AN ANALYSIS OF MEDICAL DEVICE REGISTRATION AND MARKET ACCESS IN CHINA

By

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Declaration:

"I hereby declare that this project is entirely my own work and that it has not been submitted for any other academic award, or part thereof, at this or any other education establishment".

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Abstract

The focus of this research is in the area of medical device registration and market access in China. Such a study is important as China is one of the largest markets for medical devices in the world making it an important strategic target market for medical devices manufacturers. There were four research questions to be addressed - 1) What is the current economic environment for medical devices in China? What are the projections for the future state? 2) What has changed in the medical device regulations in China, with the updated regulations enforced in 2014? 3) What is the impact and challenges to product registration and market access in China? 4) What can the regulatory function do to ensure they create a successful regulatory strategy for Class II and Class III device approval in China that will aid market access?

This dissertation met these multiple research questions through an extensive study of relevant literature and the implementation of practical research. The practical research was carried out through a three-pronged Case Study approach which included a sample product case review from one multinational company, a qualitative questionnaire with one multinational company's senior regulatory leaders and a qualitative/quantitative questionnaire with Regulatory and Quality professionals from numerous companies.

This research produced a number of key findings. The combination of the size of the Chinese market and the projected increased demand for medical devices has positioned China as a critical market for a medical device company to gain access. The survey confirmed the understanding of the importance in accessing the Chinese market. There are however challenges with the new regulations which were implemented as per CFDA's Order 650 issued in 2014. As per the literature review and practical research one key challenge to registration is echoed repeatedly, this is the requirement for local Clinical Trials. If a clinical trial is required it will bring increased timelines, cost and resourcing to access the market in China. Understanding the Requirements, Submission & Deficiency Process, Country of Origin, Approval Timelines, Clinical Evaluation, China Specific Standards and Change Control were all also identified as key challenges to product registration. All these factors accumulate in long

lead times for product approval and ultimate market access. As per the literature review and survey conducted Copying, Lack of Local Knowledge, Product Registration, Reimbursement and Change Control were all identified as challenges to market access.

The research recommended several strategies for the Regulatory function to employ to overcome the challenges outlined and to facilitate a medical device businesses success in China. One key recommendation is ‘Communication’, a recurrent theme across the practical research. This may be communication with your Chinese colleagues or your local agent to understand requirements. It may also be communication within your own company outlining lead times and the complexity of the approval process or the regulatory advantages to the business of setting up manufacturing within China. This will help with internal strategic planning and ensure that the business is aware of the burden required to access the market in China. The regulatory function should constantly review new guidance’s from CFDA to ensure the optimum regulatory strategy is outlined for any device. New processes offered by CFDA need to be utilized to a company’s advantage. It is recommended that a regulatory function create its own internal procedures for China. It is a complex pathway that needs to be formalized rather than relying on an individual’s experience with China. It is also recommended that your company looks for opportunities for advocacy in China. There are numerous challenges and Industry should use the appropriate mechanisms to influence CFDA.

1.0 Introduction

1.1 Background

China is an immense country with many opportunities for the medical device business. China's economic growth may be slowing down, but the medical device industry is still on the rise. The Chinese medical device industry was valued at US$18.8 billion in 2016 and is projected to grow modestly through 2019, when it should reach over US$24 billion (EMERGO 2017b). China is one of the BRIC countries; BRIC countries are made up of Brazil, Russia, India and China. The BRICs cover a quarter of the world's landmass and contain 40% of its population. These increasingly market-oriented economies boast a GDP of $30 trillion (or 20% of global GDP), a figure forecast to reach $120 trillion by 2050 (Watch 2015).

China's medical device market is ranked second largest in the world at this time. Driven by both an increase in discretionary income and a population that is aging faster than any other nation's population, the market has been growing at about 20 percent since 2009. By 2020, China will have 400 million people who are 60 years-old or older, and 100 million older than 80. By 2050, a third of the 1.4 billion Chinese will be at least 60 (MAINE 2015). The combination of the size of the China market and the projected increased demand for medical devices has positioned China as a critical market for a medical device company to gain access to. The faster a company can gain approval for their medical device product in China, the faster it can reap the awards of the revenue the China market will bring. However, companies interested in entering the Chinese market realize they must overcome existing barriers in an uncertain and changing regulatory environment. Whilst the regulatory pathway is well established for the other leading regions i.e. the EU and US, China is a region that brings uncertainty and less predictability.

The rise in income in China is also coupled with a rise in the incidence of cancer, heart, diabetes and other chronic diseases among China's population. According to a report by the World Health Organization (WHO), China accounted for over three million newly diagnosed cases of cancer, almost 22 percent of the global total, and 2.2 million cancer deaths, 27 percent of the world's total, in 2012. In addition to being hard hit by cancer, the WHO also estimates that approximately 230 million Chinese currently suffer from cardiovascular

disease, and that annual cardiovascular events will increase by 50 percent between 2010 and 2030 based on population aging and growth alone (WHO n.d.). The incidence of diabetes tells a similar story. Almost one-in-three global diabetes sufferers today are in China, with approximately 114 million adults afflicted by the disease.

In order to combat these growing health issues, many of China's 27,000 plus hospitals will need to be substantially upgraded or replaced in the coming years. In addition, the Chinese government is counting on foreign-owned hospitals, the ownership of which was previously highly restricted or forbidden, to fill some of the void. In August 2015, China announced a pilot project whereby overseas investors can establish wholly foreign-funded hospitals, either by acquisition or greenfield, in seven of its cities and provinces (MAINE 2015). This is one of many ongoing initiatives in China. China's first comprehensive five-year blueprint for the healthcare sector, the National Planning Guideline for the Healthcare Service System (2015–2020), sets out clear targets for 2020 including one clinic and one medical service centre for each community with a population of over 30,000 and 1.2 hospital beds for every 1,000 residents within the community (FULBRIGHT 2016).

This increased investment in hospitals, clinics and medical centres presents a massive opportunity for medical device companies to establish substantial contracts for their health care technology. Medical device firms are benefiting from the market dynamics that are encouraging hospitals to seek out and acquire new technologies (Daemmrich 2013). A critical piece to this is gaining regulatory approval to access the market in China for your company's medical device and maintaining compliance to keep the medical device on the market. The focus is on the regulatory affairs professional to create and execute a regulatory strategy that provides the business with the fastest time to market and predictability of that time to market. In the current environment, this is challenging to the Regulatory professional.

China's State Council released "Regulations for the Supervision and Administration of Medical Devices" which was enforced on the 1 June 2014. This was the first update to the regulations since January 2000 and sets out the new framework for how medical devices will be governed in China going forward. The new regulation contains some very clear changes from past legislation. There are various concerns within industry regarding the new regulation but one major concern is the requirement for domestic clinical trials of imported

medical devices. In addition, the regulation also clarifies and adds stiffer penalties for lack of conformance with medical device laws and regulations. In the past penalties were based on the manufacturers' profit, whereas the new regulation bases it on product value, making it easier for the government to enforce. The new regulation adds fines and blacklisting to manufacturers, testing centres and clinical trial sites so that for serious violations, such entities will lose their license and be unable to manufacture, test or conduct clinical trials for five years or 10 years (Michael Apler 2014).

Above describes just two of the concerns with the new regulations and the impact to the business. Companies dealing with medical devices in China need to familiarize themselves with the new regulations and determine how it affects their business and business strategy. The Regulatory professional is responsible for working to decipher the new regulations and communicating this back to the business to ensure projects are planned successfully. As the regulations are new this presents challenges to Regulatory professionals who are managing the pressure from the business to access and maintain their company's medical devices on the Chinese market. The combination of the value of the Chinese market to the business and the obstacles set out by the new Chinese regulations makes this dissertation a topical and current subject of high importance to the medical device business.

1.2 Overall Research Aim and Individual Research Objectives

The medical device market in China is one of the largest markets for medical devices in the world, making it an important strategic target market for medical devices manufacturers worldwide. All medical devices marketed or sold for use in China must be registered with China's Food and Drug Administration (CFDA). There have been many recent changes to the medical device regulations in China. This dissertation will address the following main questions:

- What is the current economic environment for medical devices in China? What are the projections for the future state?
- What has changed in the medical device regulations in China, with the updated regulations enforced in 2014?
- What is the impact and challenges to product registration and market access in China?

- What can the regulatory function do to ensure they create a successful regulatory strategy for Class II and Class III device approval in China that will aid market access?

1.3 Value of this Research

The Business cannot ignore the criticality of a company's success to gaining approval of its medical devices in China.

- Senior Leadership Strategic Planning – Time to market is critical for strategic planning where regulatory approval is a critical piece to this timeline
- Marketing – Regulatory approval timeline is important to marketing so they can plan there marketing strategy including preparing marketing materials, engagement with hospitals/physicians and ensuring tenders are in place to launch the medical device product successfully in China
- Operations - Regulatory approval timeline is important to ensure product launch quantities are available to meet the projected China market demands
- Supply Chain, R&D, Quality etc., all functions will have a vested interest in the success of gaining access to the China market
- Process Development Project Team – The team are accountable for developing to commercialising a pipeline medical device product. It is their responsibility to commercialise the latest technology product and are contacted to getting the product to the critical regions within a certain timeline. Requirements for the China submission are key to the project team, so that they can be built in the project timelines, resourcing etc. If a clinical trial is required in China, this has major implications on time to market and the cost of the project. Predictability for accessing the Chinese market is also critical as this is communicated to senior leadership so its accuracy is vital.
- Regulatory Department and Regulatory Professionals – Regulatory professionals are struggling with the requirements under the new regulations in China. For many they are seeking product approval for the first time under the new regulations whilst there still remains uncertainty around the actual requirements. This makes the regulatory pathway for China challenging in the current environment.

- End user, Physicians/Patient – It is in the interest of the end users in China that the latest healthcare technologies is available to them. As explained previously cancer, diabetes and cardiovascular diseases are on the rise in China. Therefore, China needs to get the latest technologies into their market in a timely manner to meet the demand and ensure patients are provided the best health care.
- Regulatory Authorities – It is in the interest of industry and individual companies that efforts are made to meet the requirements of the Chinese authorities. It is in the interest of the authorities that they can approve devices making than available to the China population. A company's reputation could be influential when it comes to approval.
- Competitors – Companies within industry can learn from each other. Individual experiences provide learnings as industry as a whole tackles the new regulations.

Chapter 2 reviews the literature with respect to China's medical device market, healthcare sector, the medical device regulations and the challenges to device approval and market access. Chapter 3 outlines the Methodology used to continue the research China's medical device market, approval process and challenges. Results and findings will be presented in Chapter 4 and these will be discussed and analysed in Chapter 5. Finally, Chapter 7 will outline conclusions and recommendations.

1.4 Glossary of Terms and Acronyms

Acronym	Definition
AQSIQ	Administration of Quality Supervision, Inspection and Quarantine of the People's Republic of China
BURA	Business Unit Regulatory Affairs
CCC	China Compulsory Certification
CER	Clinical Evaluation Report
CFDA	China Food and Drug Administration
CIF	Cost Insurance Freight
CMDE	CFDA Medical Device Technical Evaluation Center
COG	Cost Of Goods
COO	Country Of Origin
CTA	Clinical Trial Application

Acronym	Definition
DV	Design Verification
FIE	Foreign Invested Enterprise
GCP	Good Clinical Practice
GDP	Gross Domestic Price
GMP	Good Manufacturing Practice
HQ	Head Quarters
IEC	International Electrotechnical Commission
ISO	International Organization for Standardization
IVD	In Vitro Diagnostic
MDSAR	Medical Device Supervision and Administration Regulations
MOHRSS	Ministry of Human Resources and Social Securities
NCBI	National Center for Biotechnology Information
NDRC	National Development and Reform Commission
NHFPC	National Health and Family Planning Commission
OEM	Original Equipment Manager
PDP	Product Development Process
PTR	Product Technical Requirement
R&D	Research & Development
SAC	Standardization Administration of the People's Republic of China
SKU	Stock Keeping Unit
TM	Test Method
UDI	Unique Device Identifier
WHO	World Health Organisation

2.0 Literature Review

2.1 Introduction

This Literature Review will examine the current and future status of the Chinese Medical device market, the impact of the new regulations and the challenges to companies in gaining medical device approval and market access. In order to address the objectives as outlined in Section 1.2 of this thesis we will review the following major categories of literature with respect to China:

- The Country, Medical Device Market and Opportunities
- The Healthcare Sector
- The New Regulations and their Impact
- Challenges to Medical Device Approval
- Challenges to Medical Device Market Access

By exploring the above areas of literature, a significant contribution will be made to this research. At the end of each major section it is hoped that a critical understanding of each category is exhibited. The categories have been chosen and sequentially presented in order to firstly give the context of China's economy, healthcare sector and regulations followed secondly by the challenges to medical device approval and market access. The literature was collated and reviewed as per the Literature Protocol and Report provided in Appendix A.

2.2 The Country, Medical Device Market and Opportunities

2.2.1 Market Overview

China is the most populous country in the world with approximately 1.3 billion people (Boyer *et al.* 2015). It has become the world's second largest medical device market with an average growth of 20 per cent year-on-year since 2009 (FULBRIGHT 2016). The sales of medical devices in China have increased rapidly over the last decade, reaching a total value of 36 billion euro in 2014 (Centre 2015) and 45.3 billion euro in 2015 (Tang 2016). By 2020 the market is expected to be 50 billion euro (Council 2016). There are a number of reasons behind the burgeoning market for medical devices in China including the aging population, a more affluent population and the growing need to provide adequate healthcare

to rural areas and migrant workers (Boyer *et al.* 2015). This will be reviewed further in the next section.

2.2.2 Reasons for Market Growth

2.2.2.1 Population Demographics

China's market growth is due to several factors, firstly its due to China's demographics in particular China's aging population. In 2010 8.9% of its population were aged 65 or older, in 2015 the figure reached 10.5% (Tang 2016). By 2020 this figure is expected to grow to 17% and by 2040 the elderly population is projected to increase to 400 million (Boyer *et al.* 2015). This population shift towards a high percentage of the elderly is mainly due to the one child policy, the controversial legislation which was enacted by the Chinese government in 1979. The one-child policy resulted in fertility rates decreasing from between 5.6% and 6.3% in the 1950s and 1960s, to 2.2% in the 1980s (Boyer *et al.* 2015). Reforms to the country's one child policy came into effect in early 2014 and allowed couples to have two children if either parent is an only child. The long-term effects in this policy change will not be known for years to come (Centre 2015). As per the Chinese culture the elderly are often given care as a matter of tradition in China by family members and the community; however, this will not cover the anticipated 500% increase in the number that will require nursing home-level care. Currently, only 0.8% of China's aging population receives this care, far less than international standards, and to increase that capacity to even 3%, an investment of US$200 billion would be required (Boyer *et al.* 2015). With an aging population comes the increase of diseases associated with aging and in turn the requirement for new medical treatments and devices. The ophthalmic, cardiovascular and orthopaedic device markets are all influenced by China's growing elderly population (Council 2016). See Figure 2-1 below for visual representation of the Chinas birth rate, death rate, life expectancy and fertility rate from 1950 and projection to 2050. The data from (DESA 2013) 'World Population Prospects: The 2012 Revision' was used as the source data for Figure 2-1 (WHO 2015).

