirements; and secondly, the kind of qualifications and the cost of the skilled personnel that a firm needs to employ. Chief Operations Officer of Foxtrot Ltd had the following to say on this issue:

"It is very difficult to find people who are skilled software engineers and used to comply with the medical device standards. We have been looking across the whole

area here on the South Coast, and I have to say that we haven't found anybody that is looking for the job and has got the experience." [Res 059 (MAN), Jan, 2017]

Majority of interviewees pointed out that firms have to invest significantly in training of their engineers involved in product development with diverse aspects of the regulatory documentation. This emerged as a time-consuming exercise as it was argued that approximately 70% of the project (time and cost) has been spent on regulatory documentation and recording for audit purposes. However, some MNCs' recruitment and training needs were scarcely affected by the new regulation as remarked in the following quote from Lima Medical's Head of Operations:

"As a MNC, the recruitment of personnel was not a big issue for us; we actually remained static even after the new changes" [Res 069 (MAN), Apr, 2017].

7.1.2 Effects of the first regulatory change (software) on firm level production capabilities

Production capability consists in the ability to operate production processes and adapt them to changing market circumstances (Malerba and Mani, 2009, p.162). The functions of the production capabilities range from basic skills such as quality control, operation, and maintenance, to more advanced ones such as adaptation, improvement or equipment "stretching" (Lall, 1992).

Innovation in production

The OECD (2009) highlights the direct relation that exists between regulation and innovation. Innovation capability consists of the ability to carry out activities for creating and implementing changes in techniques and organizational processes (Lall, 1992, Malerba and Mani, 2009). The MDD 2007/47/EC stringent regulatory change affected innovative efforts of the medical device manufacturers by imposing the fulfillment of rigorous safety and quality requirements for the commercialization of any medical device software. The Technical Director of Hex Ltd said,

"Well, after the strict 2007 regulatory change, our innovation activities and focus moved towards improving our old products instead of introducing new ones because the requirements were too costly for us" [Res 063 (MAN), Jan, 2017].

This quote indicates that the increased regulation has made some innovative firms more risk averse and adopt incremental instead of radical innovation approach. Incremental innovation does not bring fundamental change in a treatment, nor does it bring about a crucial change in the product (Schumpeter, 1942). While radical innovations are generally defined as breakthroughs that create discontinuity in the technology trajectory, and destroy the existing equilibria (Dosi, 1982). The Managing Director of Indigo Ltd highlighted the challenges they faced in trying to develop a radical innovation while at the same time trying to meet the new software requirement on risk assessment in the remark below:

"A big dilemma we face is, you can't simply sit down and upfront say what problems you are going to encounter and this is really the risk assessment part of the regulation which asks you to exactly to state what risks are associated with a particular approach to solutions and particular approach to software and sometimes you simply don't know because you haven't tried that before [Res 064 (MAN), Jan, 2017].

Stringency relates to how difficult and costly it is for firms to comply with new regulatory requirements using existing ideas, technologies, processes and business models (Baldwin et al., 2012). The technical constraints required by the regulation were imposed by the standards such as the ISO 13485 and IEC 62304 which are uniformly applied to an entire medical device software development process. These requirements have imposed direct constraints on firm conduct, lowering product innovation. According to Ashford (1985) stringency is the most important factor influencing technological innovation. The Medical Devices Principal Consultant of Bravo Ltd commented,

"Having been in this industry since the 1990s from my personal experience I feel that the new regulations were too stringent for us small companies to create new products" [Res 054 (MAN), Jan, 2017].

Further, some of the firms agreed that the new regulations imposed certain requirements on product development such as requiring clinical data regardless of device classification and that has limited the exploitation of their opportunities to introduce new devices. The Chief Operation Officer of Foxtrot Ltd noted,

"The new regulation slowed down product development time and innovation substantially" [Res O59 (MAN), Feb, 2017].

This supports D'Este et al., (2012), who suggested that regulation barriers limit the drive for innovation. Further, some small firms could not able to comply with the requirements and therefore, dropped off potential ideas and opportunities due to the risk of not meeting the regulatory requirements. This stringency in the first regulatory change was considered a barrier to the innovation as reflected in the remark below by the CEO of Echo Ltd:

"The 2007 regulatory changes have definitely affected innovation to a very large extent because they are now so strict especially with the fact that most of the innovation comes from small companies and also the compliance level if you want to develop a new product, the clinical data requirements, the evaluation requirements, the need for transparency and so many more regulatory requirements are really affecting our innovation capabilities". [Res O58 (MAN), Jan, 2017].

There was also evidence of positive impact of first (software) regulatory change on the innovation in some firms. The senior managers from these firms argued that the strict regulations fostered innovation by creating opportunities for change and improvements through mandatory requirements. For instance, the introduction of a new regulation enhanced the creation of completely new processes or products because it was too costly to fulfill the regulatory requirements with the existing technology, and significant technological change was required. Two respondents remarked the following on this issue: First, the Associate Director Regulatory Affairs of Delta Ltd said,

"In 2007 we actually improved our operations by launching our innovative genome analyser and cluster station" [Res O57 (MAN), Jan, 2017].

And second, the Chief Operation Officer of Foxtrot Ltd noted,

"At the moment innovation is a good. It might in some instances mean that the innovation is slower to appear as a commercial product but then again I think that is a good thing because its ensuring safety for the patient" [Res 069 (Man), Jan, 2017].

The controversy in the impact of regulation on innovation among the firms had been discussed earlier in academic literature. On the one hand, complying with regulations is likely to increase costs or restricts firms' freedom of action (Palmer et al., 1995). On the other hand, well-designed regulation may guide or even force firms to invest in innovative activities, implement innovative processes or release innovative products (Porter and Van der Linde, 1995).

According to Porter and Van der Linde (1995) regulation can yield progressive effects when it fulfills three characteristics: First, it must create the maximum opportunity for innovation, leaving the approach to innovation to industry and not the regulation-setting agency. Second, it should foster continuous improvement, rather than locking in any particular technology. Third, the regulatory process should leave as little room as possible for uncertainty at every stage.

Some stakeholders indicated that the first regulatory change (software) has directly affected the innovative process, while others argued that innovation and technological change have also significantly impacted regulation. The co-evolution of these elements are worth mentioning since the analysis of sectoral systems requires a careful understanding of the processes of interaction and cooperation (Malerba and Mani, 2009). Over time, a sectoral system undergoes the process of change and transformation through the co-evolution of its various elements (ibid). Thus, it is not surprising that industrial technological capabilities have also a reverse influence on government policies and regulation. Head of Global Medical Device Services of a regulation-setting agency noted that:

"In terms of innovation, I think we have had situations where a manufacturer brings in a truly innovative product. We all had to scratch our heads a little bit and figure out how we were going to regulate this because for example, sometimes the product does not naturally fall within classification and then there isn't a standard to compare to" [Res 068 (NB), Jan, 2017].

Quality control

The software controlled by the first regulatory change has increasingly emerged as an integral part of modern medical devices and affects the diagnosis or treatment of patients. Therefore the software itself and its development are scrutinized to ensure its quality, safety and efficacy (Sudershana et al., 2007). When asked about the effects of regulation on software development quality control, the Medical Devices Principal Consultant of Bravo Ltd remarked:

"Quality system regulation states, that software which is used in medical device production or in implementation of the quality system must be validated for its intended use. So yes the introduction of the 2007 regulation has improved the quality of our products" [Res 054 (MAN), Jan, 2017].

The Quality Management System (QMS) in the new regulation required that whenever the firms update their software, they have to potentially perform a re-evaluation of that software. If there is a major change in the way that the software runs the product, they might even have to re-CE mark the product. This process was considered costly and slowed down product entry into the market as reflected in the quote below by the Technical Director of Hex Ltd:

"After the introduction of the new regulation, we were asked to gather additional clinical evidence for our software update for quality purposes and this process slowed down the launch our new software version into the market, the approval process was very long" [Res 063 (MAN), Jan, 2017].

The quality system regulation requires more skilled personnel to deal with documents and records to be maintained of practically everything that is related to the quality system compliance i.e. device history, design history, complaints, procedures, reviews etc. and it was seen as the positive development by some firms. The Medical Devices Principal Consultant of Bravo Ltd comments:

"These records are needed to prove to regulatory authorities that quality system regulations have been fulfilled and to me that is a positive move" [Res 054 (MAN), Jan, 2017].

One of the key findings of this study is the primary advantage associated with the introduction of the MDD 2007/47/EC (software) regulation is that it ensured quality and safety of the new as well as existing medical devices entering markets. The CE marked software brought positive reputation to the product quality and helped it gain confidence among customers as captured in the two quotes below from the Senior Quality Assurance Director of Garner Ltd and the Managing director of Indigo Ltd:

"The software we produced under the new regulation provided a competitive advantage for our firm, because it had a harmonized standard EN/IEC/62304 associated with it. That meant producing products with improved quality, increased safety and efficacy" [Res O61 (MAN), Jan, 2017].

"One of the positive outcomes of new requirements is that if you adhere to regulation and you have done testing, evaluation according to the standards as a company you also gain confidence in the quality of your products" [Res O64 (MAN), Jan, 2017].

In general, although the new regulation imposed certain compliance cost to the innovation activities, there were usually compensating benefits elsewhere. The empirical results from the sixteen firms interviewed in this study demonstrated that, in a transition period of regulatory environment change, firms experienced adverse consequences. However, in the long term, the regulatory framework for medical device software had affirmative effects on the industry with respect to the quality of new product offerings.

Compliance cost

The changes in medical device industry regulation did not come without cost. Compliance cost refers to the cost for demonstrating compliance with regulation before entering the market (Baldwin et al., 2012). As indicated by the interviewees, the MDD 2007/47/EC (software) regulation increased costs, resulting in firms needing to divert resource outflows to meet regulatory requirements reducing their

availability for innovation activities within the firms. Compliance cost consists of expenditures for developing, manufacturing and testing of products to pass the regulatory requirements. The Senior Quality Assurance Director of Garner Ltd indicated:

"Due to a series of harmonised standards which go alongside the MDD 2007/47EC, we had to increase the appropriate level of software testing and the complexity of setting up and validating all the appropriate test methods, that meant increased compliance cost" [Res O61 (MAN), Jan, 2017].

Amid all the other differences in views of the effects of MDD 2007/47/EC regulation, all the firm respondents shared one view that the costs of compliance were too significant. Compliance with the new regulation targeting software safety and efficacy was viewed as a costly venture before a firm receives certification or accreditation to export to the European and the global market. The cost factor was mostly in the due diligence and massive documentation procedures. Thus, the changes tightened the medical device software specifications by requiring medical device manufacturers to provide additional documentation to prove compliance with further safety and efficacy standards. One Director of Optics Ltd remarked:

"In complying with 2007/47EC regulation, we had extremely low tolerance for risk. So our firm's compliance budget went up" [Res O73 (MAN), Apr, 2017].

Some respondents reported that changes in regulations limited how they design, develop and market their products, services or solutions for their customers. The firms incurred unique costs such as forgone opportunity costs associated with much longer product approval times; requirements for conducting additional clinical trials to acquire safety data equivalent to that obtained in previous trials and accepted by regulators in other markets. The Associate Director Regulatory Affairs of Delta Ltd and the Managing Director of JM Medical reflected on this issue in the two quotes below:

"The increased regulatory costs means that we have to take our costs elsewhere in the business and that includes who is too smart in the production" [Res 057 (MAN), Jan, 2017].

"In 2010 our product development expenses increased due to investment in clinical trial studies and regulatory cost to bring new products to the market" [Res O65 (MAN), Apr, 2017].

Business Operations capabilities

The nature of regulation significantly influences the structure and dynamism of the sector, firm level strategy and types of firms that can succeed. The first regulatory change had opposing impact on firms' operating conditions depending on their approach towards the regulation and resources to manage the change. Some firms with strong resources such as MNCs had proactive approach to regulations and managed to adjust when the change in the regulations were introduced. These firms became successful in the market evidenced by following responses:

"Because we invested more in R&D and regulatory compliance, we improved the overall company performance and turnover increased over the years after 2007 regulatory changes" [Associate Director Regulatory Affairs of Delta Ltd, Res 057 (MAN), Jan, 2017].

"Our firms' production and sales capability increased in 2010. We sold 14,415 products compared to 10, 440 in 2009, an increase of 38% in the number of patients treated. A remarkable strong performance in a very difficult regulated market" [Chief Operations Officer of Foxtrot Ltd, Res 059 (MAN), Jan, 2017].

"Even though complying with the new regulation was burdensome, we were proactive and we increased our medical devices export sales. Our highest export sales growth was from 2007 to 2013. Eventually, in 2013 we received the Queen's Award for Enterprise – International Trade" [Chairman of Kilo Ltd, Res O66 (MAN), Jan, 2017].

In contrast, some firms with limited resources that failed to realise the possibilities inbuilt in regulatory change requirements, ended up as failures in the market. The CEO of Echo Ltd remarked:

"Our products' speed to market was reduced, thus the time to market got longer, and the net present value of our products went down" [Res O58 (MAN), Jan, 2017].

This shows that regulatory change affected business operations of both the SMEs and the MNCs as well as the structure of the entire industry. This dualistic impact of regulation is also observed in the literature. For example, a contemporary study by Hansen et al. (2013) showed that regulatory change can hamper opportunity but can also be the springboard for new firms and solutions in the market. Similarly, Tee and Gawer (2009) point out that regulations can constrain the launch of a new business in a market and thereby influences firms' ability to develop a business.

7.1.3 Effects of the first regulatory change (software) on firm level linkage capabilities

This section focuses on the impact of regulatory change on the firms' linkage capabilities. Linkage capability refers to the ability to transmit technological information and receive it from other organizations (Malerba and Mani, 2009, p.162). These linkages are supposed to assist the firm to improve its productive efficiency and also the diffusion of technologies (Lall, 1992). They are also grouped as supporting activities and signify to the ability to link up with other actors in the economy (Bell and Pavitt, 1995).

The majority of medical device firms outsource certain aspects of operations to independent firms to reduce operating costs and focus on core strength. The MDD 2007/47/EC amendment stipulated that the manufacturer must be able to demonstrate that adequate controls over the whole chain of development of the software concerned have been put in place including outsourced work and supplier network (European Commission, 2007). Therefore, medical device manufacturers required a well-organized network of subcontractors and suppliers, who had the capacity and proficiency to supply quality products or components, in order to meet regulatory standards and also keep pace with global market demands. The Medical Devices

Principal Consultant of Bravo Ltd and the Managing Director of Indigo Ltd reiterated the need for strong links within the sector in the remarks below:

"It became increasingly necessary for us to develop relationships with all the links in their supply chain after the 2007 changes" [Res O54 (MAN), Jan, 2017].

"We had to learn how to collaborate better and by collaboration, I mean we had to find out how to share resources" [Res O64 (MAN), Jan, 2017].

Most of the firms interviewed successfully broadened their outsourcing models to include foreign firms with offshore production facilities. With the new regulatory requirements in place (MDD 2007/47/EC), establishing an effective supplier relationship became an important issue for medical device firms and it was one of the ways through which the firms could improve their performance. However, monitoring the supplier base as required by new regulation was considered a huge challenge for the manufacturing firms as reflected in the remark below by the Quality Manager of Alpha Ltd:

"Since software validation of our critical supplier required a lead auditor of which we did not have, we were forced to link up with local consultants in order to validate and monitor our supplier" [Res O53 (MAN), Jan, 2017].

In fact, the outcomes suggest that the capability of a country to benefit from cross-country linkages is influenced by its internal network structure. Thus, changes took place in the interactions between different layers of the industry, and between firms within those layers, placing demands on businesses' ability to integrate.

7.1.4 Summary: Effects of the first regulatory change (software) on firms' technological capabilities

In summary, introduction of the first regulatory change drove most UK-based firms to invest substantial resources in R&D to standardize their software products. Most manufactures of medical devices software that were proactive had positive income returns that improved after they invest towards compliance with the regulatory change.

It is clear that the software product-focused regulatory change was an important step to guarantee the acceptance of products in a broad geographical market. The regulatory change repositioned medical device software in a more transparent manner because manufacturing standards, procedures, tests, validation, and accountability were all improved to reduce device recall statistics. However, one of the biggest weaknesses of product regulation governing medical device software is that compliance costs are very high. For example, clinical tests are very expensive to conduct. The expected return on a device limits the amount of testing that a firm is willing to perform. A summary of the effects of the MDD 2007/47/EC on medical device firms in the UK is presented in Table 7.1.

Table 7.1: Effects of EU Directive 2007/47/EC on medical device firms in the UK

Firm	**EU Directive 2007/47/EC** Introduction of software as a medical device, Risk and quality management, Outsourced Design and Manufacturing		
	Affected Capability		
Alpha Ltd	INVESTMENT	PRODUCTION	LINKAGE
	• Validation of software production line costing the firm about £15-20 000. Thus increased compliance costs • The firm complained about the process of conformity assessment, and called for reducing clinical data requirements • Due to skills shortages firm outsourced design therefore increasing the need to externally monitor the supplier's QMS	• Due to increased risk management paper work, design times increased and slowed down products' time to market • The firm increased the workforce training on the EN/IEC 62304 standard for efficiency and competitiveness in operations. • Validation of critical supplier requires a lead auditor of which they were and are in short supply	Validation of critical supplier requires a lead auditor of which they were and are in short supply
Bravo Ltd	INVESTMENT	PRODUCTION	LINKAGE
	• The firm's software developers took quite long to catch up and understand that they were developing not just an ordinary software but a software regulated as a medical device, therefore increasing the need for more in-house training and recruitment of skilled personnel	• Demonstration of risk assessment of products including hazard analysis and mitigations that the firm put in place to resolve issues during the design and development process improved. • Increased the cost of producing a safer device	Increased reporting obligations for manufacturer
Charlie Medical	INVESTMENT	PRODUCTION	LINKAGE
	• Increased scrutiny during conformity assessments	• The firm's expected acceleration of its embedded software product "XXXX" was limited due to the continued time taken to get product registration through the regulatory agencies due to internal processing delays. • The firm had a general belief that the 2007/47/EC, EN/IEC/62304 and the rest of the applicable standards had met expectations in enhancing the safety of medical devices.	Created an additional burden of paying for the cost of new supply agreements
Delta Ltd	INVESTMENT	PRODUCTION	LINKAGE
	• Created more jobs within the firm and increasing in-house training. • Invested more in R&D and regulatory compliance. • R&D expenditure increased by 9% in 2007 • The directors regarded investment in this area as a prerequisite for the success in the medium to long-term future	• In 2007 the firm improved its operations by launching their genome analyser and cluster station. • Increased market share • Improved the overall company performance	•
Echo	INVESTMENT	PRODUCTION	LINKAGE

Ltd	• Firm has been facing some liquidity problems because the investment into R&D and the cost of compliance to EN/IEC/62304 are expensive.	• Products' speed to market was reduced, thus the time to market got longer therefore, net present value of their products went down. • Firm did not take on board the regulatory system. • Developed the software in an unstructured way, therefore resulting products that were not safe and effective.	Due to increased regulatory cost in the UK the firm moved production to China however the quality of their products reduced
Foxtrot Ltd	INVESTMENT	PRODUCTION	LINKAGE
	• In response to the new regulation, in 2008, the firm took in-house responsibility for training of personnel while engaging the help of a distributor for regulatory support. • R&D efforts on the firm's (xxxx) monitor improved • The company recruited an additional 4 regulatory affairs personnel in 2007 adding the total number of employees to 49 • The costs of trialling the firm's products increased	• In 2007 the firms' production and sales capability increased. They sold 14,415 surgical probes compared to 10, 440 in 2006, an increase of 38% in the number of patients treated. A remarkable strong performance in a very difficult regulated market • New regulation slowed down product development time and innovation substantially. • The quality of the firm's probe they made in 2007 remained the same as the one they made 1998, thus, the new regulation did not improve product quality.	An encouraging result in product sales in international markets saw a growth of around 30% as a result of strong international linkages
Garner Ltd	INVESTMENT	PRODUCTION	LINKAGE
	• Due to a series of harmonised standards which go alongside the 2007/47EC, the firm had to increase the appropriate level of software testing and the complexity of setting up and validating all the appropriate test methods, that meant increased cost opportunity of products, time and manpower. • Decreased the firm's return on investment.	• The revision to the risk management life cycle of devices (expectable level of risk) has made the firm to question to the interpretation of what is expectable risk for a device and that slowed down the release of new products	
Hex Medical	INVESTMENT	PRODUCTION	LINKAGE
	• Training cost increased • Number of employees went up.	• The software produced under the new regulation provided a competitive advantage for the firm, because it had a harmonized standard EN/IEC/62304 associated with it. That meant producing products with increased safety and efficacy. • The changes made the manufacturers to gather additional clinical evidence	Re-negotiate supply chain agreements, and alter documentation and quality management systems.
Indigo Ltd	INVESTMENT	PRODUCTION	LINKAGE
	• The firm had to increase their in-house training needs to meet the requirements of EN/IEC/62304 such as software devices planning, requirement analysis and implementation, verification, integration and software release at different stages within the firm. • Due to the fact that the environment is an open market with no price control regulation. The firm saw a lot of discrepancies in the costs of getting the ISO 13485	• The risk assessment part of the regulation requires the firm to exactly state what risks are associated with particular approach to software and in many cases the firm simply didn't know because they would not have tried the new technology. • The regulation added quite a lot of complications to firm's product development because it required a lot of scrutiny on the risk assessment, required lot of documentation to be prepared when they were writing software.	•
JM Medical	INVESTMENT	PRODUCTION	LINKAGE
	• In 2007, the firm's investment on R&D activities reduced to £45.8m from (2006 £54.1m). The decrease was due a reduction of projects in pre-clinical trials. • Their return on invested capital increased by 39.9% from (2006 27.9%)	• The firm performance increased. • In 2010 the product development expenses increased due to investment in clinical trial studies and regulatory cost to bring new products to the market	•

Kilo Ltd	INVESTMENT	PRODUCTION	LINKAGE
	• Increased medical devices export sales growth from 2007 to 2013. • In 2013 Received the Queen's Award for Enterprise – International Trade •	• New regulation has not affected the firm's market entry capability apart from the costs of getting the CE mark • The new regulation increased the level of documentation for the technical files from 4 to 78 and maintaining those files was said to be burdensome and taking a lot of time and manpower for the firm. Therefore, slowed down products' time to market.	The firm outsource its medical devices software from USA and China therefore faced cost implication challenges of externally monitoring its critical supplier's QMS.
Lima Medical	INVESTMENT	PRODUCTION	LINKAGE
	• The firm's operations were not seriously affected by the regulatory change. Even though turnover fell to £392m in 2011 from £394m in 2010 and (2009 £449m). This was primarily driven by loss income from wound care division and restructuring their supply chain. • As a MNC, the recruitment of personnel was not a big issue; they remained static even after the new changes.	• Managed to stabilize and improve expenditures on R&D each year after the new regulation. • Commended the new regulation as a positive move as it ensured that products are safe and effective • Innovation was made slower to appear as a commercial product but they took that as a good thing because it was ensuring safety for the patient	•
Med Tec Ltd	INVESTMENT	PRODUCTION	LINKAGE
	• After the new regulation, the firm continued to increase its level of investment in R&D commensurate with its objective of its market place and enhancing its competitive position. • Employee numbers increased to 453 in 2007 from (2006 439).	• Business operations consisting principally of the manufacture and sale of medical equipment and associated software increased and 2007 saw a turnover of £149m compared to (2006 £145m).	•
Neiva Medical	INVESTMENT	PRODUCTION	LINKAGE
	• After the new regulation, the firm continued to increase its level of investment in R&D. The firm also dedicated 5% of its revenue towards innovation. • In complying with new regulation, the firm had extremely low tolerance for risk. The firm's compliance budget went up.	• The new regulation increased the firm's requirements for a lot of regulatory and quality functions. Thereby increasing in-house training needs. • The firm however felt that 2007 changes did not have a huge impact on them, as things such as clinical evaluation and validation of software were not necessarily new and they were actually there in the existing guidance, however they were just not very clear.	•
Optics Ltd	INVESTMENT	PRODUCTION	LINKAGE
	• One of the firm's products is the infusion pump that has embedded software within it. The 2007/47/EC requires this to be validated and verified to show that the embedded software runs the product as intend. The overall process has increased costs, time a lot. • Usability software standards have been fed into process of criticality, thereby increased need for highly qualified software engineers	• The QMS in new regulation demand that whenever they update that software they have to potentially perform a re-evaluation of that software. If there is a major change in the way that the software runs the product, they might even have to re-CE mark the product. This process was considered costly and slowed down product entry into the market. • Upgrading quality systems to the new regulatory environment required significant investment as well as increased senior management involvement in both the upgrade process and on-going management of the QMS	•

Compiled by author from empirical data

7.2 Effects of the second regulatory change (unannounced audit visits) on firms' technological capabilities

After analyzing the effects of the first regulatory changes covering medical device software on firms' capabilities in the previous sections, this section delves into the analysis of effects of the second regulatory change regarding unannounced audit visits on firms' technological capabilities categorized under three main themes; investment, production and linkage capabilities.

7.2.1 Effects of the second regulatory change (unannounced audit visits) on firm level investment capabilities

In-house technological effort seems to be essential for firms' performance, starting from their investment capabilities. However, when regulations have the unintended effect of discouraging or disrupting investment, they need to be identified and reviewed.

Research and Development (R&D) capabilities

Innovation and a strong commitment to R&D were the principal competitive factors most frequently cited by the firms as critical to their success. The medical device industry is R&D-intensive, driven by constant innovation and short product life cycles (Altenstetter, 2012). The introduction of the EC 2013/473/EU, the second regulatory change on unannounced audit visits was radical in nature. This provision was not entirely new but effective enough to eventually disrupt some existing medical device firm's investment capabilities. The unannounced audits placed additional obligation on both manufacturers and NBs. Some firms became more risk adverse and reluctant to invest in radical innovations. The Technical Director of Hex Ltd and the Director of Regulatory Affairs of Charlie medical noted:

"I think less innovation is coming from within the big medical devices companies now, we had a couple of engineers working on process development and developing new ideas and in reality what they actually produced was a manufacturing process upgrade" [Res 063 (MAN), Jan, 2017].

"We reduced innovation and the R&D department has gone down from 12 to 3 members. Now we invest more in smarter production due to regulatory cost and for

the first time, we are going to other markets in search of return on investments due regulatory change" [Res 056 (MAN), Jan, 2017].

These quotes indicate that the significant R&D expenses for majority of MNCs were used to modify and enhance existing products, while lesser proportion of resources are devoted to the invention of a new product completely from scratch. This innovation investment strategy protected firms from the rejection of products by the new regulation and also facilitated market acceptance of much improved existing products. However, those firms that increased their innovation activities and R&D investments in spite of the strict regulated environment improved their business financial performance and operational efficiencies. The Chief Operation Officer of Foxtrot Ltd and the Director of Optics Ltd commented:

"At the onset of the new regulation we invested highly in R&D and innovation thereby maximised our return on investment and had a strongly increased cash generation. 'The investments was focused on our new innovative monitor as a result we improved our company operations and the turnover increased to £6.8 million and this was in 2013" [Res O59 (MAN), Jan, 2017].

"Some of the bigger players do have relatively large R & D budget similar to a pharmaceutical companies and therefore would bring some innovation in that respect through the R & D" [Res 073 (MAN), Jan, 2017].

Some firms indicated that the second regulatory change did not have a significant impact on their innovation activities. Instead these firms started setting up more suitable and appropriate quality agreements and commercial contracts in place to make sure they identify the roles and the responsibilities for those within the supply chain.

Recruitment and training of skilled personnel

In accordance with new recommendations on the audits and assessments by NBs, auditors now visit firms, their critical subcontractors or suppliers without any prior notice, and at any time (European Commission, 2013a). The manufacturers, contractors and suppliers need to host NB teams and facilitate the audit in satisfactory

conditions. One such provision is to invest in qualified persons to function such as 'person responsible for regulatory compliance', or appoint qualified persons already in their organization, who may need additional training for the tasks required of that person (ibid). The new regulation therefore, induced some firms to invest more in the recruitment and training of skilled personnel. The CEO of Med Tec Ltd and the Director of Neiva Medical mentioned that:

"Well, our firm depend on our capability of producing advanced medical equipment, which require highly qualified personnel. So we managed to attract and retain qualified personnel and that had a significant impact on the success of the company. In fact, in 2013 our turnover increased to £442m from £352m in 2012)" [Res O72 (MAN), May, 2017].

"The introduction of the random NB audits prompted us to increase training programmes for all employees responsible for regulatory compliance" [Res O73 (MAN), May, 2017].

According to the interviews, the introduction of EC 2013/473/EU had mixed consequences for recruiting employees because the managers were seeking highly qualified personnel, and their compensation had high cost implications. Some firms ended up making some of their workers redundant as they pursue efficiency and cost-cutting goals. One Director of Regulatory Affairs of Charlie Medical remarked:

"Last year, our firm made 9 people redundant as a result of the regulatory change" [Res O56 (MAN), Jan, 2017].

In case of outsourcing of the production via subcontractors or suppliers and importing and exporting of products, expertise in regulatory affairs, reimbursement and import/export was reportedly critical in the new regulation. Some firms had to implement new recruitment strategies that would have to factor recruitment of staff with international regulatory exposure as the Director of Regulatory Affairs of Charlie Medical highlighted:

"We had to invest in additional human resources with international regulatory affairs experience to cope with the impact of the new regulations, because of inadequately qualified personnel to deal with the impact" [Res O56 (MAN), Jan, 2017].

7.2.2 Effects of the second regulatory change (unannounced audit visits) on firm level production capabilities

The scope of unannounced audits is to include all the medical devices covered by the CE marking certificates issued by the NB. Therefore during the audit, sampling is to be carried out among these medical devices to verify that legal obligations are respected on a daily basis by reinforcing the evaluation of the coherence between the provisions in the quality system and the data in the technical documentation (European Commission, 2013a).

Quality control

The EC 2013/473/EC audits and assessments led to more rigorous product assessments and more frequent post-market inspections. Unannounced inspections required a commitment to the implementation and maintenance of effective QMS. Firms were required to establish a fully comprehensive QMS covering all aspects of their business. Accordingly, over their audit, the NB inspects the adequacy of the manufacturer's QMS and the technical file of their products (European Commission, 2013a). The new regulation impacted some firms' QMS processes. Due to the requirements governing unannounced audit inspections, firms had to formulate new strategies including altering QMS safety and performance processes, processes for the device design and development, subcontracting, manufacturing, etc. The Medical Devices Principal Consultant of Bravo Ltd reflected in the quote below:

"The continuous changes in the regulation led to our firm not only have to alter our QMS processes to comply forward going but also to retrospectively ensure the existing product meets compliance" [Res 054 (Man), Jan, 2017].

Creating a full QMS requires skills, expertise and resources. According to the interviews, it is estimated that for a small company, it requires from five to twelve months of full-time work of around two employees to create a QMS appropriate for producing medical devices that conform to the relevant regulations. The Chief

Operation Officer of Foxtrot Ltd noted:

"The new regulation increased the level of QMS scrutiny and documentation for the technical files and maintaining those files is too burdensome and taking a lot of time and manpower for the firm" [Res 059 (Man), Jan, 2017].

The QMS consists of NBs verifying whether the manufacturer's business organisation is appropriate for ensuring the conformity of the quality system and of the medical devices. In particular, the following aspects were to be examined: the organisational structure, the qualification of managerial staff and their organisational authority, the qualification and the training of other staff, the internal auditing, the infrastructure, and the monitoring of the quality system in operation, including with regard to involved third parties such as suppliers or subcontractors (European Commission, 2013a). The manufacturer's business organisation requirements had a huge impact on management responsibilities. These verifications of management responsibilities were welcomed by some firms as they induced the strengthening of their in-built management systems as remarked in the two quotes below:

"Our company has had to ensure even before these additional checks or unannounced visits that these things were in place so we interpreted the changes as re-enforcing" [Head of Operations - Lima Medical, Res 069 (Man), Jun, 2017].

"We actually welcomed unannounced audit visits positively as we were already committed to implementing programmes and supporting resources to ensure product quality and regulatory compliance, including analysis of customer complaints and adverse event data" [Director - Neiva Medical, Res 073 (Man), Jun, 2017].

The audit of medical device manufacturers also includes suppliers of services, which are needed for compliance with QMS or regulatory requirements, e.g. internal audit contractors. The second regulation (2013/473/EC) extended the unannounced audits to cover critical suppliers and led to: reduced firms' product errors, less cited non-conformities, less product recalls and encouraged better collaborations in the supply chain as reflected the two quotes below:

"The extension of the regulatory scope helped to create a close network between us manufacturers and our suppliers and since the new regulation, our margin of error has gone down and we have less product recalls but remember this also came with huge compliance cost implications. So it's a catch 22 situation" [CEO – Med Tec Ltd, Res 072 (Man), Jun, 2017].

"Our reviews and monitoring of their critical suppliers increased due additional peripheral regulations" [Senior Quality Assurance Director – Garner Ltd, Res 061 (Man), Jan, 2017].

The QMS further addressed the after-sales measures by defining adequate processes for measurement, analysis and improvement including the definition of how to handle the internal and external feedback, to control nonconforming products and what measures should be taken for improvement for example corrective and preventive actions (European Commission, 2013a). These new changes had an impact on the manufacturing firms, as they now required new QMS training initiatives and education of both their employees and their medical device customers. Some firms had to address customer feedback and relationship through communication efforts, which were performed in collaboration with the external providers of both products and processes.

Compliance cost

It is stated in the EC Recommendation 2013/473/EU that the costs associated with unannounced audits are paid for by the manufacturer, including the audits performed on the premises of its critical subcontractors/crucial suppliers. In case the manufacturer refuses to pay, the contract between NB and the manufacturer may potentially be breached, resulting in a suspension, or even the withdrawal of certificates. To fulfill the regulatory requirements on effectiveness, sometimes, firms needed to collect additional clinical data to meet CE mark certification expectation, which leads to the substantial amount of additional investment to obtain approval. The Medical Devices Principal Consultant of Bravo Ltd reflected on the high cost of compliance associated with new regulation in the following quote:

"The additional scrutiny in the new regulation increased the difficulty of new product introductions due to indeterminate timescales and additional costs" [Res 054 (Man), Jan, 2017].

One criticism particularly from the SMEs was that of the costs associated with unannounced audits, not only the NB fees, but also the need, ability, and resources to be able to support the on-site audit along with the issue of a potentially disproportionate audit duration to the size of company where a limited range of devices are produced. For example, a small company with less than five employees manufacturing one device still is subject to a minimum audit of one day by two people. The Quality Manager of Alpha Ltd reflected on this issue in the quote below:

"And if you think in the medical device industry, there are a lot of SMEs where innovation is happening, they just cannot afford this kind of cost at the beginning" [Res 053 (Man), Jan, 2017].

The stakeholders highlighted that in general MNCs have strong financial strength and a high degree of credibility, which makes it easy to obtain loans from the international financial institutions. The Managing Director of JM medical remarked:

"As the regulations get stricter it costs more money to comply with those regulations, and for the MNCs, we can absorb those costs and carry on. For the medium sized companies it is not that difficult but the small companies it has a huge impact so that would be my answer. Yes, the small companies are really struggling with the increasing level of regulation." [Res 065 (MAN), Jan, 2017].