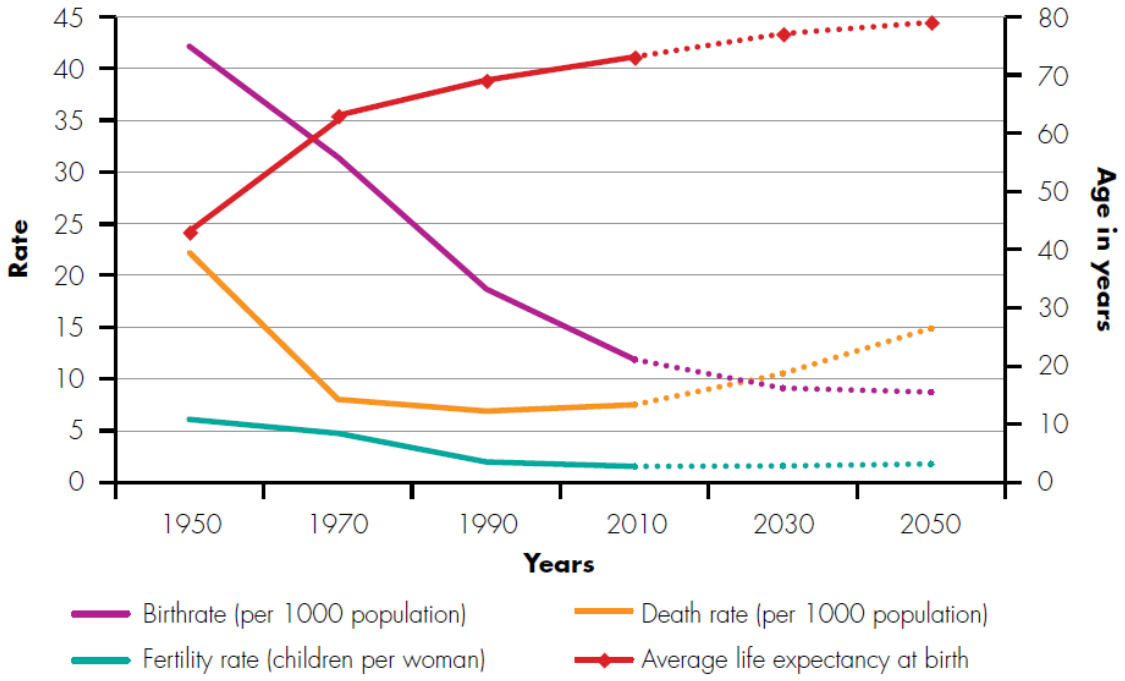

Figure 2-1: Projected Population Demographics in China (WHO 2015)

Another demographic influencing the market growth is the great number of people that are facing serious health concerns across the whole of the 1.3 billion population. According to the World Health Organization (WHO), more than 80% of deaths in China are attributable to chronic diseases, with an annual estimated 400,000 premature deaths linked to air pollution and 800,000 relating to injuries. A 2012 report suggested that 35.2% of Chinese men and 39.5% of Chinese women are overweight, compared with 14.7% averaged across both genders in 2002. In addition, 55.5% of men and 5.5% of women are currently smokers (Boyer *et al.* 2015). Currently there are 300 million people in China with chronic diseases including cardiovascular ailments, tumours, diabetes and respiratory diseases. The control of such diseases is one of the key tasks of the Chinese government (Tang 2016). With such figures and focus it is apparent China is an enormous market for the medical device industry. Access to medical devices is a key component to maintain and improve the standard of healthcare for such a population.

2.2.2.2 Healthcare Reform

China's medical device market growth has been stimulated by China's aggressive healthcare reform plan from 2009 to bring all its citizens under basic medical coverage and modernize

its health infrastructure has had an effect (Council 2016). The medical device market is growing to provide adequate healthcare to rural areas and migrant workers who traditionally have not been provided with it. The metropolises of Beijing and Shanghai have high doctor-to-patient ratios in contrast to rural areas. Individuals living in rural areas make less than a third of those that live in the city, which not only means that they are less likely to be able to afford adequate healthcare, but it also encourages a huge number of workers to migrate to urban areas, which places an increased expectation and demand for healthcare services and products. Between 2004 and 2012, the number of migrant workers in urban areas rose from 200 to 260 million, accounting for approximately 40% of the population in these urban areas. China's urban residents number about 500 million, where 80% of China's medical resources are located. In contrast, there are approximately 850 million rural residents where only 20% of medical resources are located. It is primarily for these reasons that China ranks 101st out of 187 countries in the 2013 Human Development Report, an international measure of healthcare quality. The opportunities for the medical devices market are strongly dependent on the area of the country as some areas have extremely high capabilities whereas others lack even basic care (Boyer *et al.* 2015).

2.2.2.3 County and Population Increased Wealth

The rapid increase in the wealth of the country and its people is a major force for the market growth of the medical device market is. From 1980 to 2000, the average income increased fivefold in urban areas while it increased threefold in rural areas. There has been a more than 10-fold increase in Gross Domestic Product (GDP) since 1978, with China becoming the second largest economy in the world. China now has annual expenditure of US$136 billion on research and development, and there are 263 medical research institutions with an estimated 926,000 researchers. In all of these measures, China is second only to the United States. This expansion in economy and research has primarily been due to China becoming a market-oriented economy. The needs of the healthcare industry, including medical devices, will likely continue to grow with the age and wealth of its population. The rapid growth in the Medical Device sector has not kept up with strong demand driven by an increasingly aging population and a growth in the number of affluent consumers who seek better quality medical services. Currently, there is a lack of resources and underdevelopment in relation to medical devices in rural areas and it is anticipated that the demand for medical devices will also increase from second and third tier cities and villages in the coming five to ten years (FULBRIGHT 2016).

2.2.3 Market Environment in China

China's growing old-age population and economic presence on the international stage, has made it more important to evaluate its domestic and foreign market contribution to medical devices (Boyer *et al.* 2015).

2.2.3.1 Domestic Manufacturers

The main conventional medical devices in China are manufactured by domestic manufacturers, the majority of these being low tech devices (Lueddemann *et al.* 2016). The numbers of domestic medical device manufacturers vary according to sources but as per (Lueddemann *et al.* 2016)) in 2013 there was 16,000 manufacturers of which 17% manufactured Class III devices, 54% manufactured Class II devices and 29% manufacture Class I devices. Although the growth rate of China's trade in medical devices is significantly higher than other economic powers, this has slowed in recent years, mainly because of such factors as weak global demand due to recession and rising domestic labour costs diminishing China's competitive advantage (Boyer *et al.* 2015). In recent years, Chinese governments have released a series of policies and guidelines to support the development of the medical device industry, covering medical device registration, manufacturing, distribution, and recalls, as well as hospital procurement. The medical device industry is one of the 10 key sectors of the Made in China 2025 program, which was released by China's State Council in May 2015 with the aim of promoting manufacturing in the country. The program supports the innovation and industrialization of the medical device industry, which includes medical imaging equipment, medical robots, cardiovascular stents, and mobile health, as well as 3D printing. Earlier in January 2012, China's Ministry of Science and Technology released the 12th Five-Year Plan for Medical Device Development, designed to support innovative medical device products, especially medical imaging products. A panel discussion for the plan was held in Beijing in 2016, covering the topics of development segments, innovative technologies, and key products, as well as policies. It is quite clear that local medical device products will be strongly supported in the next five years (Tang 2016).

2.2.3.2 Foreign Manufacturers

Foreign companies investing in high technology areas such as medical devices have in the past approached the Chinese market with reservation. In the past few years there has been a reduction on tariff rates on foreign medical products. China has entered into the World

Trade Organization (WTO) therefore the Chinese market system is more desirable due to the restrictions and requirements placed upon them as a result. Foreign companies are attracted to the Chinese market due to the low cost of labour. High technology firms will develop their production lines in China where expenses can be minimized before exporting their products to the international community where they can take advantage of competitive pricing. This is one of the main reasons for low patenting productivity in China because companies will conduct R&D in more developed nations with more patent protection and use their Chinese counterparts for the manufacturing portion of their business. The Chinese government has been implementing reforms in this area to make research and development within China a more attractive enterprise. The focus of foreign companies in China has been the high-technology and high-cost market. The contrast is even more apparent in the high-end medical device market as foreign firms have come to dominate with an 80% share; seven out of the top 10 largest firms are foreign companies or are joint ventures with domestic companies. These companies are catering primarily to the best hospitals in China where the clientele is generally of the wealthier upper class and government officials, who have created demand and are willing to pay for the highest quality of care. However, there are growing opportunities in rural areas for foreign firms to develop a market base as the current series of government reforms are allowing for the construction of new hospitals and upgrading old ones, encouraging them to invest in new and better-quality equipment, primarily in medical diagnostics. The strongest areas of foreign investment in medical devices in the Chinese market include medical imaging (X-ray, magnetic resonance imaging, ultrasound), products related to more advanced surgical procedures, and equipment for treatment of chronic disease. This equipment should ideally be competitively priced with domestic companies for those firms interested in catering to the rural and urban poor, and it is recommended that foreign companies provide the training and maintenance of these devices to increase market reliance and to ensure lasting profitability (Boyer *et al.* 2015).

Medical devices present large market opportunities, as well as a lowered entrance hurdles for medical device start-ups looking to enter China. Currently 92% of China's medical device technologies hail from foreign companies (Council 2016). Out of 200 countries/regions, Europe was the largest medical device exporter to China in 2014, accounting for 39% of China's total import value of such products. In comparison, North America accounted for 32% and Asia for 25%. The top six EU countries exporting medical devices to China in 2014 were Germany, Ireland, Switzerland, the UK, the Netherlands and Italy. The overall

top five exporters of medical devices to China in 2014 were the US, Germany, Japan, Ireland and Switzerland; these five countries provided 68% of China's total import value for medical devices (Centre 2015).

2.2.4 Opportunities for Medical Device Manufacturers

China is an immense market with many opportunities in the field of medical devices as indicated by its rapid growth in the medical device sector both for domestic and foreign firms. The current series of government reforms that are to be completed in 2020 and the rapid pace of economic growth are making the country more attractive to foreign investment. China has been one of the most important medical device markets in the world for many multinational companies such as GE Healthcare, Philips Healthcare, Medtronic, Boston Scientific, and Stryker, which have been actively expanding their China business via a series of strategic actions, including investments, mergers and acquisitions, localization, and partnerships. Medical imaging scanners, in vitro diagnostics, cardiovascular devices, and orthopaedics are the main segments in the Chinese medical device market, which together accounted for more than 60% of the total market size (Tang 2016).

Procurement is conducted through a centralised tender process. Public hospitals are not prevented from importing medical devices; however, in practice, public hospitals are encouraged to purchase domestically manufactured and domestically branded products. The National Health and Family Planning Commission (NHFPC) is in the process of establishing an incentive scheme to encourage the use of domestically produced medical devices and it is creating a series of lists of qualified products. In light of this incentive scheme, a number of foreign companies are moving or considering moving their production to China so that their products can meet the qualifications under the incentive scheme in order to remain competitive in the Chinese market.(FULBRIGHT 2016)

15% of the medical devices currently in use have been deemed obsolete and marked for replacement, and according to the reforms, US$250 million has been allocated by the Chinese government to subsidize new purchases. This may provide an opportunity for foreign manufacturers and investors (Boyer *et al.* 2015).

2.3 The Health Care Sector

2.3.1 Overview

There are nearly 1 million healthcare institutions in China, composed of hospitals, grassroots healthcare institutions, and specialized public healthcare institutions. The total number of Chinese hospitals increased from 19,712 in 2008 to 27,226 in 2015, this was mainly due to the growth of private hospitals, which increased from 5,403 facilities in 2008 to 14,049 sites in 2015 (Tang 2016). The total number of patient visits in China in the first half of 2016 reached 3.85 billion, a growth of 2.3% over the corresponding period of 2015. Patient visits to public hospitals and private hospitals reached 1.38 billion and 190 million, respectively, representing growth of 4.6% and 18.5% over the period, respectively. The total number of sick beds in Chinese healthcare institutions increased from 4.8 million in 2010 to 7 million in 2015, a CAGR of 7.9%. Sick beds in hospitals accounted for 76% of all hospital beds, and in 2015 more than 90% of new sick beds were added in hospitals. The ratio of sick beds per 1,000 people increased from 4.83 in 2014 to 5.11 in 2015, and it is expected to reach 6.00 by 2020, according to the government guideline (Tang 2016). The number of healthcare institutions has increased and the population are availing of the healthcare service.

Public hospitals in China spend more than 200 billion RMB every year purchasing low to mid-end medical devices from domestic manufacturers and import mid to high-end products from foreign manufacturers (FULBRIGHT 2016). Public hospitals are expected to cover 70–90% of their expenses due to the government providing very low funding. Hospitals have been forced to turn to user fees and drug mark ups as major sources of revenue. The result has been “over prescription of medicines and unnecessary and expensive medical testing with evidence that C/T scans are being performed at a rate 100 times higher than in comparable U.S. hospitals.

The largest hospitals in big cities (about 1,350 institutions in all) tend to have the highest quality physicians and equipment, and capture the lion’s share of patient flows. By contrast, grassroots facilities such as urban community health centers (CHCs) and county hospitals tend to be underdeveloped, poorly funded, and disconnected from larger hospitals. This gap impedes the achievement of the strategic goal of broad and effective care. Patients are inclined to visit the best hospitals in the largest cities, regardless of the severity of their

illnesses; this causes overcrowding at the big hospitals and underutilization at the grassroots facilities (Tang 2016).

The clinical skill of Chinese doctors is a challenge to the Chinese healthcare system, improving this will decrease unnecessary or repetitive laboratory or imaging examination, to avoid over-treatment. The poor quality of junior doctors' residential training is probably one of the weakest links in Chinese healthcare system. China senior doctors are reluctant to coach and in some hospitals the key surgical operations are monopolized by a small number of senior surgeons who obtain huge prestige and various other benefits (Wáng 2014). Chinese doctors are also living hard times. Over the last few years patient-on-doctor violence has become startlingly common, mostly when treatments fail. Stabbings and mob-style attacks have risen 23% a year on average since 2002, according to the China Hospital Management Association. This situation is a huge mental burden for doctors with an average of an incident every two weeks. China lacks healthcare professionals, including both physicians and nurses, and there are expected to be 2,500 physicians and 3,140 nurses per million people by 2020 (Tang 2016).

As concluded in (Deng *et al.* 2017) as China's population ageing trend intensifies, China should focus on the core goal of its health reform policy, which is disease prevention. China should also focus on the strengthening public health systems to effectively prevent and control key epidemic diseases. Finally China should increase the number of public health personnel, improve the level of education and training of public health personnel and increase the input of funds into the field of public health as soon as possible (Deng *et al.* 2017).

2.3.2 Health Insurance

Medical technologies and practices are expensive making them prohibitively accessible to the majority of the Chinese population unless they receive government assistance. To address health insurance coverage problems, the Chinese central government has initiated several health insurance plans since 1988. Since its inception in 2003, the New Cooperative Medical Scheme (NCMS), one of China's three main health insurance schemes, has vastly improved access and health insurance to rural residents. The initiative "Health China 2020" began in 2009, with funding of US$125 billion with the goal of providing healthcare

insurance coverage for all of China's citizens by 2020. The result of these reforms showed that by 2011/2012, insurance coverage (combined urban and rural) achieved between 92 and 95.7% of the population, which very nearly meets the government's goal of universal coverage by that time. Furthermore, reforms have been shown to have significantly reduced individual co-payments for both outpatient and inpatient healthcare. Previously, the Basic Health Insurance Scheme, the primary source of insurance in urban areas, did not cover migrant or sector workers, and as a result was accessible to only 28% of the total urban population. The rural population had the least health insurance coverage at only 25% of the total rural population. Those suffering from serious health problems did not avail of the healthcare services due to financial concerns. For the ones who did avail of the healthcare services the vast majority did so by paying themselves from 'out-of-pocket' funds instead of utilising government assistance (Boyer *et al.* 2015).

2.3.3 Healthcare Sector Initiatives

China's first comprehensive five-year blueprint for the healthcare sector, the National Planning Guideline for the Healthcare Service System (2015–2020), sets out clear targets for 2020 including one clinic and one medical service centre for each community with a population of over 30,000; and1.2 hospital beds for every 1,000 residents within the community (FULBRIGHT 2016).

The 11th and 12th 5-year plans (2006–2010 and 2011–2015) have been enacted with the intention not only to provide further healthcare reform, primarily by vastly increasing the number of care centres and providing subsidies to rural residents, but also to increase government promotion of industries such as biotech. A third of this funding will come from government at the national level, and the remaining two-thirds will come from local governments (Boyer *et al.* 2015).

In May 2014, the State Council released guidelines and a timetable to reform public hospitals. Publicly-funded hospitals that join the reform are required to sell medicines at the price they bought them, so they won't be able to overcharge patients and doctors will be much less likely to prescribe excessive medicines. On the other hand, the publicly-funded hospitals are allowed to readjust the price charged on their medical services, such as doctor consultation, so that the hospitals and their medical staff will be decently paid for their work instead of relying on selling medicines. Moreover, the State Council has decided that the

authorities should allow the market to determine the price of most medicines, and should turn to negotiations to bring down the price of certain medicines, such as proprietary medicines (Nofri 2015). Through the reform of public hospitals the State Council reiterated the need to improve the service's quality and the competence of grassroots healthcare institutions, so that more patients can turn to these institutions for small and common illnesses, and be transferred to large hospitals in time if their conditions worsen (Nofri 2015).