Another respondent points out that their firm might go out of business because their business operations have been heavily strained by regulatory costs. The Director of Regulatory Affairs of Charlie Medical had the following to say:

"Regulation has increased significantly the cost of compliance and the type of firms that have been affected the most are the SMEs because they don't have that huge amount of cash flow. It has cost our company about £400 000 just to implement these

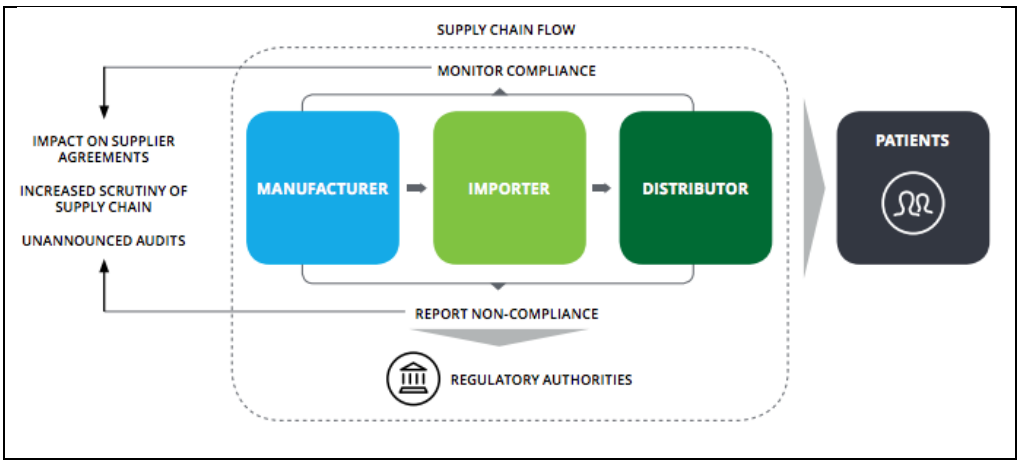
new changes. The company is small enough to go out of business because it is very unfair" [Res 056 (MAN), Jan, 2017.

7.2.3 Effects of the second regulatory change (unannounced audit visits) on firm level linkage capabilities

Some firms indicated that before the introduction of the second regulatory change (EC 2013/473/EU), they had an adversarial type of relationship with their critical subcontractors[27] and crucial suppliers[28]. The Senior Quality Assurance Director of Garner Ltd confirmed that the linkages were weak before the strengthening of regulation as reflected in the quote bellow:

"There is no doubt that since the inception of the new approach in the 1990s the relationship between manufacturers, suppliers and notified bodies has been more professional and more separated" [Res 061 (Man), Jan, 2017].

The second regulation (unannounced audit visits) also regulated operations of suppliers and that forced firms to move towards collaborative relationship with their suppliers. This regulation also brought more scrutiny and responsibility to diverse set of medical device sector actors including manufacturers, suppliers, sub-contractors, authorized representatives, importers and distributors, Figure 7.1 shows the impact of EC Recommendation 2013/473/EU on the supply chain.



[27] A critical subcontractor ensures all or part of the medical device's design, or performs all or part of the manufacturing processes, or carries out all or part of an activity in relation to regulatory requirements (e.g.: post-market data collection)

[28] A crucial supplier provides finished devices, or key sub-assemblies essential to the performance of the MD, or critical raw materials.

Figure 7.1: The EC 2013/473/EU Supply chain flow and compliance. Source: BSI (2015)

The new regulations compelled each actor in the supply chain to independently verify compliance of the previous actor (figure 7.1). Each actor became responsible for implementing vigilance, notifying authorities of non-compliant devices and taking corrective action if required. As a result, the previous responsibilities in the supply chain for medical devices changed considerably, and firms now needed to reflect this in their distribution contracts. This regulatory requirement forced to firms to move away from short-term arrangements with suppliers and contractors to deeper relationships with them that involved assistance to perform for the benefit of the entire supply chain. This investment of time and resources became vital and emerged as key source of competitive advantage and improved market positioning. The collaborative, win-win relationship between the manufacturer and the supplier is one where both parties communicate more regularly, cooperatively share relevant business information and resolve conflicts through dialogue (Bastl et al., 2012). This link is not solely restricted to the purchase of products, components and services from the suppliers, but also necessitates a high degree of commitment by both parties (Lall, 1992). Such relationship leads to higher levels of performance and economic benefits over the long-term as reflected in the quote bellow from the Managing Director of JM Medical:

"We chose to collaborate with our critical suppliers on long-term basis so that we could achieve lower cost through shared problem solving and also to ensure that our components would be readily available whenever they are needed" [Res O65 (MAN), Jan, 2017].

The introduction of the unannounced audits had a huge effect on supplier agreements between actors and throughout the whole supply chain as the level of scrutiny had increased. For example, if a subcontractor(s) and/or supplier(s) refuse access to the audit team, then this could result in a suspension, or even the withdrawal of certificates. The actions of NBs thereby influenced the level of integration between firms as well as the conditions for integration. The Director of Regulatory Affairs of Charlie Medical noted:

"A lot of our suppliers are not entirely medical device suppliers so they have all had hard times. So what we had to do is change our supplier agreements. So our legal agreements with those suppliers ensured that there was a clause in there that they will be inspected any time and they are to notify us of any dates of which they are not available" [Res O56 (MAN), Jan, 2017].

The exchange of information between the local and international regulatory bodies improved considerably. Notified bodies introduced the use of a co-end system whereby if one NB feels that they can't issue a certificate to a manufacturer or if they have issued a refusal, they then notify the rest of NBs around Europe and all the member states. This had an effect on manufacturers as the system stipulated tighter regulations and stopped them from shopping around for an alternative NB after certificate refusal and that was considered as a huge improvement. The Technical Manager of one the Notified Bodies summed up the regulatory effect on firm linkages with the following remark:

"*Certainly the regulatory changes have had an impact globally on the network of actors who are interested in the CE certification system" [Res 060 (NB), Jan, 2017].*

Operational efficiencies are the results of better relationships in the supply chain that allows processes to be streamlined and simplified (Lall, 1992). Therefore, the introduction of the EC 2013/473/EU enriched the medical supply chain relationships which in turn, stimulated better understanding of partner activities, and enhanced exchange of information and resources, reducing operational down-times, product recalls and more cited non-conformities as reflected in the two quotes below:

"Changes within the new regulation requirements fundamentally changed the way NBs interact with us as more rigorous audits has resulted in more cited non-conformities" [Director – Optics Ltd, Res 074 (Man), Jun, 2017].

"After the new regulation, we developed linkage capabilities in close collaboration with other key research leaders in the field to secure the proceeds of our product portfolio research investments" [CEO – Med Tec Ltd, Res 072 (Man), Jun, 2017].

7.2.4 Summary of the effects of the second regulatory change (unannounced audit visits) on UK firms' technological capabilities

Most firms were active in understanding the view of the new regulation and thereby managed to implement new requirements in their business, in turn, they became successful. The development of new capabilities and resources in the turbulence created by the EC 2013/473/EU regulatory change contributed to the firms' success. These firms pursued implementation of the regulatory change as a central element of gaining competitive advantage. Products and processes were designed with significant support from external providers, and linkages were formed between new and existing products and processes.

On the other hand, some firms especially the SMEs struggled to implement requirements related to the EC 2013/473/EU regulatory changes due to organizational constraints. These firms criticized the need, ability and resources required to support the on-site audit along with the issue of audit duration for a company with limited product range. Furthermore, some firms failed to see the possibilities inherent in regulatory change requirements. These firms ended up as losers in the market because they addressed the changes only as factors restricting them and not as new opportunities.

Some big manufacturing firms even though they had the market advantage felt more risk averse and put less completely radical innovations on the market. Here, some firms were torn between the desire to introduce new and innovative solutions and the need for safe and secure implementation. This innovative behavior protected firms from the rejection of products by the new regulation and also promoted easier acceptance by the market, due to the fact that the new product is an improvement of a previous one, already in use. The following table shows the summarized effects of EC Recommendation 2013/473/EU on medical device firms in the UK.

Table 7.2: Effects of the second regulatory change (unannounced audit visits) on medical device firms in the UK

Firm	EU Recommendation 2013/473/EU Ensuring that the notified body carries out a proper verification of the fulfilment of the legal requirements by the manufacturer. **Affected Capability**		
Alpha Ltd	INVESTMENT	PRODUCTION	LINKAGE
	• The changes affected the firm's operational costs, and staff competency requirement and therefore affecting the firm's medical device product lines. • The company had to invest in additional human resources to cope with the impact of the new regulations, and reported that the organization was inadequately qualified to deal with the impact.	• The new regulation slowed down firm's product development and innovation substantially. • The duration of the approval process increased	The firm had to re-negotiate supply chain agreements, and alter documentation and quality management systems.
Bravo Ltd	INVESTMENT	PRODUCTION	LINKAGE
	• The firm had to recruit additional qualified staff to help manage the transition, ensuring that the organization has comprehensive clinical and technical data for their product families.	• The additional scrutiny in the new regulation increased the difficulty of new product introductions due to indeterminate timescales and additional costs.	The organization had to improve their well preparedness for audits, and review the arrangements for post-market surveillance. All this had to be done at high cost
Charlie Medical	INVESTMENT	PRODUCTION	LINKAGE
	• In 2016, the firm made 9 people redundant as a result of the regulatory change • The firm's return on investment was almost immediate prior to the regulatory change but now because it is taking between 8-12 months to get CE approval of the same type of product, thereby only seeing the return after one and half years.	• The amount of inspection days when the auditors come on sight doubled after the new regulation, therefore increased in compliance costs • Firm's Technical files scrutiny after the new regulation increased, before they used to be reviewed in a day but now it takes three days to review. Thus, the increased review time is also paid by the manufacturer • The firm has reduced innovation and their R&D department has gone from 12 to 3 members • Now invest more in a smarter production due to regulatory cost • For the first time, the firm is now going to other markets in search of return on investments due regulatory change	As one NB's license was revoked due to changes in regulation. This has cost the company about £400 000 just to implement these new changes (drawing in a new NB required an admin fees, re-inspection fees, transfer fees, and on-going surveillance cost).
Delta Ltd	INVESTMENT	PRODUCTION	LINKAGE
	• While operating in a competitive and increased regulatory environment the firm improved innovation performance. R&D expenditure increased by 50% £ 123, 699, 262 in 2013 and increased its headcount by 71% to 229 employees	• Regulation increased the production process efficiency • Company products reduced life cycles because of development of competitive technologies and increased time to market due to new regulatory huddles • Increase the product safety • Increased regulatory costs • Tighten up the firm's processes and make them robust and more reliable	• Re-negotiate supply chain agreements
Echo	INVESTMENT	PRODUCTION	LINKAGE

Ltd	• Complex standards and regulatory requirements added to the cost of bringing products to market and delayed product approval, and thus, impeded the success of firm in that market	• Issued a notice for compulsory strike-off in Jan 2015 in March the same year suspended the strike off. In Dec 2017 the firm issued another notice for compulsory strike-off. This strike offs have been attributed to increased regulatory costs.	• Re-negotiate supply chain agreements
Foxtrot Ltd	INVESTMENT	PRODUCTION	LINKAGE
	• Firm invested highly in R&D with total expenditure of £727,000. The investment was focused on new innovative (xxxx) monitor. • The number of employees remained the same (63) in 2013 compared to 2012. Thus, there was no effect of regulatory change on recruitment of skilled manpower • The new regulation increased the level of documentation for the technical files and maintaining those files was said to be burdensome and taking a lot of time and manpower for the firm.	• Improved operations and the turnover in 2013 increased to £6.8 million. • Increased innovation thereby maximised return on investment and strongly increased cash generation. • Received NBs visits three times in a year, one to do a technical audit, one to do a re-certificate audit and one to do a microbiology audit was onerous and increased compliance cost. • The continuous change in the regulation led to the firm not only have to alter their processes to comply forward going but also to retrospectively ensure the existing product meets compliance.	2013 International revenues increased by 26% to £1.537,000 compared to £1,223, 000 in 2012 partly due strong international links.
Garner Ltd	INVESTMENT	PRODUCTION	LINKAGE
	• -The core regulation did not have a big impact on the firm, apart from the fact that they ended up with a suitable and appropriate quality agreement and commercial contract in place to make sure they identify the roles and the responsibilities for those within the supply chain.	• The new regulation did not affect the firm's innovation processes • The firm's reviews and monitoring of their critical suppliers increased due additional peripheral regulations	-Linkages through educational establishment grow
Hex Medical	INVESTMENT	PRODUCTION	LINKAGE
	• The regulatory change affected both training and administrative costs linked to preparation of contracts and auditing. • The regulation affected the level of available skilled personnel necessary to carry out innovation	• Timelines for reporting serious incidents were reduced from 30 to 15 days under the new regulation. The firm had to ensure they have sufficient staff and adequate internal systems to meet the new requirements.	The firm increased their focus more on post-market surveillance and vigilance.
Indigo Ltd	INVESTMENT	PRODUCTION	LINKAGE
	• The firm highlighted instead of investing £20 000 on the regulation they would rather spend it purely on materials.	• The financial impact of the new regulations was significant for firm. The new regulation increased cost of compliance. • Extended product's time to market	Because the regulation allowed critical supplier audits. The firm's linkage capabilities were heavily affected as they had to put systems in place to accommodate new terms and new supply contracts.
JM Medical	INVESTMENT	PRODUCTION	LINKAGE
	• The firm continued to invest heavily in R&D their product pipeline continued deliver innovative profitable products in spite of the stringent regulated environment. The firm spend £46m on R&D projects	• In 2013, the firm's operations and performance remained static. The product sales were £181.7m (2012 £181.6m)	The firm had strong linkage capabilities with its suppliers and proactively reviewed its customer contracts to leave the company well placed to maximise supply.
Kilo	INVESTMENT	PRODUCTION	LINKAGE

Ltd	• The new regulation has added at least a year before the firm can launch new products having to go through the regulatory approval tests	• Innovation capability increased. In 2017, Her Majesty Queen presented the company with another award under the Innovation category, for its technical and clinical excellence	The unannounced audits have heavily increased regulatory cost on the firm; on top of that they have to pay first class plane tickets for auditors who would have gone to their critical suppliers in China.
Lima Medical	INVESTMENT	PRODUCTION	LINKAGE
	• Overall companies operation and performance continued to increase with a turnover of £610m in 2014 from (2013 £562m)	• The company has had to ensure even before these additional checks or unannounced visits that these things were in place so they interpreted the changes as re-enforcing.	After new regulation, the company did spend more money in making sure that they are complying with the unannounced visits
Med Tec Ltd	INVESTMENT	PRODUCTION	LINKAGE
	• The firm depended on their capability of producing advanced medical equipment, which required highly qualified personnel. • The firm managed to attract and retain qualified personnel and thus had a significant impact on the success of the company. • In 2013 the turnover increased to £442m from (2012 £352m)	• Change in regulations increased the firm's costs and delayed the development and introduction of new products. • The firm's production site depends on a number of suppliers for components. After the new regulation, there was a high risk that those suppliers might change their terms. The firm therefore increased their follow-up strategies on critical suppliers regarding delivery precision and quality of components. •	After the new regulation, the firm developed their linkage capabilities in close collaboration with other key research leaders in the field to secure the proceeds of their product portfolio research investments.
Neiva Medical	INVESTMENT	PRODUCTION	LINKAGE
	• Increased training programmes for all employees responsible for regulatory compliance. • The firm took on board the regulatory changes and recognised that the cost of non-compliance with policy, regulation and standards governing products and operations regarding registration, manufacturing and distribution was higher than complying. •	• The firm increased its strategy on reviewing product safety and compliance data. • Welcomed unannounced audit visits positively as they had already implemented programmes and supporting resources to ensure product quality and regulatory compliance, including analysis of customer complaints and adverse event data. • The new regulation slowed down the time to market of the firm's products. The NBs moved away from offering the CE 45 or CE 90 where a manufacturer could get a quicker approval by going for a 45 or 90 days approval.	The new regulation forced the company to have appropriate technical agreements, quality agreements as well as the commercial contracts with their suppliers
Optics Ltd	INVESTMENT	PRODUCTION	LINKAGE
	• The firm's R&D and innovation was not affected • Increased regulatory affairs personnel •	• The review of technical files and design dossiers by NBs has also resulted in more comments that must be addressed before the reviews are completed. Leading to longer review times at the cost of the manufacturer • The firm had to change supplier agreements and in some cases re-assess some of the key critical suppliers at a relatively high cost for these additional scope of services and liability	• Changes within the new regulation requirements fundamentally changed the way NBs interact with the manufacturer as more rigorous audits has resulted in more cited non-conformities

Compiled by author from empirical data

7. 3 Detailed Analysis of Three UK-based Firms

This section will analyze three studies in more detail within the context of the two regulatory changes i.e. the MDD 2007/47/EC and the EC 2013/473/EU regulation. The actions are derived from the descriptions presented by knowledgeable respondents through interviews and in published or archival documents.

7.3.1 Alpha Ltd

Alpha Ltd was established in 1975 as a family run business set up to provide medical equipment and services to a wide range of customers, including the UK NHS and private hospitals. The company had a turn over of £1.3 million in 2016 and wide range of in-house designed products. Over the years Alpha has established a strong reputation for design, manufacture, quality and excellent customer service with full technical support and advice. The firm can be categorised as a SME with an employment size band of 20-49 people and has an international reputation for supplying medical equipment and exports its products to over 28 countries. Alpha's international operations played a crucial role for its long-term growth. In 2005, Alpha entered a joint venture agreement with another company. Alpha held 60 percent share of this joint venture and provided technical knowledge for the production and sales of the products. Alpha manufactures medical devices with a focus on oxygen-therapy products and electrical magnetic products. The purpose of the joint venture and the move away from export and sales representation, Alpha's Quality Manager argued, was less about the cost savings aspect and rather a change to be in closer contact with the growth in UK.

"The real reason for starting this joint venture was that we wanted to strengthen Alpha's presence in UK. The drive was to tap into UK's production competence" (Quality Manager - Alpha, 2017).

The joint venture factory in the UK was inaugurated in 2005, but after a year of operation the joint venture was still not running smoothly. Alpha soon realized that the management team assigned by the other partner to manage the factory was spending more time inspecting Alpha to make sure it did not double-cross them, than supervising factory operations. Alpha then decided to buy out its joint venture partner

in 2006 and turned into a wholly owned family run business again. Although it had to invest more financial capital and bring in professional management, Alpha was able to gain complete control over operations and build direct contacts with the international suppliers. By 2009, the business operations had improved.

The firm outsourced some parts of its software to a company in the USA up till 2011 when compliance related problems arose. Consequently, the firm terminated its supply contract with their USA based supplier and that led to changes in their production processes. Their assembly is now carried out in-house by their fully trained engineers, enabling full control from component conception right through to the finished product. In addition, Alpha began local sourcing activities for basic materials, and gradually expanded the sourcing activities in the UK in terms of volume and sophistication. The Quality Manager of Alpha remarked:

"We started from very basic items and now we can source relatively complicated units. Our sourcing team has grown and become more competent along with these suppliers. It has been an experience of mutual learning" (Quality Manager - Alpha, 2017).

Alpha provides personal monitors, which offer a unique method of determining individual risk to harmful exposure from waste anaesthetic gases in a clinical environment. It has been known for many years that exposure to waste anaesthetic gases may be harmful to the health of exposed employees (Guirguis et al., 1990). The areas of potential significant exposure include: operating theatres, recovery rooms, dentistry, maternity units and veterinary surgeries (ibid).

The firm also has a long history of supplying medical device systems components to nearly every NHS hospital department, which has earned the company a reputation for providing a friendly, flexible service with competitive pricing. Moreover, the firm operates a comprehensive schedule of maintenance contracts to ensure continued accuracy and reliability of its range, together with a recalibration service, so its customers can always have complete confidence (Alpha, 2017).

All products of Alpha are CE marked and is annually audited and fully meets the

requirements of the medical device quality system – ISO 62304, ISO 13485 and conform to Directive 93/42/EEC as amended by the software regulation (MDD 2007/47/EC). Alpha adhere to regulations and procedures for raising equity for expansion and research, however, they face some challenges in maintaining the ISO 13485 and IEC 62304 standard, which they viewed as too aggressive. To that effect, the Quality Manager Alpha commented:

"We are a small company therefore struggling a little bit to maintain ISO 13485 because it is really a strong requirement which cover the design phase and everything else" (Quality Manager - Alpha, 2017).

Effects of the first regulatory change (software) on Alpha Ltd.'s investment capability

The introduction of the software regulation (MDD 2007/47/EC) required that safeguards pertaining the risk management be put in place to ensure that such software is safe and fit for purpose (European Commission, 2007). Alpha emphasized that risk analysis mandated by the software regulation start at the initial R&D phase and cover supply chain, manufacturing, design transfer, software integration, and also aligns with the post market surveillance. The introduction of the risk management led to a reduction of the firm's device recalls. However, due to massive documentation procedures such as additional technical reporting and provision of information concerning validation and verification introduced in the new regulation, the new requirements were seen as limiting investment opportunities and increasing the responsibilities for the firm. The Quality Manager of Alpha said:

"The validation of software production line costing us about £15-20000. This has increased compliance costs and also limited our investment opportunities as a company (Quality Manager - Alpha, 2017).

Alpha management also raised some concerns about requirement of clinical data for conformity assessment. Conformity assessment entails clinical evaluation of medical devices which includes a process of compiling clinical data in form of the safety and/or performance related data that is generated over the use of a medical device (Chowdhury, 2013). It can be obtained from clinical investigation(s) of the device

concerned or from clinical investigation(s) or other studies of a similar device reported in scientific literature if the equivalence of the device to the one concerned can be demonstrated (Fiedler, 2017). Nelson and Winter (1982) suggest that internal R&D activities look to regulations and changes in regulations for guidance and evaluation of new solution. Alpha described the guidance and evaluation process requirements as too complex resulting in the firm having to increase its expenditures on R&D compliance activities and increased design times and ultimately slowing down products' time to market. The Quality Manager of Alpha mentioned that:

"We complained about the process of conformity assessment to the competent authorities, and called for reducing clinical data requirements" (Quality Manager - Alpha, 2017).

The software regulation (MDD 2007/47/EC) led the firm to redefine the training needs for innovations, prototyping, design, testing, validation, and release processes. A highly skilled workforce, which included researchers, engineers, and staff with regulatory expertise, was an important competitive factor for the firm. Expertise in regulatory affairs was critical, as each new and improved product had to be approved through the new regulation. An increased number of staff devoted to regulatory affairs was needed to help the firm boosts its returns. The Quality Manager of Alpha commented:

"We were forced to increase the workforce training on the EN/IEC 62304 standard for efficiency and competitiveness in operations" (Quality Manager - Alpha, 2017).

However, the need to devote substantial resources to regulatory matters reduced resources that would have otherwise be available to support product development and commercialization. The firm had to increase the workforce training on the IEC 62304 standard for efficiency and competitiveness in operations and training of the risk management system process activities. The firm indicated that it had spent approximately £100,000 per year on training of small teams. The Quality Manager of Alpha stated,

"We are always happy to evolve existing product ranges, or create new ones to meet customer and new regulatory requirements, however during manufacturing you need to validate your validation line which is very expensive, to validate a production line it costs about £15-20 000 and that is affecting us" (Quality Manager - Alpha, 2017).

The following table shows the firm's turnover from 2010 to 2016.

Table 7.3: Alpha's turnover from 2010 to 2016

Year	2010	2011	2012	2013	2014	2015	2016
Turnover	£413,560	£522,491	£185,907	£282,989	£495,496	£656,327	£1,356,593

As shown in the table above, Alpha's financial performance in 2012 was below expectations, as reflected in its revenue growth at £185,907 compared to £522,491 in 2011. The firm attributed the turnover reduction partly to high cost of compliance. To improve the company's revenue performance, the firm had to cut cost in various operational areas such as shortening the research life cycles.

Effects of the first regulatory change (software) on Alpha Ltd.'s production capability

The influence of the software regulation (MDD 2007/47/EC) in product development created significant changes in Alpha's allocation of inventive efforts to meet market requirements. The new regulation established disruptive requirements for the firm since they could not be met with existing products and technology (Bell and Pavitt, 1995). They forced the firm to establish new initiatives to develop new solutions and introduced the need to consider integration between the new and existing products. The new standards and regulatory requirements added to the cost of bringing products to market and delayed product approval, and thus, impeded the expected success of the firm in that market. The Quality Manager of Alpha remarked:

"For us to meet those requirements we needed to spend huge sums of money recruiting more people in terms of production because of a lot of new regulatory paperwork involved and new control measures. The changes affected the product development process and our existing product" (Quality Manager - Alpha, 2017).

At the same time, the firm echoed that the MDD 2007/47/EC regulation facilitated better understanding of products by demanding product content transparency and

reliability of same products through the validation processes. By requiring increased transparency, the new regulation drove the demand for the unbundling of the medical device software lifecycle process into smaller parts relevant to each production process phase. As a consequence, the IEC 62304 standard associated with the 2007/47/EC led to the firm's software development process improvement. The Quality Manager of Alpha highlighted:

"So you create a procedure, you create a quality manual you create a form then you invite the notified body in. All that helps of transparency in the production line" (Quality Manager - Alpha, 2017).

Furthermore, empirical results demonstrated that, in a transition period of regulatory change, the firm experienced adverse consequences. However, in the long term, the regulatory framework for medical device software had affirmative effects on the firm with respect to the quality of new product offerings.

Effects of the second regulatory change (unannounced audit visits) on Alpha Ltd.'s production capability

The unannounced audit visits regulation (EC 2013/473/EU) put an extra burden on Alpha's costs associated with the process of complying with these audits. The firm highlighted that medical device manufacturers are required to pay for the audit and the current cost in the UK is approximately £5000 per visit. The firm expected at least one unannounced audit during a three-year period and two auditors are typically involved in the audit. The Quality Manager of Alpha remarked:

"The calculation of the cost were too high and depended on several parameters including the number of days the audit lasted, the number of auditors, the place where the audit took place (travel expenses), the administrative and report fees, tests performed for any samples taken and the safety measures of the auditors" (Quality Manager - Alpha, 2017).

The firm indicated that their unannounced audit identified potential concerns with the management of critical suppliers, which then triggered a second unannounced audit to that supplier. The cost of this second audit was also charged to Alpha increasing the

compliance cost even more. This also led to delay in getting approval due to lengthy process associated with audit. According to the interview with the CEO of Alpha the new regulation limited the number of innovations, delayed entry for products in the market and adversely influenced the expected rate of return. But the new regulation also created opportunities for firm to improve the production process and stimulate creativity as mentioned earlier.

Effects of the first regulatory change (software) on Alpha Ltd.'s linkage capability

The new regulation demanded changed conditions for firm's collaboration due to new challenges in the interface between actors. Alpha had to change their linkage processes with their suppliers and contractors as a result of the new regulation. Alpha initiated development parts of the software design through outsourcing to bridge skills shortages and these software parts were then integrated into the medical devices manufactured by Alpha. The Quality Manager of Alpha said:

"Yes we have one software related product and we use a contract manufacturer to develop the software because there are not a lot of skilled people out in the medical device industry" (Quality Manager - Alpha, 2017).

In response to software regulation, the firm took certain precautions to ensure its control over the whole chain of development of the software concerned.

"We needed to approve our USA based supplier, by approving them we needed the time to go and audit them onsite bearing in mind that we didn't have the lead auditor. Also, we needed to create what is called a quality technical agreement so that agreement covers our relationship" (Quality Manager - Alpha, 2017).

Alpha ensured that the development process of the software fits the requirements imposed by the annexes to the MDD 2007/47EC and the applicable standards, such as EN 62304 by documenting all the elements of software development process. This process proved extremely onerous for the firm as the supplier was based in the USA and was accustomed to FDA regulations that were different to the software regulations. This led to termination of agreement with US based suppliers and forced

Alpha to identify local sources. The Quality Manager of Alpha had the following to say:

"Because of some regulatory complications we had no choice other than to terminate our contract with the international supplier and looked for another option" (Quality Manager - Alpha, 2017).

Effects of the second regulatory change (unannounced audit visits) on Alpha Ltd.'s linkage capability

Alpha's delivery of products and processes was dependent on complements in the chain of production and new regulation prompted the inclusion of external process or product providers in audits. From a contractual point of view, the new provisions had an impact on the content of contracts. The firm had to revisit their procedures for planning and execution as well as set up new contracts with the NB and external providers at a higher cost.

Summary of Alpha's implementation actions

Evidence presented in Alpha case study highlights that the firm viewed the changes in the regulation as new restriction on business practices and found regulatory requirements costly, time consuming and restrictive. This put additional pressures on firm's limited resources impacting its competing advantage through the loss of agility.

7.3.2 Bravo Ltd

Bravo Ltd was launched in 2006 as an innovative, medical technology focussed, and standards driven company. It can be categorised as a small firm with an employee size of less than ten people and had a turnover of half a million pounds in 2017. Bravo products include, orthopaedic restorative devices, dental restorative composite, and biosensor medical devices. In addition, the firm is involved in providing expert technical advice in medical and healthcare technology industries worldwide, including environmental management and related sustainable technologies (Bravo Ltd, 2017).

From 2007 Bravo was involved in providing both on and off-site support with regulatory affairs, quality assurance and product development on long term and

interim projects to a variety of clients and taking product innovations to the EU market. By 2012, Bravo had extended its product innovations to the USA and other global markets. The firm is made up of scientists, engineers, and business innovators, with in-depth industry expertise, working closely with their clients to turn great ideas into innovative products and services.

Since its foundation, Bravo's business development experts have played a pioneering role in a broad spectrum of sectors including biotechnology, pharmaceutical and medical technology. In many cases, the firm's core technology is created in-house but it also outsources some of its products components. The scope and variety of their projects can be very different, but involves usual business processes of identifying the need, assessing the market opportunity, creating the solution and then transferring the output into a manufacturing supply chain (Bravo Ltd, 2017).

Effects of the first regulatory change (software) on Bravo Ltd.'s investment capability

Bravo's success was built on innovation and a strong commitment to R&D with R&D emerging as key part in the life cycle of their products. The introduction of the software regulation (MDD 2007/47/EC) led to increase in Bravo's operational expenditures. Approximately 20% of the increased expenses were for legal services, compliance submissions, and supply chain development. The firm's viewed the new regulation as quite stringent thereby affecting all the processes involved in the developing new products. The Principal Consultant of Bravo Ltd remarked:

"The UK regulators are quite stringent but they are just as the German regulators, perhaps not as stringent as Eastern European countries because of resources and that entire thing" (Medical Devices Principal Consultant - Bravo Ltd, 2017).

In some cases the firm lacked in-house capability to test clinical safety of their device and these devices were then sent to a university or a research and development institution to conduct those tests. Preclinical investigation is the stage in the product life cycle that incorporates and resolves conflicts between requirements and manufacturing capabilities (Fiedler, 2017). While in this stage, the product is

subjected to verification and validation (V&V) processes as required by the MDD 2007/47/EC.

Product development from the earliest phases requires active involvement of practicing clinicians. These clinicians are essential to conduct animal testing (or clinical studies, as needed) while engineers will focus on bench testing (Fiedler, 2017). Bravo could not manage to meet these new regulatory requirements on its own; the firm didn't have the capacity and capability. The Principal Consultant of Bravo Ltd revealed that:

"These days you are obliged to do some sort of clinical testing to produce some sort of data for the notified bodies to be confident to say yes you have done enough to convince us that the medical device is clinically safe to use" (Medical Devices Principal Consultant - Bravo Ltd, 2017).

Moreover, the preclinical investigation activities permit Bravo's engineers to obtain the required knowledge about product performance, failure modes, and risk mitigation strategies. Bravo's safety concerns during first clinical use and pilot phase mandated collaboration between engineers, inventors, and clinicians. At this phase, the clinician frequently takes on the leadership role but needs support of regulatory expert. Thus, the new regulations kept up the firm's cost of producing a safer device for the market but enhanced strong collaborative relationships. The Principal Consultant of Bravo Ltd elaborated:

" As the manufacturer you have to do some sort of testing to support the literature review route and say yes even if it is similar and all that, I have also done this clinical testing to support what is being published out there before it is accepted" (Medical Devices Principal Consultant - Bravo Ltd, 2017).

Despite Bravo's increased investment in regulatory compliance, the firm's management was efficient in resource management and took on board well the implementation of the new regulation. The Principal Consultant of Bravo Ltd underscored that:

"The MDD 2007/47EEC enhanced the clinical evaluation, the depth of risk management and the emphasis on batch reconciliation so that we should be able to account for every device that has been manufactured within certain given periods" (Medical Devices Principal Consultant - Bravo Ltd, 2017).

From an overall industry context, Bravo placed strong emphasis beyond the impact of regulatory change on investment in recruitment and training of skilled personnel as reflected in the quote below by the firm's Principal Consultant:

"To start off, the industry really needed education to accept that software was now a medical device and as such, has to be regulated as a medical device and it even took quite long for software developers to catch up to the understanding that now what they were developing wasn't just an ordinary software but is a software regulated as a medical device" (Medical Devices Principal Consultant - Bravo Ltd, 2017).

The MDD 2007/47/EC created new firm needs for retraining of staff to improve the success rates of the respective software-embedded devices. The changes called for recruiting staff members who would provide the company with skills and productivity to propel profitability.

Effects of the second regulatory change (unannounced audit visits) on Bravo's investment capability

Bravo had to implement the provisions needed to provide answers to the auditors' questions. This meant the firm had to increase their investment budget in recruiting and training of additional "key regulatory affairs" staff members and define procedures regarding temporary replacements and delegations required for the unannounced audit to be performed in satisfactory conditions. The Principal Consultant of Bravo Ltd noted:

"Now when we produce the technical file that governs the medical device, the people that perform the testing and the processes are required to produce a CV and attach to that particular piece of work that they have done. Such that when the auditors come to review what we have done they will also have the confidence that the person that did it is competent enough to have been able to do a successful work, previously it

wasn't like that, anyone could just do anything with a little bit of training" (Medical Devices Principal Consultant - Bravo Ltd, 2017).

Effects of the first regulatory change (software) on Bravo Ltd.'s production capability

The MDD 2007/47/EC forced the firm to change their practices to create safe and quality software. The firm had a general belief that the IEC 62304 had met expectations in enhancing the safety of medical devices. Before the software regulation (MDD 2007/47/EC) there was a minor flaw for the company's software systems that were not in straight contact with patients. There was not any regulation for finding out the possible risks and fix them. With the introduction of the new regulation, the Principal Consultant of Bravo Ltd commented:

"*Now every software that is to be developed as a medical device has to go through a process of analysing the risk associated with the software, the disability of that software and the risk associated with the disability and not just the use of it but the end output of it" (Medical Devices Principal Consultant - Bravo Ltd, 2017).*

The regulatory change influenced the firm's process of manufacturing their products, leading to improvements in quality. The firm applied the external new regulation and standards as guidelines to modify their own internal regulatory compliance processes. In this way, the firm exerted their regulatory processes across their different products, thereby improving the quality of all their product offerings. However, the changes in regulation increased the time required to introduce new products and technologies to the market.

Effects of the second regulatory change (unannounced audit visits) on Bravo Ltd.'s production capability

The 2013/473/EU regulatory change influenced Bravo's organizational practice associated with manufacturing of devices since the delivery of their product innovation required input beyond the internally available components. The regulation thereby influenced businesses' consideration of whether to make or buy parts of their products. In the end the firm decided to make 95% of its products parts, thus the change opened up space for the firm to take full responsibility for most of its different

parts of their products and experienced fewer product recalls.

To get the ISO 13485 certification for QMS, the firm had to go through the process of initial audits and then certification audits. One concern mentioned by the Principal Consultant of Bravo Ltd was impact of these audits on the firm's compliance cost associated with the 2013/473/EU audit process:

"*The initial audit alone cost us around £5000 and then the actual certification audits cost a little bit extra. A day's work for an auditor will cost between £1 300 to £1 700. That is the time that they have spent on site, but extra costs do come on top. They are several times as a manufacturer we had to pay the auditor's travel and hotel expenses. The writing of the report can take about one and half days and again we had to pay for that also. By the time they finished, the whole certification cost us about £12 000" (Medical Devices Principal Consultant - Bravo Ltd, 2017).*

Effects of the second regulatory change (unannounced audit visits) on Bravo Ltd.'s linkage capability

Unannounced auditing and monitoring procedures raised issues in the relationship between the Bravo and audited suppliers. Reported issues include reduced trust and commitment and also increased coordination efforts. It was very important that as part of Bravo's preparation for compliance with the 2013/473/EU Commission Recommendation that the firm review and revise as applicable, the contracts/agreements to ensure their sub-contractors and suppliers understood their obligations. However, the management had to disintegrate their interactions with one of their crucial suppliers at a very high cost due the suppliers' nonconformities that affected the safety and performance of Bravo's products.

Furthermore, Bravo revealed that the overall medical device industry collaborative linkages efforts were so weak and not enhancing the firm's innovation process. Therefore, the firm took a pro-active approach and wrote to the competent authorities requesting them to give actors in the industry access to a system called EUDAMED. EUDAMED is an information system database for exchanging legal information related to the application of the EU Directives on medical devices and information about products of manufacturers but it is only accessible to the competent authorities.

By giving access to actors, the firm considered that this would increase efforts to communicate and improve collaborative linkages within the medical device industry network. The Principal Consultant of Bravo Ltd remarked:

"We wrote about this because Europe tends to use a database run and managed by the FDA called the MAUDE. This database houses information about any complaints that have been launched against the medical device on any market, which the FDA regulates. So if we are to develop a new device, and be able to check on the database system and see something wrong against a device that is similar to ours then we will know how to design the new device to eliminate problems that might come later (Medical Devices Principal Consultant - Bravo Ltd, 2017).

Summary of Bravo's implementation actions

Adopting the new regulation contributed to Bravo's products safety improvement, better product quality, efficacy, and reliability, while company experienced fewer product recalls. Since Bravo is a firm that is both a manufacturer and a critical subcontract to other MNCs and SMEs, the EU 2013/473/EU subjected them to two unannounced audits according to its two activities. This however had a huge impact on the overall firm's compliance costs. Bravo was a proactive proponent after the regulatory change, both facilitating contacts between regulators and the companies in the market and making direct contact with the persons at the regulatory agency who would be responsible for supervising implementation.

7.3.3 Charlie Medical Ltd

Charlie Medical Ltd is a creative development, engineering, production and research company. Founded in 1978, the company design and manufacture a wide variety of wound care products, all of which are packed and sterile and constitute 80% of the business. As well as wound care dressings, the firm also design and contract manufacture airway management products such as Laryngectomy Protectors, Voice Prosthesis Brushes and Endotracheal (Charlie Medical, 2017).

In addition, the company specialises in the development of innovative blood-processing equipment. The firm develops embedded software or firmware in their

ground-breaking blood recycling devices "XXXX" (product name) in collaboration with one university. The devices recover blood spilled during open heart and major trauma surgery, cleans and concentrate the blood cells and return them to the patient. This meant reduced risk, quicker recovery, better outcomes and potentially huge savings for hospitals, because less donor blood is required (Charlie Medical, 2017). The firm is a SME that has an employment size band of between 100 to 249 people. The following table shows the firm's key financial highlights:

Table 7.4: Charlie Medical's key financial highlights from 2011 to 2017

	2011	2012	2013	2014	2015	2016	2017
Turnover	£13.4m	£14.8m	£15.3m	£14.5m	£14.8m	£14.9m	£17.2m
Gross Profit margin	46%	49%	42%	43%	42%	36%	40%
Operating Profit/Loss	733K	1,030K	826k	392k	1.364k	(224k)	644k

In 2017 the company's turnover grow by 15% to £17.2 million. Other areas of growth for the firm were in export and medical device development of £0,5million. On the onset of the MDD 2007/47/EC the firm was investing more in R&D, as it believed that the way forward was the continued development of its existing product lines as well as expansion into new product areas. In 2012, despite the national and global medical devices continuing to be in a depressed state, Charlie Medical had a very successful year. Turnover increased in excess of 10%. With the level of uncertainty in the global market, the firm continued to maintain strong links with customers and suppliers as well as maintaining active control over operational costs (Charlie Medical, 2017).

Crucial to the company's success was the development of new innovative products, thus in 2013 the firm launched a new surgical trading division around its new blood recovery system "XXXX" product. In 2014, a year after the EU Regulation 2013/473/EU was introduced, the firm's turnover fell back to £14.5m from £15,3m as a result of expected reduction in third party sales and unexpected length of time taken to get product registration. This was down to processing delays within different governmental regulatory agencies. By then, the firm's ground-breaking blood

recycling innovative device was subjected to unexpected delays that had cost the company 12-18 months (Charlie Medical, 2017).

By end of 2014, the firm's "xxxx" product had already received Canadian national approval following highly successful clinical trials, however, at the same time there were still on-going clinical trials at several UK hospitals. Turnover grow by 2% in 2015 and a difficult decision was made to close down two of their subsidiaries and move across to a distribution model. The decision was essential to get back on a sound footing because their key product was still subject to regulatory approval delays. Yet again four years later in 2017 the firm's "xxxx" product still had on-going trials at UK hospitals. Their product went through minor design changes to facilitate better growth going forward and was anticipated that the launch of a significant improved CE marked product would be in early 2018 (Charlie Medical, 2017).

Effects of the first regulatory change (software) on Charlie Medical Ltd.'s investment capability

The implementation of the new regulation forced Charlie Medical to change its investment strategies, as such, the firm started to invest more in a smarter production, because they were getting a lot of regulatory costs. The increased regulatory costs meant that the firm had to reduce costs elsewhere in the business. Charlie Medical took a radical decision to reduce R&D spending and invest more into smart automation production. The regulatory changes forced the firm to reduce the innovation; their R&D department reduced from 12 to 3 members. The introduction of the MDD 2007/47/EC had mixed consequences for recruiting employees because the firm was seeking those with top skills, and their compensation had cost implications on the project for each EN/IEC/62304 compliance software release.

Effects of the second regulatory change (unannounced audit visits) on Charlie Medical Ltd.'s investment capability

The firm had to lay off many workers as they pursued efficiency and cost-cutting goals. The employee layoffs trend was further heightened by the introduction of 2013/473/EU regulation, which caused the firm to make nine people redundant in 2016. The Director of Regulatory Affairs of Charlie Medical commented:

"In 2016, the firm made 9 people redundant as a result of the regulatory change" (Director of Regulatory Affairs - Charlie Medical, 2017).

The firm highlighted the its return on investment was almost immediate prior to the introduction of 2013/473/EU but after changes it was taking between 8-12 months to get CE approval of the same type of product, thereby only seeing the return after one and half years.

Charlie Medical had historically been active in placing multiple new products on the market. The EU Regulation 2013/473/EU caused the firm to consider investing on one product offering at a time. Moreover, the firm's target market focus changed after the new regulation, and for the first time they took their products directly to the USA first because their regulatory pathway (FDA 510k) process for products on the market was considered far simpler and cheaper in the long run than the UK regulatory framework. The Director of Regulatory Affairs of Charlie Medical noted:

"Because of the high cost of compliance we are now working on one product at a time and bring it to the market place and in fact now we are actually going to other markets first, which is the first time it has ever happened and the reason for that is we are looking at the return on investment" (Director of Regulatory Affairs - Charlie Medical, 2017).

Effects of the first regulatory change (software) on Charlie Medical Ltd.'s production capability

Charlie Medical indicated that the MDD 2007/47/EC amendment made them to be more consistent in practices of software material designs and created widespread commitment within the firm to improve device quality, thus resulting in lower device recalls and failure incidences that cause harm to the users or the medical device operators. The firm had a general belief that the MDD 2007/47/EC, EN/IEC/62304 and the rest of the applicable standards had met expectations in enhancing the safety of medical devices. However, the firm also had a growing sense that overly burdensome and complex regulations threaten to choke off continued innovation and limit the exploitation of their opportunities to introduce new devices. The firm's expected acceleration of its embedded software product "XXXX" was limited due to

the continued time taken to get product registration through the regulatory agencies due to internal processing delays. The Director of Regulatory Affairs of Charlie Medical remarked:

"We do not disagree that there should be increased scrutiny for the public health but the level at which they are going has a huge impact on us" (Director of Regulatory Affairs - Charlie Medical, 2017).

Effects of the second regulatory change (unannounced audit visits) on Charlie Medical Ltd.'s production capability

The impact on production capabilities following the 2013/473/EU regulatory change was mostly inherent in the unannounced audit processes. The firm highlighted that frequency of audits that they must accomplish to ensure compliance had increased. The amount of inspection days when the auditors came on their site doubled. Furthermore, the firm's Technical files scrutiny after the new regulation increased, before they used to be reviewed in a day but now it takes three days to review. The increase in audits review times means additional cost to the firm and extended periods of bringing new products to the market. In 2016, Charlie Medical had their eight-man day's scheduled annual audit and received an unannounced inspection visit at the same time. As a small team, the firm had to comply with both visits but the huge strain was said to be unbearable. The Director of Regulatory Affairs of Charlie Medical highlighted that the approval process of new products has increased since the introduction of the 2013/473/EU regulation.

"Prior to the new regulation, a product review by the NB would take two months, thus making the firm's return on investment to be almost immediate but now because it is taking between 8-12 months to get CE approval of the same type of product, thereby only seeing the return after one and half years" (Director of Regulatory Affairs - Charlie Medical, 2017).

Effects of the second regulatory change (unannounced audit visits) on Charlie Medical Ltd.'s linkage capability

The firm had to reassess decisions across the supply chain involving external providers. The new regulation required actions concerning both relationships with

external providers and the business's internal technological focus. The company explained that the new changes increased its responsibility to establish relationships with the stakeholders in the network. This was fundamental as the firm wanted to have an impact on the uptake of its medical devices. Regrettably, the firm's NB had their license revoked after the introduction of the 2013/473/EU regulation due to its inability to demonstrate that they were able to assess appropriately. The revoke of the NB license did not only affect the links and collaborative efforts between the NB and Charlie Medical but it also affected about 305 other clients. In addition, Charlie Medical revealed that the new regulation had cost the company about £400 000 just to implement these new changes, which include: drawing in new contractual agreements and establishing new relationships with a different NB and new critical suppliers, meeting the required administration fees, re-inspection fees, transfer fees, and on-going surveillance cost.

This evolution resulted in the firm creating new processes of sharing tasks in the firm's supply chain. According to the interviewee, collaborative relationship with new key suppliers helped improved the quality of both the supplied components and the firm's products, since Charlie Medical and its critical suppliers were both now working towards achieving zero defects. The Director of Regulatory Affairs of Charlie Medical reflects this regulatory effect in the quote below:

"The relationship with our new key supplier afforded us to audit their quality system, as such quality defect on matured products are more or less non-existing" (Director of Regulatory Affairs - Charlie Medical, 2017).

The firm further indicated that collaborative relationship with the key suppliers has helped them to have reliable components supplies with little or no disruption in their production operation, since the firm operates a just in time product delivery with the suppliers, which reduces unnecessary product and components inventory stock and improves the lead time.

The collaborative relationship provided the critical suppliers with knowledge of Charlie Medical's production processes. The firm and their critical supplies were engaging in frequent communication and information sharing on product

improvement. This gave the suppliers good understanding of Charlie Medical's business and enabled them to contribute to the improvement of the production process, through joint research and design of quality and innovative products. The relationship had positive effect on time to market of the company's products.

This wide-ranging impact of regulatory change involved the firm's various organizational units and called for various types of implementation resources. Despite the operational complexities around the new regulation, the firm leaders had a view that did not seek to avoid but rather embraced and implemented the changes in an effective manner.

Summary of Charlie Medical's implementation actions

Despite continued regulatory changes, the firm kept the business on a sound footing to continue their growth and expansion plans. The continued uncertainty in the global market and specifically the austerity regulatory measures affecting the firm were a major concern. This was seen in the ever increasing regulatory and registration requirements not only affected the time to market for new products stifling innovation and patient care but also added considerable overheads to the day-to-day costs of maintaining compliance. By strengthening the firm's internal regulatory department and staying at the absolute forefront of technology both for products and manufacturing techniques the firm minimised principal risks. By maintaining strong links with their customers, critical suppliers, and crucial sub-contractors as well as retaining tight control of operational costs the firm positioned itself to withstand any future risks and changes in regulations.

7.4. Summary of the empirical accounts

7.4.1 MDD 2007/47/EC – Software as medical device summary

The influence of the MDD 2007/47/EC regulatory change crossed over the entire cycle of firm level technological capabilities. The extension of regulatory reach into software added cost. The MDD 2007/47/EC introduced new requirements. The first impact was on the products provided, since the regulation introduced a framework within which medical device companies could offer a new set of CE marked standalone or embedded products. The product requirements included a new set of processes such as validation and verification procedures, provided new harmonized

standards such as EN/IEC/62304 and new functionalities, which influenced the development process of products. Firms responded to this opportunity by taking subsequent actions concerning the development processes. To reach customers with the new products, distribution processes were modified. The continued evolution of these processes involved employee education as well as the design modifications.

The MDD 2007/47/EC opened new software market opportunities to companies that invest heavily in R&D because the safety and efficacy standards outlined in the EN/IEC 62304 had emerged as a global standard for the software development life cycle and thereby achieved global harmony. This amendment further empowered oversight authorities to take firm action against nonconforming companies and their products. The empirical data revealed that MDD 2007/47/EC enlightened the medical device industry on procedures for conforming to international regulations to reduce incidences of device recalls.

Data from some firms showed that MDD 2007/47/EC has helped SMEs in the medical device manufacturing to catch up with larger organizations because the same quality standards apply all. The MDD 2007/47/EC has enhanced collaboration efforts within the supply chain of the medical device industry. However the interview findings indicated that the training cost significantly increased as leaders of firms were seeking compliance with the Directive and its applicable standards. The study established that the training needs were at the quality and operational level. As such, the first regulatory change had proactive effects on most firms that led to the development of organizational capabilities and resources that may be potential sources of competitive advantage and that affect a firm's ability to gain financial benefits from improved business operations.

7.4.2 EC Recommendation 2013/473/EU-routine unannounced audits summary

The introduction of EC Recommendation 2013/473/EU increased the surveillance, not just through the unannounced audit visits but also through internal audits of the medical device manufacturing systems to minimize device recalls and failure incidences that put the lives of the users in danger. One responded described an unannounced audit as nerve-wracking for even the most buttoned-up organizations.

The EC 2013/473/EU forced the manufacturers to create or update procedures that cover supplier quality. The manufacturing firms had to identify which suppliers are critical subcontractors, which are crucial suppliers, and define the criteria for evaluation. The EC 2013/473/EU prompted the manufacturing firms to apply more stringent criteria to suppliers of products and services that have a direct impact on the safety and performance of their medical devices.

Compliance to the EC 2013/473/EU created widespread commitment among the medical device manufacturers to improve device quality and communication among the stakeholders. It was expected by the regulatory authorities that intensified control on NBs would increase the quality of conformity assessments and reduce approvals lacking sufficient clinical evidence. This had a direct effect on manufacturers, whereby the regulations required increased involvement of competent authorities when conformity assessing high-risk devices. This in turn increased costs and the duration to reach market approval and consequently, patient availability. The EC 2013/473/EU enriched the medical supply chain relationships, which in turn, stimulated better understanding of partner activities, and enhanced exchange of information and resources, reducing operational downtimes, product recalls and more cited non-conformities. Compared to the first regulatory change that had proactive effects on most firms, the second regulatory change seem to have had more reactive effects on most firms as they did not need extensive expertise in dealing with new unannounced audit processes. Rather the firms needed to change their in-house strategies such as developing strong collaborative links with their critical suppliers.

Overall, the two different but significant types of regulations led to negative effects, such as increased barriers to entry and decreased investments in R&D on SMEs, which were counter balanced by positive effects, such as reduced risk in investments, enhanced collaborative relationships and minimized turnovers. The results of the research indicated overwhelming competitive advantages for the complying device firms, including certification and quality marks on the products preferred by both private and public hospitals. Additionally, according to the empirical data and literature, medical devices that comply with the MDD 2007/47/EC had less product recalls, which often trigger huge income losses to the medical device manufacturers.

7.4.3 Investment capability empirical account summary

The case studies established that leaders of the medical device manufacturing companies invest substantial resources in R&D to standardize their products. The findings from this study indicated that manufactures of medical devices software had positive income returns that improved after they complied with the MDD 2007/47/EC. The findings indicated the changes of the MDD 2007/47/EC led to redefining of the training needs for innovations, prototyping, design, testing, validation, verification and release processes.

Staff training was needed to ensure better efficacy and accountability from the medical devices firms. The interviews established that MDD 2007/47/EC created new needs for retraining medical device manufacturers to improve the success rates of the medical device software. The interview responses included the extended training costs that the firms factor in their R&D going forward. The other impact of introducing the MDD 2007/47/EC was demand for highly skilled personnel or specialized employees. The changes called for recruiting staff members who could provide the companies with skills and productivity that would propel profitability.

This case study revealed that some firms struggled with recruitment of highly skilled personnel such as software engineers and lead auditors. The synergy of skills such as software design and development was crucial for medical device manufacturers to nurture for research sustainability and better returns on investments.

7.4.4 Production capability empirical account summary

The empirical accounts revealed that regulatory changes yielded some positive effects on innovation in some firms: For example, it created the maximum opportunity for innovation, leaving the approach to innovate in the hands of the firms and not the regulation-setting agency. It also fostered continuous product improvement, rather than locking in some particular technology.

The other effects of introducing the MDD 2007/47/EC include: increased product market entry time and lengthened the R&D life cycles. The manufacturers called for improvements of these affected areas as they in turn, affect their competitiveness in the market. The empirical data further revealed that compliance criteria introduced by

the new regulations were slowing down many operations among the medical device manufacturers who pursue industry innovations at the same time.

Additionally, some medical device manufacturers tend to view the EC Recommendation 2013/473/EU as a bureaucratic system that imposes additional cost through increased random and scheduled audit visits. The firms criticized having two different types of the audits (unannounced and scheduled) in the same regulatory framework and called for a substitution strategy. However, and in line with substitution approach, we also argue that regulation should always include a small element of random audit inspection in order to check on the validity of the risk assessment system. A value of random inspection, on this view, is that it holds out the prospect of uncovering new risks and risk-creators in a way that is unlikely to flow from a scheduled audit inspection that is based on analyses of previously identified risks.

7.4.5 Linkages capability empirical account summary

The changes in regulation introduced by the MDD 2007/47/EC promoted strong linkages between the manufacturers and the rest of the actors involved in the whole chain of development of the software. With the introduction of the MDD 2007/47/EC, most of the firms interviewed successfully broadened their outsourcing models to include foreign firms with offshore production facilities. The firms established strong supplier relationships to enable them have access to resources outside of their organization, reduce costs of manufacturing and operation, shorten product development life cycle, and improve product quality, and productivity. To some extent, this regulatory reach into software changed the expected profitability by providing a guarantee of product quality.

The EC Recommendation 2013/473/EU regulatory demands changed conditions for firm collaboration due to new challenges in the interface between actors. Some firms indicated that before the introduction of the EC 2013/473/EU, they had an adversarial type of relationship with their critical subcontractors and crucial suppliers. After the new regulation, firms were forced to move from adversarial relationship towards collaborative relationship within the network. The move was driven by the fact that the supply chain operations of medical device industry were now much more

regulated than it used to be before the introduction of the unannounced audit visits.

The collaborative relationships further developed from short-term to long-term. A long-term relationship with critical subcontractors and crucial suppliers enhanced the firms' efficiency in procurement and also enabled the medical device manufacturers to be more effective in delivering quality products. The strong linkages also facilitated diffusion of their technologies. Exchanging information, keeping industry actors informed was considered very important for generating technological changes and transfers.

The empirical accounts described the actions taken by the industry actors when implementing the new requirements arising from the regulatory change in the UK. The case studies revealed both common patterns and individual differences in how each firm addressed the new regulatory requirements. To explore these patterns and differences further, the empirical accounts will be viewed through the lens of the theoretical framework in the cross-case chapter 9. The next chapter presents an analysis of the effects of the third regulatory change on the capabilities of firms based in South Africa.

CHAPTER EIGHT
THE EFFECTS OF REGULATORY CHANGE ON TECHNOLOGICAL CAPABILITIES OF MEDICAL DEVICE FIRMS IN SOUTH AFRICA

8.0 Introduction

This chapter, like chapter 7, addresses research sub-question number three, this time using empirical data from a group of sixteen medical devices firms in South Africa (SA). This chapter is focused on firm level effects in a national environment where the regulatory authorities were not so equipped to assess the hidden costs of regulation or to ensure that regulatory powers were used cost-effectively and coherently. The objective was investigated through the following research question: *How have regulatory changes affected firm level investment, production and linkage capabilities of medical device firms in the SA?*

The analytical evidence from SA presented in this chapter also comprises two kinds of empirical data. As in chapter seven, the first type of empirical evidence involves comparative analysis of sixteen SA manufacturing/distribution firms that supply medical and dental diagnostics. This section focuses on the effects of radiation emitting devices regulation and its successive changes on firm level technological capabilities on these sixteen firms. Thereafter, a more comprehensive narrative of three purposefully selected firms will be presented. This chapter concludes with the summary of the findings focusing on the key characteristics of the firms' responses to the new regulation.

8.1 Effects of the third regulatory change (Radiation emitting devices) on firm level technological capabilities

The effects of the third regulatory change on the technological capabilities of the SA-based firms are analysed by looking at various dimensions of the production system in which local manufacturers of medical devices operate. The analysis starts with the effects of regulatory change on investment capabilities.

8.1.1 Effects of the third regulatory change (Radiation emitting devices) on firm level investment capabilities

The manufacturing and supplying radiation-emitting devices such an X-ray puts financial burden on firms. These high-margin medical devices require high investment in R&D and the development time up until clinical testing takes around 2-

3 years and costs between 1 to 20 million US dollars (Fiedler, 2017). All this determines that such type of medical devices rely on more investment funding.

Research and Development (R&D)

The effects of regulation under the Hazardous Substances Act 15 on R&D elicited various responses among the medical device firms. The majority of respondents echoed that the regulatory changes introduced within the product category of radiation emitting devices had little impact on a large number of local SMEs firms' R&D capabilities. Some respondents reflected this notion in the following quotes:

"Not much R&D is done here because it's an importers market dominated by distributors or importers. Where you will find some pockets of R&D happening locally, it would be with a few local manufacturers that are truly innovative." [Executive Officer – Industry Association, Res 005 (IS), Oct, 2016].

"We do very little R&D ourselves, we do some products but it is just merging up of some components into a bigger solution. So from an R&D point of view it's just merging components into a bigger solution if I can put it like that" [Director – TM Africa, Res 028 (MAN), Nov, 2016].

"So there is no R&D done in SA in that regard. We only have the specialists and the professors that are specifically doing patient research or clinical research but not research on the machines" [Strategic and Key Account Manager – SSA Ltd, Res 014 (MAN), Oct, 2016].

The underpinning argument why there is less R&D as reflected in the above quotes is the limited local manufacturing base that, following the reasoning of most respondents, is an existential criterion to have in place for R&D. Because of this base being so small, no critical mass is created for R&D investments to result in a positive Return-On-Investment (ROI). For example, the South African Medical Technology Industry Association (SAMED) indicated that in 2014 total spend on R&D amounts to approximately USD1.5 million on R&D. This equates to less than 1% of their total average operational expenditure (SAMED, 2016).

A majority of respondents pointed out that the regulatory changes did not directly influence investment in R&D of MNCs as most of their R&D activities were conducted in the advanced countries. The CEO of CR Medical remarked:

"I don't think that regulation has had that much of an impact on us in that respect because our company being a multinational, the R&D take place from an external perspective and not in South Africa so I think that's something that would be better asked to the local manufacturers and to SAMED as an industry" [Res 008 (MAN), Oct, 2016].

SAMED, the medical device industry association in SA indicated that currently SA medical device industry is dominated by MNCs and typically these firms depend on their parent company to develop new products using R&D resources close to headquarters. Therefore, there was much less regulatory impact on investment capability in R&D in the SA medical device industry.

On a more positive note it was mentioned that, specifically the MNCs, could draw upon local skills and can contribute to medical device R&D in the country through collaboration with academia and tertiary hospitals. Indeed, some few MNCs indicated they already have R&D projects with several universities in the country and contribute to learners at academic institutions. Others indicated that regulation increased the quality and safety of products and the design process as a result of their increased R&D investment, which in turn gave them a competitive advantage in the market. The Managing Director of Southmed and the CEO of DK medical supplies remarked:

"Regarding R&D, regulation helped our company to focus on upfront design process before bringing a product to market. [Res 003 (MAN), Oct, 2016].

"The change in regulation has actually added R&D investments because it has allowed us to have inspections and to do modifications to systems and upgrade" [Res 009 (MAN), Oct, 2016].

The quotes above reinforces the notion that regulatory change in SA came about not just as an obligation requiring compliance, but instead as a possibility for firms to improve their products and competitive position in the market.

The lack of trained local human capital and absence of venture capital funding were echoed as critical concern by some firms in terms of access to appropriate skills to perform R&D to an internationally required standard. The Managing Director of Southmed notes:

"It's hampers us to a certain extent because funding that could have gone to R&D now goes into flying auditors from Europe to here and also from a timing perspective things get slowed because we can't speak to the auditor in Johannesburg we have to speak to somebody in Europe, and we may not be their highest priority" [Res 003 (MAN), Oct, 2016].

"The problem has been we don't have a venture-funding environment" [Res 003 (MAN), Oct, 2016].

Recruitment and training of skilled personnel

The introduction of accreditation and compliance monitoring system through the South African National Accreditation System (SANAS) enhanced the need for firms to recruit skilled personnel or the need to provide adequate periodic staff training. According to SAMED, the total expenditure on training on medical technology was USD2.1 million in 2014. The expenditure on training by MNCs was significantly higher (USD1.4 million) when compared with local companies (USD758 thousand) (SAMED, 2016). However, most respondents in the interviews emphasized that there was a shortage of skilled and semi-skilled personnel in SA. These senior managers argued that as long as the lack of skilled and semi-skilled personnel is not resolved, manufacturing of even the simplest of low technology products would not be viable. The Senior Manager of Medtronic and the Managing Director of Southmed expressed concerns about this regulatory requirement in the two quotes below:

"We supply a lot of high end technology or high-risk medical devices so we are operating in those fields. We are in the AIMD field, we are in surgical technologies

where we supply electromagnetic medical equipment that are high tech and we have to have well-qualified people for that and we do look actively for highly qualified people but unfortunately there a massive shortage of skilled people" [Res 004 (MAN), Oct, 2016].

"That is also difficult because we have to use accredited companies to do our validation. So if we get audited, and we have used a piece of equipment they want to see that the people that audited the equipment or validated the equipment are themselves skilled to be able to do that and in a country like South Africa where the skill set is growing from a low base but isn't improving all time that has been part of the challenge" [Res 003 (MAN), Oct, 2016].

On the local front, many of the high level skill shortages in SA are blamed on the education system, which is still struggling to overcome decades of "neglect and dysfunction" under apartheid, when the education of black people was under funded and of poor quality (Breier and Wildschut, 2006). A Senior Quality & Regulatory Systems Manager of PH Healthcare reflects:

"I think there is now a massive scramble for highly skilled regulatory affairs people here in SA. They have never been more needed before and all of a sudden, people such as clinical engineers, field service engineers, people who have got a background like yours who have studied formally regulatory science are on high demand. At the moment there is nowhere here in SA you can get a Regulatory Science Degree" [Res 012 (MAN), Oct, 2016].

However, even though the respondent above cited shortage of highly skilled people, South Africa has established institutions for biomedical/clinical engineering education and research as well as training programs for medical device technicians. For example, biomedical/clinical engineering training exists at the leading SA universities such as Tshwane University of Technology, University of Cape Town, University of Stellenbosch, and Witwatersrand University (WHO, 2015). The Clinical Engineering Association of South Africa also provides training to medical device technicians (CEASA, 2018). The role of the government is significant in ensuring support for local production, but equally critical is the role of academia to train biomedical

engineers, clinical engineers and other professionals capable of translating local needs into action and finding appropriate local solutions based on international best practices.

Further, regulatory changes have prompted firms to invest in training and development of people who work with these devices more seriously. For instance the authorised representative responsible for adhering to regulation has to have advance level of understanding of the medical devices and of the regulatory landscape in SA. Moreover, the Department of Health (DoH), Directorate Radiation Control (DRC), lists the responsibilities of license holders of medical X-ray equipment in the Code of Practice for users of medical X-ray equipment. The license holder and responsible person, apart from complying with equipment requirements, must ensure that radiation workers are identified and issued with Personal Radiation Monitoring Devices (PRMDs). The code further requires every radiation worker to receive education regarding the risks and safety rules of ionizing radiation (DRC, 2011). The education and or training pertaining to ionising radiation safety of these staff members is the responsibility of each license holder. In that sense regulatory changes has raised the bar for the firms' training requirements. The Regulatory Affairs and Quality Officer of SISA comments,

"Because we do export to Europe and so now we make sure that we do get the competent people involved and our company also do spend a lot of money on training. I mean I have been sent overseas a couple of times to go and get training there" [Res 015 (MAN), Oct, 2016].

The quote emphasises that, after the regulatory changes, it was important for medical device firms personnel e.g. biomedical engineers to be appropriately trained and knowledgeable not only in matters related to technical specifications and performance, but on how to evaluate products and manufacturers to be in compliance with regulatory standards and processes (e.g. manufacture, process, marketing, post-market surveillance).

Some firms indicated that the introduction of inspection bodies induced enormous challenge for local firms given that the regulatory environment in SA lack regulatory

affairs human resources and that there is quest for skilled manpower. The Director of TM Africa and the Strategic and Key Account Manager of SSA Ltd summed up:

"Basically what the inspection body added was a fair amount of stress because all of a sudden you had a specific number of your engineers doing the service and maintenance of spares on a big installed base now you suddenly had to find time and more people to be able to do all the inspection testing which puts the service under a very large amount of stress" [Res 028 (MAN), Nov, 2016].

"The drain on organisations is that suddenly you have got a significant amount of regulatory labour that has to be performed by highly qualified people. So staffing issues are now suddenly a problem" [Res 014 (MAN), Oct, 2016].

The regulatory change exposes the South Africa's lack of trained human resource challenges and specifically country's inability to sufficiently retain highly trained individuals.

8.1.2 Effects of the third regulatory change (Radiation emitting devices) on firm level production capabilities

South Africa's trade of medical devices experienced strong growth from 2004 to 2013 (BMI, 2016a) as discussed in section 2.3 of Chapter 2. However, healthcare provision remains inequitable and challenges in access to quality, affordable healthcare technologies persist in large parts of the country. The medical devices sector plays a critical role at each stage of the healthcare continuum. Although it has been instrumental in improving access and affordability of healthcare services, a number of regulatory constraints have led to a high dependence on imports for addressing domestic demand.

Innovation in production

The regulatory environment or lack thereof, is a key issue for manufacturers in South Africa. It should be considered an issue of vital importance to be addressed for the development of the medical devices sector. The regulatory environment in the country affects innovation because it determines the ability of firms to operate freely

(Malerba, 2005). However, it is also worth mentioning that innovation in the context of developing countries and in particular African countries is not so much a matter of pushing back the frontier of global knowledge, but more the challenge of facilitating the first use of new technology in the domestic context (Dahlman, 2007). Innovations should be considered broadly as improved products, processes, and business or organizational models. Development strategists ought to think not only of R&D and the creation of knowledge, but also attend to the details of its acquisition, adaptation, dissemination, and use in diversified local settings (ibid). It is useful, therefore, to view innovation activities in the African context as this taxonomy will help to understand the structure this analysis chapter.

The majority of respondents indicated that regulation of radiation emitting devices did not bring about radical or disruptive innovations into the market, which involves discontinuities in innovation pathways (Tait and Banda, 2016) but instead it had an influence on incremental innovations. Product development and commercialization in SA currently involves local improvements of technologies developed elsewhere; modifying imported technologies to suit local conditions (usually focused on cost reduction); or less commonly, novel product development. CEO of Gabler Medical comments:

"We don't do much of that, so we have a product range where we improve the products and bring out new designs but these new designs are of products that are already on the market. So this isn't new product innovation it's more about repackaging old products in a better way, more pleasing, and easier to use as opposed to new product development" [Res 006 (MAN), Oct, 2016].

Even though manufacturing remains limited to producing low technology products, a few domestic companies and MNCs with manufacturing facilities in SA have successfully developed low cost products that are on par in terms of quality with existing products that require complex technical know-how to manufacture. One Regulatory Affairs and Quality Officer of SISA noted:

"We recently introduced a new product into the market. So there are some innovations in SA, but the only thing is you can't design a new product today put it on

the market tomorrow. You have to make sure that the device is safe, the clinical trial is done and get the IP rights. You have to get approvals which can take a long time, so that creates a delay in the innovation output" [Res 015 (MAN), Oct, 2016].

The first regulatory licensing condition "Code of Practice for industrial radiography - X-ray Equipment" was drawn up in order to limit the risk of overexposure of workers and members of the public, and to keep radiation doses as low as is reasonably achievable. This requirement has forced firms to formulate new strategies when innovating including altering Quality Management System (QMS) safety and performance processes as reflected in the following quote by the Chairman of SAMED:

"I think from an innovation perspective, the regulation is now saying that you need to comply with many levels regarding safety, so it forced the companies when innovating to take the safety aspect into consideration. So it has guided the way innovation takes place. On the one hand, you have to control, monitor, evaluate and keep products safe" [Res 002 (IS), Oct, 2016].

Majority of SMEs argued that the bureaucratic protocols caused by the regulatory environment slowed the process of innovation. These firms stated that there are lots of documentations and administrative procedures to bring a product in to the market that inevitably impede innovative outputs. The Health Economics & Government Affairs Manager of BS Medical Specialists and the Projects Manager for BV Medical noted:

"Sometimes regulations slow down innovation because you find that you have too many requirements which you need to comply with before you can bring a product into the market and like in our current situation that is the case" [Res 032 (MAN), Feb, 2017].

"Innovation is going down a little bit because at least you could develop the product sell it in SA without those requirements but now you are at that stage of regulatory change" [Res 013 (MAN), Oct, 2016].

Majority of MNCs in SA emphasized that regulation had no effect on their innovation activities as that phase in the product lifecycle was done by their parent companies based outside SA. Some respondents note,

"Well our innovation is done by our company oversees in German, so no effect" [National Sales Manager – ESA, Res 025 (MAN), Nov, 2016].

"No, not at all. Regulation has not affected our innovation. I mean our companies overseas are developing products all the time. The only problem, the impact that we have is the price" [Reimbursement and Regulatory Affairs Manager - AA Biomedical, Res 027 (MAN), Nov, 2016].

"We really don't do the innovations, we don't do the R&D ourselves on the bigger forms of devices like the CAT scan, MRI and the ultra sound and the like are innovated outside SA" [Director – TM Africa, Res 028 (MAN), Nov, 2016].

Quality control capabilities

The introduction of regulatory change led to introduction of new processes concerning effective accreditation and compliance monitoring system in SA. The new SANAS players entered the market as control actors and certifiers of quality, a central role after changes in regulations. The regulatory change triggered new technical requirements for the industry, as has been similarly observed in the history of the UK medical device industry. There has been a strong focus on upgrading medical technology by manufacturers, hospitals and laboratories to comply with quality and accreditation requirements.

An ineffective quality assurance program can lead to poor quality radiograms that can impair diagnosis, increase operating costs and contribute to unnecessary radiation exposure to both patients and staff (Fiedler, 2017). Most of stakeholders in SA were in agreement that the introduction of the acceptance test and annual Quality Control (QC) tests plays an important role in diagnostic imaging to limit the population dose growth, thereby improved quality control. Three respondents comment,

"It has improved our quality control and innovation also so it's given us more scope

so it has enabled us to work a little bit out of our boundaries but for a newcomer trying to come into the field this makes almost impossible [CEO – DK Med Supplies Res 009 (MAN), Oct, 2016].

"I think quality control is part of ISO and the regulatory process and I think that it would keep one honest in terms of quality control" [Programme Director - PATH, Res 010 (MAN), Oct, 2016].

"I think that when it comes to quality control we have been "forced" to actually step up our game. Now we are all being sat down and get told to do this and I think it is a good thing because even if it is something simple like ISO 9001 it just once again comes back again to the customer and its ensuring that the customer is getting adequate service" [Projects Manager – BV Medical, Res 013 (MAN), Oct, 2016].

The quotes above reinforce the notion that the regulatory change led to upgrading medical technology and better-quality products for the consumers. The QC tests include periodic quality tests, preventive maintenance procedures, administrative methods and training. They also includes continuous assessment of the efficacy of the imaging service and the means to initiate corrective action (Fiedler, 2017). The tests however come at a high cost and some respondents indicated that the implications of the increased regulatory cost was over burdensome for firms. The National Medical Physics Manager of Netcare noted:

"When you look at the cost involved in quality control, it has increased since the changes were made in 2009-2010. When they said that you have to have accredited inspection body test the machines in most cases, of the suppliers and send the result to the DOH. They are expensive no doubt about that. It's an expensive test, so an annual quality control for a unit can vary from a few thousand Rands to twenty thousand Rands depends on the type of the machine" [Res 007 (HF), Oct, 2016].