2.4 New Regulations and Impact to Medical Device Registration

Multiple government agencies are responsible for policy-making as well as monitoring the medical device industry in China. These include as follows:

- National Health and Family Planning Commission (NHFPC)
- China Food and Drug Administration (CFDA)
- Ministry of Human Resources and Social Securities (MOHRSS)
- National Development and Reform Commission (NDRC)

(Medical 2015)

The China Food and Drug Administration (CFDA), previously known as the State Food and Drug Administration (SFDA), is the administrative and supervisory authority for medical devices in China. CFDA oversees the administration of food, drugs and cosmetics. The CFDA drafts regulations for medical devices, draws up standards, classifies medical devices, and inspects the manufacturing, sales and distribution of medical devices in China. In addition to this, the CFDA also manages the import of medical devices (Centre 2015). The CFDA is broken into the State Municipal CFDA that has responsibility for local Class I medical devices, the Provincial CFDA that has responsibility for local Class II medical devices and the State CFDA that has responsibility for Imports and local Class III medical devices. See Figure 2-2 below for CFDA structure (Brandwood 2016).

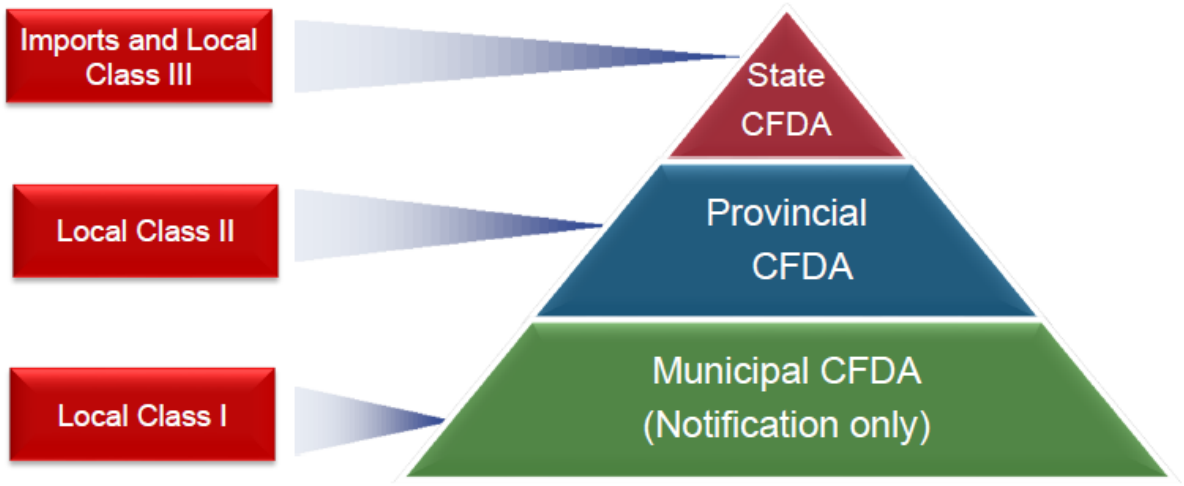

Figure 2-2: CFDA Structure and Responsibility(Brandwood 2016)

China's State Council released its new Administrative Regulation on the Supervision and Administration of Medical Devices in March 7, 2014 (CFDA 2014c) and this came into effect on June 1, 2014. This is commonly known as Order 650, the "New Regulation" which replaced Order 276 the "Old Regulation". The State Council Legislative Affairs Office worked more than six years revising the old regulation Order 276 which had been effective since 2000. The revisions are intended to establish a more efficient and scientific regulatory regime for supervision and administration of medical devices. The New Regulation addresses research and development, clinical trials, product approvals, manufacturing, business operations, sales, and advertising. In general the New Regulation moderates the oversight of low-risk medical devices and strengthens the supervision on high-risk devices (Yan *et al.* 2014).

As per Ropes&Gray (2016) Order No. 650, stands out as a landmark policy update in China. Prior to Order No. 650, there was Order No. 276 which was created from scratch. This was created when there was less the 5000 manufacturers marketing in China, by 2013 there was greater than 15,000 manufacturers. As of the end of December 2013, of the 15,698 medical device manufacturing companies with licensed certificates, 35 companies were listed either in China or overseas. A total of 93,592 types of medical devices were licensed as well as 34,655 types of imported medical devices (Centre 2015). Order No.650 was implemented as an improvement to Order No.276. Overall, the new framework emphasizes both premarket

approval and postmarket surveillance, indicating China's intent to harmonize with international standards and practices. The new framework adopts a risk-based approach in medical device classification and supervision; uses simplified premarket approval procedures for Class I medical devices (filing instead of registration); extends the time allowed to submit supplemental documents (deficiency process); and extends license validity from four to five years. In addition, the reform opens a channel for new, unclassified products to be submitted as Class III medical devices (Wenyan 2014). Since its announcement in 2014, Order No. 650 has brought a series of profound changes to the industry and impacted both local and multinational corporation Medical Technology players in China. In the past few years, the CFDA has issued dozens of guidelines for technical reviews and mandatory standards for medical devices, urging the industry to upgrade device safety and effectiveness (Ropes&Gray 2016). With the new regulations the number of Class III devices requiring the mark for product safety has reduced but this is still a requirement for certain medical devices such as x-ray equipment and pacemakers (Zhang *et al.* 2016). The CFDA have also implemented a number of measures to streamline product approval and foster innovation. More recently, the CFDA issued '*Good Clinical Practice for Medical Devices (GCP)'* (CFDA 2016), a new revision imposing higher compliance standards on the conduct of clinical trials by medical device companies (Ropes&Gray 2016)

2.5 Changes in Medical Device Registration and Filing Requirements

All Class I medical devices, including those manufactured in foreign countries, can enter the market through a filing with CFDA or its local counterpart. A registration or pre-market assessment is no longer required. Class I devices require technical documentation including a Declaration Of Conformity to Chinese regulations and standards which will be submitted to the relevant CFDA office Class II and Class III devices still require registration. Registration certificates for Class II and Class III devices have five year validity. An application for renewal should be submitted six months prior to certificate expiry (Theisz 2015).

Under the Old Regulation, a material change in a registered device required a new registration as a new device. By comparison, under the New Regulation, a material change only requires a change in registration. Generally, a material change in a registered medical device is when the device's safety and/or efficacy might be affected by any change in its

design, raw material, manufacturing procedure, etc. In practice, CFDA's local counterparts have wide discretion in determining what changes constitute material changes.

A minor non substantial change in a registered medical device is no longer subject to the approval by the original registration authority; filing a notification of the change with the authority is sufficient. The term of a medical device registration is five years instead of four, and the registration can be extended through renewal, instead of re-registration. If there is a change requiring registration, the change registration cert is attached to the initial registration cert and the expiration date remains unchanged(Yan *et al.* 2014). See Table 2-1 below for a summary of old versus new for medical device registration.

Table 2-1: Registration Old versus New

OLD	NEW
Registration – Class I, II & III	Notification – Class I Registration – Class II & III
- Initial Registration - Re-registration due to the license expiration - Re-registration due to product changes	- Initial Registration - Registration Extension for license expiration with no product change - Permission Amendment due to product change - Notification Amendment due to notification change

2.5.1 Changes in Regulation of Clinical Trials

Under the New Regulation, a clinical trial of low-risk medical devices no longer requires the approval of CFDA or its counterparts, but a filing is required. Certain Class III medical devices that involve very high risks must still obtain the necessary approvals. Clinical trials for Class II and Class III medical devices that have a proven record of safety can be exempted in accordance with the New Regulation if they are on the Clinical Trial Exemption list as published by CFDA. Certain Class II and Class III medical devices may also be exempted if the Safety and Effectiveness can be proven via analysis and evaluation of the data obtained from trials or clinical use of the substantially equivalent device already marketed and approved in China. In this instance a China specific Clinical Evaluation Report is required to be filed for registration. If your device does not fall into either of these categories then a local clinical trial will be required. Prior to the new regulations domestic manufacturers required a clinical trial for all Class II and Class III devices. Foreign

manufacturers could use the clinical package that supported product approval in the Country of Origin for registration in China unless the device was deemed high risk e.g. a combination device. See Figure 2-3 below for the three possible Registration Pathways for Class II & III Medical Devices under the New Regulations (Brandwood 2016).

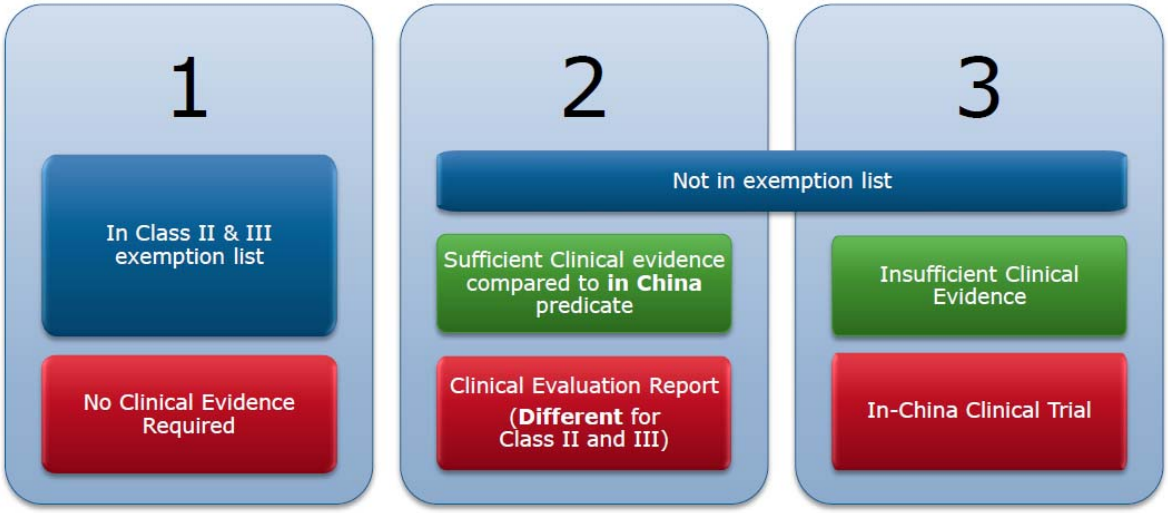

Figure 2-3: Registration Pathways for Class II & III Medical Devices under the New Regulations (Brandwood 2016)

2.5.2 Changes for Manufacturers

As per the new regulations medical device manufactures shall comply with good manufacturing procedures (GMPs) for manufacturing, operating conditions and quality control systems. Manufacturers must conduct self-inspections on a regular basis and submit self-inspection reports to CFDA's counterparts at the municipal level. CFDA and its counterparts can make regular and random inspections to check on compliance (Yan *et al.* 2014).

As per the new regulations a manufacturer of Class II and Class III medical devices must apply for registration of its medical device first and then apply for its product specific manufacturing permit. Under the old regulations a manufacturing license was required first. The manufacturer can now submit the product registration certificate when applying for the manufacturing permit. The manufacturer can ensure their device will be approved prior to investing in production facilities.

Figure 2-4: Old versus New Regulations for the Manufacturer

OLD		NEW	
Domestic Device	Imported Device	Domestic Device	Imported Device
Product specific Manufacturing Permit + Device with registration license	Device with registration license (based on Country of Origin Approval)	Device with registration license + Product specific Manufacturing Permit	Device with registration license (based on Country of Origin Approval)

The New Regulation stipulates what information must be included in the specifications and labels of medical devices. Medical devices manufactured in foreign countries must have their Chinese labels attached before they are imported into China. The New Regulation contains a section (Chapter V of Order 650) on monitoring adverse incidents, re-evaluating registered medical devices, and recalling defective medical devices. Every medical device enterprise must now establish an adverse incidents monitoring system to monitor and report adverse incidents(Yan *et al.* 2014).

2.5.3 Changes for Distributors

Distributors of Class II medical devices may file with CFDA's counterparts at the municipal level instead of obtaining a permit as required by the Old Regulation. Distributors and other sellers of medical devices are required to verify and inspect the qualifications of their manufacturers or providers, as well as the certificates of conformity of the devices they will purchase. Wholesalers of Class II medical devices and all Class III medical devices sellers (wholesalers and retailers) shall also establish a system to maintain their sales records (Yan *et al.* 2014).

2.5.4 Enhanced Postmarket Surveillance

The new regulations set out enhanced post market surveillance. There are mechanisms for recording stocking and sales, systems for adverse event monitoring, safety re-evaluation and product recall (Wenyan 2014). The old regulations did not have requirements for medical device adverse events and recalls until 2011 when CFDA issued two provincial Decrees, one for tracking adverse events and one for managing recalls. The new regulations have now stepped up. For adverse event reporting there are clear responsibilities outlined for manufacturers, manufacturer personnel, distributors, patients and users, each having rights to

report. CFDA have set up a monitoring system and information network to allow for adverse event reporting, analysis and control (Zhang *et al.* 2016). Death related events must be reported within five days and injury related events must be reported within fifteen days either to regional monitoring institutions or as required to CFDA (Lueddemann *et al.* 2016).

There are challenges with the post market enforcement lacking consistency and the dependence on how local enforcement authorities interpret the statutory requirement (Ropes&Gray 2016). There is concern that this may lead to inappropriate penalties being applied in Chinese provinces and regions and also a lack of professional knowledge and expertise on the part of inspection personnel. For example the General Administration of Quality Supervision, Inspection and Quarantine (AQSIQ) has authority to perform inspections including product testing and checking Chinese language packaging, IFU and labeling (Wenyan 2014).

Industry recommends CFDA further optimize the adverse event monitoring system over the long term to use the postmarket surveillance (PMS) system to provide supporting data for product registration extensions (Wenyan 2014).

2.5.5 Increased Legal Penalties and Liabilities

The new regulations have increased the liabilities and penalties for manufacturers. certain serious violations under the old regulations saw fines based on two to five times of the illegal proceeds (Yan *et al.* 2014). With the new regulations comes an increase on sanctions and penalties for various violations (Zhang *et al.* 2016). Under the new regulation fines will be calculated on the value of the medical devices concerned in its illegal activities. Manufacturing costs and other expenses for the particular medical device will not be deducted from the proposed fine. Depending on the violations it could be five to twenty times the value of the involved medical devices(Yan *et al.* 2014). For example, administrative penalties of up to twenty times the value of the manufactured product may be imposed on medical devices produced without the proper permits. In extreme scenarios a company may be suspended from application for any permits of licenses for five years and may be subject to criminal proceedings (Zhang *et al.* 2016).

2.6 Challenges to Medical Device Approval

2.6.1 Overview

From the new regulation, four keys areas have emerged as high impact to manufacturers seeking medical device approval in China:

- Clinical Trials
- Country Of Origin
- Submission Process
- Enhanced Post-Market Surveillance

(Wenyan 2014)

On a functional level, Regulatory Affairs leaders have been most exposed to the new regulation, while at the same time taking an important role in shaping the implementation and interpretation of the new policies. Order 650 poses numerous challenges to the Regulatory Affairs professional to navigate to medical device approval.

Among all the regulatory changes, clinical evaluation is consistently rated as the most relevant topic by all participating RA leaders. Interpreting and following the highly complex clinical trial authorization and the clinical trial exemption policies have presented the most challenges to their work. RA leaders also expressed their concerns about the costs and benefits associated with fast-track applications, the differences between the China GMP and ISO standards, and the unpredictability of post-market enforcement (Ropes&Gray 2016).

A survey conducted with AdvaMed members (AdvaMed being the Advance Medical Technology Association is a trade association that leads the effort to advance medical technology in order to achieve healthier lives and healthier economies around the world) identified China specific issues including the length of the registration process, regulatory costs and the volume of information that is required to be translated as part of the submission process. The single greatest concern for medical technology companies operating globally was the duplication of clinical trials and its cost and time for product registration (Limited 2015).