Due to the cascading effect of the high cost involved in setting up of a quality management system and annual quality assurance, some firms indicated that consequently, this affect affordability of the devices for the patients. These firms usually transfer increased cost of regulatory compliance to the patient. The Managing

Director of UMC summed up this cascading regulatory effect in the following quote:

"At the moment you have a regulation cost of QC and not necessarily the amount but the accreditation and cost involved and making sure that the QC is up to date. That eventually comes down to the patient, and their fees go up, and their medical aids go up, and they end up paying more, so it's a bad cycle. We have had to complain to SANAS about the calibration of QC devices which we use in chambers to measure out the radiation and the energy that the machines produce" [Res 035 (Man), Oct, 2016].

The introduction of the QC test not only improved quality control practices but also created need for appropriate training for all personnel with QC responsibilities and effort was required by management to ensure that adequate financial provision be available to meet this requirement. The CEO of Gabler Medical noted:

"The annual QC test developed our quality control because we had very little so we have a lot more staff in quality control, and in those areas, there is and will be a lot more training. But skills development for our manufacturing is too low-tech for a lot of skills development" [Res 006 (MAN), Oct, 2016].

Compliance cost

Some stakeholders considered compliance costs in South Africa as relatively high with implications for competitiveness of the local medical device industry in the international markets. Higher cost had an impact on the decision of firms to continue the project and eventually bring the product to the market. It emerged that obtaining the license to operate was considered as the first hurdle to firm entry and had a significant effect on the industry structure, competition, and on firm level profitability. Some of the interviewees also raised their concerns about the higher cost associated with stricter QMS requirements from the regulatory change. One Executive Officer of SAMED based on her experience from the industry, mentioned that:

"And one of those requirements is that you have to have a QMS in place in your company. That is not necessarily inexpensive, it cost money to put those systems in place, and to maintain them but it ensures that the company is credible and it is doing what it should be doing concerning the risk category of devices that they are selling.

The licensing fee for the manufacturer at the moment is USD1500, and you hold that license for five years and distributors its USD896, but there are also renewal fees and annual retention fee as well" [Res 005 (IS), Oct, 2016].

The introduction of the licensing conditions through the code of practice for industrial radiography (X-ray Equipment) called for a number of administrative and medical requirements from those applying for the license and enforced annual quality assurance tests. These regulatory requirements had an effect on prices. Higher safety standards and other additional regulatory requirements required manufacturers to generate more (clinical) data to prove the safety of products, and required manufacturers to further invest in production facilities and thus reach the necessary quality standards. As a consequence, higher regulatory standards increased the level of investment needed to comply with the new requirements and contributed to higher prices for end products. The CEO of MDG stated:

"Well so that's the challenge for the small companies because the cost of compliance is too high" [Res 002 (MAN), Oct, 2016].

Market size of South African industry is small, therefore the introduction of new licencing conditions were considered by many firms to be inhibiting local companies from investing in R&D and clinical trials. Moreover, the compliance cost even goes high if for example as a local manufacturer you intend to export. The CEO of Gabler Medical noted:

"Compliance just goes with regulation if you don't, nobody here can afford to produce a product and not intend to export that product, and if you are going to export it, compliance with safety standards are the requirements. If you don't have that you will not export, nobody is going to buy it. Nobody can afford to manufacture medical devices for the SA market only; the South African market is tiny. If you are producing it here and it's for the South African market, it will also be for the Middle East, Africa and hopefully Europe; you just can't afford to produce for South African market only, it's much too small" [Res 006 (MAN), Oct, 2016].

Local device and diagnostic manufacturers all spend significant time and financial

expense to obtain CE registration from European certified bodies. This is because South African medical device regulations have an affinity to European directives, despite the fact that the latter are particularly strict (De Maria et al., 2018). As most of the SA firms' notified bodies are based in Europe, the challenge in this as indicated by most the firms is an increased burden of compliance cost especially when it comes to bringing in auditors for CE certification purposes. Currently, they must cover transportation and accommodation costs to fly representatives from these notifying bodies to South Africa for facility and product inspection. CE Mark requires annual ISO 13485 auditing. There is limited local capacity for auditing facilities for this ISO certification and the SABS certification has no recognized value outside of South Africa. The CEO of Gabler Medical and the Managing Director of Southmed points out,

"It's much too expensive because the notifying bodies are based in Europe. We are billed based on European prices. Our currency is in a bad state. If I say guys come in out of Europe and the auditor is buying an air ticket out of Europe, and then he is maybe putting 10 % onto his costs, and then he is converting that to our currency, we get hammered. It's too expensive" [Res 006 (MAN), Oct, 2016].

"From an industry association side, we are negotiating with regulatory bodies to have local auditors, but you must remember that the field is so wide. If I have a spinal disc they can't have an auditor that understands spinal discs here, so what happens is that my documentation still has to go to the expert in Europe and often that expert has to fly out to come and audit us, up till now we have not succeeded in having local auditors for any of our products, so our regulatory cost for the group are well in excess of 2 million rands a year" [Res 003 (MAN), Oct, 2016].

Another challenge most manufacturers are facing is lack of calibration[29] authorities. The respondents highlighted that if they have equipment that might needs to be calibrated, the firms will have to send the equipment oversees and this process is very

[29] Calibration according to SANAS means a set of operations that establish, under specified conditions, the relationship between values of quantities indicated by a measuring instrument or measuring system, or values represented by a material measure or reference material, and corresponding values realised by standards whatever their uncertainty

expensive. This tall challenge is having an enormous challenge on many firms especially when they have to send the product once every year or two years. The CEO of DK Med Supplies and the Strategic and Key Account Manager of SSA Ltd explained this dilemma in the following quotes:

"The biggest problem in SA we don't really have calibrations authorities here..,. All these calibrations authorities are all in the UK all in Europe all in America and for us to send the equipment from here to there is a very large cost to get it calibrated is a large cost and then the down cost that you have with the equipment being oversees is also a massive cost so it becomes very expensive" [Res 009 (MAN), Oct, 2016].

"If one has equipment that needs to be calibrated. It cannot be calibrated locally in SA so once every year or two years depending on the equipment you have to ship it overseas crossing rates of exchange to be calibrated so you don't get the use of that machine for that time period. You can't do a recovery on your cost so it's a very costly exercise with no return on the investment" [Res 014 (MAN), Oct, 2016].

The CEO of CR Medical explained how the regulatory challenges and high cost associated with regulatory compliance are creating problems of survival and growth in SA in the following quote:

"Compliance is costly, for example in order for us to get a CE mark we have to have our system independently tested for the electronic magnet compatibility and electrical safety. There are no companies in SA that have the necessary certification in place to do that testing and to issue us with a certificate. There are some laboratories that can do the testing but they are not necessarily licensed. We have to send our system to Germany, France, and Britain and to the United States. We have a system sitting in the United States that has been there for a couple of months it got damaged on the way but they have to get the testing done it's going to cost us over a million rand. A million rand in the deflated value of a pound so it's over 50 000 pounds just to get the certificate and we cannot get the CE mark unless we have got that independent certificate. So for us to do business in medical devices in SA dealing with some of those issues like that is very expensive" [Res 008 (MAN), Oct, 2016].

Business Operations capabilities

An Executive Officer from the SAMED industry association highlighted the implications of the SA regulatory system on overall business operations in the following quote:

"Well it is very costly to manufacture locally because we still don't have a comprehensive regulatory system for medical devices and the international quality management standard for the manufacture of medical devices is ISO 13485. Because we don't have regulations, there is limited capacity here in South Africa to audit companies to ISO 13485 which is what you need if you are going to manufacture. As a result, the local manufacturers have to pay for auditors to come from either Europe or America. They pay them in US$ or Euros; they fly business class, and this is extremely expensive [Res 005 (IS), Oct, 2016].

Most firms echoed that SA still lags behind most countries in terms of ease of doing business. Due to complex hazardous substances regulatory requirements, products now require multiple agency approvals and more skilled manpower to address the quality assurance requirements. This leads to time delays at multiple layers, at both the national and international levels. The Projects Manager of BV Medical noted:

"The operations lines become a lot more process focused, because we started off as a small company, as a start-up and a lot of tasks were performed by the same person but now there is regulatory changes and implementation of a QA system which requires more skilled personnel" [Res 013 (MAN), Oct, 2016].

8.1.3 Effects of the third regulatory change (Radiation emitting devices) on firm level linkage capabilities

Understanding the effects of regulation on linkages and interactions among the institutional actors involved in innovation activities or processes is crucial to improving SA's technological performance. Two divergent and often conflicting discourses emerged when asked about the effects of regulation on linkages. On one hand, some firms reported that there were no formal structures for regular collaborative engagement between government and the private sector. As a result, interactions between government and the industry were often disjointed and

opportunities for effective collaboration for the benefit of stakeholders on both sides are limited. The Health Economics & Government Affairs Manager of BS Medical Specialists noted:

"I think what has happened is that the regulator has not always been very good at communicating the intentions or the requirements and that caused a lot of panic and when people panic then; relationships do suffer so it has affected relationships negatively" [Res 032 (MAN), Feb, 2017].

On the other hand, some firms expressed that the new regulatory requirements fostered target-based collaboration between government and private sector, harmonized the industry actors and facilitated growth of the industry. The Programme Director of PATH offered explanations to this regulatory outcome as,

"I think at the moment regulatory changes have harmonised the industry a lot because everyone is pulling in the same direction and everyone is making sure that the regulations do provide safety, information and efficacy" [Res 010 (MAN), Oct, 2016].

Partnerships are key to accessing the new technologies, markets and skills that make growth possible. Even though most of the South African medical device firms interviewed were involved in at least one domestic or international partnership, many highlighted the difficulty of forming collaborations. Reasons for this included geographic isolation, the small size of the local industry, lack of knowledge overseas about private sector activity in South Africa and, particularly, the perceived lack of credibility of 'made in Africa' products. The Compliance Officer of AEC Amersham remarked:

"We have entered into several partnership agreements to bring innovated products to market in collaboration with different stakeholders some of those worked some of those didn't work but we are very well engaged with all stakeholders" [Res 031 (MAN), Nov, 2016].

Most of the firms interviewed had domestic partnerships with universities and research institutions. Some of these partnerships were developed and driven by the need to meet new regulatory requirements in respect of conformity assessment, calibration and monitoring of good laboratory practice (GLP). A Projects Manager of BV Medical and a National Sales Manager of ESA commented,

"The MCC is actually urging companies to be part of the SAMED association because it is their only mode of communication with us as companies, so it has affected us greatly but more to our benefit to be part of SAMED" [Res 013 (MAN), Oct, 2016].

"I wouldn't say that it hasn't really affected I think because we are part of these bodies and the like SAMED and SALDA there is a lot of linkage capabilities between the organisations that has been going on for many years now. I think now with the implementation of regulatory affairs its really bought us maybe closer together and really see what each of the challenges are in each every company there is such a diversity with the different companies not everybody is doing the same thing" [Res 025 (MAN), Nov, 2016].

International company-to-company partnerships, usually with European companies, were much more common, and South African medical devices firms put significant effort into establishing these relationships after the introduction "routine" tests/inspections are performed by IBs. For a sector that needs to reach global markets to grow, such partnerships are vital, particularly for accessing necessary technologies and markets and raising local companies' international and domestic reputation. Common alliances cited by companies were in the areas of manufacturing, distribution. The CEO of Gabler Medical said,

"It has forced manufacturers to be more aware of purchasing, importing of components, importing from suppliers with some form of accreditation and better quality management systems themselves" [Res 006 (MAN), Oct, 2016]

8.2 Detailed Analysis of Three SA-based Firms

This section will analyze three case studies in more detail highlighting the specific actions of the firms within the context of the SA regulatory changes. The actions are

derived from the descriptions presented by knowledgeable stakeholders through interviews and in published or archival documents.

8.2.1 Southmed

Southmed is a private company that was founded in 1987, with a focus on the electrophysiology and respiratory markets. It is a distributor of electro-medical devices and medical consumables throughout Southern Africa. Southmed provides specialized equipment to meet the stringent expectations of specialist physicians, private clinics and hospitals including: operating theatres, critical care, high care units, trauma and emergency care. The company has a workforce of over 200 people, generated an estimated revenue of £20m - £50m in 2016 and owns 4 subsidiaries.

By 2000, the company's position as one of the leading distributors of electro-medical devices in Sub-Saharan Africa was firmly established. Southmed had expanded its product base to include ultrasound imaging such as Cart-Based Ultrasound, Handheld Ultrasound, Tablet Devices and medical consumable products. The firm also provides radiology devices including: Digital Radiography Systems, Analogue Radiography Systems, C-Arms, Fluoroscopy Tables, Mammography, Specimen Radiography Systems and MRI Products.

The company's well-developed infrastructure and experienced team of clinical and technical specialists allow it to deliver a comprehensive range of products for an extensive array of medical applications. Southmed has a strong team of experienced national product managers who ensure that their product ranges are kept up-to-date with the latest advances in medical technology. Each national branch is self-sufficient, offering prompt service and full local technical and sales support. Southmed places an emphasis on a well-trained and highly proficient product development and sales team. As a result, the firm has managed to develop highly skilled and knowledgeable team of managers.

Southmed is proficient in the installation and commissioning of medical devices including the provision of on-site and off-site clinical training and full technical support. With over 27 years of experience in the field, Southmed's engineers are able to deliver on the most technically challenging and complicated installations, including

patient monitoring networks in intensive care units, Cardiac haemodynamic laboratories, Ultrasound DICOM networks and private practice diagnostic device networks. Southmed's consumable products are assembled and sterilized in-house and conforms to the ISO 13485 global standard certification.

In 2004, Southmed contracted another local company to manage its warehouse, logistical and technical support requirements nationally. The contracted local company was dedicated to incremental innovation of new products and technologies. The company was also undertaking activities related to development of several novel products in partnership with a local university. In May 2006 the two companies merged with the aim of improving efficiency and now trade as Southmed. The new company is fully compliant with industry standards at all levels including the requirements of the Health Care Charter and Broad Based Black Empowerment regulations. The firm scorecard according to B-BBEE Codes of Good Practice (Gazette Number 36928) in 2013 indicating that the firm is a level 3 contributor with 51% of the company being black owned and 7.32% is women black owned.

The firm's client base spans the entire Southern African region. This is accomplished by strategic alliances in the African continent with direct representation in SA. The firm's market comprises three segments: hospitals (which include all state, academic and private clinics and hospitals), blood transfusion services and medical practitioners. Over the last two decades Southmed has built a healthy partnership with leading suppliers, in order to guarantee compliant, state-of-the-art technology.

Effects of the REDs regulation on Southmed's investment capability

Southmed indicated that REDs regulation to some extent impeded innovation by creating unnecessary barriers and cost but less efficient. The Managing Director of Southmed remarks,

"So radiation control basically requires QC certification every year…. in the past it was just once for that product now it is every single year you have to get radiation control at some particular point in time. The amount that we pay for these annual tests could otherwise be invested in R&D activities" (Managing Director - Southmed, 2016).

The DoH, South Africa applies the international standards as legal requirements and guidelines through the DRC. The DRC issues a license if the product and usage comply with the legislative and international requirements for safety and performance (RSA DoH 1973). The firm further indicated that demonstrating compliance with the international standards in order get the product license as one of the biggest regulatory challenges. The Managing Director of Southmed articulates,

"Introducing a new product to a market that needs radiation control approval here takes longer compared to other countries because of the unnecessary demands from the regulator. The RCD requires a CE mark and yet we don't have local accredited CE auditors" (Managing Director - Southmed, 2016).

The REDs regulation had a significant effect on the firm's human resources. Southmed was forced to develop targeted training programs, and recruit highly trained personnel from overseas to fill in shortage of regulatory affairs personnel. The Managing Director of Southmed comments,

"After the new regulatory requirement, we started offering on-site product demonstrations and level-one technical training, in the form of lectures and workshops, to our workers and to the end-user, where required" (Managing Director - Southmed, 2016).

Efforts by the firm to train personnel domestically were not only time-consuming but faced challenges of their own. As a result, the firm developed a strategy of empowering individuals by identifying and then further developing their unique abilities and skills through educational support. The Managing Director of Southmed emphasizes:

"A major focus of the company to meet the licencing condition was to empower individuals, by identifying and then further developing their unique abilities and skills. This is achieved through an on-going in-house skills development programme, tertiary degree and diploma support, and international training courses" (Managing Director - Southmed, 2016).

Many training programs relevant to health technologies in SA are based in university systems, which have been traditionally isolated from industry. As a result they are not perceived to be effective at detecting and addressing changing industrial demands (Blankley and Booyens, 2010).

Southmed highlighted that it was required to undertake a well-reasoned and documented risks and benefit analysis of device use for the patient or user of the medical device. These analyses have to recognize that a patient or user's safety is paramount. The work, therefore that had to be undertaken by Southmed involved: demonstrating that a well-reasoned and documented risk analysis has been done, producing a documented review of relevant published literature, a review of manufacturer's experience with device, assessing and documenting compliance of the device and its packaging with specifications and standards, reviewing and documenting the labeling and instructions for use of the device and reviewing and documenting final release procedures. All these processes increased the firm's R&D investment budgets.

Another regulatory effect that negated the strength of the firm in clinical research was the significant delay in research ethics approval. The firm echoed that, SA is an attractive location for conducting clinical investigations in Africa. However, delays in the ethics approval process, estimated at six months on average, are thought to be a significant stumbling block preventing the industry from reaching its potential in clinical research. The involvement of multiple bodies, such as Southern African Radiation Protection Association (SARPA), the Medical Research Council (MRC) Ethics committee and Radiation Control Directorate (RCD) are contributing factors to these delays, with the last two perceived as primarily responsible.

Effects of the REDs regulation on Southmed's production capability

Southmed indicated that lack of practical experience on the part of many health product regulators leads to the delays in the ethics approval process for clinical trials. This along with issues related to radiation safety remain major obstacles to medical devices commercialization in SA. The Managing Director of Southmed points this out this in the following quote,

"On the x-ray devices, we have waited 8 months to get a product approval for the device that hasn't failed so timing is a problem. I think two reasons for this situation are: one, it's a normal government bureaucracy and two, it might be that they under staffed in terms of what needs to happen. But if they are telling us it should happen in 30 days then done months down the line. If there is a reason like the product failed registration because of x, y, z that is fine but if you give them all the documentation and you have to keep fighting and begging for product approval, then something is wrong with the system. I won't mention people's names" (Managing Director - Southmed, 2016).

The respondent even went further and remarked:
"The wheels are slow really, really slow in radiation control" (Managing Director - Southmed, 2016).

Although the firm acknowledged that some regulators were highly educated and accomplished professionals (mainly in the pharmaceutical field), they cited lack of necessary medical device product development and manufacturing experience as a significant challenge. The Managing Director of Southmed captured this sentiment by stating:

"MCC and the Radiation control department has hired highly educated people, but they lacked experience in the field or experience in production.... I think they will be ready in years to come and we will in the meantime have to bear the consequences" (Managing Director - Southmed, 2016).

Recognizing that MCC and the Radiation Control Department have made some important strides forward in recent years, the broad consensus is that the competent authorities needs to improve the efficiency of its decision-making process as the current situation was slowing down the firm's products market entry.

It emerged that the regulatory requirement has enhanced Southmed's quality control systems and safety of their products. The firm had to demonstrate compliance by doing a risk and benefit analysis, produce evidence of appropriate testing to confirm

the design and production decisions resulting from the risk analysis, and produce evidence of appropriate radiation shielding. Further, the firm was able to demonstrate that appropriate control and indicator mechanisms have been incorporated into the device to ensure the operational consistency of variable parameters relevant to the emission of the radiation and the operation of the device.

Effects of the REDs regulation on Southmed's linkage capability

The new regulations had a huge influence on Southmed's entire approach to business collaboration and led to a restructuring of the firm. The changed structure had an effect on the firm leading to adoption of different competitive strategies and consolidation of business. For example, Southmed merged with another local firm and consolidated their business with the aim of improving efficiency and became fully compliant with industry standards at all levels including the requirements of the Health Care Charter and Broad Based Black Empowerment regulations. The inter-firm co-development interactions involved joint ventures, in an attempt to share, regulatory cost, development costs and minimize risks associated with innovative activities.

Summary of Southmed (Pvt) Ltd.'s implementation actions

Southmed indicated that REDs regulation to some extent impeded innovation, R&D efforts, created unnecessary barriers, and is very costly but not so much efficient. Demonstrating compliance with the international standards in order get the product license was one of the biggest regulatory challenges for the Southmed. On a positive note, REDs regulation played a significant role in facilitating the need to have more training of radiation workers. The firm in turn developed a strategy of empowering individuals by identifying and then further developing their unique abilities and skills through tertiary and degree and diploma support. Lastly, the REDs regulation led to the Inter-firm co-development interactions that involved joint ventures, in an attempt share, regulatory cost, development costs, minimize risks associated with innovative activities and ultimately contributing to meet to meet the B-BBEE regulatory requirements.

8.2.2 Northmed Healthcare

Northmed Healthcare is one of the leading MNC in the world operational in vivo diagnostics market. The firm was established in the late 1800s. Northmed holds more than 60,000 patents, has presence in 130 countries and two Nobel Prizewinners. The firm is a diversified multinational company, which has a set of technical, manufacturing and service industries as a whole, and is committed to be a global leader in each industry to obtain their business. The company has been supplying X-ray machines since 1896 and developed a series of CT scanning, ultrasound, MRI as the representative in vivo diagnostics equipment, and gradually became the industry leader. The company has demonstrated proven expertise in medical imaging and information technologies, medical diagnostics, patient monitoring systems, performance improvement, drug discovery, and biopharmaceutical manufacturing technologies.

In SA, the firm has over 1100 employees and participates in various business sectors of which healthcare is one of the sectors. The firm's presence in SA can be dated back to 1898, with the first office having been opened in Johannesburg in that year. In 2016 Northmed opened a R500M Africa Innovation Centre in Johannesburg, SA. This is Northmed's center of excellence for innovation and technology transfer in Africa. It is the first for Northmed in Africa and the 10th Northmed innovation Centre globally. In November 2015 Northmed completed an acquisition of another local healthcare supplier company. This acquisition has now positioned Northmed as a strategic and value adding partner to South Africa.

The firm has a strong commitment to contributing to SA's sustainable development especially in skills and small medium enterprise (SMEs) development. Their commitment to localization focuses on expanding local supplier's capabilities through skills development and technology transfer. Further to this, Northmed Healthcare has embarked on a Supplier Development Vehicle (SDV) program that is focused on the development of black owned SME's through business development services and technical development services. This program was implemented in respond to the SA government's B-BBEE regulatory requirements. Beyond this company program, their overall goal is to incorporate these suppliers into the Northmed supply chain.

Northmed Healthcare is transforming healthcare delivery in SA with 6000 clinical devices installed such as anaesthesia equipment and monitor. Northmed Healthcare ships over $2 million worth of parts per year to other Africa countries, Europe and the US. In 2017, the firm donated $1million to the Nelson Mandela Children's Fund for the construction of the Nelson Mandela Children's Hospital. The hospital's radiology division is a showcase of Northmed Healthcare technology designed to make imaging more inviting for paediatric patients.

Effects of the REDs regulation on Northmed Healthcare's investment capability

The introduction REDs regulation provided protection to radiology segment of medical devices and prompted investment from the Northmed to develop local business operations by bringing in more foreign direct investment, one example being the shipment of over $2 million worth of parts per year. The Projects Manager of Northmed comments,

"Well, because the radiology devices to some extent are now well protected than the rest of the devices in SA from a regulatory point of view, it became less risk for us to invest more in such machines" (Projects Manager - Northmed 2016).

As a result of REDs regulation, the firm is now one of the key producers and disseminators of applied knowledge in SA's medical devices industry. Northmed disseminate knowledge directly through licensing agreements and through its operations in SA. The operations include: the acquisition of another local firm in 2015, which had a progressive impact on skills development and technology transfer and its involvement in the SDV program that is focused on the development of black owned SMEs. The Projects Manager of Northmed comments,

"As I have mentioned earlier, I think the regulatory change worked well to our advantage, we are now considered as one the big key players in knowledge transfer as far as sharing medical diagnostics production and regulation information is concerned, maybe because we have been in this field for quite some time now or because of our policy company strategies" (Projects Manager - Northmed 2016).

In addition, the firm is now often the first to introduce new products, processes, or business and management methods in SA, providing examples and ideas for imitation by domestic companies. Due to REDs safety requirements, the license holder must ensure that persons who perform routine tests are competent to execute the tests. As a result, Northmed now strongly support and offer training to its radiation workers, managers and researchers and creates a potential for local knowledge transfer. The Projects Manager of Northmed noted,

"It is important for us to have people that would be able to interpret the QC tests, and adjust specific parameters" (Projects Manager - Northmed 2016).

The radiation safety training contributes substantially to attaining the critical cross-field outcomes by promoting effective and safe patient care practices to fulfil the patient's needs by taking into consideration medical law requirements. The training further promotes total quality management in the radiography profession by planning the frequency and executing the QC tests. The training is in line with international trends - the QC testing was only implemented in 2008 (DRC 2012)

Effects of the REDs regulation on Northmed Healthcare's production capability

Northmed Healthcare highlighted that even though additional regulatory requirements increased the time and costs associated with bringing new products to market but their innovation activities actually increased. As a result of increased innovation activities, the firm opened a R500 million Africa Innovation Centre in Johannesburg, SA. The Projects Manager of Northmed mentioned that:

"Regulation helped to increase our innovation as it removed uncertainty, so we have to be constantly innovating to avoid falling behind because there is a lot of competition out there (Projects Manager - Northmed 2016).

The quality control measures of Northmed healthcare significantly improved with the additional requirements of Essential Principle 11.5 that addresses medical devices intended to emit ionising radiation. The requirements means that if the device is intended to be used for diagnostic radiology, the device must be designed and produced in a way that ensures that, when used in relation to a patient for a purpose

intended by the manufacturer: the device achieves an appropriate image or output quality for that purpose; and the exposure of the patient, or the user, to radiation is minimized. The requirements for quality control tests were implemented in SA by the DoH only on 31 March 2009 (DRC 2012).

Effects of the REDs regulation on Northmed Healthcare's linkage capability

In respond to the SA government's B-BBEE regulatory requirements, Northmed Healthcare has embarked on a Supplier Development Vehicle program that is focused on the development of black owned SME's through business development services and technical development services. This is a relatively recent trend that is becoming more viable and noticeable in the growing interest on the part of large MNCs to partner with domestic firms. These linkages or relationships are primarily driven by the B-BBEE regulatory requirements and reduction of product development costs by tapping cheaper scientific labor in South Africa. The benefits to domestic firms included; access to financing for innovative projects, technological learning, and reputational advantages of working closely with major global enterprises.

Summary of Northmed Healthcare's implementation actions

After the introduction of the REDs regulation, Northmed's investment activities and/or mergers and acquisitions in SA give good indicators of how the firm and the market is developing. All these activities contribute to SA's medical device industrial growth. Therefore, foreign investment made a positive contribution to SA by supplying capital, management resources and technology that would otherwise not be available and this increased the country's economic growth rate, enhanced technology prowess, which in turn stimulated further economic development and industrialization. This firm supported the 2011 Code of Practice and the QC test requirements by determining the specific capability outcomes needed to attain to comply with the guidelines, in order to develop the company further.

8.2.3 Medtech Solutions

Medtech Solutions is a private group of bio-technology companies that was launched in 1987, originating from the work of two South African mechanical engineers. The company had revenues of $31.9 million for 2016. The two engineers first started a Cardiac devices company which was focused on developing a heart valve. As young

engineers in those days, the founders changed their devices focus because they needed some form of cash flow or income since the heart valve was long in generating funds, and there were no venture funds in those days available, so they had to fund themselves. The company's innovative activities have led to the commercialization of several other products, with other candidates at various developmental stages.

In 1988, the company founders saw an opportunity in dental implants, so they changed the name of cardiac devices company to Medtech Solutions. When Medtech Solutions was established, dental implant science on a worldwide basis was in its infancy. The company has been one of the pioneers in this field contributing extensively to the enhancements with respect to implant devices, surgical techniques, patient education and options of treatment. The firm is not only one of the leading dental implant companies in South Africa, but is an international player in the USA, Europe and Australia.

The parent company develops and manufactures dental implants and associated prosthetic devices. It focuses on the more specialized section of the market, not the generic implants but on the bespoke solutions, on high-end solutions and working with the specialists. The firm has directly owned offices in UK, Australia and USA. In addition they are represented in most parts of the world. In recognition of its role and activities in the medical device sector in SA, Medtech Solutions received the Gauteng export of year award and SABS innovation award for innovative design. Medtech Solutions has FDA approval and CE Mark, and was the first biomedical company producing locally to have those qualifications or those registrations.

In 1994, the founders, decided to also relook at the heart valve, and they established an associate company called GY (Pty) Ltd. GY became the second company in the group of companies and was established to manufacture and develop the applications for cross-linked collagenous membranes. Products include hernia repair patches, dural membranes, and cardio-vascular patches. Successful implementation of international quality standards enabled the establishment of a plant for the processing of pericardium tissue, and the development of heart valves, and patches. These are class 3 products that are more difficult from a CE regulatory perspective and has FDA approval.

In 1998 they started manufacturing pedicle screws for spinal use within Medtech Solutions. The development of orthopaedic implant devices benefited from the extensive experience of Medtech Solutions with respect to precision machining and processing of implantable materials, as well as knowledge of surface treatments for enhanced integration. This prompted the formation of the third spinal company in the group in 2001 which is dedicated to the development of orthopedic and neurosurgical implantable devices. The company is comprised of spinal surgery, foot surgery, maxillofacial surgery, and neurosurgery, as well as equipment divisions.

The third spinal company designed a disk replacement for spinal use and that product is a class 2B in Europe but is a class 3 in the USA. In the USA they took the product through the Pre-market Approval (PMA) trial. It was a very expensive trial, but the firm raised venture funding for that trial in the order of approximately $100 million, a hugely expensive trial, but they did prove their superiority. In parallel to the time of the firm's PMA trial, there was a (Johnson & Johnson and its subsidiary, DePuy Orthopaedics) recall of the Articular Surface Replacement (ASR) metal-on-metal hip replacement system. This was one the events that triggered regulatory reform in Europe. Medtech Solutions' design was also metal-on-metal, so they decided at the end of trial not to commercialize but to change materials, so at the time of the interview, the firm was in the process of doing a secondary trial based on what they did the first but this time around with poly framing materials.

Then the fourth company in the group was formed in 2002. It's originally an Australian company which manufacture electronic implantable hearing aids, x-ray units, x-ray machines and the accessory devices. Medtech solutions group has a successful partnership with them. It's not products that the SA firm produce but products they represent, and for that, they work together with their UK branch as their representative. This company is therefore a proud distributor of the electronic implantable hearing aids, x-ray units, x-ray machines and conforms to the highest standards of quality and biocompatibility.

Furthermore, the Medtech group of companies in 2002 formed MDSA (Pty) Ltd. MDSA develops advanced wound care products. The wound care products range

from honey-based ointments to nanofiber temporary skin substitutes. Tissue engineers have successfully implemented a cellular expansion facility for fibroblasts, keratinocytes and chondrocytes. Other successes in the SA market have been the development of the first South African hyaluronic acid visco-surgical device and also the most advanced partial and full thickness biological skin replacement devices. So the fifth company in the group is a specialized wound care focused firm.

With a team of R&D scientists in the wound care, skin care line, and human resources that span the disciplines of bio-medical engineering, tissue engineering, bio-technology, bio-chemistry and microbiology Medtech Solutions dedicated a team to develop the foremost skin rejuvenation products that are also medical devices according to regulations.

Medtech Solutions has representation in the United States through its affiliate companies and is firmly committed to ensuring not only excellence in medical devices, but ensuring that these devices are cost effective. The group's employees count in excess of 150 staff, which includes strong R&D departments. Currently, the company commits 5% of its annual budget for R&D. The group is developing and evaluating numerous devices to ensure that it remains the leading biotechnology group in South Africa. It has recently built a state-of-the-art manufacturing facility according to international standards to allow good manufacturing practice production of devices, especially those targeted to export markets.

Product licensing is a central component of Medtech's growth strategy in the short term, which it hopes will allow the company to access proprietary products and build on its technological capability. Medtech adhere to the highest medical device quality standards. The firms are ISO 13485 certified companies with many of the products bearing CE marks. The skin rejuvenation products are ISO 9001 certified with products registered for sale in the UK and the United Arab Emirates.

Effects of the REDs regulation on Medtech Solutions' investment capability

One of the regulatory obligations in the Code of Practice 2011 is that, the license holder of medical X-ray equipment is responsible for the education and training of radiation workers. As a license holder, this regulatory requirement forced Medtech

Solutions to increase its in-house training as well as sponsored some of the workers to go to the universities and be trained in targeted radiography courses in order to comply with the new requirements and stimulate its business development. This result is in line with a study by Audretsch (1995) that suggest that while technology and knowledge transfer from universities and research institutes to companies has been a major stimulator of technology development, in-house training within companies is also considered an important factor for innovation. The author has shown that overall R&D expenditure is associated with knowledge production and innovation within firms (Audretsch, 1995). Medtech has even received compliments from their international auditors about their high standards of regulatory affairs as a result of increased in-house training. The Director of Medtech summarised this issue in the following quote:

"We had the first skilled regulatory people who were in-house trained, and from us, I think a lot of expertise has gotten into the industry from the Medtech group because our regulatory people have trained other regulatory people and are constantly busy sharing their knowledge to try and up to the whole regulatory knowledge. So we have the regulatory manager who is also in the regulatory committee of SAMED. She is a microbiologist by trade, but have done the auditing courses and has been in our regulatory side for 10-12 years, so she very well trained, and we get quite a lot of compliments when we are audited from Europe about the standard of our regulators" (Director - Medtech, 2016).

The firm acknowledged the importance of education and training in reducing patient doses while maintaining image quality of their products. However the firm identified Diagnostic Radiography as a scarce skill in SA, indispensable in both the public and the private sectors as part of a multidisciplinary team providing a holistic health care service. The qualification is recognised by the relevant Professional Health Council as a requirement for registration to practise in the field of Diagnostic Radiography. According to the South African Qualifications Authority (SAQA), the exit-level outcomes for this qualification describe the foundational, practical and reflexive competencies required for Diagnostic Radiography regulatory requirements. The Director of Medtech summed up this issue by saying:

"Training must be considered at different levels, not only for entry users but also for retraining and certification" (Director - Medtech, 2016).

Effects of the REDs regulation on Medtech Solutions' production capability

The REDs regulation influenced the group of companies' arrangements and processes established to produce and distribute products since the delivery of their products needed them to be at least fast adopters, use and improve new technology in order not to fall behind and meet local conditions. This did put a great deal of pressure on firms' technological capabilities. Moreover, innovation is not just a matter of the simple creation and launching of new products. It is also about how services, are delivered, how business process are integrated, how companies and institutions are managed, how knowledge is transferred, how public policies are formulated and how enterprises, communities, and societies participate in and benefit from it all (Palmisano, 2006). The Director of Medtech captured this sentiment by stating:

"Well yes we were affected operationally in that we had to revisit our production process and changed some of ways of doing business so that we could meet our local regulatory conditions" (Director - Medtech, 2016).

SA's September 2000 regulatory requirement that suppliers and users of diagnostic x-ray equipment, for example medical and dental facilities, must ensure that a series of QC tests are done on all diagnostic x-ray units and processors was highlighted as one of the best regulatory requirement for the industry as it resulted in increased product and process safety. The aim of radiation safety is to minimize the potential harmful effects of radiation to patients, radiation personnel and the general public. This is necessary to enable suppliers and practitioners to comply with the mission statement of the DRC, which is *"the promotion and maintenance of health within the framework of the National Health Plan and specifically the protection against injury or disease caused by technological devices, including hazardous sources of radiation, by furthering the safe and legal use of such devices"* (DoH South Africa, 2011). Medtech indicated that the REDs influenced the firm's process of supplying their products, leading to improvements in quality and safety of their products. This in turn gave a competitive advantage of the firm in the local and international markets. The Director of Medtech commented that:

"Clearly the safety of our products increased and I think that's how it should be. So that provided us with a market competitive advantage, now we are an international player in the USA, Europe and Australia" (Director - Medtech, 2016).

Due to mergers and acquisitions, Medtech Solutions group was forced to adhere to the local and international medical device quality standards. The firms are ISO 13485 certified companies with many of the products bearing CE-marks. According to Deloitte (2014), the implementation of the EN ISO 13485 QMS is the critical path for CE-mark approval and must be taken into account. In addition, to QMS requirements, Medtech was faced with increased scrutiny by regulatory authorities in forms of inspections and audits in order to ensure compliance to the requirements. This had an implication for the manufacturer as well to emphasize more product testing.

Effects of the REDs regulation on Medtech Solutions' linkage capability

As from 31 March 2009 an Inspection Body (IB) approved by the Department of Health (DoH) or an appropriately trained professional registered with the HPCSA as a medical physicist must be used to perform all the acceptance tests as well as the routine test. New equipment acceptance tests are the responsibility of the company that installed the equipment and in most cases it's the manufacturer or distributors who install their product offering. If they don't have the capability to install they subcontract these services.

These new requirements called for close collaboration of not only Medtech's group of companies (internal linkages capabilities) but also of different actors within the supply chain of the diagnostic medical systems (external linkage capabilities). The new requirements called for better support infrastructures. In this respect we agree with the Director of Medtech that:

"Strong collaboration was needed in this innovative industry. As a group the introduction of SANAS and IBs inspections just made us to work together more closely. More to that and in a way it has harmonised the industry" (Director - Medtech, 2016).

We would extend Medtech's observation to suggest that when it comes to medical devices innovation it is not only competition among firms that matters, but also increasingly cooperation among them. In fact, the external or networking technological capabilities involved in the new requirement include:

- Accessing external knowledge - for example, the license holder was required to have an in depth knowledge of the x-ray unit (make, model, system ID and product license number) in order to implement the requirements with proof of compliance (DoH: QC Diagnostic).
- Managing the producer/user relationship, which is central to successful innovation.
- Accessing other partners who have useful complementary assets and capabilities such as the use of medical physicist to preform QC tests

Summary of Medtech Solutions' implementation actions

Medtech was a proactive proponent of the REDs regulatory changes. The REDs regulation was a major stimulator of firm in-house training. The firm emphasized that training must be considered at different levels, not only for entry users of radiology devices but also for retraining and certification. Overall, adopting the new REDs regulation contributed significantly in enhancing the safety of the firm's products, the safety of radiation workers, and the compliance of the Medtech as a license holder of medical X-ray equipment and as result, safety of the patients**.**

8.3 Summary of empirical accounts

8.3.1 REDs regulation summary

The analysis shows that REDs regulation was a major milestone in SA's medical device history. The "Regulations" laid down the legal status of REDs' supervision and management. They also gave the DRC authority to oversee medical devices that emit radiation and ensure their safety and effectiveness, and protect human health and life. In fact, an earlier study suggested that regulative institutions represent the legal aspect of the institution and exert a coercive pressure on the participating organizations through formal mechanisms, including rule-setting, monitoring, and sanction (Scott, 2005, Scott, 1995). SA government, International bodies and directives have confirmed the need for education and training of manufacturers, distributers, medical staff and other healthcare professionals in the principles of

radiation protection. From a regulation and policy dimension the third regulatory change was perceived by many domestic firms as constraining and discriminative as it was selective in its targeted products (i.e. only targeting radiation emitting devices).

The current criticism surrounding the implementation of third regulatory change regarding radiation protection in South Africa in the light of human error reiterates the need for standardized training of manufacturers, radiation workers, and also potential license holders. The consultation of experts to establish comprehensive objectives for a radiation safety controls ensured that the licensing conditions, which included the code of practice and annual QC test, were implemented. From an institutional theory point of view, the two licencing conditions were transitional and not turbulent changes.

Transitional change in regulative institutions involves new laws and regulations that can be traced back to an overall governmental policy and plan, which are issued to facilitate the development of a market (Kingston and Caballero, 2009). They reflect a long-term orientation, focused on ensuring the market will follow the prescribed development plan; therefore changes tend to be gradual. As such, the occurrence of the transitional change can be better expected or predicted, as it is most likely to follow a timeline established in the policy and plan (ibid). In contrast, turbulent change which, some scholars refer to as “revolutionary” occurs in response to market shocks, or certain unexpected incidents that disrupt the market (Tihanyi et al., 2012). New laws and regulations that are considered turbulent change are issued with the aim of fixing the situation quickly by controlling the negative impact resulting from these shocks and ensuring a fast recovery. Turbulent change is therefore short term oriented, and may involve the implementation of many laws in rapid succession. As a result, the market order may be completely altered. Since market shocks cannot normally be anticipated, the occurrence of turbulent change is also not easily expected or predicted

8.3.2 SA firms – Investment capability empirical account summary

A growing number of firms viewed product R&D as an important component of their business models. However, the extent of commitment to R&D and the nature of their involvement varied across the firms. The effects of regulation under the Hazardous

Substances Act 15 on R&D elicited various responses among the medical device firms. A common view, however, amongst respondents was that, compared with the UK, which has a large number of R&D investments, most of SA's SMEs do not have strong product R&D capabilities as it is an importer's market, therefore regulation had little effect on a large number of local manufacturing SMEs firms. The underpinning argument why there is less R&D is the limited local manufacturing base and following the reasoning of most respondents that is an existential criterion to have in place for R&D. Because of this base being so small, no critical mass is created for R&D investments to result in a positive Return-On-Investment (ROI).

On the other hand, for a few MNCs that were involved in R&D activities, the introduction of REDs regulation induced them to start investing more in radiology devices. A good example was Northmed Healthcare, a MNC that was proactive to REDs regulatory change and in turn became one of the firms that brings in a lot of foreign direct investments to SA, over $2 million shipment worth of parts per year.

One of the most common challenges faced by innovation-inspired firms in SA was related to clarity and effective enforcement of regulations governing health products. Again, while the outcome mainly manifested in delays in regulatory approval, the underlying causes varied across the firms. Lack of practical experience on the part of South African regulators was thought to make product approval challenging. Other challenges in South Africa were primarily related to delays in approval of clinical trials, which was perceived to detract from a major competitive advantage possessed by the country.

On key finding of this analysis is that REDs regulation enhanced the need for more training of radiation workers in almost all firms interviewed. What is clear is that SA's ambitious regulatory infrastructure building policies, as part of its overall goal to build an innovative and globally competitive technological environment, will continue to create demands for specialized skills in the REDs segment and other various healthcare technological areas. It remains to be seen whether current initiatives will be sufficient to meet this demand.

8.3.3 SA firms – Production capability empirical account summary

The analysis focused on capabilities of firms across the health product development value chain that firms used to advance their innovation objectives. The analysis collectively reveals various degrees of regulatory effects across different firms. A common strategy however, for entrepreneurs in SA has been to begin with technologically and financially less demanding products and/or services and to venture into more sophisticated areas as capabilities and revenues improve. Since REDs such as X-ray, CT, and MRI are on high end of technology, also the falling on the product category that is heavily regulated, very few SMEs were willing to or had the capability to invest in such products.

Most firms indicated that REDs regulation did not have a significant effect on radical or disruptive innovations into the SA market, which involves discontinuities in innovation pathways but instead it had an influence on incremental innovations. This was because product development and commercialization in SA at present mostly involves local improvements of technologies developed elsewhere and modifying imported technologies to suit local conditions.

Overall, this analysis on production capability reveals a striking similarity across the firms with respect to how REDs regulatory changes affected the firms' R&D and innovation capabilities. These commonalities include; less regulatory impact on R&D and innovation on most of SMEs due a low manufacturing base and their preference for collaboration with international firms.

8.3.4 SA firms – Linkages capability empirical account summary

The REDs regulation enabled a strong collaborative relationship in the SA medical device industry. As a result, the collaboration of SA medical devices and diagnostics value chain which include; the product role players, the regulators, funders, government departments and the industry associations facilitated the development of the new regulations relating medical devices and In Vitro Diagnostic Medical Devices (IVDs) published on December 9, 2016. Some stakeholders within the medial device sector in SA have been lobbying for this regulatory effect in the past years.

In order to meet the clinical evidence regulatory requirements, the firms involved in

R&D activities tend to have increased reliance on partnerships with domestic universities and research institutes as well as foreign entities. Firm-university linkages typically served to fill in gaps in internal R&D capabilities and access facilities/equipment and, to a lesser extent, to the transfer of new technologies to firms. There appears to be a strong correlation between the levels of R&D interest among firms and their linkages with domestic universities and research institutes.

In the same vein, these results were predicted in literature that supports the notion that, strong collaboration or close interactions between manufacturers and regulators in niche markets lead to the creation of knowledge, innovation and regulatory solutions (Malerba, 2007). In fact, the sectoral systems of innovation (Malerba, 2004) places interaction between heterogeneous actors at the centre of the focus where firms interact with non-firm organizations such as government agencies and universities in processes of learning and knowledge accumulation (Metcalfe, 1998).

8.4 Conclusion

Most MNCs indicated that the third regulatory change (REDs) influenced their process of supplying their products, leading to improvements in quality and safety of their products. This in turn gave them a competitive advantage in local and international markets. SA domestic firms were expected to have a capability to import, manufacture or fully refurbish any listed electro-medical device on a global basis, to comply with radiation emitting device regulatory requirements. Respondents argued that it is a tall challenge for most firms. Such stringent requirements made it more difficult for domestic suppliers in SA to enter the supply chain. The next chapter presents a cross-case analysis of the three regulatory change cases selected for this study.

CHAPTER NINE
CROSS-CASE ANALYSIS

9.0 Introduction

In the previous two chapters, individual case analyses of regulatory changes and their impact on firm technological capabilities were presented. As discussed in chapter 6, there were three regulatory change cases, two in the UK context and one in a South Africa context. This chapter will present a cross-case analysis of these regulatory change cases using empirical data from the UK and SA based firms. In this regard, the chapter addresses research sub-question 3.

To achieve the above intention, this chapter will be structured as follows. Section 1 sets out the analytical approach undertaken during the analysis of regulatory change effects. In addition, the three regulatory changes that have been identified will be briefly described, before the cross-case analysis is summarized and presented in Table 9.1. The chapter will then proceed (in sections 2-4) to present data relating to investment, production and linkage capabilities. Within these capabilities, the chapter will analyze in some depth each regulatory change case looking for generalizable conclusions from the study's various empirical firm data. At the end of the chapter, the results will be summarized so as to provide an overall empirical and conceptual perspective.

9.1 Analytical Strategy

The data analysis strategy discussed in Chapter 5.5.3 is employed to build an understanding of the effectiveness of the three regulatory changes in achieving their aims and also their impact on firms' capabilities. This simplified analytical structure is designed to facilitate identification of similarities and differences between the effects of the three regulatory changes. For example, the analysis shows that while REG1 (Software) was perceived as discriminating and enabling because the changes drove most UK-based firms to invest substantial resources in R&D to standardize their software products, REG3 (REDs) was perceived as discriminating and constraining through its indirect influence on R&D investment decisions as described in section 4.7. Based on this analytical model, the thesis argues, with empirical evidence, that a more enabling and discriminating regulation that takes into

consideration firms' technological capabilities can achieve intended goals more efficiently and effectively, than a constraining and indiscriminate regulation.

9.1.1 Identified regulatory change cases in the United Kingdom and South Africa: brief overview

This section starts with a brief summary description of the three specific regulatory changes influencing the two national medical device industrial systems.

As discussed in chapter 6, the European directive (REG1: MDD 2007/47/EC) introduced software into medical device regulation and tightened the specifications by requiring manufacturers to validate software whether integrated or standalone, regardless of device class and to provide additional documentation to prove compliance with further safety and efficacy standards. The ultimate objectives of this regulatory change were to ensure medical devices produced and used in the EU region not only are effective and safe but also provide more benefits to users (European Commission, 2007).

REG2: EC 2013/473/EU: As of January 2014, UK Notified bodies were required to conduct unannounced production audits on manufacturers at least once every three years and more often for high-risk devices, frequently non-compliant devices or in case of suspected nonconformities. The unannounced audit involves checks on a recently produced adequate product sample for its conformity with the technical documentation and with legal requirements. Also included is a file review and verification of the traceability of all critical components and materials and of the manufacturer's traceability system (European Commission, 2013a).

In respect to REG3: Radiation emitting devices (REDs), the SA government imposed additional restrictions by introducing two licensing conditions guidelines, namely the *"Code of Practice for industrial radiography - X-ray Equipment 2011"* and the *"Requirements for license holders with respect to quality control tests for diagnostic X-ray imaging systems"*. The first licensing condition was drawn up in order to limit the risk of overexposure of workers and members of the public, and to keep radiation doses as low as is reasonably achievable (DoH South Africa, 2011). The second licensing condition enforces annual quality assurance according to a prescribed list

(Herbst and Fick, 2012). The REDs regulatory changes called for a number of administrative and medical device requirements from those applying for the license as discussed in chapter 6. These requirements have a significant impact on the license holders, as they must show that they possess the necessary equipment, facilities and trained personnel to ensure that the radiographic work will be performed in a safe manner. Table 9.1 summarizes how each regulation has influenced firm level technological capabilities.

Table 9.1: Summary of the firms' responses to the three regulatory changes

INVESTMENT CAPABILITIES	UK REGULATION 1 (Software) Product regulation	UK REGULATION 2 (Unannounced Audit visits) Process regulation	SA REGULATION 3 (Hazardous Substances Act) Product and process regulation
Research and Development	• Created substantial shifts in the distribution of inventive efforts to meet market requirements • Some firms indicated that this regulatory change curtailed R&D considerably. • Other firms' R&D expenditure increased as new inventive efforts to meet market requirements were now needed	• The core EC 2013/473/EU did not have a big impact on firms' innovation activities, apart from the fact that they ended up with a suitable and appropriate quality agreements and commercial contracts in place to make sure they identify the roles and the responsibilities for those within the supply chain • Influenced R&D investment decisions	• Little impact on R&D as the environment is an importer's market. • MNCs tend to depend on parent companies to develop new products using R&D resources close to headquarters.
Recruitment & training	• Created competitiveness among the firms as the staff members received training to keep up-to-date with emerging rules and standards regulating software design processes, and technological scalability. • Increased the cost of the skilled personnel that firms needed to employ. • Created more jobs within the firm and increased in-house training efforts.	• Increased training programmes for employees responsible for regulatory compliance. Creating a full QMS requires skills, expertise and resources. • Forced implementation of new recruitment strategies that would have to factor recruitment of staff with international regulatory exposure for most firms that outsource production via subcontractors	• Enhanced the need for firms to recruit skilled personnel or the need to provide adequate periodic staff training. • Increased technology transfer • Induced a tall challenge on firms given that the regulatory environment in SA lack regulatory affairs human resources and that there is quest for skilled manpower
Standard procurement	• Technical constraints were imposed by the standards e.g. ISO 13485 and IEC 62304 which are uniformly applied to an entire medical device software development process. • Brought positive reputation and helped to gain confidence among customers	•	• Procurement of ISO standards e.g. ISO 13485 in order to get CE certification proved very costly for most of the firms • Brought positive reputation and helped to gain confidence among customers • Enhanced firm positioning • Increased competitiveness
PRODUCTION CAPABILITIES	**UK REGULATION 1 (Software)**	**UK REGULATION 2 (Unannounced Audit visits)**	**SA REGULATION 3 (Hazardous Substances)**

Innovation	• Some innovative firms became more risk averse towards novelty. Thus, they became incremental instead of radical innovators. • Slowed down product development time and innovation substantially. • Forced some firms to drop off potential ideas and opportunities due to the risk of not meeting the regulatory requirements. • Enhanced the creation of completely new processes because it was too costly to fulfill the regulatory requirements with the existing technology, and significant technological change was required	• Indirectly influenced investment decisions whether to innovate new medical devices	• Enabled modification of imported technologies to suit local conditions. • Some firms argued that the bureaucratic protocols caused by the regulatory environment slowed the process of innovation
Safety and Quality control	• Improved the quality and ensured the safety of products entering the market. • Brought positive reputation to the product quality and helped it gain confidence among customers	• Firms had to formulate new strategies including altering QMS safety and performance processes, processes for the device design and development, subcontracting, manufacturing, etc.	• Most firms were in agreement that the introduction of the acceptance test and annual Quality Control (QC) tests plays an important role in diagnostic imaging to limit the population dose growth, thereby improved quality control.
Operations	• Although complying with the new regulation was burdensome, some firms that were proactive increased their sales. • Firms that failed to realise the possibilities inbuilt in regulatory change requirements, ended up as failures in the market	• Business operations disrupted by the multiple visits (scheduled and unscheduled) and staff having to spend time with inspectors or auditors (substitution approach recommended).	• Business operations affected by the discriminating BBBEE regulation or preferential procurement policy.
Cost of compliance	• Due to a series of harmonised standards which go alongside the 2007/47EC, the firms had to increase the appropriate level of software testing and the complexity of setting up and validating all the appropriate test methods, that meant increased cost of products, time and manpower. • Coerced compliance cost and in turn resulted in firms needing to divert resource	• Increased NB inspection cost (Inspection time spent with inspectors by staff or management of the firms, during which they were not able to perform other work) • Increased costs of putting the business in compliance following the inspection's findings and inspector's improvement notice. • Increased auditor's travelling costs and	• Increased SANAS inspection cost (Preparation time when visit scheduled, Inspection time spent with inspectors by staff or management of the firms, during which they were not able to perform other work) • Increased burden of compliance cost especially when it comes to bringing in auditors for CE certification purposes

	outflows to meet regulatory requirements • The firms incurred unique costs such as forgone opportunity costs associated with much longer product approval times	costs of sampling and testing all of which are incurred by the manufacturer • Lost turnover or profit as a result of delayed or suspended operations.	
Product market entry	• Approval time increased, the delay was considered more critical to the firms' decisions and operations. This was because regulatory approval directly determines when the product can enter the marketplace, and determine the return on investment for businesses. • Products' speed to market reduced, thus the time to market got longer therefore, net present value of their products went down.	• Delayed product market entry when firms are putting the business in compliance following the inspection's findings and inspector's improvement notice or suspension of its certification.	
LINKAGE CAPABILITIES	**UK REGULATION 1 (Software)**	**UK REGULATION 2 (Unannounced Audit visits)**	**SA REGULATION 3 (Hazardous Substances)**
Local linkages	• It became increasingly necessary for firms to develop relationships with all the links in their supply chain. • Some firms had to learn how to collaborate better and how to share resources	• Forced firms to move from adversarial relationship towards collaborative relationship with their suppliers. • Enhanced a long-term relationship with critical subcontractors and crucial suppliers.	• Fostered improved collaborative and target based interactions between government and private sector, harmonized the industry actors and in turn ignited growth of the industry.
International linkages	• Most firms successfully broadened their outsourcing models to include foreign firms with offshore production facilities. • Increased outsourcing denoted more dependence on suppliers and implied the need to manage the supplier base and develop relationships with suppliers.	• Increased the firms' focus on the development of close collaborative relationships with their suppliers in search of competitive advantage and improved market positioning • Forced some firms to re-negotiate supply chain agreements, and alter documentation and QMS. • Improved the exchange of information between the local and international regulatory bodies.	• Enabled international company-to-company partnerships, usually with European companies.

Compiled by author from research data

In order to analyze in some depth each regulatory change case and have a better understanding of how the changes influenced the firms, I adopted a regulation and policy instrument proposed by Chataway et al. (2006), presented earlier in Chapter 4. "Its focus is on the effectiveness and efficiency of the governance achieved by a particular policy or regulatory instrument". First the authors categorized policies and regulations according to whether they are perceived as enabling (providing encouragement or inducements to undertake a desired course of action) or constraining (creating disincentives to undertaking undesirable actions) by industry managers. The second category of policies and regulations was based on whether they are indiscriminating or discriminating among products" (Chataway et al., 2006, p. 177). Figure 9.1 allows us to map the enabling, constraining, discriminating and indiscriminating within the Medical devices regulation and policy dimensions. The next three sections present empirical data showing the effects of the three regulatory changes on investment, production and linkage capabilities.

9.2 Effects of regulatory change on Investment Capability: cross-case analysis

Investment capability involves the ability to prepare for the identification and acquisition of design technology, equipment, management, and to develop a new product or upgrade the current one. This initial stage is crucial for defining the goals and objectives or the strategy that the firm should follow. Below is an analysis of the effects on firms' R&D, human resource training and standards capabilities.

Research and Development (R&D)

R&D capability is an important investment contributor to financial, marketing and innovation performance. The analysis summarized in Figure 9.1 highlights that from a regulation and policy dimension, REG1 was perceived as discriminating, enabling and constraining in relation to R&D. REG2 was seen indiscriminating and constraining and the REG3 was perceived as discriminating and constraining. The cross-case analysis indicates that all regulatory change cases had some form of influence on the R&D capabilities of some firms in both the UK and SA.

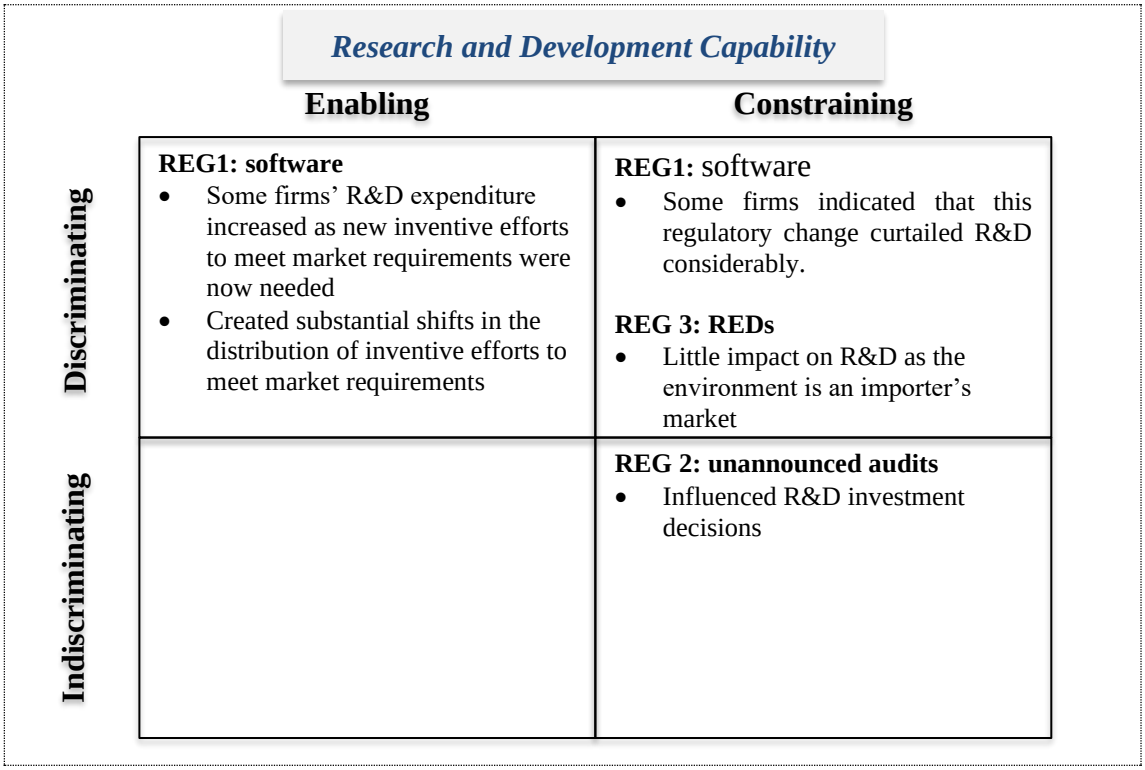


Figure 9.1: Medical devices regulation and policy dimensions: Effects on R&D
Compiled by author

The product regulation REG1 has been observed as a driver of requirements for new technology. This comparative review of the firms' actions has unearthed clear patterns that firms that invest in R&D extend their technical knowledge base, which allows them to design and develop new innovative products or services. Some firms' R&D expenditure increased after the new regulation. Some respondents argued that investment in this area should be a prerequisite for the success of their companies in the medium to long-term future. Other firms indicated that the regulatory change created substantial shifts in the distribution of inventive efforts to meet market requirements. Thus, from the regulation and policy metrics in Figure 9.1, REG1 was mainly perceived as enabling.

On the contrary, some firms perceived this regulation as constraining due to the fact that before the changes, the process of R&D and placing of a medical device on the market, as long as it was safe, was fairly easy to do. After the regulatory change, almost any product change or new product development has to go through a series of regulatory hoops before one can get a CE mark. For example, clinical evaluation: REG1 emphasized the need for manufacturers to provide clinical evidence for all

devices. All devices were now in need of such data, including devices for Class I. Additionally, this imposes more stringent requirements for what constitutes "clinical trial" and calls for a stronger attention from the authorities. Annex X on clinical evaluations was changed (European Commission, 2007). Consequently, manufacturers must now analyse and review the clinical part during the planning stage to identify any problem that needs further investigation. Such control measures are then inserted in the document risk analysis at the design stage and also after the commercialization of the product in order to keep updated on the state of the art of all the technical data of the medical device. In fact, for a better demonstration on the compliance of the medical device, manufacturers are obliged to implement a procedure to review the production of the device even after its commercialization, with the duty to report to the authorities any accidents or withdrawal from the market. Such regulatory hoops were perceived as constraining, especially at the R&D stage of the products as compliance costs limited the R&D budget of some firms.

In contrast to the product regulation REG1, the product and process regulation REG3 was perceived as constraining through its indirect influence on investment decisions. Subject to debate, the most important effect of regulatory inspections is not through the direct amount of administrative burden it creates, but through its impact on investment decisions whether to engage in an R&D activity, to expand, procure or innovate new medical devices, hire staff etc. All these decisions are affected by many factors of the investment environment and regulations but it is clear that the way enforcement and inspections are done or perceived has a significant role. Indeed, one of the most important aspects of regulatory changes for firms when making investment decisions is predictability. Some of the SA firms referred to the introduction of the SANAS inspections under *the Hazardous Substance Act* as ambiguous and constraining in which case they called for transparent enforcement that could help their businesses to understand what they actually mean, and what to expect. The CEO of MGD Health Solutions noted:

"SANAS inspections are so complex and technical that we do not know how to understand them. If no official guidance clarifying what to expect is available, we will often refrain from investing in R&D or introduce new products altogether" [Res 002 (MAN), Oct, 2016].

The quote above reinforces the notion that R&D investment in new equipment or new activity, be it by existing or new businesses, MNC or SME, will be significantly reduced if the manufacturing firms are not sure of how the regulators will assess compliance, and if they cannot get appropriate guidance. In many developing countries, not only is an officially published guidance not available, but also regulators will even refuse to give any prior consultation or visit that would be binding on them, thus leaving the whole risk on manufacturing firms (Monk, 2012). The cross-case analysis revealed that good regulatory delivery that is enabling and discriminating can improve confidence and control. This simply means firms need to understand how regulatory inspections impact upon them to enable them to identify the most cost-effective means of compliance for their business context. Good risk assessment should be transparent to the business and should be supported by assurance that enables investment decisions to be made on a sound understanding of future inspection and enforcement compliance requirements.

SA firms faced a wide diversity of regulatory challenges related to investment and innovation activities. One important and common barrier that hinders innovation activities in the context of SA is the ability to finance innovation activities. In terms of business investment in R&D, the analysis reveals that SA spends very little, compared to the UK. SA's investment as reflected by its Gross Expenditure on R&D (GERD) has always been very small, it has never exceeded 1% (SAMED, 2016).

Respondents in SA were in general agreement that government policies and regulatory changes did not directly influence the type of innovation in their firms (e.g. R&D of multinational companies were influenced by their corporate strategy rather than be subjected to the policies of the emerging country). According to SAMED (2016) the underpinning argument why this is the case is the limited local manufacturing base that is an existential criterion to have in place for R&D. Because of this base being so small, no critical mass is created for R&D investments to result in a positive Return-On-Investment (ROI) (SAMED, 2016). Most MNCs confirmed this by stating that most of their R&D was done in developed countries where their head offices are located, mainly in the US, the UK, Switzerland, France, and German. The cross-case analysis revealed that only a few MNCs have control of their product

development activities and spending on R&D is inadequate. Since investment in R&D has a direct effect on output, if output is to be increased then investment will have to be increased proportionately (Cullmann et al., 2012). Unfortunately, most respondents indicated that there was lack of R&D funding, whether it be through universities, subsidies from government or medical schemes. Some firms argued that the R&D investment climate is more business friendly in other African countries like Kenya thus resulting in decisions to move R&D activities outside South Africa. Lastly, other respondents feel there is no true R&D culture in the country and there is little appetite and uptake from universities to invest in the medical device industry.

It can be argued without equivocation that product regulation had a huge impact on the UK firms' R&D capabilities compared to SA firms, but there were both affirmative and negative impacts in classification. This can be attributed to the fact that UK innovators had more access to resources and capabilities available to them compared to those in SA. This also goes to show that, in high-income countries, R&D efforts may result in innovations driven by technology, despite the stringency of regulation or a high degree of uncertainty. From a regulation and policy perspective as shown in Figure 9.1, a discriminating and enabling regulation REG1 produced desired outcomes effectively and efficiently for the case firms even though more favorable regulatory conditions should be created for the introduction of appropriate technology to vitalize the industry.

Training and Recruitment

Successful industrial production requires a range of different skills. Figure 9.2 captures the key findings related to the effects of regulatory changes on training and recruitment. The findings indicate that all regulatory change cases have composite training and recruitment implications. The findings indicate all regulation whether categorized as discriminating or indiscriminating, they all were perceived by the stakeholders interviewed as enabling and constraining.

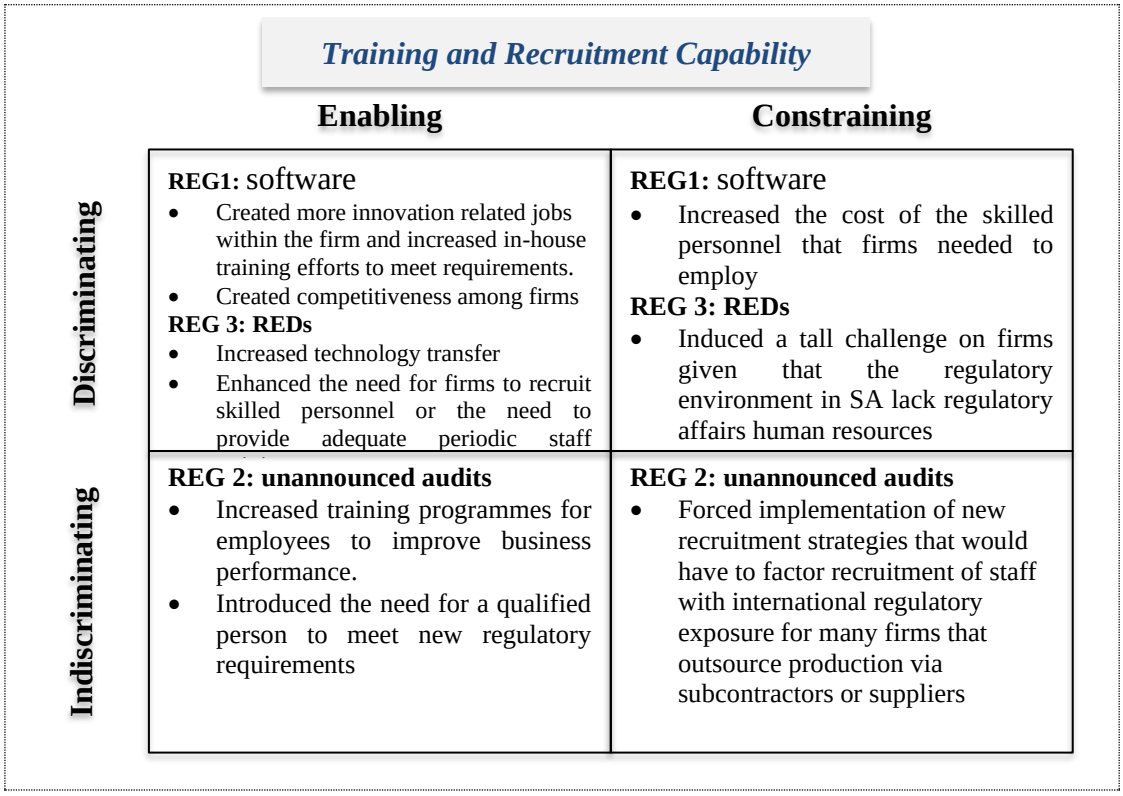


Figure 9.2: Medical devices regulation and policy dimensions: Effects on training and recruitment. Compiled by author.

It is evident that all regulatory change cases enabled all firms to acquire experts and skilled personnel as vital sources of knowledge and learning to fill their inherited knowledge gap in order to address the new regulatory requirements and the demand for innovative products, processes, and further organization-wide change. Moreover, such engagements not only support new product development, but also help firms' R&D teams provide innovative ideas and future products concepts to upgrade existing products and processes.

For engagement with experts, Figure 9.2 captures the four most important reasons across firms. The findings identified "ability to innovate", "improve business performance", "improvement in medical devices production," and "ability to meet new regulatory requirements" as the predominant motives for engaging with experts.

The findings showed that REG1 enabled the creation of new job opportunities related to innovation and regulatory affairs management, a good example being the industry of medical consulting. In terms of readability of the clinical evaluation guidelines,

they have changed from a document that was fairly easy to comprehend by any medical device manufacturer representative to a heavy document that requires expert knowledge on the regulatory background of the EU medical device policy and experience in working with EU legislative documents. This is a clear sign from the European Commission that the clinical evaluation process was not to be taken lightly and a significant addition to the skillset of the enterprise was needed, as most firms had to choose between leveling up their knowledge of the new requirements or use the help of external consultants.

Institutional theory has traditionally been concerned with how organizations better secure their positions and legitimacy by conforming to the rules (such as regulatory structures, governmental agencies, laws, and other societal and cultural practices that exert conformance pressures) and norms of the institutional environment (DiMaggio and Powell, 1991). For the firms to be able to conform to the rules as suggested by the theory, expertise in regulatory affairs become vital in the medical device sector. Expertise in regulatory affairs is critical to the medical device industry, as each new and improved product must be approved in every country in which it is to be sold and the requirements for approval are constantly evolving.

The cross case findings as depicted in Figure 9.2 indicated that on one hand, REG1 forced firms to devote a large number of staff to regulatory affairs after its introduction. On the other hand, REG2 forced implementation of new recruitment strategies that would have to factor recruitment of staff with international regulatory exposure for many firms that outsource production via subcontractors or suppliers. However, some firms echoed that the need to devote substantial resources to regulatory matters often reduced resources that would otherwise be available to support product development and commercialization therefore perceived the two regulatory changes as constraining. The Quality Manager of Alpha Ltd noted:

"Due to skills shortages firm outsourced design therefore increasing the need to externally monitor the supplier's QMS" (Quality Manager - Alpha Ltd, (UK), 2017).

In addition, Figure 9.2 reveal that REG3 was perceived as constraining because it induced a tall challenge on firms given that the regulatory environment in SA lack

regulatory affairs human resources. Unlike in the UK, official reviews (KPMG, 2014) and interviews suggest that there is a scarcity of South African nationals with knowledge and expertise in the area of ISO certifications and regulatory systems. The Strategic and Key Account Manager of SSA Ltd noted:

"The rigorous rule-following, documentation centered culture required by regulatory changes is unfamiliar for some of our staff and that slows us down so we have embarked on a series of in-house training" [Res 014 (MAN), Oct, 2016].

On a positive note, REG3 was also perceived as enabling from the regulation and policy dimensions, due to the fact it enhanced the need for firms to recruit skilled personnel or the need to provide adequate periodic staff training. The Director of Medtech Solutions reflected on the increased training needs in the following quote;

"In response to the new regulation, we took in-house responsibility for training of personnel while engaging the help of another distributor for regulatory support" Director - Medtech, (SA), 2016.

Finally, from a regulation and policy dimension as displayed in Figure 9.2, all the three different regulatory change cases placed some huge training cost constrains on firms as all the firms were forced to increase their in-house training. However the two product-focused regulations REG1 and REG3 were perceived as discriminating and enabling, because they created more innovation related jobs, upgraded quality of in-house talent, increased technology transfer, and enhanced the knowledge base of the regulation targets.