Complexity in Product Registration remains given the ambiguous nature of Chinese policies and regulations, transparency and consistency have been the most significant challenges for industry. Although clear interpretations of the new order are desired, detailed

implementation rules have not yet been released. Industry is urging the Chinese government to allow a reasonable transition time to implement these changes, and not to make them retroactive. The new framework abolishes previous articles beneficial for imported devices and requires an incremental number of detailed technical dossiers during the product registration process. This additional documentation will demand greater support from sponsoring companies and will necessitate better and more-strategic internal planning, particularly for new products entering China (Wenyan 2014).

2.6.2 Local Clinical Trials

Overall costs also are expected to rise due to Order 650 expanding requirements for local clinical trials and calls for per-submission product registration fees. Order 650 requires both domestic and imported Class II and III medical devices and in vitro diagnostic (IVD) products to undergo local clinical trials (previously, only domestic products were required to undergo local clinical trials). In addition to an ethics review, high-risk Class III devices will require preapproval for initiating clinical trials. Overseas clinical trials will not be recognized, and in-country clinical trials must follow China Good Clinical Practices (GCPs) (Ropes&Gray 2016). The requirement for local clinical trials will be the most significant premarket approval challenge facing a foreign-invested enterprise (FIE) and undoubtedly will increase registration uncertainty, timelines and investment, particularly when registering innovative products. Setting up an FIE is a common method of creating an operation in Asian countries, especially in China. Exemption from the clinical trials requirement is feasible for products listed in the Catalogue of Clinical Trial Exemptions maintained by CFDA. In addition, Order 650 lists three general criteria for clinical exemptions: mature products having no severe adverse events safety and efficacy can be proven by nonclinical performance evaluation safety and efficacy can be proven by evaluation and analysis of data on similar products from clinical trials or clinical use. In the US, the definition of "me-too" devices includes technology that is identical or very similar to that of the predicate device; an identical indication; and labeling containing equally stringent warnings and precautions. When assessing and conducting a risk evaluation for the Chinese market, however, companies may lack the knowledge or expertise necessary to create a competitive yet similar product or convince the reviewer of its similarity to a device currently on the market. Industry has asked CFDA to issue detailed regulations with clear guidance for clinical trials, GCPs and site qualification, to establish a dynamic clinical trial exemption amendment mechanism (e.g., update the list every six months), to publish the clinical trial exemption list

on the CFDA website in a timely manner and to work out a clear definition of “device of same category” (or me-too) with industry experts (Wenyan 2014).

2.6.3 Country of Origin

Imported Class II and III medical devices to be registered in China are required to gain market approval in the country of legal manufacture, a prerequisite for CFDA submission. Alternatively, a US Food and Drug Administration (FDA) 510(k) clearance can be used to meet the CFDA prerequisite. This Country of Origin (COO) requirement applies to both new registrations and changes or extensions to registrations. This requirement creates another barrier for imported devices and is expected to cause significant registration delays and may cause companies to change launch strategies and timelines. It is problematic for many FIEs, as approval requirements vary widely across Chinese regions and provinces. For example, companies making medical devices and equipment solely for export or for designated Chinese regions often do not file in the Country of Origin or country of legal manufacture. This new requirement may prevent FIEs from introducing advanced technology products into China in a timely manner and could prevent patients from receiving the benefits of the latest technologies. Industry asked CFDA to accept registration applications from countries where the manufacturing sites are located to accelerate the process of registration while ensuring product safety and effectiveness (Wenyan 2014).

2.6.4 Submission Process

Submission of technical files (similar to the Summary Technical Document (STED)) now requires companies to provide more detailed documentation and explanation compared with the current practice of submitting product registration standards. For medical device products, it is necessary to include data such as research and manufacturing information, as well as packaging and labeling samples of the smallest sales unit, in the medical device technical files. There may be an increase the risk of intellectual property leaks. A Chinese label should be on the product before it clears customs, and the manufacturing site address, manufacturing date and contact information are necessary on either the Chinese label or Chinese instructions for use (IFU, sometimes called directions for use, or DFU). Stringent penalties for labeling noncompliance, up to and including the revocation of a medical device distribution license may be imposed. Documentation for Class I devices will be more extensive under the new order, requiring additional time and resources for dossier preparation. Class I applications currently under evaluation or pending supplementary

documentation will have to be withdrawn and resubmitted according the new documentation requirement, even if they were submitted prior to the 1 June effective date for Order 650. Evaluation timelines for Class II and III devices are longer under the new framework: 60 and 90 working days, respectively (Wenyan 2014).

2.6.5 Change Control

CFDA Decree No.4, Chapter VI Change of Registration (CFDA 2014b) sets out the requirements for changes to medical device post registration approval. As per Article 49 of CFDA Decree No.4 –

'For the registered Class II and Class III medical devices, if medical devices registration certificate and the contents listed in the attachment have changed, the registrant shall apply for change of registration to the original registration department and submit the declaration materials according to the related requirements.'

For changes a Registration Amendment application is required. If the amendment is approved the license expiry date of the initial product registration remains the same. For changes that are categorized as a "Notification Amendment," the CFDA will conduct a quick review and issue amendment approval documents within 10 business days. For changes that are categorized as a "Permission Amendment," the CFDA will conduct a technical review regarding the changed technical files. The review timeline for "Permission Amendment" is the same as the initial registration timeline of a medical device. Change control post initial approval of a medical device in China is challenging and there is significant impact to the business due to the timelines. There is a lack of clarity around what type changes are notification amendments versus permission amendments. A permission amendment may require a clinical trial dependent on the change.

2.7 Summary of Challenges to Market Access & Success

China is an immense market with many opportunities in the field of medical devices as indicated by its rapid growth in the medical device sector both for domestic and foreign firms. The current series of government reforms that are to be completed in 2020 and the rapid pace of economic growth are making the country more attractive to foreign investment (Boyer *et al.* 2015).

Presently, the best opportunities for foreign company investment are in high-technology devices, but this is gradually changing due to the rising demand by the rural and urban poor for better healthcare and as enforcement of intellectual property rights improve, with similar market increases anticipated in the area of chronic healthcare as China's society ages. Despite improvements by the Chinese government, there still remain substantial social and economic concerns, but if correctly implemented the benefits and opportunities for profits and expansion in locating a medical device company in China outweigh the inherent risks**.**

2.7.1 'Copying'

Other than catering to the wealthy elite, foreign firms are most heavily invested in high-tech because it is more difficult for local firms to reproduce these devices. In developed countries, the prohibition of so-called "copying" of an intellectual property is rigidly enforced, whereas in China the patent laws are weakly enforced. Foreign firms must resort to other measures for protection, including design secrets and focusing on more complex high tech products that require a significantly greater knowledge base than is typically available to domestic companies. Protection has improved since China joined the WTO; however, there is still a view that increasing protection of intellectual property (IP) rights would stifle economic growth. The culture of imitation is gradually being replaced by the realization that to maintain competitiveness in the global marketplace, domestic firms must be capable of innovation. If there is innovation this must be protected by stronger patent laws. Fortunately, it has been stated that the recent trend appears to be in favour of stronger IP protection (Boyer *et al.* 2015).

2.7.2 Lack of Local Knowledge

Another difficulty often faced by foreign companies entering the Chinese market is lack of local knowledge. This may include such considerations as social factors, intermediate suppliers, and policy changes. One way that these difficulties have been addressed is to locate companies in industrial clusters where strong local business linkages are already established, which can have the added benefit of shared supply lines and lowered production costs. Several such clusters for medical devices are located in the metropolis of Shanghai, which also happens to be one of the largest markets for premium medical devices, along with Beijing, Shenzhen, Guangzhou, and Hong Kong. Partnering with local distributors, in particular, appears to be a viable method of entry into the Chinese market, but it should be

noted that there are over 10 000 distributors of medical devices in China, most of which are extremely small outfits, which necessitates the employment of a large sales force by the marketing or development firm. It is also advisable to be open to partnerships with various levels of government, hospitals, and even the Chinese army (Boyer *et al.* 2015).

Getting your Chinese distributor to excel in conceptual sales is often challenging. Chinese distributors, like other distributors around the world, often focus on easy-to-sell products where conceptual sales are not required to maximize commissions. Setting up your own subsidiary operation or entering into a joint venture is more complicated now than ever before (Gross 2016).

2.7.3 Product Registration

There are significant regulatory procedures for foreign-made medical devices, which are governed by the China Food and Drug Administration (CFDA) (see Challenges to Medical Device Approval Section 2.6). According to CFDA regulations, approval of registration of medical devices takes between 60 and 90 days for a US$500 fee; however, it has been stated that a majority of companies wait for up to a year to receive approval to move to clinical trials. This lengthy approval time discourages both foreign and domestic businesses in medical device development. This is thought to be partially owed to the execution of the head of the SFDA in 2007 due to corruption charges, leading to a more thorough and lengthy evaluation process with the intention of being “more careful”. However, regulatory restrictions for devices undergoing clinical trials are extremely relaxed, possibly due to the long approval process and pressure to generate revenue or lack of expertise in regulatory staff. The Chinese central government has recently taken steps to mitigate these problems, in particular, implementation of new registration requirements intended to make it easier for foreign companies to export medical devices to the Chinese market, as well as price caps and reduction of tariffs (Boyer *et al.* 2015). A survey conducted with AdvaMed members showed that 60% stated that the regulatory environment had worsened in 2014 versus 2013 and more than 60% registering medical technologies in China rated the regulatory environment in China as more difficult than other major markets such as the US, EU and Japan (Limited 2015).

2.7.4 Reimbursement

Even when registration is completed, reimbursement is not easy to obtain and this has become a lot more difficult with the 2014 reforms (Gross 2016). Foreign companies must go through a complex, lengthy, and uncertain process in order to receive reimbursement. This process includes CFDA approval, patient price approval (including national and provincial medical device reimbursement), and provincial bidding (Medical 2015). Most medical device reimbursement takes place at the provincial-level pricing bureaus, and negotiating with these bureaus can be tricky. Reimbursement for foreign-made devices is normally low, and cash supplements from patients are often required. The government also incentivizes Chinese hospitals to buy locally made products (Gross 2016).

The NHFPC, NDRC, and MOHRSS are the three bodies responsible for determining pricing and reimbursement at the national level. In general, medical devices must pass through the following steps:

1) Patient-Price Application Approval - Before entering the bidding process, the manufacturer needs to submit and receive approval for the highest allowable patient-price. The manufacturer must submit sensitive information on COGs, CIF, and other patient-price items in select reference countries. It normally takes three months to receive price approval in the province in which the company is registered or at the port of importation.

2) Provincial Bidding & Approval - Brands must undergo a bidding process before they are allowed to pursue hospital listing regardless of whether the product code is in the National/Provincial Reimbursement List. The bidding time window is unpredictable in all provinces and manufacturers must pass through the bidding process province by province. If the manufacturer wins and accepts a bidding offer it can then go to individual hospitals for listing.

3) Hospital Listing - The manufacturer needs to pursue hospital listing with each targeted hospital individually. The provincial bidding and approval does not guarantee that the brand will enter hospitals automatically. The manufacturer can lobby for special procurement with hospitals while undergoing or awaiting the bidding.

4) The Tendering and Bidding Process - Tenders are done at the provincial level and are generally issued once a year; however, this process has become more unpredictable in many provinces due to new regulatory changes.

Manufacturers can rely on local distributors for help throughout the bidding process. Ultimately, if a manufacturer loses the bid, it cannot enter hospitals in that province. If an asking price is too low, the manufacturer can choose not to accept the bid and give up reimbursement and market access in that particular province (Medical 2015).

Reimbursement is primarily done at the provincial level. The provincial reimbursement normally includes three lists:

- List A devices are generally reimbursed 100% with a co-pay less than 10%
- List B devices have a 20-60% co-pay. Deductibles may also apply in the case of imported products.
- List C devices receive no reimbursement and must be purchased at 100% cost

There are various "ceilings" for reimbursement. Ceilings are applied to each patient individually in a particular province or city based on the average annual income. Ceilings are also applied to each patient for each diagnosis code and each hospital stay. Supplemental reimbursement is another key issue. This includes an insurance policy purchased by the employer or employee from a commercial insurance company. Local government and commercial health insurance are mainly designed for "catastrophic diseases"(Medical 2015).

In late 2014, China instituted a series of healthcare reforms designed to reduce the burden on the healthcare system and patients, squeeze out mark-ups in the value chain, push for consolidation of distribution for medical supplies, and favor local innovation. Over time, the central government will likely remove itself from price setting somewhat, although high-value medical supplies will continue to be tightly controlled for the coming years. Reimbursement policies are undergoing changes. Hospitals, which are constantly under funded by local governments and are under pressure to implement a "zero mark-up" scheme. They are limited by complicated reimbursement and formulary restrictions including a monthly quota on the use of certain products. For device products and manufacturers, the reimbursement process and Chinese government outlook means that future price-cuts are certain. Obtaining medical device reimbursement in China requires a strong market access team to successfully navigate the complex local reimbursement process (Medical 2015).

2.8 Conclusion

For those not already in the market, deciding whether now the right time to enter is and negotiating a tricky and sometimes idiosyncratic product registration process can be daunting (Lack 2016). Order 650 demonstrates China's determination to develop regulations more closely harmonized with international practices, as does CFDA's move to a risk-based assessment system for classification. However, while the new order greatly simplifies Class I medical device registration, Class II and III device registrations remain complicated. New requirements for local clinical trials greatly increase the time and cost of importing products. The medical device industry in China is looking toward clean guidelines and consistent interpretation and practice across the nation in the future (Wenyan 2014).

Despite the factors discussed in both the medical device market access and medical device registration, it is possible for medical device companies to succeed in China. The best way to go, despite the fact that it may take a long time to get approved, is to produce a unique product that is not easily copied. Companies should continually upgrade their innovative products so that the Chinese copycat producers have trouble keeping up. Medical device companies that wish to acquire IP protection can also register their patents in China, although normally only large companies can afford to pay for expensive IP lawyers in the country (Gross 2016).

Some device companies may take advantage of the cheap local labor and manufacture their products in China. This labor is not as cheap as it was in the past. A company can make its Class II products in China, they generally only need to apply for provincial approval not national CFDA approval which is faster. However, if a Chinese manufacturer is to be the Original Equipment Manager (OEM), the product must be registered under the local manufacturing company, not the foreign device manufacturer. If the foreign manufacturer has its own Chinese facility and Good Manufacturing Practice (GMP) certificate, it may outsource some of the manufacturing and then register directly in its name with the CFDA. Furthermore, by manufacturing in China, companies may also be able to export to other markets in the fast-growing Asia region more easily (Gross 2016).

There is an additional opportunity that lies within sourcing medical devices or medical device components from China. For many Class I and II products, the quality of the devices

manufactured in China by local manufacturers is acceptable for global export, including to the West. Some foreign companies are now beginning to import locally made Class III products for global distribution. Of course, Class III products made in China will need to be approved there, go through local Good Clinical Practice (GCP) clinical trials, and meet Chinese Good Manufacturing Practice (GMP) standards before they can be registered in the West(Gross 2016).

Most companies that are serious about China are setting up their own operations in the country, including representative offices, branch offices, or Wholly Foreign-Owned Enterprises WFOEs. It is up to the foreign companies to make sure their local Chinese employees know the difference between right and wrong and to outline punishments for violating intellectual property rights. Foreign companies are no longer setting up joint ventures in China, generally because they become too problematic over time (Gross 2016).

3.0 Methodology

3.1 Introduction

This chapter describes the research strategy to address the following interrelated dissertation questions:

1. What is the current economic environment for medical devices in China? What are the projections for the future state?
2. What has changed in the medical device regulations in China, with the updated regulations enforced in 2014?
3. What is the impact and challenges to product registration and market access in China as per the new regulations?
4. What can the regulatory function do to ensure they create a successful regulatory strategy for Class II and Class III device approval in China that will aid market access?

In Chapter 2, the extensive literature review spoke to all five objectives. To further substantiate the literature review completed, elements of all the five objectives were researched further. As per Chapter 2 the global perspective on China is understood. The research strategy outlined below will describe how data was gathered to understand the experiences and perspective of the regulatory professional in relation to China. The research strategy will describe the collection and analysis of data. The combination of the literature review findings and the 'real life' experiences will ensure a greater understanding of the challenges to regulatory approval and market access in China.

This chapter will provide the details of the research strategy adopted to further address and answer the objectives outlined above. This chapter will also detail the method for collecting data for analysis and the analysis approach to be adopted. Potential limitations of the strategies chosen will also be discussed.

3.2 Research Methodology

The research methodology is the general philosophy or principle that guides the research. The research may be quantitative, qualitative or a mixture of both (Dawson 2001). Quantitative research is research that is concerned with quantities and measurement whilst

Qualitative research on the other hand is linked to in-depth exploratory studies (Biggam 2015). As per Creswell (2014) –

'Mixed methods research is an approach to inquiry that combines both qualitative and quantitative forms of research. It involves philosophical assumptions, the use of qualitative and quantitative approaches, and the mixing or integrating of both approaches in a study.'

The research methodology that was adopted to address the dissertation objectives was mainly qualitative research but with an element of quantitative research therefore a mixed method approach. Qualitative research explores attitudes, behaviour and experiences of the contributors involved. It is more in-depth and usually requires a smaller sample in comparison to quantitative research. This is suitable for the subject matter and objectives outlined, whilst medical devices are a large industry in Ireland the number of regulatory professionals that have interacted with the Chinese regulatory system would be limited. A quantitative only methodology was deemed too challenging. There would be difficulty in identifying individuals and quantities of individuals to generate any statistically relevant data. Qualitative research focused on my own in depth experience in addition to qualitative and quantitative research by reaching a smaller sample size of relevant people was deemed an appropriate methodology.

An exploratory sequential mixed method was chosen as the research methodology starting with a qualitative phase first followed by a quantitative phase. An exploratory sequential mixed method is a design in which the researcher first begins by exploring with qualitative data and analysis and then uses the findings in a second quantitative phase. Like the explanatory sequential approach (reverse of the exploratory sequential approach) the second database builds on the results of the initial database. The intent of the strategy is to develop better measurements with specific samples of populations and to see if data from a few individuals (in qualitative phase) can be generalized to a large sample of a population (in quantitative phase). For example, the researcher would first collect focus group data, analyse the results, develop an instrument based on the results, and then administer it to a sample of a population. In this case, there may not be adequate instruments measuring the concepts with the sample that the investigator wishes to study. In effect, the researcher employs a three-phase procedure with the first phase as exploratory, the second as instrument development, and the third as administering the instrument to a sample of a population (Creswell 2014). Figure 3-1 below illustrates the research methodology; the

qualitative data gained through collection and analysis of the case study builds to the quantitative/qualitative data collection and analysis of the peer survey for overall interpretation.

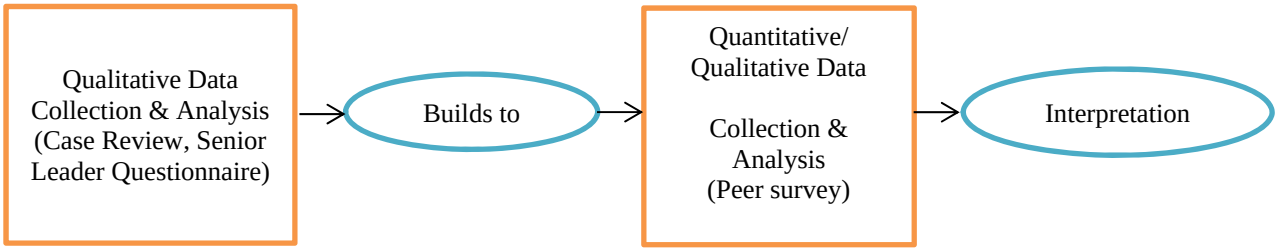

Figure 3-1: Exploratory Sequential Mixed Methods(Creswell 2014)

3.3 Research Strategy

This study would adopt a case study strategy in answering the research questions posed. A case study quite simply is a study of one example of a particular type. Case studies are an approach to gain a richer and deeper understanding of the research. Yin (1994) cited in (Rowley 2002)defines a case study thus:

'A case study is an empirical inquiry that:

• *Investigates a contemporary phenomena within its real life context, especially when*

• *The boundaries between phenomenon and context are not clearly evident.'*

The research questions are all 'What' questions. Who, what and where questions can be investigated through documents, archival analysis, surveys and interviews. Typically case study research uses a variety of evidence from different sources, such as documents, artefacts, interviews and observation, and this goes beyond the range of sources of evidence that might be available in historical study (Rowley 2002). Case study research can be based on any mix of quantitative and qualitative approaches. Typically, it uses multiple data sources including two or more of: direct detailed observations, interviews, and documents.
The research strategy involved the research methods as outlined in Table 3-1.

Table 3-1: Research Strategy and Research Method

Research Strategy	Research Method
Literature Review	An in-depth literature review to present an overview of the Chinese medical device market current and future state including the opportunities to medical device manufacturers.
	An in-depth literature review to present an overview of the Chinese Healthcare Sector and the reforms in progress. An in-depth literature review to describe the principles of the new Chinese medical device regulations and to discuss the key changes versus the old regulations
	An in-depth literature review to describe the challenges to medical device registration and market access for a medical device in China
Case Study	Sample product case review to discuss the challenges and considerations for medical device registration under the new Chinese regulations and the Strategic Regulatory Planning involved for getting the product to market in China
	Qualitative Questionnaire with internal multi- national company regulatory subject matter experts to discuss their experiences and challenges with China's regulatory approval process
	Qualitative and Quantitative Questionnaire to understand Regulatory professionals perception of the medical device registration in China and market access to China

3.4 Literature Review

Chapter 2 is the output of the in-depth Literature Review as listed in 1, 2 and 3 of the research strategy above. Three databases PubMed, Medline and Embase, were utilized. PubMed is a free resource developed and maintained by the National Centre for Biotechnology Information (NCBI) at the National Library of Medicine. PubMed comprises more than 25 million citations for biomedical literature from MEDLINE, life science journals, and online books. Medline is a database of the U.S. National Library of Medicine and includes over 17 million citations from life science journals related to biomedical, medical and clinical issues. Embase, published by Elsevier, contains over 11 million records with $500{,}000^{+}$ citations added annually. The Embase journal collection is international with over 5,000 biomedical journals from 70 countries. The use of these three major international

databases provides a comprehensive collection of peer-reviewed literature. Other sources included outside of the scientific databases included Google search, internal company presentations and conference material. The databases were searched over either a 5 year or 10 year period. The Literature Review Protocol and Report available in Appendix 1 outlines the search criteria and the inclusion/exclusion criteria as well as the results of the searches.

3.5 Case Study Mixed Methods

3.5.1 Regulatory Approval Case Review

A strategy that meets the needs of this research is an in depth case review. As discussed previously, the case study approach provides the focus that is required, emphasizes depth of study, is based on the assumption that reality can only be understood through social constructions and interactions, and that the context in which the phenomena under study is situated is complex (Biggam 2015). A case review of a recent medical device approval pathway in China was completed and will be presented and discussed. This strategy was chosen in order to complete a deeper analysis of a 'real life' device approval in China. This will be discussed in Chapter 5 as a comparative to the literature review and the data derived from other case study methods. To guide and control the focus of the case review a mini protocol was developed.

Table 3-2: Case Review Protocol

CASE REVIEW PROTOCOL
Purpose – Gather data from a specific real life example to answer the Research Question Research Question – What is the impact and challenges to product registration and market access in China as per the new regulations? What can the regulatory function do to ensure they create a successful regulatory strategy for Class II and Class III device approval in China that will aid market access? Unit Of Analysis – Regulatory pathway for approval of a medical device in China Boundaries – From device development to device approval in China Data Collection and Management Techniques – Collect the following data for review: • Early Regulatory Strategy Plans • Project Presentations developed for internal senior leadership • Presentations from Regional Subject Matter Experts

- Translated Regulations
- Email communications with geography colleagues
- Deliverables requested and provide to geography

Management of data:

- Align all data chronologically
- Categorise data into relevant sections/themes e.g. classification, type testing

Describe the Full Case –

Write up the case from my perspective as a regulatory professional managing device approval in China, outline:

- Device and Manufacturer Background
- Present case under relevant sections/themes

Analyse the Full Case –

Present key findings, outline:

- Challenges to registration
- Important considerations during registration

Recommendations –

Present recommendations based on the case review, outline:

- Important considerations for future registrations
- Suggested strategy to aid successful product approval and market access

3.5.2 Internal Industry Questionnaire

Regulatory senior leaders from various different business units within one multinational company were consulted on the main challenges they have encountered with gaining Regulatory Approval in China. This strategy was chosen to understand the regulatory challenges experienced for one multinational company. This will be discussed in Chapter 5 as a comparative to the literature review and the data derived from other case study methods.

3.5.3 Questionnaire with Industry Peers

Regulatory and quality professionals from various companies were surveyed on their perception and experience with regulatory approval and market access in China. This strategy was chosen for a broader understanding across different companies. The survey was provided to all students of the MSc. Medical Technology Regulatory Affairs and a number

of additional regulatory professionals. This was deemed appropriate as all students are working in industry in a scientific discipline. The companies of individuals in the survey distribution included but were not limited to the following – Boston Scientific, Medtronic, Johnson & Johnson, Nypro, Aerogen, Vistamed, Merit Medical, Teleflex, Fleming Medical and Filtertek. The findings are discussed in Chapter 5 as a comparative to the literature review and the data derived from other case study methods.

3.6 Data Collection

3.6.1 Regulatory Approval Case Review

A case study of a recent medical device approval pathway in China will be reviewed in detail. Internal documentation and communications will be collated, reviewed and summarised in order to accurately document the case study. The regulatory pathway will be structured in the applicable steps to get a medical device approved in China. For each step it will be detailed the strategy taken for this particular device and how this is in compliance with CFDA regulations and guidance. In addition to this, the learnings from the literature review will be applied to the case study. The key findings and challenges of the case study will be reviewed and other considerations for various scenarios documented.

3.6.2 Internal Industry Questionnaire

Regulatory senior leaders (Director Level and above) from various business units within a multinational company were contacted via email to outline their top challenges with gaining regulatory approval in China. The email communication was limited to one requirement/question only i.e. outline the challenges to regulatory approval in China. This was identified as the single most important question for senior leadership in order to answer the objectives of the dissertation. To ensure a detailed response and 100% response rate the request was limited to the one requirement/question. All data was collated, summarised and redistributed for review for consensus with the senior leaders. The summarised data was bucketed into common themes.

3.6.3 Survey with Industry Peers

Regulatory and quality professionals from various companies were surveyed on their perception and experience with regulatory approval and market access in China. The survey was created and distributed via Survey Monkey™. Survey Monkey™ is survey software

used within industry and academia; it is a professional and easy to navigate. The survey included a combination of both open and closed ended questions. Closed ended questions are questions where the participant chooses and answer and there is no follow up descriptive. Open ended questions are where participants are asked to answer a question with text. The majority of the closed ended questions in the survey included a text box where the participant could add text for a scenario not considered in the multiple choice options. The survey was limited to 10 questions and multiple 'tick box' options included ensuring a successful response rate by keeping the participant engaged over a short period of time. The survey was broken into several themes:

1) Workplace – Q1
2) Perception of China – Q1, Q2, Q3, Q4
3) Interaction with China – Q6, Q7
4) Challenges and Lessons Learned – Q8, Q9, Q10

The following questions were asked in the survey:

Table 3-3: Research Survey

No.	Question	Response	Question Type
1	What type company do you work for and what is the size of your Regulatory Affairs (RA) Department?	(Please select one option for the company size and one option for the RA Dept. size) - Small Company (< 50 employees) - Medium Company (>50<249 employees) - Multi National Company - Small RA Dept. (< 5 employees) - Medium RA Dept.(>5<20 employees) - Large RA Dept.(>20 employees) - Other - Please specify	Closed Ended
2	What is your perception of the importance to your business of accessing the Chinese market?	Scale – Not Important to Extremely Important	Closed Ended
3	What is your perception of the level of difficulty in gaining market access for a medical device in China?	Scale–Easy to Extremely Difficult	Closed Ended
4	What is your perception of	Scale–Easy to Extremely	Closed Ended

No.	Question	Response	Question Type
	the level of difficulty in gaining Regulatory Approval of a medical device in China?	Difficult	
5	Does your company have a local manufacturing facility within China?	Yes, No, Don't Know	Closed Ended
6	Has your company received approval for a device in China?	Answer Choices - Yes (as per new regulations in China – Order 650 in effect since 2014) - Yes (as per old regulations in China – Order 276 in effect since 2014) - Yes (as per new and old regulations in China – Order 650 and Order 276 respectively) - No - Don't Know	Closed Ended
7	Who is your local agent in China?	- Local Agent - Subsidiary of your company - Consultant - Don't know - Other – Please specify	Closed Ended
8	Can you rate your Top 3 challenges (as applicable) to receiving medical device approval in China?	- Local Clinical Trial Requirements - Compilation of China specific Clinical Evaluation Report - Submission Process for CFDA Review & Deficiencies - Compliance to China Specific Standards - Country Of Origin Approval Requirement - Understanding the Requirements - Other – Please specify	Closed Ended/Open Ended
9	Can you rate your Top 3 challenges (as applicable) to accessing the medical device market in China?	- Cost and Time for Regulatory Approval - Potential for Device 'Copying'	Closed Ended/Open Ended

No.	Question	Response	Question Type
		- Requirements for a large Marketing & Sales Team - Reimbursement Challenges - Other – Please specify	
10	What is the biggest lesson learned when dealing with the Chinese market?	Open Response	Open Ended

Convenience sampling was used to select the participants. The survey was distributed to all students undertaking the MSc in Medical Technology Regulatory Affairs both Year 1 and Year 2. It is convenient because of the access to the mailing list. Convenience would not normally be perceived to claim a representative view of the targeted population but the demographic of the MSc students suggests otherwise. The majority of MSc students are quality and regulatory professionals already working in the medical device industry. It is fortunate that the convenient sampling will also be representative of the wider population.

3.7 Data Analysis

As per (Creswell 2014)'*They found the purposes of mixed methods studies to be based on seeking convergence (triangulation), examining different facets of a phenomenon (complementarity), using the methods sequentially (development), discovering paradox and fresh perspectives (initiation), and adding breadth and scope to a project (expansion)'*

More than one technique was used as per the research strategy to allow for triangulation of results. Geertz (1973 cited in (Biggam 2015) said triangulation occurs when you use different sources of data to get a range of perspectives (particularly useful in qualitative research) and so achieve a more rounded picture, or 'thick description' of what you are looking at. An important part of this case study research is to analyse the case review data, comparing and contrasting different stakeholder perspectives obtained from the questionnaire/survey, and to reflect on the case study results with respect to the findings in the Literature Review. Figure 3-2 shows the flow of data analysis for the research question categories – challenges to product registration and market access, regulatory strategy, economic environment and changes in regulations. This figure also presents the comparative process for each category across the research methods used. In terms of data analysis, there will be a multi-pronged approach as follows -

For Research Question 1 – *What is the current economic environment for medical devices in China? What are the projections for the future state?* The case study findings as per the peer survey are described and analysed (Perception of China – Q1, Q2, Q3 and Q4). A comparative and contrast was made between the literature review findings and the peer survey findings.

For Research Question 2 - *What has changed in the medical device regulations in China, with the updated regulations enforced in 2014?* No further data was required in addition to the literature review documenting the changes in regulations

For Research Question 3 - *What is the impact and challenges to product registration and market access in China as per the new regulations?* The case study findings as per the case review, senior leadership questionnaire and peer survey (responses for Challenges and Lessons Learned – Q8, Q9, and Q10) were described and analysed. A comparative and contrast was made between the literature review findings and the case study findings.

For Research Question 4 - *What can the regulatory function do to ensure they create a successful regulatory strategy for Class II and Class III device approval in China that will aid market access?* The case study findings as per the case review, senior leadership questionnaire and peer survey (responses for Challenges and Lessons Learned – Q8, Q9, and Q10) were described and analysed. A comparative and contrast was made between the literature review findings and the case study findings. This analysis provided the source for recommendations.

The essence of this qualitative analysis paradigm reflects accepted practice in dealing with qualitative data, and is perhaps more succinctly described by Bogdan and Biklen (1982) cited in (Biggam 2015) as ‘working with data, organizing it, breaking it into manageable units, synthesizing it, searching for patterns, discovering what is important and what is to be learned, and deciding what you will tell others’.