Standards Procurement

In terms of the effect of regulatory change on standards procurement, it has been argued that good-quality and affordable products, whether imported or locally produced, depend largely on the outcome of standards-based competition (Narayanan and Chen, 2012). Figure 9.3 captures the key findings related to the influence of regulatory changes on standard procurement. The findings indicate that the REG 1 and REG 3 had enabling and constraining effects on standards procurement. It is important to note that international standards play a very significant function in the

regulatory systems of the two study countries, and in product safety. Standards are core components underpinning firms' operational strategies. They are developed in respect of each directive in order to provide manufacturers with a set of technical specifications recognized in the directive as giving a presumption of conformity to the essential requirements. Use of international standards remains voluntary: manufacturers are able to put on the market products, which either meet other standards or no standards at all, subject to fulfilling the procedures for assessment of conformity laid down by the Directive.

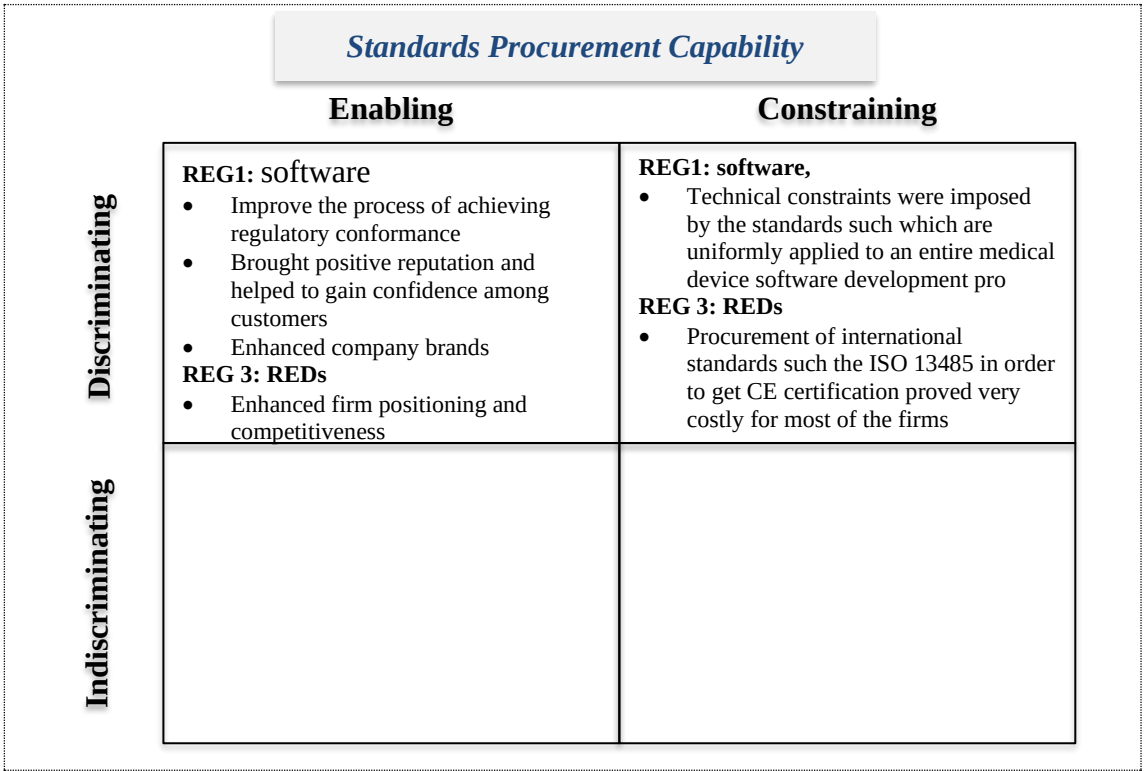


Figure 9.3: Medical devices regulation and policy dimensions: Effects on standards procurement. Compiled by author.

The analysis revealed to us that some firms perceived the REG1 as constraining when it comes to standards procurement. The respondents in the UK were in general agreement that the technical constraints were imposed by the Directive's aligned standards such as the ISO 13485 (Quality Management Systems), IEC 14971 (Application of Risk Management) and IEC 62304 (Software Lifecycle Processes) which are uniformly applied to an entire medical device software development process. Requirements contained in these standards have imposed direct constraints on firm's conduct, foreclosing product innovation. The processes involved in order to

procure these standards were viewed as constraining and stringent in production of medical device software especially for the small companies. The financial cost involved in complying with software standards proved to be a significant barrier for small companies in UK to upgrade their innovations.

Furthermore, the cross-case analysis indicated that the content of standards was highly technical thereby required expert knowledge of technology and practice in the medical device sector. Accordingly, experts inevitably come predominantly from industry, although academics and consultants are also involved. The involvement of personnel from competitors or companies making different products within the same sector produced uncompetitive results in some cases. Also, the increasing length and complexity of standards meant that manufacturers need sufficient understanding in how to apply them.

In SA, the requirements with regard to the application for a licence to import, manufacture or fully refurbish any listed electro-medical device under REG3 mandates that "the manufacturer of a particular electro-medical device in South Africa will be permitted to manufacture but not distribute that device in any way until the applicable and valid EC compliance documentation[30] has been submitted to and accepted by the Directorate: Radiation Control" (Doh South Africa, 2012). The acquirement of a CE Mark requires ISO 13485 standard procurement and annual auditing. However, the cross-case findings indicated that there is limited local capacity for auditing facilities for this ISO certification and the SABS certification has no recognized value outside of South Africa. Therefore, the cross-case analysis indicated that most firms faced daunting challenges in order to procure the standards required for the smooth flow of their operations. Most companies experienced unexpected delays on product registration and license renewal, and bureaucracy hurdles. Manufacturers spend significant time and incur financial expenses to obtain

[30] The following documentation must be submitted by the manufacturer in South Africa in order to get a licence to import, manufacture or fully refurbish any listed electro-medical device:

- Completed application form 41BM-1(MAN); and
- Colour brochure (including technical specifications); and
- Copy of the EC Certificate(s) issued by a recognised Notified Body to the manufacturer in South Africa in terms of EC Directive 93/42/EEC or 90/385/EEC (whichever one is applicable); and
- Copy of the EC Declaration of Conformity issued by the manufacturer in South Africa in terms of EC Directive 93/42/EEC or 90/385/EEC (whichever one is applicable).

CE registration from European certified bodies. Moreover, they must cover transportation and accommodation costs to fly representatives from these Notifying Bodies to South Africa for facility and product inspection. Implementation of these higher standards by local firms and achieving certification requires high investments. Against this backdrop, standard procurement was perceived as constraining.

On the positive side, the cross-case findings as indicated in Figure 9.3 show that REG1 was perceived as discriminating and enabling with regard to standards procurement. The findings identified that firms that had evidence of the applicable standards improved the process of achieving regulatory conformance. This finding resonates with an earlier study by Mugwagwa et al. (2015) that argued that when regulatory standards or mechanisms conflict, they may prevent one another from achieving their intended benefit. For instance, manufacturers that attained ISO 13485 compliance argued that they had an easier time bringing their products to international markets. Compliance streamlined the processes and ultimately helped to run a more efficient, profitable and risk-averse operation. Compliance with ISO 13485 helped firms with overall quality control, traceability, process validation and risk management. Furthermore, there was an increase in acceptance and demand for new products among consumers and promotion of barrier free trade throughout the global trade markets. The Director of Neiva Medical reflected on this notion in the following quote:

"*The introduction of software products standards has been crucial to the success of the 2007 regulatory changes in promoting barrier free trade throughout the European Community and in international markets. These standards have also enabled products to reach the high levels of safety achieved in the sector" [Res O73 (MAN), Apr, 2017].*

The analysis indicated that SA firms that managed to procure standards and CE certifications enhanced their legitimacy in the local market. Standards procurement enabled positive reputation, helped the firms to gain confidence among customers and ultimately increased competitiveness. Institutional theory places emphasis on how organizations establish their positions and achieve legitimacy in order to survive and make profit (Scott, 2008). These standards legitimized the operations of the case firms

and gained acceptance of their offerings even in the international market. Therefore, under these circumstances and from a policy and regulation dimension, REG3 was viewed as enabling. The Director of Bioweb Ltd noted:

"In order to work with international clients, we have to comply with their international standards as well. We acquired certifications. We are certified by ISO-13485" [Res 001 (MAN), Oct, 2016].

9.3 Effects of regulatory change on Production Capability: cross case analysis

Firms' technological capabilities are core determinants of their ability to compete (Lall, 1992). Many of the regulatory challenges faced by firms concern production capabilities, and the ability to manage and document the work processes following the Essential Principles of Safety and Performance guidelines. For medical devices firms, such capabilities determine their market access, both locally (achieving product registration and sustaining quality when products are tested) and for access to regional and international markets. This section analyses four elements of production capability: production itself, quality control, operations, and regulatory compliance.

Innovation in production

Regulatory changes may impact products, processes, marketing or organizational innovations. The changes may be incremental or disruptive, enabling or constraining. The analysis summarized in Figure 9.4 highlights that product-focused regulations REG1 and REG3 enabled new products to substitute older ones, which had been banned by regulation or as imported products were modified to suit local conditions in the case of SA firms. Thus, it is clear that product regulation can have a positive effect and has been a key driver of many innovations.

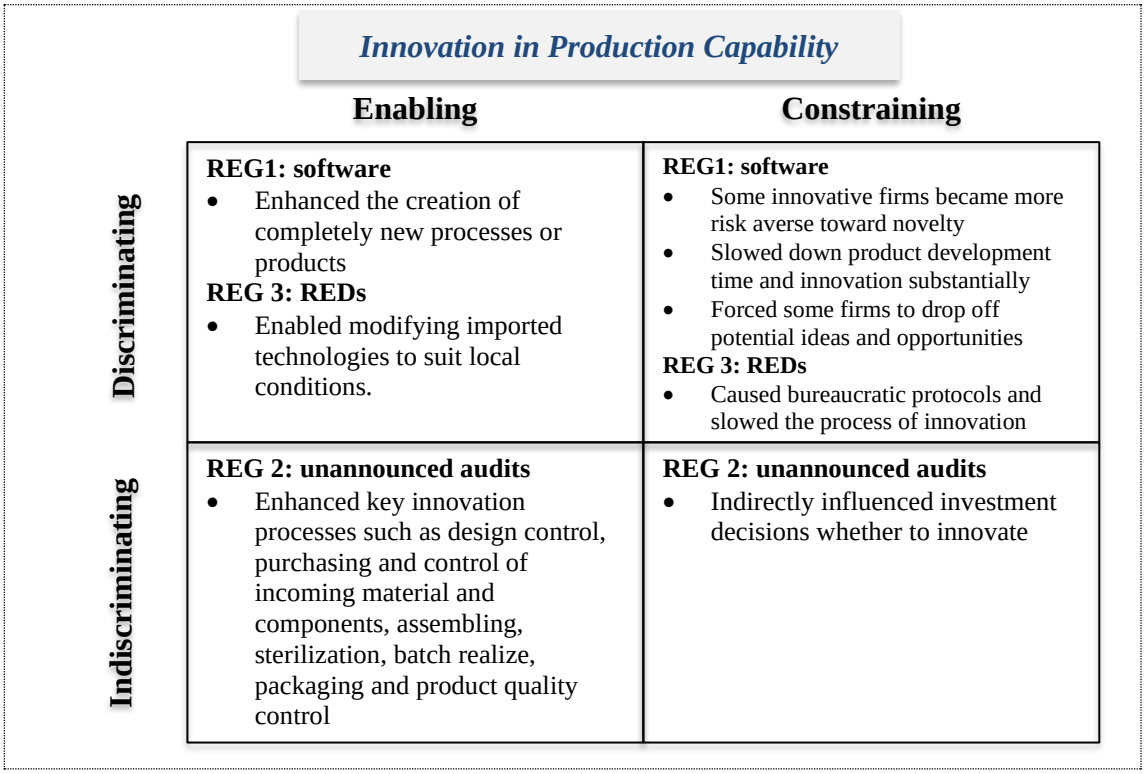


Figure 9.4: Medical devices regulation and policy dimensions: Effects on innovation in production. Compiled by author.

The cross-case analysis revealed that, on the one hand, REG1 was perceived as discriminating and enabling. Perhaps the most significant influence of this regulatory change was that it enhanced the creation of completely new innovative processes because it was too costly to fulfill the regulatory requirements with the existing technology, and significant technological change was required. The new innovative process included validating medical device software according to the state of the art taking into account the principles of development lifecycle, risk management, validation and verification. This meant developing new software in accordance with international harmonised standards.

On the other hand, the analysis indicated that REG1 was seen as discriminating and constraining. Some firms became more risk averse towards novelty and in turn became incremental innovators instead of radical innovators. The analysis indicated that regulatory change forced some firms to even drop off potential innovative ideas and opportunities due to the risk of not being able to meet the new software regulatory requirements. Moreover, there was a general consensus by respondents that to some extent, the changes in regulation restricted market entry of innovative newcomers.

Examples of requirements that were perceived as constraining innovation in order to prove compliance with further safety and efficacy standards include: 'clinical data requirement'[31] that must be supplied when seeking regulatory approval regardless of device classification, the 'evaluation' requirements, 'transparency' requirements and design changes[32] in software requirements.

Furthermore, some firms highlighted that innovative development of medical device software, was hugely constrained by "software localization". Under the REG1, software sold or used within the EU must be localized into the language of each of the EU countries that the product will be marketed i.e. MDD 2007/47/EC, Article 4.4. Essentially, if a UK medical device manufacturer wishes to market a medical device into France, the graphical user interface (GUI) must be available in French. A number of difficulties can arise when attempting to perform a software translation such as differing file formats, different character encoding, character size constraints and errors caused in code caused by repossessing. Thus, REG1 was perceived as constraining in this regard by some firms.

As indicated in Figure 9.4, REG2 was viewed as indiscriminating and enabling regulation. The regulatory change had a significant impact on firms' innovation processes. The respondents indicated that the key mandatory process affected by unannounced audits include: design control, establishment of material specifications, purchasing and control of incoming material and components, assembling, sterilisation, batch release, packaging, and product quality control. This list is not an exhaustive list and other relevant processes may be examined as well. The ultimate goal of this regulatory change was to ensure that innovative products that enter the market are safe and of good quality.

[31] Clinical data is defined as safety and/or performance information that is generated from the use of a medical device MCCAFFERY, F., CASEY, V. & MCHUGH, M. How can software SMEs become medical device software SMEs. European Conference on Software Process Improvement, 2011. Springer, 247-258.

[32] Design changes may necessitate notification to the notified body that audited the software before it was altered and should be included in the manufacturer's technical file KLÜMPER, M. & VOLLEBREGT, E. 2009. Navigating the New EU Rules for Medical Device Software. *RAJ Devices,* 17**,** 1-8. ibid.

The low level of manufacturing capacity in SA made the REG3 changes have less impact on firms' innovation activities. The cross-case analysis revealed that, regulation did not have a significant effect on radical or disruptive innovations, which involve discontinuities in innovation pathways but instead had more impact on incremental innovations as discussed in chapter 8.1.1 and in section 9.2 of this chapter under research and development capabilities.

To sum up, the regulated environment plays a significant role on the level of regulatory impact or effectiveness. If the regulated environment is subjugated by low product manufacturing capacity, the effects of any regulation irrespective of its nature or type will also be of little impact. Further, it can also be argued from a regulation and policy dimension that discriminating and enabling regulation as indicated in Figure 9.4 above can attain better and desired industry outcomes. Based on this cross-case analysis of the medical device innovation system and the interplay of regulation, there were more constraining effects than enabling ones, key affirmative impact being the creation of completely new innovative processes. These need to be addressed in order to improve regulation effects on innovation. Policy-makers should be aware of the various effects. Political decisions, including those on regulation, need to be increasingly based on evidence. This holds true for new regulation as well as for those under scrutiny, which may face an amendment, replacement or abolishment. Each decision will almost inevitably bring about different incentives and thus also have different innovation consequences for different stakeholders.

Quality control

With respect to quality control, Figure 9.5 captures the key findings related to the effects of regulatory changes on quality and safety. It is interesting that the cross-case findings show that there was no constraining regulation when it comes to quality and safety of products. Quality assurance was therefore considered to be the most important concern in outsourcing by most firms in the UK and SA. The findings indicated that most firms emphasized the importance of a sufficiently robust and effective regulatory enforcement policy that is clear from the safety perspective. The firms considered that rigorous inspections have contributed to the high quality of authorized medical devices.

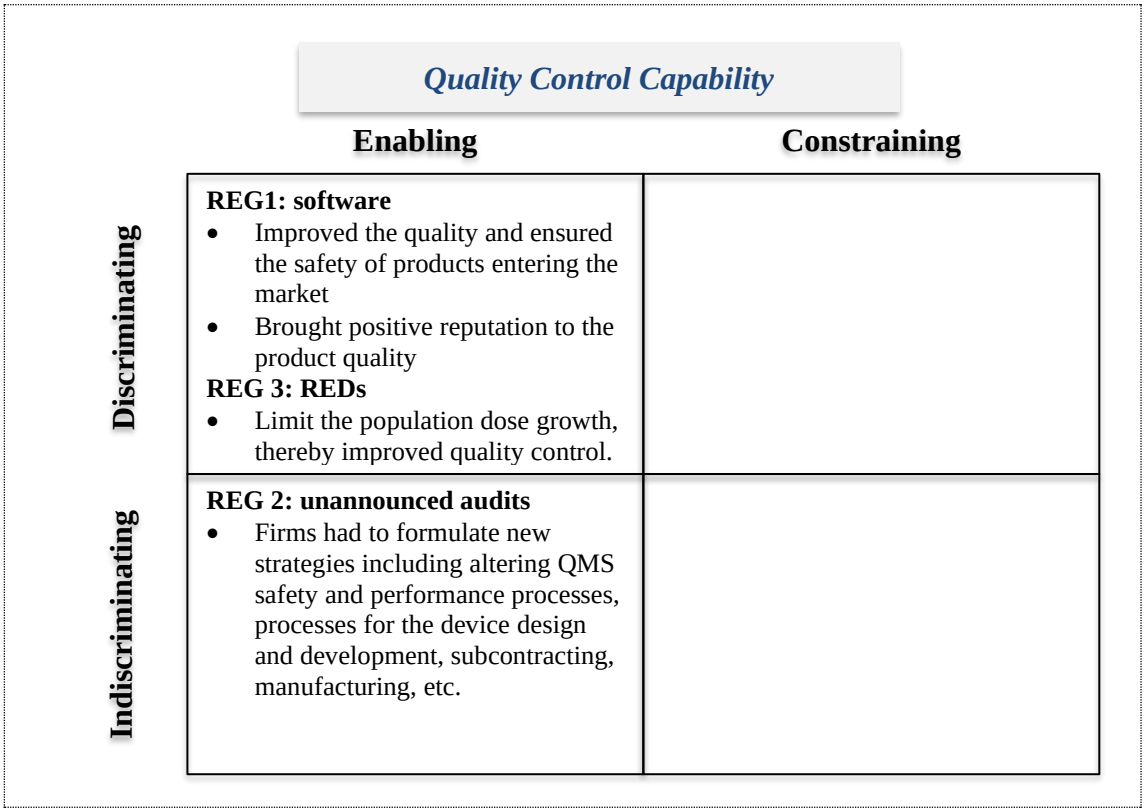


Figure 9.5: Medical devices regulation and policy dimensions: Effects on quality control. Compiled by author.

Firms perceived the product-focused REG1 as discriminating and enabling because it created incentive to develop new processes with higher work safety. It improved the quality and ensured the safety of products entering the market. The new regulatory changes further placed emphasis on supplier compliance for any part of the manufacturing process which in turn resulted in better quality outcomes. Firms were now keeping a close eye on their suppliers making sure that they were fully utilizing QMS such as the ISO 13485. To ensure patient safety, ergonomic design was now considered an essential requirement of the medical device. To that effect, the cross-case findings showed that REG1 brought positive reputation to the firms as the improved product quality helped in gaining customer confidence.

Reference to Figure 9.5 above, the analysis reveals that REG2 was perceived as indiscriminating and enabling. The regulatory change fostered firms into formulating new strategies including altering QMS safety and performance processes, processes for the device design and development, subcontracting, manufacturing, etc. The selection of suppliers occurs early in the product development process. Thus, firms

were forced to apply rigid and sophisticated qualifications to ensure quality and that suppliers must comply with complex documentation requirements and that the final product meets regulatory demands.

Furthermore, the analysis as indicated in Figure 9.5 shows that REG3 was seen as discriminating and enabling. Most firms were in agreement that the introduction of the acceptance test and annual Quality Control (QC) tests plays an important role in diagnostic imaging to limit the population dose growth, thereby improved quality control.

In brief, the findings reveal to us that, there was consensus among manufacturers interviewed on the fact that, although all the firms faced pressure for continuous improvements in terms of quality and reliability of their medical devices in a consistent manner, it appears the pressure resulted in positive outcomes. The firm managers all agreed that the three regulatory changes were engineered in such a way that quality is built-in and checked for at various stages and the evidence meticulously documented. From regulation and policy dimensions as depicted in Figure 9.5 above, all the three regulatory change cases were perceived as enabling.

Operations

Figure 9.6 captures the key findings related to the effects of regulatory changes on business operations. The summary identified that all the three regulatory change cases had enabling and constraining effects.

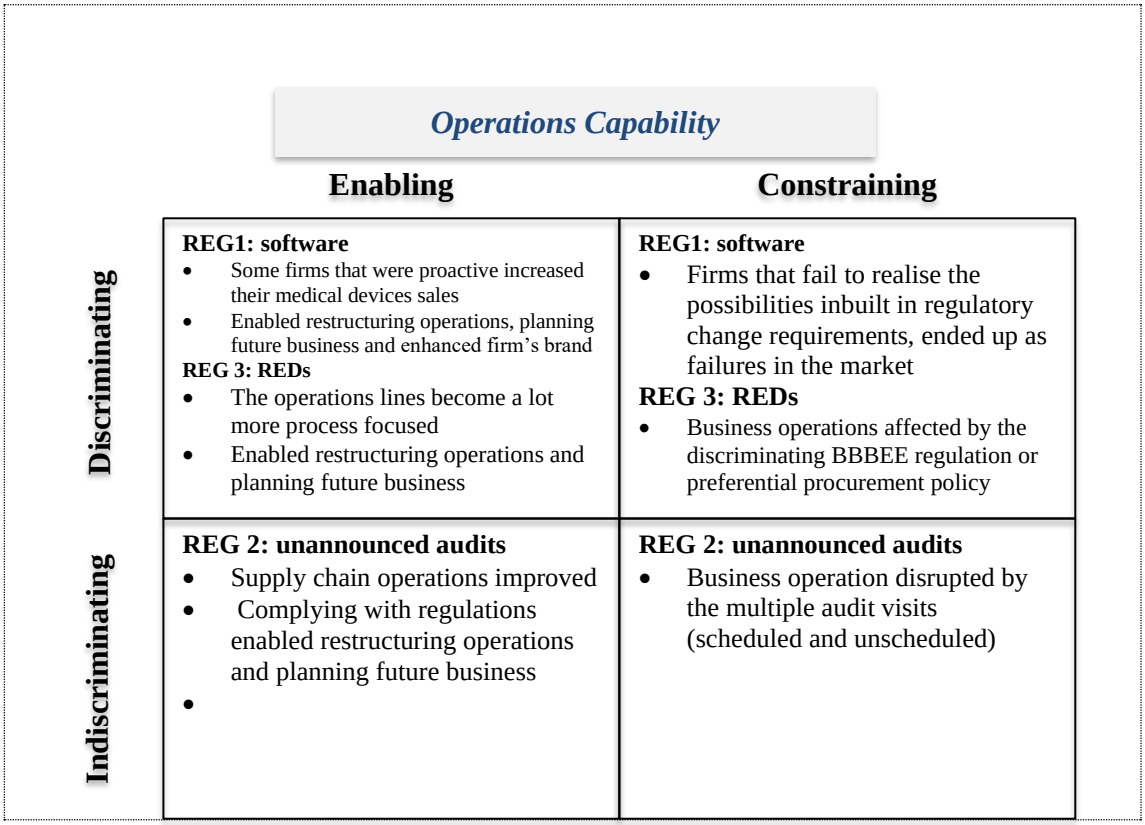


Figure 9.6: Medical devices regulation and policy dimensions: Effects on business operations. Compiled by author.

The findings indicate that REG1 was perceived as discriminating, enabling in relation to business operations. First, the regulatory change enabled brand enhancement. Compliance with REG1, with its focus on public safety, enhanced companies' standing and brand as trusted partners in their internal and external business operations in health care. Second the regulation enabled firms' competitive positioning. As different companies adopted different strategies in response to the new legislation, based on their capacity to undertake the extensive changes, this presented market expansion opportunities and or acquisition targets for the business. Even though complying with the new regulation was burdensome, the cross-case findings indicated that some firms that were proactive increased their medical devices sales. A positive approach to the regulations was a key business operations success factor. The findings indicated that firms that used the regulatory changes as a framework and process to ensure their devices are as safe as possible and perform reliably and consistently enjoyed quicker and greater commercial success. This was evidenced by the following remark from the Associate Director Regulatory Affairs of Delta Ltd:

"Because we invested more in R&D and regulatory compliance, we improved the overall company performance and turnover increased over the years after 2007 regulatory changes" [Res 057 (MAN), Jan, 2017]

On the contrary, the findings indicate that REG1 was perceived as discriminating and constraining. Some UK firms' business operations slowed down as market authorization timelines became protracted, curtailing patients' access to technology innovations and the costs of operating in Europe increased. Firms' overall operations were affected by the regulation as more regulatory and technical documentation were introduced, that meant more in-house control operations and scrutiny needed and the more the regulatory cost, the less the investors.

On the one hand, Figure 9.6 highlights that REG2 was perceived as indiscriminating and enabling by firms that had high experience of the medical device review process. Some firms indicated that an intensive scrutiny of their business practices and processes through the unannounced audits left the companies considerably better equipped for the future regulation. Complying with this regulatory change enabled restructuring of operations and planning for future business. On the other hand, the regulation was perceived as constraining because business operations were disrupted by the multiple audit visits (scheduled and unscheduled). Furthermore, the findings indicated that after the introduction of REG2, there was a shake-up of the notified body network that led to closing down of a few notified bodies and in turn led to bottlenecks in getting products to market. This had a significant impact on firms' business operations. Some respondents expressed concern about the uncertain future of their businesses operations given the ad-hoc and abrupt policy changes by the EU community. The Chairman of Kilo Ltd reported;

"We cannot properly plan how to grow our business given the current practice whereby the governments just make abrupt decisions without proper consultation" [Res O66 (MAN), Jan, 2017].

Similarly, the analysis shows REG3 *in SA* was perceived as discriminating and mainly enabling with regard to operations capabilities. The regulation enabled restructuring

operations and planning future business. Most firms expanded their business operations mainly as a means to meet regulatory requirements.

However, REG3 was perceived as discriminating and constraining with respect to the associated preferential procurement system and the BBBEE regulation. The way in which purchasing decisions are structured and regulated impact profoundly on the way in which firm operations happen. Lall (1987) identified firms' procurement capabilities, as well as those of governments, as elements of cumulative industrial improvement. Procurement can act as a financing and incentive mechanism to improve technological capabilities, a key element of medical device industry development. The findings indicate that many existing local companies without BBBEE qualification faced difficulties in competing in the procurement system and collectively called for a transparent system and a level playing field.

The case analysis shows that industry associations such as SAMED and SALDA in response, have been attempting to influence the institutional environment and its actors by lobbying for less stringent regulation in the BBBEE space. Overall, there seems to be a consensus that the cost of BBBEE regulation imposed by government has developed into a political issue over concerns about the excessive cost and administrative burden imposed by complying with regulatory requirements.

Based upon the medical devices regulation and policy dimensions model in Figure 9.6, we are able argue that a discriminating and enabling regulation is capable of assisting firms to develop better strategies, restructure operations, improve processes, implement key business initiatives, plan future business and help the firms to effectively manage regulatory changes. The importance of regulation and industrial policies that foster the operations of business into local medical devices production cannot be overemphasized. Local production of medical devices benefits local economy, such as savings on foreign exchange through import substitution, employment creation and the development of exports.

Cost of Compliance

It should be noted that most firms generally viewed regulatory compliance[33] as a driver of complexity and costs for businesses, whose regulatory teams are tasked with ensuring that their companies are compliant with legislation and minimizing the risks associated with it. The firms that seek to leverage the opportunities inherent in compliance with new regulation had fruitful outcomes for their businesses. The analysis summarized in Figure 9.7 highlights that regulatory compliance is costly and absorbs significant resources.

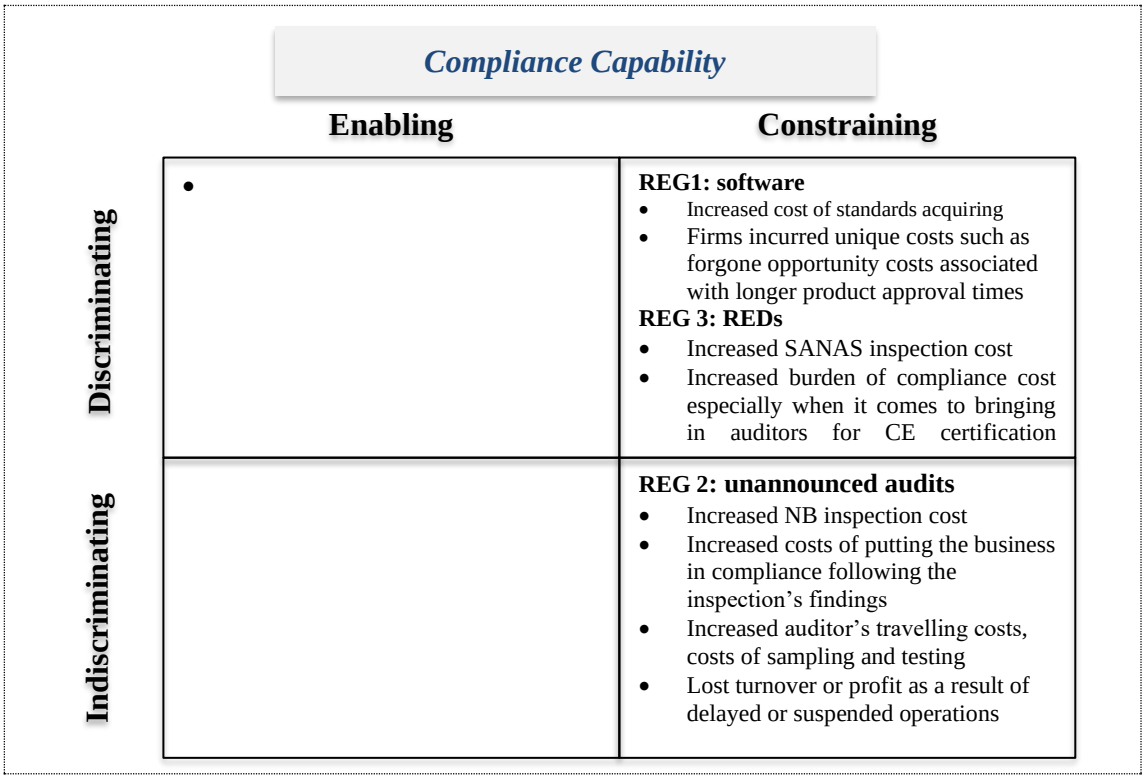


Figure 9.7: Medical devices regulation and policy dimensions: Effects on cost of compliance. Compiled by author.

The findings indicate that REG1 was seen as discriminating and constraining in relation to compliance. Due to a series of harmonised standards which go alongside REG1, firms had to increase the appropriate level of software testing and the complexity of setting up and validating all the appropriate test methods, meant increased cost of products, time and manpower. Furthermore, the firms incurred unique costs such as forgone opportunity costs associated with much longer product approval times. However, trying to reduce compliance costs by compromising on

[33] Regulatory compliance refers to organizational activities that are induced or stimulated by requirements issued by the regulatory authority.

standards would lead to fewer medical devices entering the market, instead ensuring a cost-effective and sustainable compliance with standards would be good for all the actors in sector in the short and long runs.

REG2's routine unannounced audits and REG3's SANAS inspections share some similarities in their inspection requirements. For example, they both called for technical inspections that focus on compliance with, broadly speaking, "safety requirements" (understood in a very broad sense, as social aspects of regulation), and protection of patients' occupational safety and health, safety and performance of the medical device[34], buildings and premises, market surveillance of products, etc. (Blanc, 2012).

The findings summarized in Figure 9.7 shows that REG2 audits were perceived as indiscriminating and constraining while REG3 was perceived as discriminating and constraining with regard to the cost of compliance. The findings indicated some similarities in the way in which inspections were a burden on most firms through the time lost and other direct costs of the conformity assessment procedures. Given this, manufacturers had to factor the additional costs related to inspections or audits in their budgets. These may not, in fact, always be the most important form of inspections burden, but they are the most easily quantifiable (Monk, 2012). The type of costs directly affected by regulatory inspections include:

(i) Preparation time, if any, when inspections are announced in advance (e.g. in the case of SANAS inspections), including time to retrieve or prepare specific documentation.

(ii) Inspection time spent with inspectors by staff or management of the firms, during which they were not able to perform other work.

(iii) Follow up time, if any, for all activities directly resulting from the inspection such as preparing documentation or any other administrative tasks.

(iv) The other costs incurred by the manufacturer include: auditor's travelling costs and costs of sampling and testing.

[34] Testing of device conformity in the UK is done in accordance to ANNEX III Section 4 of the European Commission's Recommendation 2013/473/EU, with the main focus on the safety and performance of the device. Possible tests include: microbiological, mechanical, packing, performance, electrical and functional safety testing

Trying to get the details of most costs through in-depth interviews was difficult especially from the SA firms as the respondents were reluctant to reveal the actual regulatory inspection cost

To sum up, as all the three regulatory changes increased compliance cost, in turn this resulted in most firms needing to divert resource outflows to meet regulatory requirements. However, firms that sought to leverage the opportunities inherent in compliance with new regulatory changes had fruitful outcomes for their businesses.

9.4 Effects of regulatory change on Linkage Capability: cross case analysis

Linkages offer benefits to foreign affiliates and domestic manufacturers/suppliers, as well as to the country in which they are forged as a whole. Linkages can also transmit knowledge and skills between the linked firms. A dense network of linkages can promote medical device production efficiency, productivity growth, technological and managerial capabilities and market diversification for the firms involved in the medical device industry. The three regulatory changes in the UK and SA had a major impact on both local and international linkage capabilities with influence across products and processes. Figure 9.8 captures the key findings related to the effects of these changes on linkages.

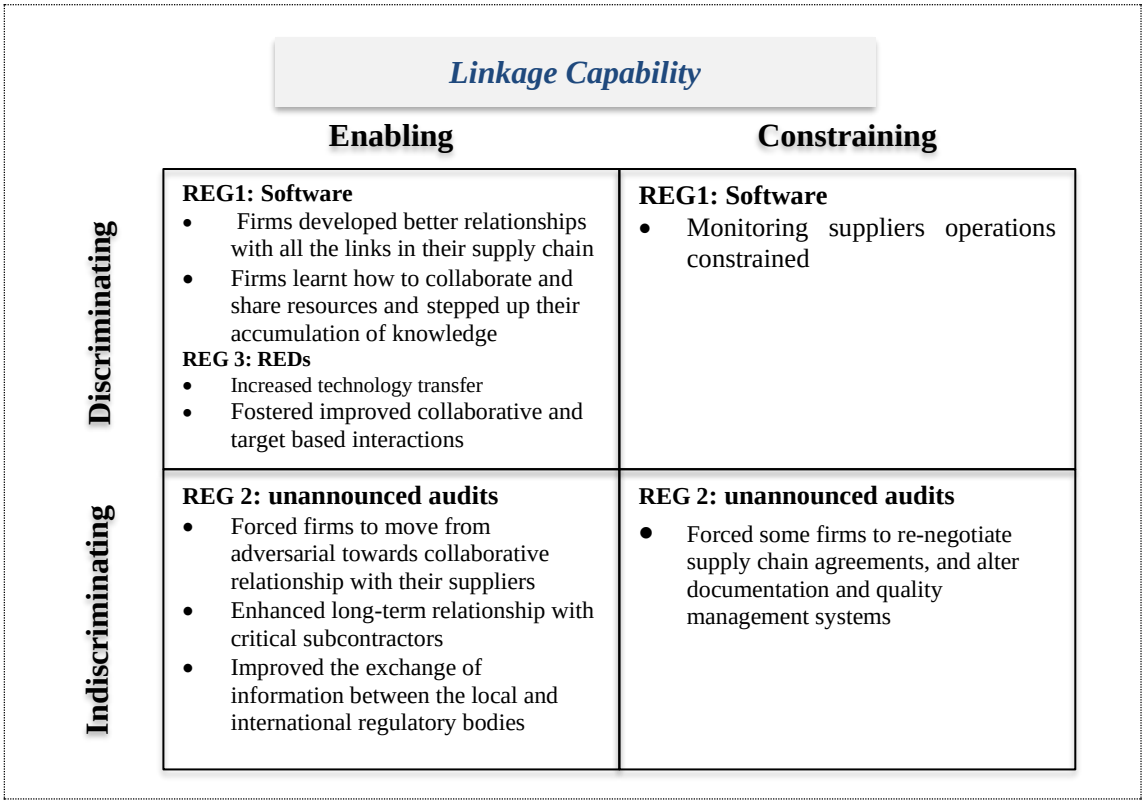


Figure 9.8: Medical devices regulation and policy dimensions: Effects on linkage capabilities. Compiled by author.

The findings indicate that REG1 was seen as discriminating and enabling with respect to linkages. There was a general agreement by the respondents from the UK-based firms that because both manufacturers and their critical suppliers were technologically strong and capable, therefore the regulatory change enabled knowledge flows to run in both directions with a focus mainly on new medical software technologies and organizational methods. Whereas in SA even though the firm respondents perceived REG3 as discriminating and enabling, they indicated that domestic manufacturers' technological capabilities were comparatively weak and the knowledge flows were more one-sided, coming from MNCs to domestic firms.

Both product-focused REG1 and process-focused REG2 regulatory changes in the UK fostered the formation of an efficient supply chain management, which is critical to the competitiveness of firms. On one hand, as part of REG1 changes, the directive mandated that, should a device manufacturer outsource any part of the design or manufacturing process, then the manufacturer must be able to demonstrate that adequate controls over the whole chain of development of the software concerned

have been put in place. This new regulatory requirement helped in the creation of an efficient supply chain management system though a few respondents argued that it was very constraining to monitor the process and the suppliers.

On the other hand, the most radical reformation within the REG2 concerns their audit policy or the modalities for conduct of assessments that mandated Notified bodies to not only audit the premises and processes of the manufacturer, but also those of its critical subcontractors or its crucial suppliers. On average, a manufacturing firm was spending more than half its revenue on purchased inputs. Some firms were contracting out the entire manufacturing process to independent "contract manufacturers", keeping only functions such as R&D, design and marketing. In these cases, as a result of the regulatory changes, supply chain management became even more important. Most of the firms interviewed indicted that they successfully broadened their outsourcing models within their supply chain networks to include foreign firms with offshore production facilities.

The analysis indicated that firms developed better relationships with all the links in their supply chain**,** learnt how to collaborate and share resources and stepped up their accumulation of knowledge in order to meet the new regulatory requirements. The motives for close collaborative relationships fostered by the product and process regulations between manufacturers and their suppliers was said to be in search of competitive advantage and improved market positioning. The supply chain linkage formation process was affected by a new regulation and policy environment. Indeed, in addition to regulatory changes being a key determinant for the formation of efficient supply chain linkages, the technological, managerial and regulatory compliance capabilities of the subcontractors or suppliers also determined to a large extent the ability of manufacturers to meet new regulatory requirements and benefit from the knowledge that supply chain linkages can transfer. Weak capabilities of the crucial suppliers increased the chances of medical device manufacturers to outsource the most sophisticated and complex parts and components from other capable or preferred suppliers within or outside the UK.

Based on Figure 9.8, it can be seen that some respondents perceived REG2 as enabling due to the fact that the changes fostered firms to move from predominantly

adversarial and transactional relationships towards collaborative relationships with their suppliers (see chapter 7). Thus, this type of linkages enhanced long-term relationships with critical subcontractors.

On the contrary, there was a general consensus among respondents in the UK that REG2 had an enormous constraining effect on supplier agreements between actors and throughout the whole supply chain as the level of scrutiny had increased. The cross-case analysis showed that a lot of suppliers were not entirely medical device suppliers so they found the new inspection regulatory requirements that had been extended to them as a market shock and had difficulties in complying with them. Moreover, changes in regulation usually have a transition period of three years but REG2 was imposed three months after the EC recommendation was passed. Most manufacturers were forced to change their supplier contract agreements. The manufacturers' new legal contract agreements with their suppliers had to ensure that there was a clause included that the suppliers will be inspected any time by NBs and they are to notify the manufacturers of any dates of which they are not available.

As mentioned earlier, in SA, there was a general consensus among the respondents that domestic manufacturers' technological capabilities were comparatively weak and the knowledge flows were more one-sided, coming from foreign affiliates to domestic firms. The types of linkages affected by REG3 were different from linkages in the UK. In section 9.3 under the subsection "operations", the analysis revealed that the BBBEE regulation was perceived as constraining business operations in the way it was implemented. However, this regulation, to a certain extent enabled the framework for linkages formation. In the search to meet the target based BBBEE regulatory requirements and increase the BBBEE company rating in order to have a competitive public procurement advantage in the SA market, some foreign affiliates merged with the domestic firms that had higher BBBEE ratings. In turn this led to upgrading of domestic suppliers' technological capabilities. Lall (1992) refer to this type of linkages as "a special linkages promotion programme" and is a proactive approach, which is typically focused on a selected number of industries and firms, with a view towards increasing and deepening linkages between foreign affiliates and domestic firm.

9.4.1 Joint ventures and strategic partnerships: fostering technology transfer

Under REG3, there are some requirements that had enabling effects on the interviewed firms' linkage capabilities. The requirements promoted the creation of joint ventures, strategic partnerships and in turn fostered technology transfer. These regulatory change requirements are in respect to the application for a licence to import, manufacture or fully refurbish any listed electro-medical device. As already established, two of the shortcomings of SA's regulatory environment are: (a) local manufacturers are organized at the secondary level and hence dependent on foreign companies for raw materials and technology sources; and (b) the country imports more than 90% of the medical devices. Yet, two of the requirements for importation of new or fully refurbished listed electro-medical devices include:

(i) Providing a copy of the EC Certificate(s) issued by a recognised Notified Body to the original manufacturer in terms of EC Directive 93/42/EEC or 90/385/EEC (whichever one is applicable); and

(ii) Proving a copy of the EC Declaration of Conformity issued by the original manufacturer in terms of EC Directive 93/42/EEC or 90/385/EEC (whichever one is applicable) (DoH South Africa, 2011).

As the SA domestic firms are expected to have a capability to import, manufacture or fully refurbish any listed electro-medical device on a global basis, to comply with the stated requirements above, the respondents argued that it is a tall challenge for most of the firms. Such stringent requirements make it more difficult for domestic suppliers in SA to enter the supply chain. In order to overcome these problems, some local manufacturers established joint ventures as a strategic partnership with foreign companies whose technological capabilities and resources are strong. Some of the specific criteria used by the SA local firms in the quest for foreign affiliates include; their willingness and potential to establish beneficial linkages, their interest in developing strong supply links with domestic enterprises, production capabilities, ISO certification and CE mark certification.

As the product and process REG3 raised its constraints, the SA firms were caught up in a situation where there are not enough technological capabilities. This dilemma led to the formation of 'horizontal linkages', which involve interactions with domestic firms engaged in competing activities and 'backward linkages' that are defined as

transactions that go beyond arm's length and involve longer term relationship with firms (Lall, 2003). Thus, external networks and support are vital to survival in the race to meet regulatory requirements, upgrade and retain or regain market access.

The analysis indicates that domestic/foreign affiliates enabled relationships that were marked by sustained exchanges of information, technology, skills and other assets. The linkages are of particular significance to SA firms, because they provided a means of diffusing valuable knowledge throughout the medical device sector. Since technical requirements to attain CE certification and associated standards are so complex, foreign affiliates' assistance was considered a huge knowledge transfer benefit. Some assistance was in the form of human resource development therefore often forming part of linkages, and expands the scope for deeper spillovers of skills and knowledge.

The benefits provided through linkages with foreign affiliates were of greater competitive significance than those among domestic firms because of the stronger knowledge and skills base of many foreign affiliates. Foreign affiliates, in turn, benefited from backward linkages as they enhanced their access to local tangible and intangible resources. Hence there was a substantial mutual interest between foreign affiliates and domestic firms to create and deepen backward linkages. Linkages are, therefore, a channel towards strengthening the competitiveness of domestic firms, and giving them a footing in the international production networks of medical devices. Fundamentally, these linkages should be seen as part of a broader set of FDI, SME regulation and policies.

Successful local SA companies have, in general, developed internal expertise through partnerships or international/multinational collaborations, whether it be manufacturing or distribution. The alliances with leading players and suppliers gave the companies access to critical skills, resources, and support when developing the latest products, processes, and international endeavors. Two examples of firms in SA that benefited from backward linkages with foreign affiliates and horizontal linkages with other domestic firms as a result of regulatory change include Medtech and Southmed (see chapter 8). Medtech successfully merged with its affiliate companies in the USA and is now firmly committed to ensuring not only excellence in medical devices, but

ensuring that these devices are cost effective. The merger enhanced Medtech's capabilities to become involved in value-added operations and offerings. Similarly, Southmed merged with another local firm and consolidated their infrastructures with the aim of improving efficiency and quality. The joint venture enhanced Southmed's capabilities and the firm's client base now spans the entire Southern African region. The Director of Medtech respondent noted:

"Our acquired sister company in the UK and USA-based consultants and designers feed us with the latest medical device global market information, help us to adopt new production and processes and training developments. Such an arrangement put us ahead of the game and improved our product quality" (Director - Medtech, (SA) 2016).

As reflected in the quote above, joint ventures/alliances and partnerships are the most dominant ways to adopt new production and processes by the firms. It is important to note that partnerships include both alliances with leading market players as well as with suppliers in co-product development, marketing, and supplies (Alexiev et al., 2016). The present findings supports existing studies showing that alliances and partnerships are the main sources of opening new opportunities and are a vital mode in firm development (Cudjoe and Ibiyemi, 2015), and learning from partners (Peng and Heath, 1996). Further, the alliances of interviewed firms with international players earned them access to critical skills and competences in their new production endeavors to overcome their inherited bottlenecks in production, processing and operations. This is in line with the learning and acquisition of knowledge from foreign partners (Meyer and Nguyen, 2005).

According to institutional theory, alliances can enhance their ability to address institutional turbulence or transitions in the business environment, market alienation, and competitive intensity (Alexiev et al., 2016). Furthermore, since institutional theory is concerned with how organizations establish their positions and achieve legitimacy in order to survive and make profit (Scott, 2005), an effect of being associated and connected with the right individuals, networks and organizations was that it increased the legitimacy for the case firms. As far as risks with

internationalizing goes, not having legitimacy and credibility can be devastating for a firm and that was highlighted from all of SA case firms.

Other common channels through which firms have gained useful knowledge in order to address regulatory challenges introduced by SANAS inspections under REG3 are exhibitions, membership of professional associations and conferences. Manufacturers also learn from each other because employees move between firms or meet and have informal exchanges at training events and seminars. Flows of knowledge also occurred through the industry associations such as SAMED and SALDA, which organize training events and other initiatives.

Finally, as previously explained, the accumulation of linkage capabilities occurs over time, and the current capabilities are influenced by past events. Because of the cumulative nature of technological knowledge, regulation and policy initiatives had a long-lasting impact on the linkage capabilities of firms and industries. In the SA's REG3 case, an example of regulation policy intervention that can be said to have helped the development of linkage capabilities in the industry is the provisions for compulsory licensing of imported new or fully refurbished listed electro-medical devices. It can be argued that the compulsory licensing has enabled local firms to reach good licensing agreements with foreign MNCs. However, obstacles and limitations remain, and the analysis in this chapter has shown that SA firms have to upgrade successfully in order to compete effectively against strong imports. There are, however, success stories of firms that have reached significant technological sophistication, as in the case of Medtech and Southmed.

9.5 Summary of the cross-case analysis

As discussed at the beginning of this chapter, Chataway et al., (2006) proposed a data matrix analytical strategy that has been employed in this chapter. Based on this analytical model, Figure 9.9 shows the overall effectiveness of the three regulatory changes from wider medical devices regulation and policy dimensions.

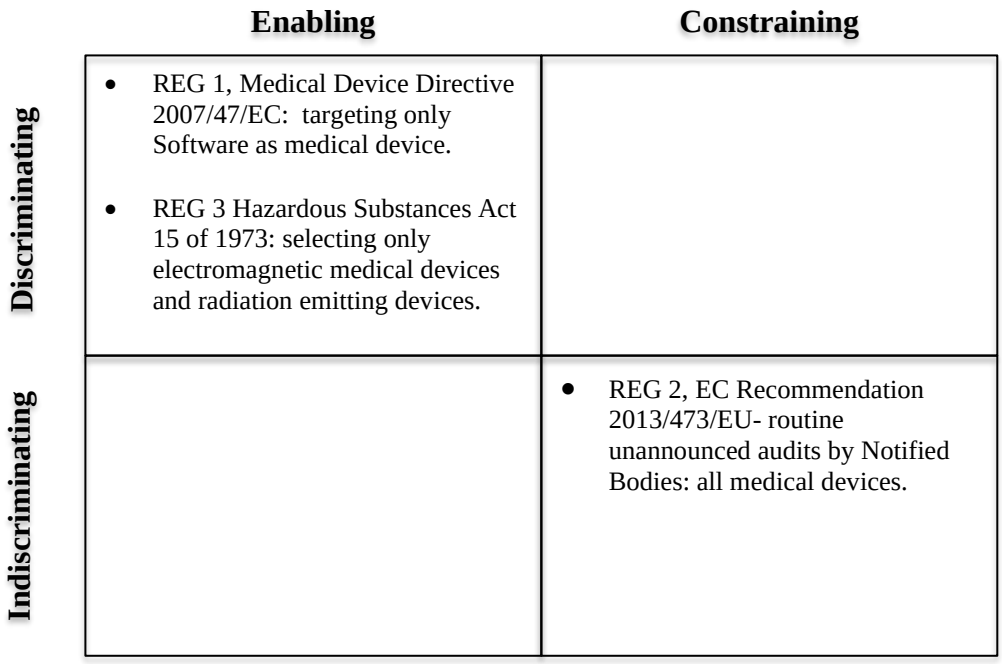


Figure 9.9: Medical devices regulation and policy dimensions. Compiled by author.

Based on Figure 9.9, one can see that overall most firms perceived REG1 as enabling and discriminating. This is because the introduction of the REG1 enhanced the creation of completely new firm processes. The regulatory change drove most UK-based firms to invest substantial resources in R&D to standardize their software products. The changes led to redefining of firm's training needs for innovations, prototyping, design, testing, validation, verification and release processes. The regulatory change improved firms' product quality and ensured safety of software products entering markets. The CE marked software brought positive reputation to the product quality and helped it gain confidence among customers. Furthermore, it also became increasingly necessary for firms to develop relationships with all the links in their supply chain.

As far as the industry managers are concerned, REG2 was seen overwhelmingly as constraining (Figure 9.9). Criticism particularly came from firms with limited regulatory review process experience or the SMEs and was mainly to do with the high costs associated with unannounced audits. REG2 had an enormous constraining effect on supplier agreements between actors throughout the whole supply chain as the level

of scrutiny increased. For most firms, the delivery of products and processes was dependent on complements in the chain of production and new regulation prompted the inclusion of external process or product providers in audits. Firms had to revisit their procedures for planning and execution as well as set up new contracts with the NBs and external providers at a higher cost. Many suppliers were also not medical device focused and the new inspection requirements operated as a market shock and in turn the firms had difficulties complying.

The analysis suggests that majority of firms perceived REG3 as predominantly enabling. The regulatory change enhanced the need for firms to recruit skilled personnel or the need to provide adequate periodic staff training. The changes enabled modifying imported technologies to suit local conditions. Most firms were in agreement that the introduction of the acceptance test and annual Quality Control (QC) tests played an important role in diagnostic imaging to limit the population dose growth, thereby improved quality control. Importantly, the regulatory changes improved collaborative and target based interactions between government and private sector, harmonized the industry actors and in turn ignited growth of the industry. Furthermore, REG3 enabled international company-to-company partnerships, usually with European companies. As such, this reinforces the notion that regulatory change in SA came about not just as an obligation or as constraining requiring compliance, but instead as a possibility for firms to improve their products and competitive position in the market through affirmative linkages.

In summary, the findings in the cross-case analysis show that regulatory changes affect firms differently according to the resources and capabilities available to the firms. In this respect, the analytical approach adapted in this chapter allowed us to have a better understanding of the effects of regulation that is more ‘resource-based’. The next final chapter presents a summary of the findings, discusses various policy implications and addresses the limitations of the study.

CHAPTER TEN
CONCLUSION

10.0 Introduction

This thesis examines the influence of regulatory changes on industrial capabilities and affordable healthcare technology development in the medical devices sector in developed and developing countries. The objective was achieved by identifying key medical device regulatory changes, the drivers behind these changes and by examining how these changes influenced the development process of novel devices in two countries, the UK and South Africa. This final chapter presents a summary of the findings, discusses various policy implications and addresses the limitations of the study.

10.1 Addressing Research Sub-Question 1

What changes have been made to regulation of medical devices and what approaches were utilised by regulators to implement the changes in the UK and SA?

This question was addressed in its two parts. We begin by summarizing each case of regulatory change from our main findings in chapters 7-9.

10.1.1 First regulatory change case: Medical Device Software in the UK

These regulatory changes marked the introduction into the EU of stricter rules for software used with medical devices. They included the following key changes:

a) The requirement for *risk-based validation* of software.
b) The requirement for manufacturers to provide precise and detailed *technical documentation* of the medical device.
c) *Clinical data* was now required on all devices regardless of classification. The regulatory change introduced stricter requirements for clinical investigations and clinical evaluation.
d) *Requirement on* manufacturer to demonstrate adequate controls over the whole chain of software development, including outsourced design and manufacturing.
e) The requirement on manufacturer' subcontractors to report any design changes in their software.

10.1.2 Second regulatory change case: introduction of unannounced audit visits in the UK

This regulatory change (on audits) involved the following key changes:

a) Notified Bodies (NBs) were mandated to audit the premises and processes of the manufacturer, and also those of its subcontractors and crucial suppliers.
b) NBs were instructed to perform unannounced audits at least once every three years.
c) The changes further instructed the NBs to pay special attention to the production of the devices and any critical processes such as subcontracting.
d) The requirement for NBs to verify the manufacturer's system ensuring traceability of materials and components. At each audit, the notified bodies were now required to verify that the manufacturer correctly applied the approved quality management system and the post-market surveillance plan.

10.1.3 Third regulatory change case: Radiation Emitting Devices (REDs) in South Africa

Key changes of this regulatory change were:

a) The requirement for manufacturers/suppliers to apply international standards as legal requirements and guidelines through the Radiation Control Directorate (DRC) and obtain a license of compliance.
b) The manufacturer/supplier was required to comply with the rules contained in two documents supplied with the license.
c) The requirements for the manufacturer/supplier/user to obtain a joint product and premises license for X-ray equipment before installation and commissioning, together with requirement to perform acceptance tests on the equipment.
d) The License holder of a diagnostic X-ray facility was made ultimately responsible for the entire scope of radiation safety.

10.1.4 Regulatory approaches used to implement change by the regulators

The second part of the research question addresses the nature of the regulatory approaches utilised by regulators in the UK and SA.

The first key finding is that the three cases used different regulatory approaches with consequent differential impact on the behavior of firms. The first regulatory change case (software product regulation) used a proactive regulatory approach. Whereas the

second regulatory change on audits was a reactive and rapid response measure mainly triggered by market shocks e.g., the Poly Implant Prothèse (PIP) scandal in 2010.

The second key finding is that the software product regulation provided firms a governance framework for development of medical devices and helped the growth of the market. In contrast, the regulatory change on audits had disruptive impact on firms' capabilities and dynamics of the industry structure. Firms, especially SMEs, found themselves facing major demands to conform to new regulations from the government.

The third regulatory change case (Radiation Emitting Devices: REDs) in South Africa was perceived as disruptive, discriminating and constraining by many domestic firms.

10.2 Addressing Research Sub-Question 2

The objective of the second research sub-question was to determine the drivers that led to changes in the regulatory frameworks in the UK and SA:

What conditions, processes and events facilitated the changes to regulation of medical devices in the UK and SA?

10.2.1 Drivers that led to the first regulatory change: Medical Device Software in the UK

Chapter six analysed the regulatory changes concerning software products. It showed that the regulatory changes were developed in response to increasing technological sophistication of devices and the need to extend regulatory reach into software, thereby toughening regulatory compliance and regulatory processes. This process was driven by the demands of member states and MNCs to establish common rules of exchange and by the supply of regulatory proposals from the European Commission. The extension of regulatory reach into software suggests that supranational forces were driving the regulatory change and activity.

10.2.2 Drivers that led to second regulatory change: introduction of unannounced audit visits in the UK

Our research suggests there were multiple drivers towards this change, albeit reaction to a scandal was a prime mover.

Need to address product failures

In chapter two we found three product failures that facilitated the introduction of the second regulatory change introducing unannounced audits in the UK and Europe. These product failures included: i) the 2010 recall of ASR metal-on-metal hip replacement systems due to a five-year failure rate of the product; ii) the 2011 U.S. FDA product warning of serious complications associated with surgical mesh for transvaginal repair; iii) and the 2012 Poly Implant Prothese scandal where breast implants made with industrial-grade silicone instead of medical-grade silicone were sold affecting about 300 000 women. These scandals or externalities (where an individual or firm's action have consequences for others) raised serious questions about regulatory systems in the EU. A flurry of regulatory activity ensued to bolster the legitimacy of the EU system of medical device governance.

External pressure and the European Commission

These product failures led to increasing demand from member states and other stakeholders for stringent regulatory framework. The EU regulatory framework for medical devices, through the Conformité Européenne (CE) marketing process was asserted by member states as inadequate to provide sufficient safeguards for technologies that affect health-related quality of life. The inadequacies cited included inferior regulatory evidence standards, non-transparent decision-making processes, and insufficient post-market surveillance to ensure devices' safety and long-term performance. The European Commission echoed such concerns, stating a need to "adapt the European regulatory framework in order to secure patients' safety while favouring innovation" (European Commission 2011). This pressure acted as one form of "external" pressure for regulatory change.

Public consultation: Influence of industry voice

The pressure from member states and other stakeholders led to the announcement of the public consultation on the "Recast of the Medical Devices Directives" by the European Commission in 2008. It received 200 responses with the industry (individual companies, mainly manufacturers of medical devices) emerging as the principal contributor with 92 responses. Most respondents confirmed that the current legal framework for medical devices left some room for improvement to strengthen the regulatory system. Some SMEs, however, were concerned that the costs of putting

a medical device on the market would multiply. There was unanimous support for improving the way in which Notified Bodies were working. Most respondents believed that there should be a tightening up of the designation and monitoring of Notified Bodies to ensure a uniform high level of competence (EU, 2008)[35].

10.2.3 Drivers that led to the third regulatory change: Radiation Emitting Devices (REDs) in South Africa

Chapter 6 details the drivers leading to regulation of REDs in South Africa.

Internationalization as a driver of regulatory change

The South African government played a major role in driving the regulatory change. The government recognized the need for an internationally recognized national accreditation system as a crucial element of a well-functioning technical infrastructure aligned with international best practice. The government therefore, assented the *Accreditation for Conformity Assessment, Calibration and Good Laboratory Practice Act*, 2006. The purpose of this Act was to provide an internationally recognized and effective accreditation and compliance monitoring system for SA by establishing the South African National Accreditation System (SANAS) as a public entity. SANAS became responsible for carrying out the regulatory accreditations in respect of conformity assessment, monitoring of good laboratory practice to comply with Organization for Economic Cooperation and Development (OECD) principles. The SA government was the major player in this internationalization process that led to the third regulatory change (see Chapter 6).

SMEs and home market conditions can push regulators to change regulation

We found that another driving force behind regulatory change were the SMEs and the complexity of the home market. Our analysis indicated that local SMEs experienced constraints when internationalizing. For example, the process of ISO 13485 certification is very expensive for local manufacturers and constraints were compounded by the lack of a comprehensive regulatory framework for medical devices in South Africa. Local manufacturers needed audit by a notified body in order

[35] Recast of the medical devices directives: Summary of responses to the public consultation. https://eur-lex.europa.eu/resource.html?uri=cellar:487acc33-213b-4fdf-bdbb-8840209a8807.0001.04/DOC_4&format=PDF

to get the certification and ended up spending significant time and financial resources to obtain CE and FDA certification from European and American certified bodies. The process is expensive and lengthy so that very few local manufacturers could afford it. Local SMEs lobbied for regulatory change that would accredit local companies to provide auditing services and change the institutional environment.

Role of MNCs in influencing institutional change

One key finding was that several established MNCs influenced the regulatory changes in South Africa. As regulatory processes pose a barrier and require conformity for firms when entering markets, they can be used to benefit established firms. Medtech and Northmed are examples of MNCs that played a role in influencing institutional change by lobbying for increased regulation. Northmed confirmed that they actively promoted the demand for CE labelling in the SA market (see section 8.3.2) with the intention to strengthen the competitive advantage of the firm as illustrated by the following quote: *"We have used our ability to influence market to push through a demand for CE labelling in order to do business" (Northmed, 2016).* The MNC was influential in the implementation of REDs changes and was proactive in lobbying for the new regulatory changes under the Medicines and Related Substances Act of 2015 that were promulgated in June 2017.

Collaboration of actors facilitates lobbying of regulatory changes

Findings from our analysis of linkage capabilities showed that the RED regulatory change enabled the development of a strong collaborative relationship in the SA medical device industry. As a result, the collaboration of the manufacturers, regulators, funders, government departments and industry associations facilitated the development of the new regulations published on December 9, 2016 (see section 8.4.4). We argue that the lesson for firms, especially SMEs that are weak alone, wishing to change regulation, is to collaborate to make a powerful entity that can truly influence regulatory change.

10.3 Addressing Research Sub-Question 3

How have regulatory changes affected firm level investment, production and linkage capabilities of medical device firms in the UK and SA?

Our detailed findings, presented in the previous chapters, show that three case studies give different but in some instances similar perspectives on the way in which regulatory changes in medical devices have affected technological capabilities.

10.3.1 The effects of the first regulatory change: Medical Device Software in the UK

As Malerba and Mani (2009) highlighted, a sectoral system of innovation approach considers a wide range of factors that affect innovation and production in a sector. In particular a sectoral system approach examines innovation as the result of firm's specific capabilities.

Regulatory change increases firm's investment capability in R&D

Chapter seven shows that this product-focused regulatory change drove most UK-based firms to invest substantial resources in R&D to standardize their software products. Adner (2002) argues that if innovators have sufficient financial support to invest in their R&D departments, they will continue innovation improvement efforts to attain a dominant position in the market. In this study, we found that most manufactures of medical devices software had positive income returns that improved after they invested towards compliance with the regulatory change. Results from this study strongly indicate that R&D capabilities are vital to the early growth of innovative healthcare technology development ventures. Firm R&D capabilities included an ability to sense and seize opportunities from compliance with the regulatory changes. Existing and enhanced R&D capabilities of these firms allowed them to develop products with higher market value.

Regulatory change and its harmonized standards enhanced and extended the medical device market

Our analysis in chapter 6 shows that the software product-focused regulatory change emerged as an important step to guarantee the acceptance of products in a broad geographical market. The changes enabled the opening of new software market opportunities to companies that invested heavily in R&D to comply with the safety and efficacy standards outlined in the EN/IEC 62304, a software development standard that emerged as a global standard for the software development life cycle. The introduction of this regulatory change repositioned medical device software in a

more transparent manner because manufacturing standards, procedures, tests, validation, and accountability were all improved to reduce device recall statistics. Our results indicate that the regulatory change on software enabled overwhelming international competitive advantages for complying device manufacturers, with special certification and quality marks on products. This finding resonates with Salvador et al., (2002) who argued that cross-national agencies and regulatory bodies promote standardization to encourage firms to sell the same product across national markets. The key finding is that product-focused regulation enabled the enhancement and extension of the market.

Software product-focused regulatory change increased firm's investment in training and recruitment capability

As Lall (1992) argued, the development of investment capabilities not only requires the improvement of existing competencies, but also the acquisition of new knowledge. In this study, in chapter 7, we found that regulatory changes for software led to redefining of firm's training needs for innovations, prototyping, design, testing, validation, verification and release processes. Staff training was needed to ensure better efficacy and accountability from the medical device firms. The changes also called for the recruitment of highly skilled specialized employees who could provide the companies with, regulatory affairs knowledge, skills and productivity that would propel profitability. This finding supports the observation by Lundvall (2000) that innovation is rooted in learning and learning is rooted in doing, using and interacting among users and producers.

Software product-focused regulatory change influenced production capability by firms' altering structures and processes

Malerba and Mani (2009) suggest that a central place in evolutionary theory is occupied by the processes of variety creation in technologies and products. In this study, we found that the regulatory change concerning software prompted most firms to alter their structures, processes and resources to adequately address regulatory threats and opportunities. In view of these findings, we argued in Chapter nine that the software product-focused regulatory change had a huge influence on firms' design structures and processes while the audit process-focused regulatory change induced a significant influence on firms' linkage capabilities and interdependencies.

Software product-focused regulatory change influenced production capabilities by creating entry barriers that locked out small firms due to high costs of compliance.

Our results indicated that one of the biggest weaknesses of product regulation governing medical device software is that approval is very costly. For example, clinical tests are very expensive to conduct. The expected return on a device limits the amount of testing that a firm is willing to perform. Clinical trials increase fixed costs and may make it unfeasible to develop devices for small markets. Analysis has revealed that this has created entry barriers that lock out small companies that cannot afford to go through the approval process.

10.3.2 The effects of the second regulatory change: introduction of unannounced audit visits in the UK

Our analysis of the effects of audits, a process-focused regulatory change, had three key findings:

Move towards collaborative relationship between manufacturers and suppliers

As discussed in chapter nine, the audits process-focused regulatory change enabled the formation of efficient supply chain management, which is critical to the competitiveness of firms. Importantly, firms that extensively utilized external providers after regulatory changes were found to be more successful in the development of affordable healthcare technologies. This finding resonates with earlier research on the importance of establishing relations between firms in the supply chain that enhances absorptive capacity, which leads to upgraded technological capabilities (Lall, 1980; Shandya et al., 2002). Wu (2008) argued that creating supply chain knowledge requires interlinked processes that enable information sharing as well as associated information technology infrastructures. In this study, we found that the regulatory changes enabled manufacturing firms to move from adversarial relationship towards collaborative relationship with their suppliers. This collaborative relationship between the manufacturer and the supplier became one where both parties communicated more regularly, cooperatively shared relevant regulatory information and resolved conflicts through dialogue. Such relationships led to operational efficiencies that allowed processes to be streamlined and simplified, higher levels of performance and economic benefits over the long-term.

Audits process-regulation affected firm's linkage by prompting the actors to alter supplier agreements

Second, as argued by Jaspers et al., (2012) regulatory demands can change conditions for firm collaboration due to new challenges in the interface between actors. As discussed in Chapter nine, we found that the second regulatory change on audits had an enormous constraining effect on supplier agreements between actors throughout the whole supply chain as the level of scrutiny increased. Many suppliers were not medical device focused and the new inspection requirements operated as a market shock and had difficulties complying.

Regulatory change created turbulence in the sector

Third, we found that the indiscriminate regulatory change was perceived by most SMEs leaders as constraining because it introduced considerable turbulence to the sector, with long-term consequences. The changes came into force three months after the EU recommendation without going through the normal three-year transition period.

10.3.3 The effects of the third regulatory change: Radiation Emitting Devices (REDs) in South Africa

Our analysis in chapter 8 found that since radiation emitting devices such as X-ray, CT, and MRI are on high end of technology and the fall under product category that is heavily regulated, very few SMEs were willing to or had the capability to invest in such products. The domestic firms were expected to have a capability to import, manufacture or fully refurbish any listed electro-medical device on a global basis, to comply with the radiation emitting device regulatory requirements, the respondents argued that it was a tall challenge for most of the firms. Such stringent requirements made it more difficult for domestic suppliers in SA to enter the supply chain.

REDs product-focused regulatory change influenced linkage capabilities by enabling overseas collaborations

As discussed in Chapter nine, we found that the REDs product-focused regulatory change enabled the creation of joint ventures and strategic partnerships which, fostered technology transfer. The stringent requirements made it more difficult for

domestic suppliers to enter the supply chain. In order to overcome these problems, some local manufacturers established joint ventures as a strategic partnership with foreign companies whose technological capabilities and resources were strong. The foreign companies involved in these partnerships were mainly MNCs.

Summary

As shown in Table 10.1, we found that the influence of regulatory change affects the entire cycle of innovation, which includes resource allocation for the innovation process, the innovation process itself, production, firm linkages and the sales/use of final products. A summary of the key findings applicable to all three regulatory changes is presented in Table 10.1 below.

Table 10.1: Summary of Key findings

	Regulation 1-Software UK	**Regulation 2-Audits UK**	**Regulation 3-REDs SA**
Investment Capability	1. Firms with limited experience of the medical device review process had difficulties adapting, and innovation activities from these firms were impeded after regulatory changes.		
	2. Increased investment in R&D		Little impact on R&D as the environment is an importer's market
	3. Firms acquired experts and skilled personnel as vital sources of knowledge and learning to fill their inherited knowledge gap in order to address the new regulatory requirements.		
	4. Introduction of IEC 62304 software standard enhanced and extended the medical device market		Procurement of ISO 13485 in order to get CE certification proved very costly for most of the firms
Production Capability	5. Regulatory change facilitated firms to create new strategies and innovation processes required to achieve efficient and effective operations within the parameters of the new requirements		
	6. The regulatory change diverted innovation direction from radical to incremental innovation considering the technical difficulties firms needed to confront		Enabled modifying or refurbishments of imported technologies to suit local conditions.
	7. Regulatory changes coerced compliance cost and in turn resulted in firms needing to divert resource outflows to meet regulatory requirements.		
	8. Regulatory changes ensured product quality and safety of products entering the market, CE-mark increased positive reputation of the firms and helped in gaining customer confidence.		

Linkage Capability	9. Regulatory changes enabled firms to develop close collaborative relationships with external providers in search of competitive advantage and improved market positioning.		
	10.	Audits process-regulation affected firm's linkage by prompting the actors to alter supplier agreements	Regulatory changes induced firms to create joint ventures, strategic partnerships.

Compiled by author

In general, the three regulatory case study analysis of firms' investment, production and linkage capabilities shows that the process of complying with the regulatory changes in the UK and SA has become more arduous as the requirements have become stricter. That is especially true for SMEs for whom the long and resource-heavy process of bringing a medical device to the market is associated with high risk. However, the regulatory changes enabled new software markets and new linkages between actors to take off, and as such they prompted the emergence of new modes of organizing firm capabilities in the medical device sectoral system of innovation. Therefore, governments and regulators can influence the development of market infrastructure and affect the role of technology, thereby influencing firms' implementation decisions (Jacobides, 2005).

10.4 Answers to the Overall Research Question

The overall research question that guided this study is:

How and to what extent has the evolution of medical device regulations in the UK and SA influenced industrial capabilities and contribution towards affordable health care technology development?

The thesis assessed the influence of changes to regulatory environments on firms' technological capability. The use of SSI as theoretical framework allows the framing of both market and non-market relations in the technological development of products and services, particularly for the "creation, production and sale of products" (Malerba, 2002, p.248). By using Chataway et al., (2006)'s policy and regulatory instrument empirically, in detail, we were able to show the often-contradictory influences of regulatory change and need for extreme care as regulation is formulated.

Our results suggest that the influence of regulation may also be enabling or facilitative. In this study, the analysis showed that enabling and discriminating regulatory changes matter immensely and that constraining and indiscriminate regulation can be very damaging, particularly to SMEs and firms in developing countries.

We summarize below some key findings in answer to our main research question.