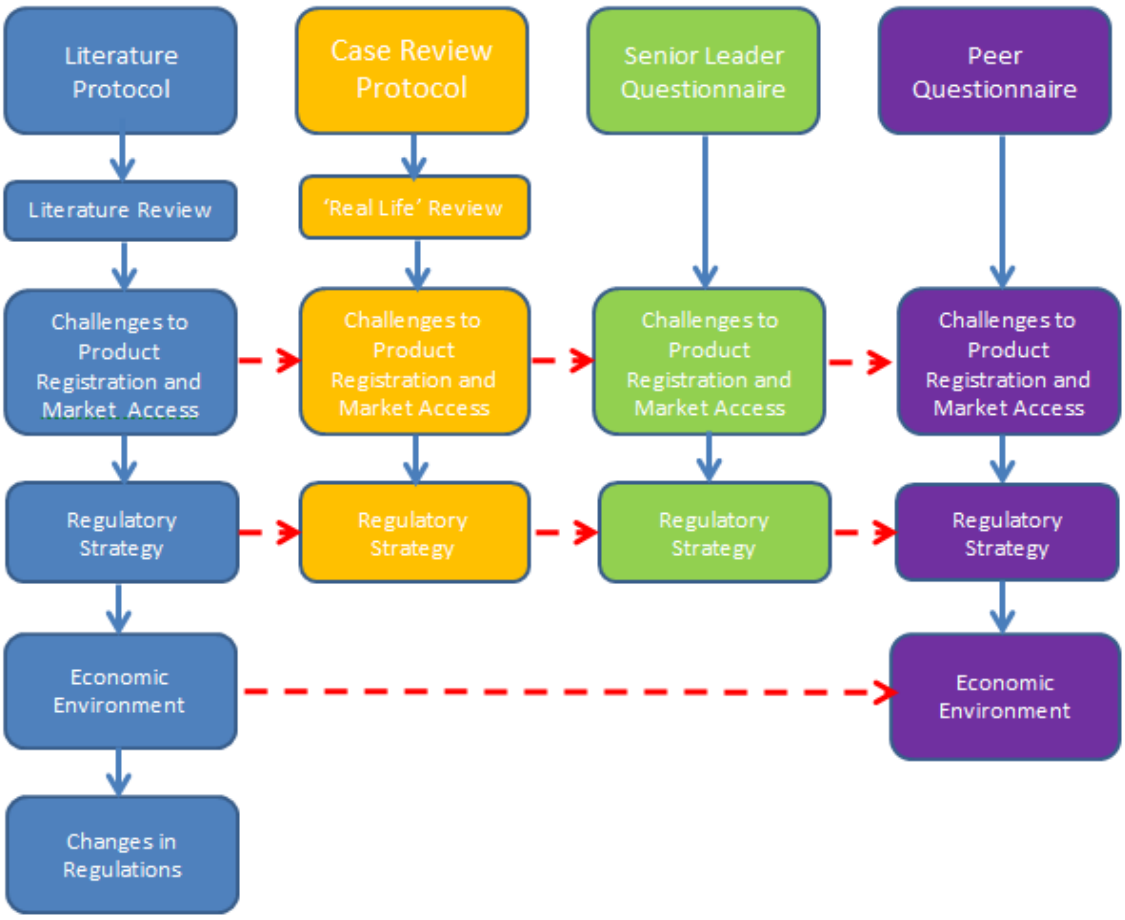

Figure 3-2: Data Analysis Flow chart

3.8 Limitations and potential problems

At a general level, mixed methods is chosen because of its strength of drawing on both qualitative and quantitative research and minimizing the limitations of both approaches (Creswell 2014). This section outlines the limitations associated with case study research and the survey data collection tool.

There are certain limitations that are inherent in case study research as well as issues related to completing a case study within a workplace where one is employed. The case study is limited by the fact it is based on the experiences within one Multi-National company. The case review is based on one specific device at one point in time. The Senior Leader questionnaire is from leaders within one company. To prevent bias seven leaders views were collected on the same issue each leader being responsible for different product lines. The mixed method approach was used to overcome this limitation and allow for generalisation across Multi-National companies. However, generalisation across other type companies would be difficult to ascertain.

The peer survey data collection tool used – Survey Monkey™ facilitates data collection from the identified participants. Although the peer survey has been identified as a quantitative tool the number of participants contacted to complete the questionnaire is not a statistically relevant sample size. This sample size was limited due to the difficulty in accessing contact lists for regulatory professionals working in Ireland. It was also deemed unreasonable to try and contact regulatory professionals who have direct experience with China as this is a relatively small subset within medical devices, The survey is reliant on the respondents underpinning knowledge either directly or indirectly. The survey is limited by the fact that it does not facilitate in-depth investigation with respondents, as in the case of individual interviews or focus groups.

4.0 Findings and Results

4.1 Introduction

This chapter presents the finding and results of the research strategy as per the methods set out in Chapter 3. In addition to the extensive literature review carried out in Chapter 2 the case study research methods are as follows:

1. Analysis of a sample product case review to discuss the challenges and considerations for medical device registration under the new Chinese regulations and the Strategic Regulatory Planning involved for getting the product to market in China
2. Questionnaire for internal multi- national medical device company senior regulatory leaders to understand their challenges with China's regulatory approval process
3. Questionnaire/Survey to understand Regulatory professionals perception and experience of the medical device registration process in China and market access to China

4.2 Case Study

The case study concentrates on the regulatory pathway in China for one specific medical device (catheter based technology) which was approved in 2016 as per the new China regulations implemented in 2014. The case study presents the steps taken and findings as experienced during the regulatory approval pathway.

4.2.1 Case Study Device Background

The medical device which was the subject of this case study was a catheter based technology widely used in the cardiovascular field, hereinafter referred to as the 'catheter'. This device is approved for sale in the EU and is classified as a Class III device; it is also cleared for sale in the US and is classified as a Class II device in the US. The manufacturing site was not EU or US based but was ISO 13485 certified. This device is a next generation device with a number of design upgrades on an existing device which is already approved in China. This catheter type has been on the market in China for several years with various foreign and domestic manufacturers approved in China. At present, the Chinese market is both dominated by foreign companies, such as Medtronic, Abbott, Boston Scientific, Goodman, Terumo, etc. and local Chinese companies including Lepu Medical, MicroPort, JW Medical, Yinyi, Neich Medical (Shenzhen), Synexmed, Sino Medical and Demax Medical (China 2014).

4.2.2 Step 1 - Device Classification

The first step in determining the regulatory pathway for the catheter device was to classify the device. CFDA published medical devices classification rules which were implemented in 2016 however this did not alter the original classification of the device identified in 2014. The new rules follow much of the precedents of the GHTF rule set, but with some significant differences – not least of which is that they are applied by the regulator and not by the manufacturer. The Rules for classifying your medical device are laid out in Decree No.15 of China Food and Drug Administration - Rules for Classification of Medical Devices (CFDA 2015). According to degree of risk (from low to high), the management classifications of medical devices are divided into class I, class II and class III in due order. As per Article 4 of Decree No.15 (2015) – 'the risk degree of a medical device shall be determined comprehensively according to the intended purpose, structural characteristics, pattern of use, status of use as well as whether the device is body contacting'.

Applying the new classification rules the catheter device in question is a non-active device which is invasive to the body to be used in the coronary vasculature. The following definitions as specified in Decree No.15 are applicable to the device and were used to retrospectively apply the classification prior to registration application.

Non-active medical device - A medical device of which the effects are achieved not relying on electric or other forms of energy, but may use the energy directly generated by human body or gravity.

Invasive device - A medical device which is wholly or partially inserted into human body through body surface by way of surgery, and contacts such parts as tissue, blood circulation system and central nervous system. It may include an interventional operation instrument, a disposable sterile surgical device and a device which may remain in human body temporarily or for a short term, etc. The invasive device in the Rules does not include a reusable surgical instrument.

Body-contacting device - A medical device that directly or indirectly contacts or can be inserted into the body of the patient.

Service life Temporarily - The intended continuous service period of medical device is less than 24h.

Blood circulation system - Blood vessels (except the blood capillary) and the heart;

See Figure 1 below for the Classification Table. The device is a Class III device in China; therefore it is classified as a High Risk device and will adhere to the strictest registration requirements.

Body-contacting device											
		Status of use / Patterns of use	Temporary use			Short-term use			Long-term use		
			Skin /Orifice (openings)	Trauma /Tissue	Blood circulation /Central	Skin /Orifice (openings)	Trauma /Tissue	Blood circulation / Central	Skin/Orifice (openings)	Trauma /Tissue	Blood circulation / Central
Non-active device	1	Liquid transportation device	II	II	III	II	II	III	II	III	III
	2	Blood and other body fluids alternation device	–	–	III	–	–	III	–	–	III
	3	Medical dressing	I	II	II	I	II	II	–	III	III
	4	Invasive device	I	II	III	II	II	III	–	–	–
	5	Reusable surgical device	I	I	II	–	–	–	–	–	–
	6	Implantable device	–	–	–	–	–	–	III	III	III

Figure 4-1: Table for Determination of Medical Device Classification

In addition to the classification rules set out in Decree No.15 CFDA have released a long-anticipated draft Classification Catalogue of Medical Devices. The Draft Catalogue updates a 2002 Classification Catalogue and is one of the final pieces in the reform of China's medical device system that has taken place since the 2014 revision of the framework regulation — the Medical Device Supervision and Administration Regulations (MDSAR) (Zhao and Balzano 2016). CFDA reviews the Class II and Class III imported medical device and issue the medical device registration certificate upon the approval.

4.2.3 Step 2 - Product Technical Requirement

The Product Technical Requirement (PTR) is a test protocol that is used by China type testing laboratory to test medical device samples. It is one of the key documents based on which CFDA Medical Device Technical Evaluation Center (CMDE) will perform their review of the product application and it also forms the basis of sampling when CFDA or provincial FDA conduct post-market quality inspection. A PTR should include the functional parameters which reflect the product features and the various performance

parameters and characteristics which shall have or shall reach to achieve the intended use of the device as well as the test methods, and meeting the requirement posed by relevant China mandatory and/or recommended standards. Medical devices marketed in China must be compliant with the PTR approved by the China regulator through the filing or registration process.

The PTR for the catheter device was developed during the Product Development Process (PDP). Business unit regulatory and China regulatory worked with the PDP team to develop the PTR. This device is a next generation device for a catheter device already approved in China. The PTR for the predicate device was the starting point in creating the PTR; however Regulations and Standards had changed in 2014 so this had to be factored into the new PTR. The PDP team were reliant on China RA to advise the applicable testing and standards and the business unit team to review against the Product Performance Specifications. CMDE do not review the PTR before testing, therefore type testing is completed on the draft PTR provided by the manufacturer.

The Product Technical Specifications should include the following:

- List all required performance specifications and safety specifications for the finished product.
- List testing methods for each specification.
- Type Testing is required for all specification items listed in this file with the method described

The Chinese standards system is administered by the Standardization Administration of the People's Republic of China (SAC), a governmental organization under the General Administration of Quality Supervision, Inspection and Quarantine of the People's Republic of China (AQSIQ). Chinese Standards can be either mandatory (i.e. compulsory, required by the Chinese government), or voluntary (encouraged or recommended, but not required by the Chinese government). Products sold in the Chinese market are generally required to have a label indicating which standards have been followed. In addition to national standards, companies may also need to follow Industry Standards. It is advised that you consult with your local contact to understand which standards need to be followed for your device and how and to obtain copies of these standards. SAC maintains a database of all

Chinese National GB Standards, which is searchable in English or Mandarin (ANSI 2017). CFDA does keep the database for industry (YY) standards, but not the national (GB) standards (Biomedical 2016a).

National Standards are consistent across all of China and are developed for technical requirements. Many Chinese national GB standards are adoptions from ISO, IEC or other international standards developers. China has also expressed a goal of significantly increasing the number of standards that are adoptions of international or advanced foreign standards. The database of Chinese national GB standards provides information on which standards have been adopted (ANSI 2017). Table 4-1 lists some of the standards required to be met by the case study device and the comparative ISO standard is applicable.

Table 4-1: Chinese Standards

ISO Standard	Chinese Standard	Standard Name
ISO 10555-1	YY 0285.1-2004	Sterile, single-use intravascular catheters—Part 1:General Requirements
ISO 14233	GB/T 14233.1-2008	Test methods for infusion transfusion injection equipments for medical use - Part 1: Chemical analysis methods
ISO 594-1	GB/T 1962.1-2001	Conical fittings with a 6%(Luer) taper for syringes, needles and certain other medical equipment--Part 1:General
N/A	GB/T 14233.2-2005	Test methods for infusion, transfusion, injection equipment for medical use-Part 2: Biological test methods
ISO 10993-1	GB/T 16886.1-2011	Biological evaluation of medical devices—Part 1:Evaluation and testing within a risk management process
ISO 10993-4	GB/T 16886.4-2003	Biological evaluation of medical devices--Part 4:Selection of tests for interactions with blood
ISO 10993-5	GB/T 16886.5-2003	Biological evaluation of medical devices--Part 5:Test for in vitro cytotoxicity
ISO 10993-10	GB/T 16886.10-2005	Biological evaluation of medical devices-Part 10:Tests for irritation and delayed-type hypersensitivity
ISO 10993-11	GB/T 16886.11-2011	Biological evaluation of medical devices—Part 11:Tests for systemic toxicity

Compliance to the Product Technical Report does not stop at approval of a medical device. The manufacturer needs to meet these requirements routinely. Any changes to the content in PTR would trigger a product change application. If there are any adverse events, injury incidents or lawsuits, the first thing CFDA or court will do is to check if your product still meets the PTR. If not, there could be significant consequence. "Non-Conforming" product is regarded as "Non-approved" products (Brandwood Q&A 2016).

4.2.4 Step 3 - Local Agent located in China

The case study company have a well-established local agent in China. This representative serves as the required local entity that deals with the China Food & Drug Administration (CFDA) regarding product registration and renewal, adverse event reporting, etc.

In Order No. 4 Administrative Measures for Medical Device Registration (CFDA 2014b) CFDA has listed the duties of foreign manufacturers' authorized representatives, known as Legal Agents, as follows:

- Managing communications between Chinese regulators and market entry applicants (manufacturers)
- Forwarding all regulatory and technical requirements to applicants
- Collecting post-market adverse event data and providing that information to applicants and regulators
- Coordinating recalls when necessary and reporting information to regulators
- Managing product quality and after-sales service activities

(EMERGO 2017c)

There are three local agents required:

1 .Registration Agent: The Company that registers the product is the registration agent.

2. After Sales Agent: The after sales agent provides technical service and support for the medical device product. The business scope described in the business license of the local legal Chinese entity must include a provision stating that the after sales agent will provide such services.

3. Legal Agent: The legal agent's key responsibilities include: a) reporting any adverse events regarding the medical device that occur inside or outside China to the CFDA; and b) handling any recall issues as they arise, as well as other regulatory matters (Medical 2017a).

Local Agent Key Points

An independent third party allows for confidentiality of technical information and less reliance on a distributor, whose primary motive may only be sales. In cases where your distributor is acting as your local agent, if your distributor does not perform well and you wish to end the relationship, the distributor may attempt to charge a large fee to transfer the existing registrations or refuse to transfer them at all (Medical 2017a).

4.2.5 Step 4 - Local Type Testing

For Class III devices, CFDA requests samples for type testing. The testing centers will use the product standard to determine what tests to conduct. Testing centers will test all specification items listed in the Product Technical Specifications as drafted in Step 3. For each specification item, testing centers will utilize the testing method described in the Product Technical Specifications. While conducting the tests, the CFDA requests that testing centers provide comments on the company's drafted Product Technical Specifications. The comments from the testing center should be submitted together with the testing report to avoid repeats and additional testing, which occurs frequently, leading to long delays in the registration process (Medical 2017b).