Firms with limited experience of the medical device review process had difficulties adapting, and innovation activities from these firms were impeded after regulatory changes.

As discussed in section 9.2, we found that when regulations were changed, firms, in particular SMEs, with limited experience of the medical device review process had difficulties adapting, and innovation activities from these firms were impeded. SMEs with limited regulatory review experience typically try to receive market approval for their products as soon as they feel that their product is ready. Such firms are under pressure to get products onto the market as they have undertaken significant investments and the development process of the product is usually long and burdensome. Of course, this is equally the case for large firms. However, we found that limited-experience firms can afford to hesitate less to see how a regulatory change might affect their approval application relative to other firms. Such firms generally have limited knowledge of Notified Bodies, particularly about the application process for market approval. The findings show that firms (MNCs), which have gained experience with the regulatory process, were able to benefit from this experience in turbulent periods of regulatory change, whereas firms with limited experience were adversely affected by regulatory shocks to the industry. This was uniformly applicable to all three regulatory changes.

Regulatory changes enabled firms to acquire experts and skilled personnel as vital sources of knowledge and learning

As discussed in section 9.2, we found that, all the three regulatory changes required greater skill, technical knowledge and experience in regulatory review processes that may not previously have been possessed by firms. Thus, the changes prompted firms

to acquire experts and skilled personnel and increase their in-house training as vital sources of knowledge and learning to fill their inherited knowledge gap in order to address the new regulatory requirements and the demand for innovative products, processes, and further organization-wide change.

Regulatory change facilitated firms to create new strategies and innovation processes

This research shows that the regulatory changes largely had a positive impact on large medical device manufacturing firms' key innovation processes required to achieve efficient and effective operations. Chapter seven emphasized that the first regulatory change introduced new set of processes such as validation & verification procedures, provided new harmonized standards and new functionalities, which influenced the development process of products. Mandatory processes influenced by regulatory change requiring unannounced audits include; design control, establishment of material, purchasing and control of incoming material and components, assembling, packaging, and product quality control. In SA the regulatory change influenced adaptations and improvement processes such as electro-medical devices refurbishment and QMS safety and performance process. The firms responded to regulatory changes by adopting a path of building technological capabilities. In short, firms conformed to the argument by Dierickx and Cool (1989) that their survival and success depended on their ability to create a set of distinctive capabilities that enable them to stand out in the competition.

Regulatory changes ensured product quality and safety of products entering the market

We found that regulatory changes improved firms' quality control systems and ensured the safety of products entering the market. The findings showed that the changes brought positive reputation to the firms and the improved product quality helped in gaining customer confidence. Most firms had a general belief that the regulatory change and the rest of the applicable standards had met expectations in enhancing the safety of medical devices.

The cascading effects of high compliance cost negatively affect the development of affordability healthcare technologies

As discussed in Chapter seven and eight, the study found that all firm respondents argued that compliance costs were significant. Compliance with the regulatory change targeting software was viewed as a costly venture. As for the compliance costs associated with unannounced audits, we found that the cost had to be met by the manufacturer, including the audits performed on the premises of its critical subcontractors/crucial suppliers. The large costs and delays associated with placing medical devices on the SA market, were found to be inducing some SMEs to withdraw from the market or ending up focusing on low end, low risk technologies that are not heavily regulated. The cascading effect of high compliance cost significantly affected affordability of healthcare technologies.

Regulatory changes enabled firms to develop close collaborations

The three regulatory changes influenced linkage capabilities by enabling collaborative relationships. Most firms increased their focus on the development of close collaborative relationships with their suppliers in search of competitive advantage and improved market positioning. Firms that extensively utilized external providers after regulatory changes in both countries were found to be more successful in the development of affordable healthcare technologies. Most small firms with higher in-house technological capabilities initiated innovative activities in collaboration with local or global subcontractors or research institutions to respond to regulatory changes. This led to production capability enhancement, such as time to market, as discussed in Chapter nine, through collaborative learning and very intense communication mechanisms. Over a period, many SMEs' production capability was enhanced by these experiences and accumulation of knowledge.

In summary, the influence of regulatory changes on firm level capabilities crosses over the entire cycle of innovation. Regulatory change adds cost to firms and causes an often-unwelcome diversion of technical and management resources away from business innovation. Regulatory approval may postpone the time a product can enter the market and negatively influence the expected rate of return. But regulatory change can also create opportunities for firms to improve the development process of affordable healthcare technology and stimulate creativity. Regulation may change the

expected profitability by providing a guarantee of product quality. Table 10.2 summaries the key findings that were uniformly applicable to three regulatory change case studies.

Table 10.2: Summary of key findings uniformly applicable to all three regulatory changes.

	Regulation 1-Software	Regulation 2-Audits	Regulation 3-REDs
Investment Capability	1. Firms with limited experience of the medical device review process had difficulties adapting, and innovation activities from these firms were impeded after regulatory changes.		
	2. Firms acquired experts and skilled personnel as vital sources of knowledge and learning to fill their inherited knowledge gap in order to address the new regulatory requirements.		
Production Capability	3. Regulatory change facilitated firms to create new strategies and innovation processes required to achieve efficient and effective operations within the parameters of the new requirements		
	4. The constraining effect of the three regulatory changes on innovation capability was that firms became more risk adverse toward novelty and in turn became incremental innovators instead of radical innovators.		
	5. Coerced compliance cost and in turn resulted in firms needing to divert resource outflows to meet regulatory requirements. Due to the cascading effect of high compliance cost, affordability of healthcare technologies was significantly affected.		
	6. Regulatory changes ensured product quality and safety of products entering the market, CE-mark increased positive reputation of the firms and helped in gaining customer confidence.		
Linkage Capability	7. Regulatory changes enabled firms to develop close collaborative relationships with external providers in search of competitive advantage and improved market positioning.		

Compiled by author

This study adopted critical realism as the philosophical position. The fundamental assumption of the realist position is that there is a reality "out there" waiting to be discovered and that reality is independent of us" (Easton, 1995, p.372). In this study, the "discoverable reality out there" is maintained and reproduced by established firms, guided by shared beliefs. Thus, from a philosophical perspective, the effects of regulatory changes on firm technological capabilities explored in this research are real. The "discoverable reality out there" was that the lengthy and demanding nature of the three regulatory changes have induced changes in firms' strategies, processes,

market environment, entry of new firms and creation of new collaborative relationships among firms and between firms and non-firm agents. These, to a certain degree, systematically transformed the medical devices sectoral systems of innovation and production of the UK and SA to be stronger and less fragmented. However, the study found that the lack of comprehensive regulatory framework in SA upsurge the likelihood of having substandard and spurious healthcare technologies that pose serious public health problems in the market.

10.5 Policy Implications and lessons

This study has shown five important factors that must be considered carefully in any discussion on policy within and also outside the UK and SA. These are discussed in points a-e below:

a) The study shows that regulatory change impacts on firm's investment and innovation capabilities. Product makers need to be aware of that, to include in their internal management policies, the opportunity cost of foregone innovation and dynamic efficiency into their benefit-cost evaluation of regulation and regulatory change. In the case of medical technologies, foregone innovations can hinder opportunities coming to fruition.

b) Our results have important implications for policymakers. When policymakers introduce strict regulation, they often think about health and security of final users. However, they should also need to consider the "side-effects" for the economy. A more stringent regulation might discourage innovative firms from introducing new health care technologies. Regulators should listen to the opinions of small companies and medical device experts in order to introduce norms that guarantee patient safety, but at the same time, meet the needs of the sectorial operators

c) To anticipate the effects of regulatory change is not an easy task. However, building awareness that regulatory change will have consequences, some unintended, is a step in the right direction. This study reminds decision makers in medical device regulation that the safety and efficacy of medical devices depends on smart regulatory governance, which requires policy measures for the effectiveness and efficiency of governance.

d) This study has implications for positive social change from regulatory compliance. This study showed that the changes in the software medical device

regulation had a positive impact on the safety and reliability of software embedded medical devices. Members of the Council on medical devices of the European Commission believed that consistent and coherent implementation of the MDD 2007/47/EC was necessary to ensure the protection of human health (European Council, 2007). As a result, the medical device manufacturers have fortified their internal management policies to synchronize with industry innovations classes and times. Thus, the MDD 2007/47/EC regulation has realigned the social technological links and methodology for medical device manufacturers.

e) This study reinforces conclusions that there is no one optimal policy in medical device regulation. A choice for one policy always excludes other alternatives and possible choices and prevents experience with other paths. It can therefore never be absolutely known which policy might offer "optimal'' solutions to a given policy dilemma.

10.5.1 Recommendations

This thesis provides following recommendations based on a limited number of case studies:

1). The SA medical device market is currently one of the most promising and fastest growing markets in Africa with market drivers such as the aging population and number of hospital visits expanding demand. SA's high-end medical device market is dominated by foreign companies, based on this market profile, the government and policy makers should pay more attention to scientific and technological innovation, give financial and policy support to companies' innovation, encourage the SA companies' R&D on medical devices. Moreover, SA firms should deepen the transnational cooperation with international companies; increase the training and the introduction of human talent.

2). The policy makers might give more attention to the development of an enabling regulation and policy framework. Enabling regulation can serve both as the legislative mandate for the competent authorities to act, and as a starting point for regulator discretion and oversight. The building of an enabling context for regulatory systems could be helped with a well-defined and focused set of objectives, perhaps focused first on the life science sectors.

10.6. Limitations of the Study

Even though the results of this study provided a robust methodological contribution and considerable empirical evidence to support our argument as pointed out in section 10.7, limitations stemming from the nature of the topic being investigated are acknowledged.

First, there is likelihood that some firms, which flout medical devices health and safety regulations, will be reluctant to truthfully answer questions. Although participants were assured that their responses would be treated confidentially and, that results of the research will not have any adverse implications on the operations of their businesses, it is difficult to assess the extent to which this allayed their fears. We addressed this problem by interviewing in a large number of firms, in three case studies and by triangulating results as described in our empirical chapters.

Second, due to obvious limitations of time, cost and relevance of context, focus was given to the regulatory changes on software, audits and radiation emitting devices subdivisions rather than the entire medical devices category within the industry. Other subdivisions might present different outcomes of regulatory changes. Thus, other scholars could conduct the similar research on other regulatory changes and compare the results to provide a broader understanding of the effects of regulatory changes in medical markets.

Third, collecting data in emerging markets, such as SA, posed challenges, as there was limited published literature on medical device regulatory changes. Moreover, the new draft proposals of medical device reforms, in both case study countries were still under debates during writing of this thesis. Therefore, some information in the papers may not be entirely reflective of the changes ultimately adopted. Nevertheless, the documents studied in literature review were published at a time when relevant developments were still unfolding, and therefore served to inform current debates in these areas.

10.7 Contributions of the Study

This thesis makes six contributions to the literature on the effects of regulatory changes on industrial technology, but particularly with respect to the medical device

software and unannounced audit regulations in the UK and radiation safety regulation in SA.

First, the thesis argues, with empirical evidence, that a more enabling and discriminating regulation that takes into consideration of firms' technological capabilities can achieve intended goals more efficiently and effectively, than a constraining and indiscriminate regulation. In this regard, this study makes important contributions to health technology regulatory science literature by answering calls for deep empirical research to examine the influence of regulation on the ability of industries to innovate (Altenstetter, 2012, Blind, 2012) and calls for more research to assess new regulatory developments and evolutions in practice (Sorenson and Drummond, 2014).

Second, the context of two very different countries has allowed investigation of in-depth regulatory changes devised and implemented in diverse socio-economic, industrial and infrastructural context. Previous studies on health technology regulation in low and middle-income countries emphasized the need to investigate health technology developments, relevant policy and regulatory systems especially in Africa to encourage a more coherent regulatory approach (Rugera et al., 2014, Saidi, 2016). In line with these studies, this research was not confined to the UK, but also included SA, a country from the global south. Such a perspective is less often included in comparative studies but offers valuable insights to the healthcare technologies (Rugera et al., 2014). The present research studied the institutions that affect actors in the medical device industry and also allowed investigation of what happens to technological capabilities when these institutions were radically changed or greatly stressed. Regarding this point, the research results point to the importance of a clear, enabling regulatory framework, coordinated science and technology policy, political stability and the gaps that policy must consider when radical change takes place.

Third, the selected regulatory changes have not previously been analyzed at this depth. Two regulatory changes have involved the collection and analysis of a rich and unique EU dataset, which offers potential for further insights into the industrial dynamics of the medical device industry, and particularly its high-risk sector.

Fourth, as methodological and empirical contribution, a regulation and policy matrix was applied (see Chapter nine) that provides a unique way of integrating diverse policies and regulations according to whether they are perceived as enabling or constraining by industry leaders and whether regulations and policies are indiscriminate or discriminating among products; or in some cases whether they discriminate on an inappropriate basis (Chataway et al., 2006). The matrix allows individuals or organizations to focus on the effectiveness and efficiency of the governance achieved by a particular policy or regulation, taking into consideration the resources and capabilities available to innovators.

Fifth, our analysis highlights the importance of compliance capabilities in firms to underlie health technology innovation process success. The study has shown that compliance capability is a crucial element that ensures medical device safety for patients, enables firms to get medical device approval from regulatory bodies and smooths medical device audits.

Sixth, the study has also contributed theoretical and methodological insights and empirical evidence to the debates on streamlined regulatory bureaucracy, safety and efficacy and the benefits of harmonized standards. Finally, to the best of my knowledge this research is the first study that makes a rigorous assessment of the innovation dynamic changes in SA radiation medical device sector, and particularly considers regulation as a defining element of these dynamics

10.8 Boundaries and generalization

The empirical material in this thesis has been collected using a multiple case study methodology. Case study methodology has been criticized as non- or weakly-generalizable. However, this thesis has used the case study methodological approach of Eisenhardt who developed comparative case study method, and Yin with his highly systematic multi-method approach to intensive investigation (chapter 5). They argue that such methods are able to build generalizable findings.

The focus of the thesis, the evolution of medical device regulation and its impact on firm-level industrial capabilities, also lends itself to case study methodology because there has been relatively little systematic research on this relationship. The use of three case studies has allowed the thesis to begin casting light on the causative

relationship between enabling or constraining regulation and the drivers/blockers of capability enhancement and particularly of innovative capabilities.

In this thesis, the use of a multiple case study approach together with the regulation and policy matrix of enabling or constraining regulation, has allowed some generalizable characteristics to be shown concerning the medical devices industry, particularly on the strongly constraining nature of some indiscriminate regulatory systems. It would be informative to further test and substantiate the methodological framework by employing it in other policy areas. For example, the matrix could be applied in full to other health care regulators (e.g. food, health care professionals), in addition to non-health regulators, and across different jurisdictions. The use of this regulation and policy matrix would, this thesis argues, lend greater understanding of what constitutes good regulation and the influence (if any) of different policy.

10.9 Future Research

Future research might be directed towards a longitudinal analysis of the governance structures of firms, which could yield further insights into the resource allocations involved in the health technologies innovation experience. Thus a longitudinal study might be undertaken using a five to ten year framework to track firms in different regions as they undertake their healthcare technology innovation activities.

Such studies would allow better understanding of the political and social considerations involved in evidence-based regulation or policy making. Such research would enable more effective analysis of decision making around health technologies, with respect to the interplay between evidence, political and institutional dynamics, stakeholder values and interests, balancing technical, social, and political priorities.

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List of Appendices

APPENDIX 1: Study Questionnaire Number 1 – United Kingdom

SECTION 1: Background information

Objective 1: The information collected in this section will not be used in any manner to identify you. The objective of collecting this information is to be able to find any patterns in demography that may have an influence on management practices.

1. Respondent details

1.1 Name (optional)……..

1.2 Organisation……..

1.3 Year of Establishment……..

1.4 Position in organisation……

1.5 Number of years with current employer……..

1.6 Number of years in the medical device sector……

1.7 What are your primary responsibilities?

- Policy making ☐
- Policy analysis ☐
- Policy implementation ☐
- Management ☐
- Other, please specify ☐ ……

1.8	**Stakeholder category:**	**Analysis code**	
	Government/Competent authority	Gov	☐
	Research and Development	RD	☐
	Academic and research institution	ARI	☐
	Health facility	HF	☐
	Medical device manufacturing	MAN	☐
	Regulatory agency/Notified body	RA/NB	☐
	Industry association	IA	☐
	Other, please specify	ORES	☐ ……

1.9 **Main products of your organisation/firm?**

(a)……

(b)……..

(c)……

1.10 **What medical device type do you manufacture?**

- Low-risk devices (Class I) ☐
- Medium-risk devices (Class IIa) ☐
- Medium-risk devices (Class IIb) ☐

High-risk devices (Class III) ☐

Other, please specify ☐ ……

SECTION 2: Understandings on regulation and regulatory changes
Objective 2: To assess the market structure, CONTENT and DRIVERS of regulatory changes.

2. How is the medical device industry structured in the United Kingdom?

3. Who are the key players involved in the medical device industry in the UK? and what role do they play?

4. Evidence/Literature suggests that the UK regulatory framework has often been viewed as superior to many countries, given its somewhat faster regulatory process for devices and earlier access to some high-risk technologies. What could be the reasons for this situation?

5. How are medical devices regulated, and what is the role of the government in the regulatory processes in UK?

6. What is your understanding of regulatory changes in the context of the Medical device sector?

7. In the last 30 years, different regulations in the medical device sector have been enacted/implemented. What are the key 2 or 3 regulatory changes that have affected your organisation's operations? And How?

8. Reflecting on your company's experience, which medical device software regulatory compliance were you required to follow before 2007?

9. What are the new regulatory requirements that control medical device software as of 2007? Could you compare quality of regulatory content in the past and the present?

10. Other than the domestic or EU regulations, are there any other international regulatory standards you required to comply with? If yes how do you comply? E.g.

    (1) ISO 13485 (Medical Devices-Quality Management Systems-Requirements for Regulatory Purposes). ☐
    (2) ISO-9001 (Quality systems-model for quality assurance in design, development, production, installation and servicing). ☐
    (3) Other, please specify ☐ ……

11. In UK's medical device's regulatory history, what events or circumstances could have led to changes in medical device regulations?

SECTION 3: Understandings of the impact of regulatory changes
Objective 3: To assess the EFFECTS of medical device regulation and regulatory changes on industry capabilities and development of medical devices.

12. How has the past regulatory changes affected your firm's Investment capability in terms of:
    - Research and Development (R&D) of new technology?
    - Recruitment and training of skilled personnel?
    - Equipment acquirement?
    - Standard procurement?

12. How has the past regulatory changes affected your firm's Production capability in terms of:
    - Innovation?
    - Quality control?
    - Operations?
    - New product technology licensing?
    - Compliance?
    - Monitoring (pre and post market)?
    - Maintenance?

13. How has the past regulatory changes affected your firm's Linkage capability in terms of:
    - Local acquirement of goods and services?
    - Exchange of information with suppliers?
    - Exchange of information with regulatory bodies?
    - Exchange of information with industry associations?
    - Importing from and exporting to other countries?

14. What steps are involved in the process of obtaining the CE mark?

15. How long on average does the approval process for medical devices take?

16. How have regulations or regulatory costs affected affordability and appropriate healthcare technologies in the UK?

17. Lastly, What can be done to ensure effective medical device regulations and at the same time affordable and appropriate healthcare technology in the UK.

APPENDIX 2: Study Questionnaire Number 2 – South Africa

SECTION 1: Background information

Objective 1: The information collected in this section will not be used in any manner to identify you. The objective of collecting this information is to be able to find any patterns in demography that may have an influence on management practices.

1. Respondent details

1.1 Name (optional)…….

1.2 Organisation……..

1.3 Year of Establishment……..

1.4 Position in organisation……

1.5 Number of years with current employer……..

1.6 Number of years in the medical device sector…….

1.7 What are your primary responsibilities?

- ☐ Policy making
- ☐ Policy analysis
- ☐ Policy implementation
- ☐ Management
- ☐ Other, please specify ……

1.8

Stakeholder category:	**Analysis code**	
Government/Competent authority	Gov	☐
Research and Development	RD	☐
Academic and research institution	ARI	☐
Health facility	HF	☐
Medical device manufacturing	MAN	☐
Regulatory agency/Notified body	RA/NB	☐
Industry association	IA	☐
Other, please specify	ORES	☐ ……

1.9 **Main products of your organisation/firm?**

(a)……

(b)……

(c) ……

1.10 **What medical device type do you manufacture?**

- ☐ Low-risk devices (Class I)
- ☐ Medium-risk devices (Class IIa)
- ☐ Medium-risk devices (Class IIb)
- ☐ High-risk devices (Class III)

Other, please specify ☐ ……

SECTION 2: Understandings on regulation and regulatory changes
Objective 2: To assess the market structure, CONTENT and DRIVERS of regulatory changes.

2. How is the medical device industry structured in South Africa?

3. Who are the key players involved in the medical device industry in SA? and what role do they play?

4. Evidence/Literature suggests that 90% of medical devices are imported and 10% are locally manufactured. What could be the reasons for this situation?

5. How are medical devices regulated, and what is the role of the government in the regulatory processes in SA?

6. Currently, only electromagnetic medical devices or radiation emitting devices are regulated through the Hazardous Substances Act, No. 15 of 1973 while the rest of the devices are not regulated. What could be the reason for this and how does this affect the whole process of medical device regulation in SA?

7. In the last 30 years, different regulations in the medical device sector have been enacted/implemented. What are the key 2 or 3 regulatory changes that have affected your organisation's operations? And How?

8. Other than the domestic regulations, are there any other international regulatory standards you required to comply with? If yes how do you comply?

9. In South Africa's medical device's regulatory history, what events or circumstances could have led to changes in medical device regulations?

SECTION 3: Understandings of the impact of regulatory changes
Objective 3: To assess the EFFECTS of medical device regulation and regulatory changes on industry capabilities and development of medical devices.
10. How has the past regulatory changes affected your firm's Investment capability in terms of:

- Research and Development (R&D) of new technology?
- Recruitment and training of skilled personnel?
- Equipment acquirement?
- Standard procurement?

11. How has the past regulatory changes affected your firm's Production capability in terms of:

- Innovation?
- Quality control?
- Operations?
- New product technology licensing?
- Compliance?
- Monitoring (pre and post market)?

- Maintenance?

12. How has the past regulatory changes affected your firm's Linkage capability in terms of:

- Local acquirement of goods and services?
- Exchange of information with suppliers?
- Exchange of information with regulatory bodies?
- Exchange of information with industry associations?
- Importing from and exporting to other countries?

13. What steps are involved in the process of obtaining the SABS, CE mark and the FDA approval?

14. How long on average does the approval process for medical devices take?

15. How has regulations affected affordability and appropriate healthcare technologies in SA?

16. Lastly, What can be done to ensure effective medical device regulations and at the same time affordable and appropriate healthcare technology in SA

Thank you

APPENDIX 3: The Open University Research Ethics Approval Letter

Human Research Ethics Committee (HREC)

The Open University

From	Marc Cornock, Deputy Chair The Open University Human Research Ethics Committee
Email	marc.cornock@open.ac.uk
Extension	(6) 55807
To	Andrew Mkwashi
Project title	Evolution of Medical Device Regulations and its Impact on Industrial Capability and Affordable Healthcare Technologies: *A Case Study of South Africa and the United Kingdom*
HREC ref	HREC/2016/2281/Mkwashi
AMS ref	N/A

Memorandum

Date application submitted: 21/04/16
Date of HREC response: 06/06/16

This memorandum is to confirm that the research protocol for the above-named research project, as submitted to the OU HREC does not require a full HREC review. However, if there is a major change with the research, or you have a new research project which may require an ethics review, please contact Research-REC-Review@open.ac.uk

Please note the following:

1. You are responsible for notifying the HREC immediately of any information received by you, or of which you become aware which would cast doubt on, or alter, any information contained in the original application, or a later amendment which would raise questions about the safety and/or continued conduct of the research.

2. It is essential that any proposed amendments to the research are sent to the HREC for review, so they can be recorded and a favourable opinion given prior to any changes being implemented (except only in cases of emergency when the welfare of the participant or researcher is or may be affected).

3. You are authorised to present this memorandum to outside bodies such as NHS Research Ethics Committees in support of any application for future research clearance. Also, where there is an external ethics review, a copy of the application and outcome should be sent to the HREC.

4. OU research ethics review procedures are fully compliant with the majority of grant awarding bodies and where they exist, their frameworks for research ethics.

Best regards,

Dr Marc Cornock, Deputy Chair

The Open University Human Research Ethics Committee

http://www.open.ac.uk/research/ethics/

APPENDIX 4: Participation Consent Form

PARTICIPATION CONSENT FORM

The Open University

Project Title:	Medical Device Regulations, Industrial Capabilities and Affordable Healthcare Technology Development: *Case Studies from the United Kingd and South Africa*
Researcher:	Andrew Mkwashi
Institution:	Development Policy & Practice, Faculty of Arts and Social Sciences, The Open University, Walton Hall, Milton Keynes, MK7 6AA (UK)
Contact Details:	Tel: +44 (0) 1908 655706 or +44 (0) 7773359364 Email: andrew.mkwashi@open.ac.uk

Name of participant: _____

1. I consent to participate in this project, the details of which have been explained to me, and I have been provided with a written statement in plain language to keep.

2. I understand that my participation will involve an interview and I agree that the researcher may use the results as described in the plain language statement.

3. I acknowledge that:

   a) The possible effects of participating in this research have been explained to my satisfaction;

   b) I have been informed that I am free to withdraw from the project without explanation or prejudice and to request the destruction of any data that have been gathered from me until it is anonymized at the point of transcription point on (31/05/2017), After this point data will have been processed and it will not be possible to withdraw any unprocessed data I have provided;

   c) The project is for the purpose of research;

   d) I have been informed that the confidentiality of the information I provide will be safeguarded subject to any legal requirements;

   e) I have been informed that with my consent the data generated will be stored at The Open University and will be destroyed after five years;

   f) If necessary any data from me will be referred to by a pseudonym in any publications arising from the research;

   g) I have been informed that a summary copy of the research findings will be forwarded to me, should I request this.

I consent to this **interview** being audio-taped □ **yes** □ **no** (Please tick)

I wish to receive a copy of the summary project report on research findings □ **yes** □ **no** (Please tick)

Participant signature: _____ Date: _____

APPENDIX 5: List of Interviews Conducted in SA

Interview Schedule SA

Respondent Code	Company Position	Stakeholder Category	Date	Place of interview
01	Director	Manufacturer.	6 Oct 2016	Johannesburg, SA
02	Chairperson	Industry association/ Manufacturer	6 Oct 2016	Johannesburg, SA
03	Managing Director	Industry association/ Manufacturer	7 Oct 2016	Pretoria, SA
04	Senior Manager	Manufacturer	10 Oct 2016	Midrand, SA
05	Executive Officer	Industry association	13 Oct 2016	Johannesburg, SA
06	Production & Quality Manager	Industry association/ Manufacturer	14 Oct 2016	Cape Town, SA
07	National Medical Physics Manager	Health facility	17 Oct 2016	Cape Town, SA
08	Chief Executive Officer	Manufacturer	17 Oct 2016	Cape Town, SA
09	Chief Executive Officer	Manufacturer	19 Oct 2016	Pretoria, SA
1o	Programme Director	Academic and research institution	20 Oct 2016	Johannesburg, SA
11	Regional Service Manager	Manufacturer	21 Oct 2016	Johannesburg, SA
12	Senior Quality & Regulatory Systems Manager	Manufacturer	25 Oct 2016	Johannesburg, SA
13	Projects Manager	Manufacturer	25 Oct 2016	Johannesburg, SA
14	Strategic & Key account Manager	Manufacturer	27 Oct 2016	Midrand, SA
15	Regulatory Affairs and Quality Officer	Manufacturer	2 Nov 2016	Centurion, SA
16	Head: Technology Innovation Programmes at Technology Innovation Agency	GOV- Department of Science and Technology (DST)	3 Nov 2016	Pretoria, SA
17	Senior Programme Officer -AU/**NEPAD** Agency.	Academic and research institution	3 Nov 2016	Midrand, SA
18	The Executive Director: Biosciences. **CSIR**	Academic and research institution	11 Nov 2016	Pretoria, SA
19	HOD: Medical Imaging and Radiation Sciences Department (MIRS) - UJ	Academic and research institution	14 Nov 2016	Johannesburg, SA
20	Director	Manufacturer	15 Nov 2016	Johannesburg, SA
21	Registrar of Medicines - MCC	Regulator	17 Nov 2016	Pretoria, SA
22	Deputy Director - Radiation Control	Regulator	17 Nov 2016	Pretoria, SA
23	The Group Executive - CSIR	Academic and research institution	18 Nov 2016	Pretoria, SA
24	SAMED/SALDA	Focus Group	22 Nov 2016	Pretoria, SA
25	National Sales manager	Manufacturer	22 Nov 2016	Pretoria, SA
26	The Projects Manager - SANAS	Regulator	25 Nov 2016	Pretoria, SA
27	Reimbursement and Regulatory Affairs Manager	Manufacturer	28 Nov 2016	Pretoria, SA
28	CEO	Manufacturer	28 Nov 2016	Midrand, SA
29	Engineer - CSIR	Academic and research institution.	1 Dec 2016	Pretoria, SA
30	Director	Department of Trade	2 Dec 2016	Pretoria, SA

APPENDIX 5: List of Interviews Conducted in SA

Interview Schedule SA

Respondent Code	Company Position	Stakeholder Category	Date	Place of interview
31	Vice President for sale	Manufacturer	17 Feb 2017	Durban - Skype call
32	Health Economics & Government Affairs Manger	Manufacturer	17 Feb 2017	Johannesburg, SA
33	NEPAD SANBio Annual event	Facilitated a session on Regulation in the diagnostic sector	21-22 Feb 2017	Johannesburg, SA
34	Regulatory Affairs Specialist/QA Manager	Manufacturer	23 Feb 2017	Durban - Skype call
35	Managing Director	Manufacturer	24 Feb 2017	Johannesburg, SA
36	General Sales manager	Manufacturer	27 Feb 2017	Johannesburg, SA
37	Area Medical Director	Manufacturer	27 Mar 2017	
38	Research and development policy officer - Path	Academic and research institution.	28 Mar 2017	Johannesburg, SA
39	Managing Director	Manufacturer	28 Mar 2017	Roodepoort, SA
40	Consultant	Other	2 Mar 2017	Durban - Skype call
41	Regulatory Affairs Manager	Manufacturer	3 Mar 2017	Johannesburg, SA
42	Quality & Regulatory Affairs Officer at Strait Access Technologies	Manufacturer	6 Mar 2017	Cape Town, SA
43	Independent Medical Devices Professional	Manufacturer	7 Mar 2017	Cape Town, SA
44	Business Developer	Manufacturer	9 Mar 2017	Cape Town, SA
45	Business Unit Manager	Manufacturer	9 Mar 2017	Cape Town – Skype Call
46	Senior Medical Representative	Manufacturer	10 Mar 2017	Midrand, SA
47	Medical Science Liason	Manufacturer	11 Mar 2017	Roodepoort, SA
48	Sales Account Manager	Manufacturer	24 Mar 2017	Midrand, SA
49	Responsible Pharmacist and regulatory affairs	Manufacturer	27 Mar 2017	Midrand, SA
50	QA Manager	Manufacturer	28 Mar 2017	Durban - Skype Call
51	Clinical research associate	Manufacturer	28 Mar 2017	Pretoria, SA
52	Focus Group	Regulator – Medical Control Authority of Zimbabwe (MCAZ)	06 April 2017	Harare, Zimbabwe Skype meeting

APPENDIX 6: List of Interviews Conducted in the UK

Interview Schedule - UK

Respondent Code	Company Position	Stakeholder Category	Date	Place of interview
53	Quality manager	Manufacturer	28 Dec 2016	Hitchin, UK
54	Medical Devices Principal Consultant	Manufacturer	29 Dec 2016	Huntingdon, UK
55	Medtech Regulatory Affairs Editor	Manufacturer	12 Jan 2017	London, UK Skype call
56	Director of Regulatory Affairs	Manufacturer	16 Jan 2017	Nottingham, UK
57	Associate Director Regulatory Affairs	Manufacturer	19 Jan 2017	Open University
58	CEO	Manufacturer	23 Jan 2017	Daresbury, UK
59	Chief operations officer,	Manufacturer	26 Jan 2017	Chichester, UK
60	Technical Manager	Manufacturer	27 Jan 2017	London, UK
61	Director Quality Assurance	Manufacturer	30 Jan 2017	Stanford, UK
62	Director, Technical & Regulatory	Industry Association - ABHI	1 Feb 2017	London, UK
63	Technical Director	Manufacturer	2 Feb 2017	Uxbridge, UK
64	Managing Director	Manufacturer	3 Feb 2017	Braintree, UK
65	Independent Consultant	Manufacturer	6 Feb 2017	Telephone interview
66	Chairman	Manufacturer	7 Feb 2017	High Wycombe, UK
67	Medical Devices, EU Policy Manager	Competent Authority - MHRA	8 Feb 2017	London, UK
68	Head of Global Medical Device Services	Notified Body	9 Feb 2017	Lync Meeting
69	Medical Device Consultant	Manufacturer	10 Feb 2017	Skype call
70	Head of Operations and Training	Notified body - BSI	10 Feb 2017	Skype call
71	Certification Manager	UK notified body	22 Feb 2017	Skype call
72	Manager	Manufacturer	4 April 2017	London, UK
73	Director and Consultant	Manufacturer	21 April 2017	Chesham Bois, UK
74	Director Global Quality	Manufacturer	26 April 2017	Oxford, UK
75	Director	Manufacturer	6 May 2017	Cleveland, UK
76	Manager, Franchise Marketing, Advanced Surgical Devices,	Manufacturer	8 May 2017	Guildford, UK

APPENDIX 7: Letter of Affiliation

Southern Africa Network for Biosciences
CSIR Campus, Building 20
Meiring Naude Road
Brummeria
Pretoria, 0001
Echakauya@csir.co.za

13 September 2016

Dear Sir/Madam

Letter of Affiliation

This letter saves to confirm that we at NEPAD SANBio agree to host and provide local affiliation for Andrew Mkwashi (a PhD student in the UK Open University's Faculty of Arts & Social Sciences, Development Policy and Practice Department) during his proposed research visits to South Africa from 30 September 2016 to 7 December 2016 and from 15 February to 31 March 2017.

The purpose of the visits is to carry out interviews with medical device industry stakeholders. We are well positioned to offer guidance to Andrew as he carries out his research project entitled *'The evolution of medical device regulations and its impact on industrial capability and affordable healthcare technologies: A case study of the United Kingdom and South Africa'*.

The Southern Africa Network for Biosciences (SANBio) is a NEPAD Agency Flagship for collaborative research and development, and an innovation platform aimed to address Southern Africa's challenges in health and nutrition. The Network is comprised of 12 of the Southern Africa Development Community (SADC) Member States and operates on a Regional Hub (The CSIR in South Africa) and Country Nodes model. The current SANBio Member States are Angola, Botswana, Malawi, Mauritius, Mozambique, Namibia, Lesotho, South Africa, Seychelles, Swaziland, Zambia and Zimbabwe. SANBio responds to the 4 Pillars and 6 Priority Areas of the Science, Technology and Innovation Strategy for Africa (STISA-2024 - a 10-year strategy which is part of the long-term African Union Agenda 2063). The STISA envisages the accelerated transition of largely commodity-based African economies to innovation-led, knowledge-based economies. Such economies are underpinned by robust science, technology and innovation (STI) systems.

We also take this opportunity to recommend the project. We express our confidence that the proposed research is both valuable and feasible, and that the applicant is qualified and motivated to complete the project as planned. The project is especially timely and important because the UK and SA have recently introduced or are currently debating reforms of medical device regulation. It is thus an opportune time to examine the current regulatory policies and practices in both countries and identify areas for additional improvement.

APPENDIX 7: Letter of Affiliation

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The applicant's research is in line with our own research agenda, and available resources and we will be able to provide appropriate guidance. We are also willing to support the applicant by providing working space and the opportunity to participate in the intellectual life of our organisation.

We look forward to having Andrew affiliated with us as a visiting researcher and will do our best to make his stay productive and mutually beneficial. We will ensure that after completion of his visit he will return to the UK.

Regards

E Chakauya

Dr. E. Chakauya
SANBio Network Manager