The testing report will be issued by a CFDA certified national testing center, which can be freely selected from the CFDA list. It is only valid for 1 year, and once it expires, a company must start again to obtain a new valid testing report. There are 10 national testing labs around the country that are CFDA certified:

- National Testing Institute (Beijing)
- Beijing Testing Institute
- School of Dentistry, Beijing University ("Beida")
- Shanghai Testing Institute
- Jinan Testing Institute
- Shenyang Testing Institute
- Tianjin Testing Institute
- Wuhan Testing Institute
- Hangzhou Testing Institute
- Guangzhou Testing Institute

The case study company chose one of the above based on historical use.

Type testing can take over 6 months to complete and then the type test report is valid for one year only so it was important that a strategy was put in place to ensure the units were shipped to China at the appropriate time for when the business wanted to pursue approval in China. For the catheter device the China market is important and there was no delay in pursuing this market. Type testing devices were shipped to China as soon as possible due to the lengthy test time. Type testing units must be the final design of the device and final labelling; the product must represent the final configuration intended for the future China market, The product configuration covers the product itself (specs, TM's, etc.), the packaging, and the labeling. It was decided to ship the type test units post Design Verification testing of the device; this would ensure that we provided a product that was representative of the product intended for market in China. An internal process was followed to ensure the product was able to move through customs in China. As this product is unapproved and intended for testing only, it was labelled accordingly. The type test centre repeated all performance related tests. In a case where the type test centre is not capable of conducting certain test they may accept the applicant's in-house test result. This would be the Design Verification testing and should align with the "representative model" submitted to the type test centre. The type testing completed for this device did not rely on any testing completed in-house but when deciding on the Representative Product Model (normally one size only) for China type testing, we considered what models were tested during Design Verification. During the type testing at the centre a number of minor queries were relayed back via the China contact. It is also common that the type test centre will require support from the manufacturer's technical product experts in China in order to complete the testing. All testing was successfully completed and the test report issued.

4.2.6 Step 5 - Clinical Trial Requirements

To determine whether local clinical trials are needed for your medical device in China, the classification of the device must be determined. As per Step 1 Device Classification the catheter device is a Class III device in China. Class I medical devices do not require local clinical trials. Class II and Class III medical devices do require clinical trials unless they have exact predicates and/or are in the CFDA's clinical trial exemption list. The devices on

the list will gain automatic exemption from doing a local clinical study in China or needing to do a full clinical evaluation. Instead, the enlisted device manufacturer only needs to identify a substantial equivalent device which is already marketed in China then make a comparison table for this substantial equivalent device. This approach significantly reduces the efforts and cost of bringing the device into China market (Wen 2016). If your product is not on the exemption list, but has sufficient evidence on a predicate device substantially equivalent device then you can submit a clinical evaluation report (CER) (Biomedical 2016b).

The Wave 1 of this exemption list had been put into effect on Oct 1, 2014 along with the new medical device registration rule Order No. 4. There were 488 Class II and 79 Class III devices on the Wave 1 list. The catheter device did not appear on Wave 1 of CFDA's clinical trial exemption list. As per the regulatory strategy developed in 2014, it was determined that a comparison with our own exact predicate substantial equivalent device would be required to negate a local clinical trial. As per the 'Technical Guidance on Clinical Evaluation of Medical Devices' the definition of equivalent medical device is as follows –
"The equivalent medical device refers to the device that has obtained domestic registration approval and is substantially equivalent to the device under application in aspects of basic principles, structural composition, manufacturing materials (manufacturing materials that come into contact with the human body for active devices), manufacturing process, performance requirements, safety evaluation, conformed national /industry standards and expected use.
The device under application can be considered as substantially equivalent with the equivalent medical device in the case that no adverse effects on the safety and effectiveness of the device are caused by the differences between the two devices."

A comparison was presented in the China specific Clinical Evaluation Report. The China specific CER was developed in accordance with the draft 'Technical Guidance on Clinical Evaluation of Medical Devices'. The final document published in 2015 sets out the requirements for the CER in Annex 8. The technical guidance outlines the requirements for 1) the clinical evaluation for the products listed in the catalogue of medical devices exempted from clinical trial and 2) the clinical analysis and evaluation based on data obtained from clinical trial(s) or clinical application of the equivalent medical device.

In order to prove the safety and effectiveness of the catheter device which was the device under application utilizing the data from the clinical application experience of an equivalent medical device, we needed to compare the catheter device with an equivalent medical device and prove the substantial equivalence between the devices. As the catheter device was a next generation device, the previous generation device which was approved for sale in China was used as the equivalent device. Annex 2 of the Guidance was followed to incorporate all the comparison items including qualitative, quantitative data, verification and validation results. The similarities and differences between the two products were described in detail. Where there were differences with the catheter device under application it was confirmed based on the data presented that the differences did not result in any negative impact on the safety or effectiveness of the device. See Figure 4-2 extracted from Annex 4 of the Guidance explaining the evaluation pathway. The data presented included non-clinical studies, clinical literature, clinical experience, and clinical trials conducted in China to address any differences.

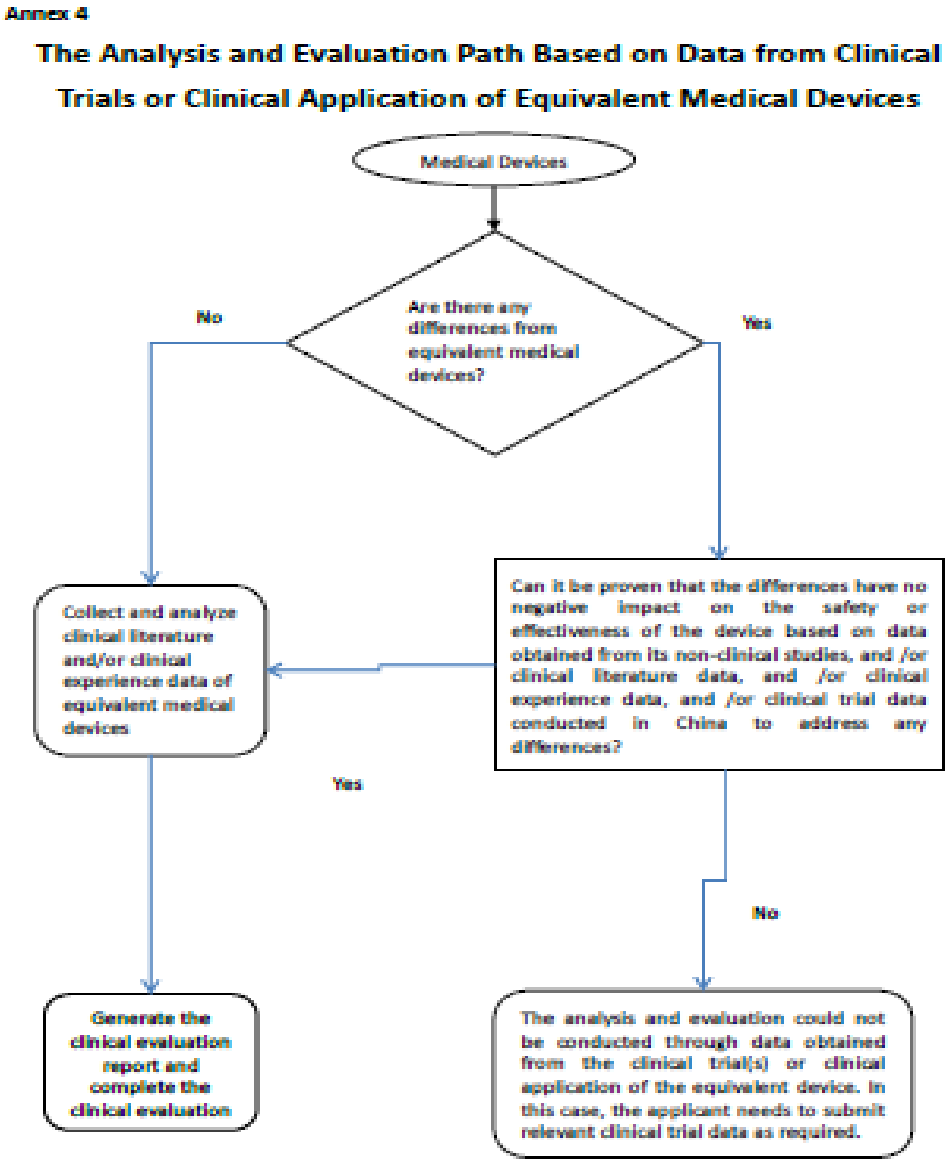

Figure 4-2: Clinical Evaluation Path as per Annex 4

On May 20, 2016 CFDA published Wave 2 the draft of the Exemption list of Class II & Class III device for local clinical study. There were 259 Class II devices and 93 Class III on the Wave 2 exemption list. The wave 2 exemption list was reviewed to see if the case study device was listed (Wen 2016). CFDA requested feedback from industry on the draft list. On the 30th September 2016, CFDA published the updated exemption list of Class II and Class III devices for local clinical study. Examples of devices included in the new exemption list included surgical instruments, silicone breast implants, pen injectors, endoscopy and

bronchoscopy devices, various ultrasound diagnostic imaging equipment and a wide range of dental equipment and devices (Tserng 2016). The case study device was included on the exemption list.

If your product is on the exemption list, there is no need to conduct clinical studies or provide a clinical evaluation report, you just need to justify your product is exactly matching the definition set in the exemption list and make a simple comparison to a marketed predicate device (Biomedical 2016b). When the Wave II exemption list was published, CFDA had already completed the technical review for the case study device post deficiency letter responses and the submission had moved to administrative review.

4.2.7 Step 6 - Country of Origin

As per Article 13 of Order 4 Provisions for Medical Device Registration – 'the imported medical device applied for registration or filing shall have been proved for market at the country (region) of the registration place or production address of the applicant or the person who files for record'. The Country of Origin (COO) for the device is outside the EU and US. A pre-requisite for device registration in the COO is EU Approval. Post EU Approval, the registration application was submitted to the COO. It took six months for Regulatory Approval of this device in the COO. Proof of authorisation for sale of device in the Country of Origin was required for the application dossier i.e. a Cert of Free Sale from the COO. A Cert of Free Sale was issued by six weeks post regulatory approval.

4.2.8 Step 7 Application Dossier

Once all the pre-requisites to application as outlined above were completed, the application dossier was prepared for submission. A total of 12 document items must be collected and submitted to the CFDA consisting of 9 legal documents, 2 technical documents, and a testing report issued by a CFDA certified testing centre. See Table 4-2 for the requirements of the Application Dossier.

Table 4-2: Application Dossier

1	Application Form
2	Legal Documents
3	Main Safety and Efficacy Specifications List
4	Summary Data • Overview • Product description • Product model • Description of the package • Intended use and contraindications • Predicated device (if applicable). • Other information
5	Research Data • Product performance evaluation data • Biocompatibility evaluation data • Biosafety research data • Sterilization and disinfection process validation data • Shelf and package evaluation data • Animal research data • Software validation data • Other data if necessary
6	Manufacturing information • Manufacturing process description for active/inactive device • Manufacturing site description
7	Clinical Evaluation Data
8	Product Risk Analysis Data
9	Product Technical Specifications
10	Registration Testing Report • Testing report issued by a CFDA certified lab • Preliminary evaluation comment from the testing lab
11	Artwork for the IFU and Product Label • Instructions for use (IFU) • Artwork of the product label for the minimum selling unit
12	Self-declaration Documents

As per Article 12 of Order 4 Provisions for Medical Device Registration the application filing was in Chinese, with the English originals also provided as the deliverables had been translated. The CFDA forwarded the application to CMDE for review where there is an allowance of 90 working days to complete the initial technical review.

4.2.9 Step 8 - Application Review with CFDA

The initial application was submitted in August 2015 and the Deficiency Letter response was received in December 2015, approximately 90 working days post submission and in line with the regulations.

Figure 4-3: Catheter Device China Submission Timeline

Deficiency Letter:

The deficiency letter was issued by CFDA approximately five months post initial submission. The letter was translated to English for the business unit team to work on the responses. A summary of the key subject matter of the questions within the deficiency letter is provided below in Table 4-4.

Information Requested
Clinical Evaluation
Product Technical Requirements versus Product Performance Specification
Supplier Purchase Agreements, COA's, Specifications
Supplementary Type Testing
Biological Test Reports
Chinese Trade Name Detail
Percentage of each Ingredient in Mixtures, Indicate pigment , dye, solder, and additive
Engineering Structure Schematics
Design Verification (including sample size, statistical method, test method & deviations)

Figure 4-4: Deficiency Letter Subject Matter

A cross functional team was assembled to work on the responses, this included Clinical, Design Assurance, R&D, Biocompatibility, China Regulatory and Business Unit Regulatory. A number of the questions were unclear on the intent so CFDA were consulted on the requirement for these particular questions. In 2015 and 2016 CFDA allowed face to face consultation on Thursday of every week. The China Regulatory representative used this 'open day' to consult with the CFDA reviewer. The singular most burdensome activity to support the deficiency letter response was the CER update. The China specific CER which was submitted as per the original application was in accordance with draft Guidelines. The final document 'Technical Guidance on Clinical Evaluation of Medical Devices' set out the requirements for the CER in Annex 8. The clinical team updated the CER as per the Annex 8 requirements, in addition to bridging the literature review and post market surveillance data since the initial release of the CER.

The deficiency letter responses were finalised and individually signed by Regulatory Management, notarised and forwarded to the China Regulatory contact for translation to Chinese prior to submission to CFDA. It took six months to finalise the responses. CFDA only issue one deficiency letter per product submission and allow for a maximum of one year for a response. If there is no response from the applicant in the one year timeline the technical review is terminated and a proposal forwarded to CFDA to refuse the application.

After the deficiency letter responses were submitted to CMDE the technical reviews continues for up to 60 working days. The technical review was completed approximately in line with the 60 working day review timeline. The submission then moved to the administration review. The administration review takes 20 days with a further 10 days required for licence printing post the approval decision. Final approval and the subsequent licence were issued as per CFDA's timelines. It took a total of 16 months from the initial submission to gain approval in China.

Application Review Key Findings

- Increased criticality of this process due to the one deficiency letter process. If the response is rejected we are back to the start.

- Access to reviewer is difficult, limited interaction increases the timeline on finalising the deficiency letter response
- Lack of clarity on questions received. The CFDA reviewer is vague regarding their requirement for some of the questions. We are unsure of the adequacy of the responses until the CFDA reviewer has commented.
- Iterative process to finalise the response, the expectation being that the CFDA reviewer will request more information as the review process continues.
- Cross functional team required to support the Deficiency Letter Response, difficult to resource. Need to reiterate criticality of these activities with the functions in order to provide support.
- Large Quantity of information required to be compiled to respond to the deficiency letter. We may see an impact with regard to post approval changes due to the increased scope of the submission

4.3 Senior Regulatory Leadership Consultation Finding and Results

Table 4-3 below outlines the collated feedback from Senior Regulatory Leaders in a large Multinational company. The challenges were categorised into common themes - Local Clinical Trials, Clinical Evaluation Reports, Unique Device Identifier, Country Of Origin Approval, China Specific Standards, Type Testing, Submission Process and Deficiency Letter.

Table 4-3: Regulatory Challenges as per Senior Leadership

GREATEST REGULATORY CHALLENGES IN CHINA - AREAS FOR ADVOCACY FOCUS FEEDBACK
Local Clinical Trials
Clinical Trial Exemption lists are not risk-based and have changed several times since the regulation was announced and many of our products are not exempted. A Clinical Trial Application (CTA) must be approved before the trial can begin in China.
There are other clinical trial exemptions offered by CFDA, based upon “substantial equivalence” to a device currently on the China market. The requirements to establish substantial equivalence are vague.

The requirements to submit the CTA are quite burdensome, including approval in the Country of Origin.
The requirement for local clinical trials extends time-to-market and delays access of medical technology.
Clinical Evaluation Reports (CER)
CER's used to support CE mark do not meet Chinese requirements. The preparation of CER's specifically for China is burdensome.
China specific CER's for Class 1 products may be required which are not currently required in the EU
CER is burdensome in the management of the preparation, the Chinese literature search is translated from Chinese to English and then back to Chinese for CER submission.
Unique Device Identifier (UDI)
China CFDA plans to require UDI. Industry would want UDI to be consistent with what the US—and other regulated nations—will require.
It is unknown what China will require for UDI. The history of releasing requirements with very short time before they go into force would be quite burdensome in the case of UDI.
County of Origin Approval
COO requirement is difficult in a global economy. This requirement extends time-to-market and delays access of medical technology.
COO approval is now needed before the local CTA commences.
COO Approval is required prior to submission. To gain approval in COO, approval in the EU, US may be required. All the pre-requisite events increase timelines and ultimately extend time to market. Given the application is assessed entirely on its own merits the need for approvals in other countries appears redundant. Also, some of these pre-requisites to filing exist for other major markets including US, Europe and Japan.
China Specific Standards
As per the revised regulation, CFDA requires compliance with specific Chinese standards instead of international (ISO) standards. This creates challenges for the BU product development teams to know the standards to which they must build and test devices. Project teams need to assess completing Mitigation Testing for new devices as per China National Standards

In renewal applications, the CFDA requires the business unit RA team to certify in writing that the device meets the Chinese standards. This is challenging for the business units which do not have knowledge of the Chinese standard. RA have to sign for compliance to Chinese standards based on China RA's confirmation that the standards had been met. The issue here is access to Chinese source/supportive documentation for sign-off by the RA.
Challenges for the BURA as standards/ expectations changed since last renewal. Type testing was required to be completed to meet new requirement as per Chinese standard, therefore extending the renewal process.
Type Testing
The tests chosen for type testing are not appropriate for the device being evaluated. As a result, there may be failures in these tests during type testing in China, preventing a device from entering the China market.
As it relates to type testing, and the need to proactively address new standards through leveraging our R&D support and building relationships with the testing labs.
Generation of erroneous data at type testing facilities is routine for novel devices leading to test engineers having to fly to China test labs to support testing.
Submission Process
The China PTRs (Product Technical Requirements) used with products are considerably inconsistent with our Technical Specifications requiring a significant amount of time for RA Specialist to track down the appropriate information to move the submission process forward.
There is no ability to implement changes during review (CFDA will not accept changes, need to repeat type testing etc.). Given that the cycle in China can be ~5 years, iterations are inevitable so businesses have to continue with a product that is several generations behind.
The process does not benefit Chinese patients. Time to market for new technology is significant.
There is a huge issue with lack of a formal consultation or pre-sub process. There is informal feedback every Thursday at CMDE which is useful, but on major strategies the feedback is only 1 person's opinion and isn't binding.
Conflicting feedback from sources on something where the guidance is actually apparently clear. The implications are huge and there is no formal way to clarify. A pre sub process would help enormously.
Access to the reviewer is difficult, as China RA can only meet the reviewer on the open day, which is Thursday of every week.

Submission Process - Deficiency Letter
The 'one strike you're out'/"one chance only" rule for the deficiency process is unmanageable. It's impossible to get an original application through the review process without any questions.
Reviewers are now starting to place phone calls to ask for additional information outside the timeframe of providing deficiency reports. This is also becoming a major issue.

4.4 Peer Survey Findings and Results

4.4.1 Introduction

Regulatory and quality professionals from various companies were surveyed on their perception and experience with regulatory approval and market access in China. The survey was created and distributed via SurveyMonkey™. The survey was forwarded to approximately 48 individuals. A total of 28 individuals participated in the survey; therefore there was an approximate response rate of 58%. All responses were anonymous. The combined results from SurveyMonkey™ are available in Appendix C. The survey results are presented below for each question. The results will be further analysed in Chapter 5 Analysis and Discussion.

4.4.2 Survey Response Q1

Table 4-4 below outlines the question, response options and number of respondents (n) for Question No.1a and 1b. The pie charts as per Figure 4-7 presents the overview of the workplace for the respondents who took part in the survey, including the company type and the size of their Regulatory Affairs Department.

Table 4-4: Q1 – Question, Response and Number of Respondents

No.	Question	Response	n
1a	What type company do you work	(Please select one option for the company size and one option for the RA Dept. size) - Small Company (< 50 employees) - Medium Company (>50<249 employees) - Multi National Company - Other - Please specify	27
1b	What is the size of your	- Small RA Dept. (< 5 employees)	18

No.	Question	Response	n
	Regulatory Affairs (RA) Department?	- Medium RA Dept.(>5<20 employees) - Large RA Dept.(>20 employees) - Other - Please specify	

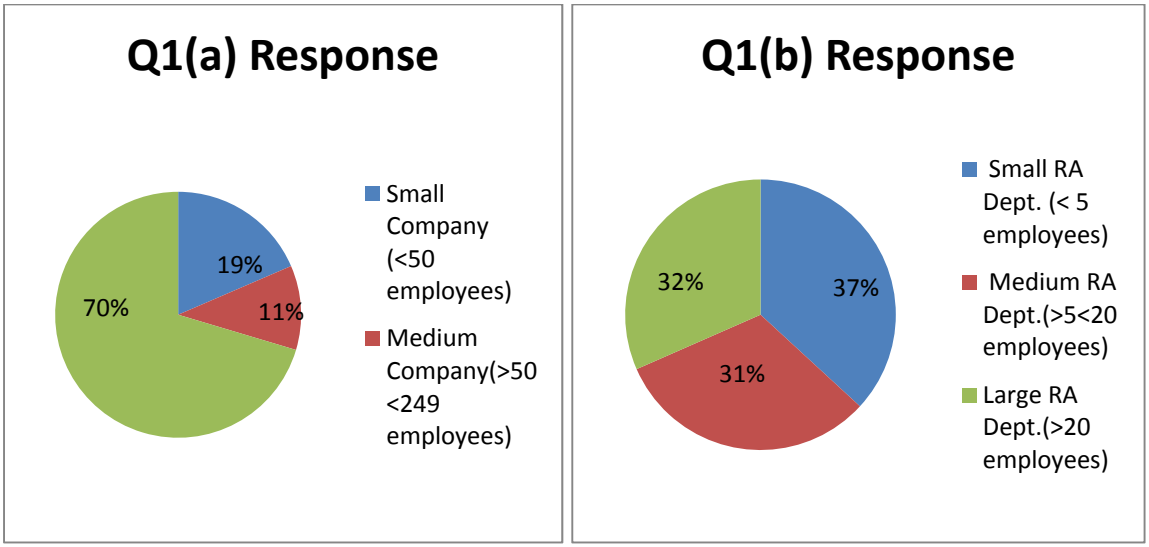

Figure 4-5: Response Percentage Breakdown for Q1a Response and Q1b Response

Three responses were included in the 'Other- Please Specify' category. Responses as follows:

- Not in RA
- Regulatory department is based in corporate divisional HQ in the US. We have only one regulatory specialist on site who reports into Corporate HQ
- Large multinational

On the basis of these responses and further review of individual responses, the response count for Q1.b was updated by 1 for the individual who specified they had one regulatory specialist onsite for their response. The response rate for Q1.b was lower than expected. Incorporating two parts to one question in the survey may have caused confusion and the respondent proceeded to Q2 after answering Q1a.

4.4.3 Survey Response Q2

Table 4-5 below outlines the question, response options and number of respondents (n) for Question No.2. The bar chart as per Figure 4-8 presents the percentage of overall responses for each category.

Table 4-5: Q2 – Question, Response and Number of Respondents

No.	Question	Response	n
2	What is your perception of the importance to your business of accessing the Chinese market?	- Extremely Unimportant - Unimportant - Moderate - Important - Extremely Important	28

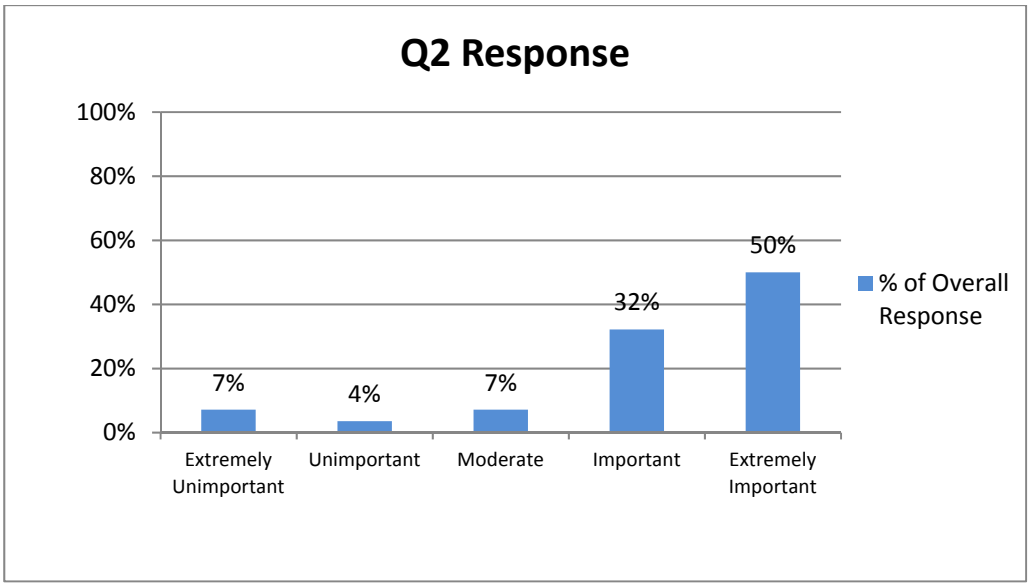

Figure 4-6: Response Percentage Breakdown for Q2 Response

4.4.4 Survey Response Q3

Table 4-6 below outlines the question, response options and number of respondents (n) for Question No.3. The bar chart as per Figure 4-9 presents the percentage of overall responses for each category.

Table 4-6: Q3 – Question, Response and Number of Respondents

No.	Question	Response	n
3	What is your perception of the level of difficulty in gaining market access for a medical device in China?	- Extremely Easy - Easy - Moderate - Difficult - Extremely Difficult	28

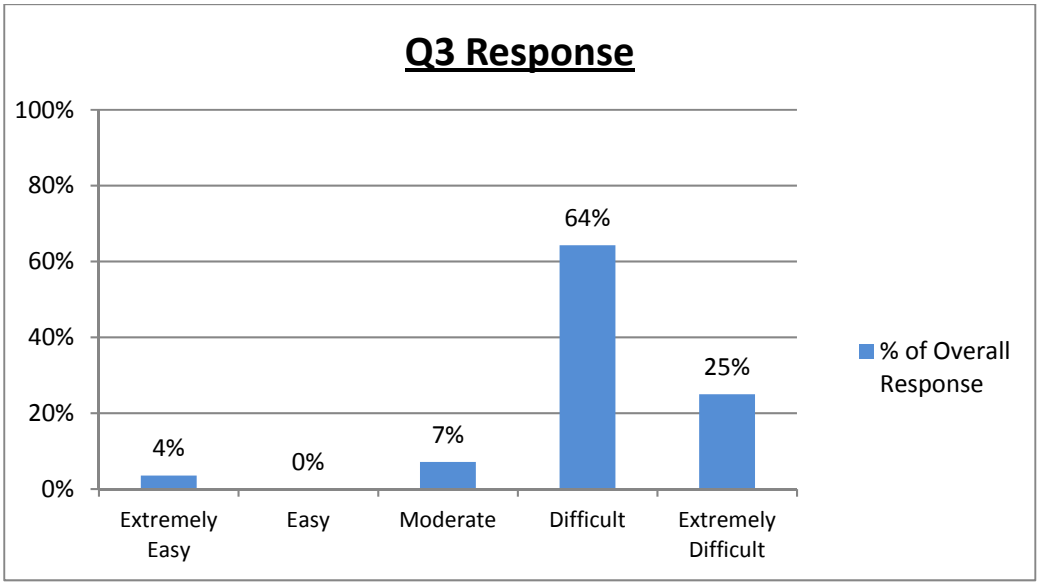

Figure 4-7: Response Percentage Breakdown for Q3 Response

4.4.5 Survey Response Q4

Table 4-7 below outlines the question, response options and number of respondents (n) for Question No.4. The bar chart as per Figure 4-10 presents the percentage of overall responses for each category.

Table 4-7: Q4 – Question, Response and Number of Respondents

No.	Question	Response	n
4	What is your perception of the level of difficulty in gaining Regulatory Approval of a medical device in China?	- Extremely Easy - Easy - Moderate - Difficult - Extremely Difficult	23

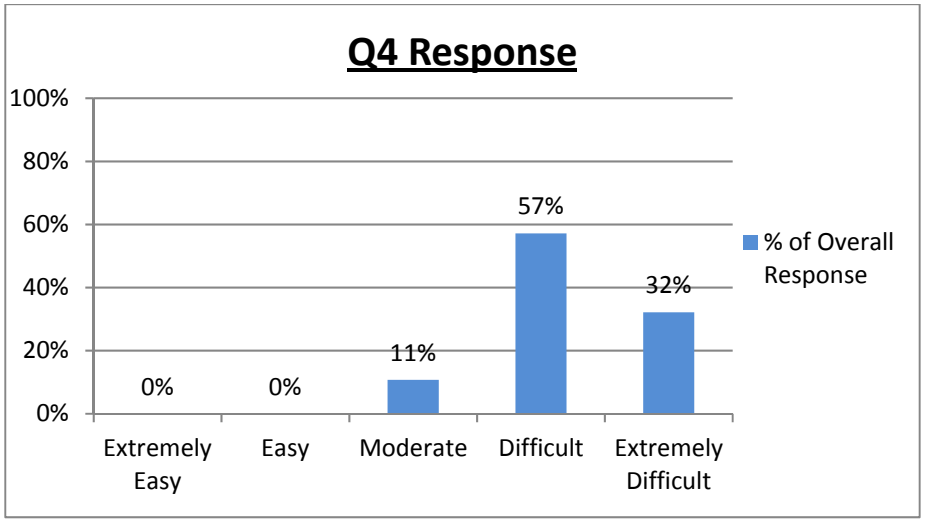

Figure 4-8: Response Percentage Breakdown for Q4 Response

4.4.6 Survey Response Q5

Table 4-8 below outlines the question, response options and number of respondents (n) for Question No.4. The bar chart as per Figure 4-11 presents the percentage of overall responses for each category.

Table 4-8: Q5 – Question, Response and Number of Respondents

No.	Question	Response	n
5	Does your company have a local manufacturing facility within China?	- Yes - No - Don't Know	27

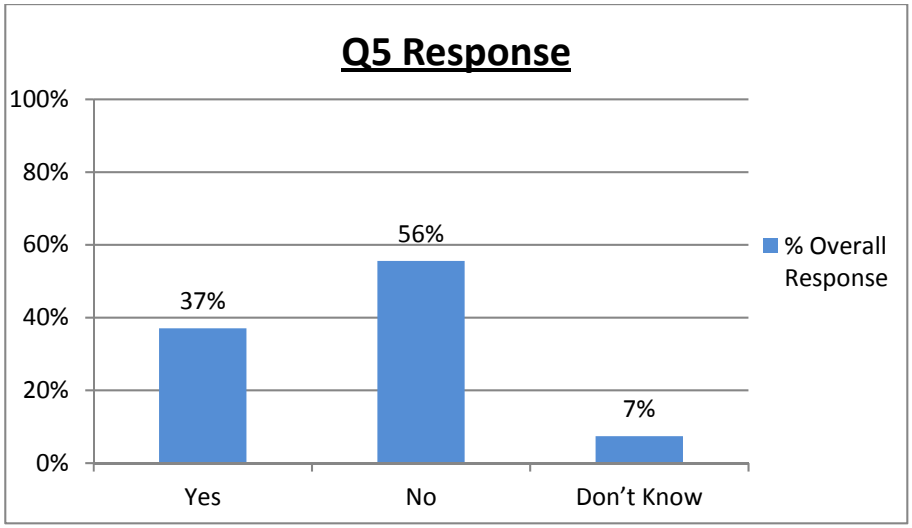

Figure 4-9: Response Percentage Breakdown for Q5 Response

4.4.7 Survey Response Q6

Table 4-9 below outlines the question, response options and number of respondents (n) for Question No.5. The bar chart as per Figure 4-12 presents the percentage of overall responses for each category.

Table 4-9: Q6 – Question, Response and Number of Respondents

No.	Question	Response	n
6	Has your company received approval for a device in China?	- Yes (as per new regulations in China – Order 650 in effect since 2014) - Yes (as per old regulations in China – Order 276 in effect since 2014) - Yes (as per new and old regulations in China – Order 650 and Order 276 respectively) - No - Don't Know	28

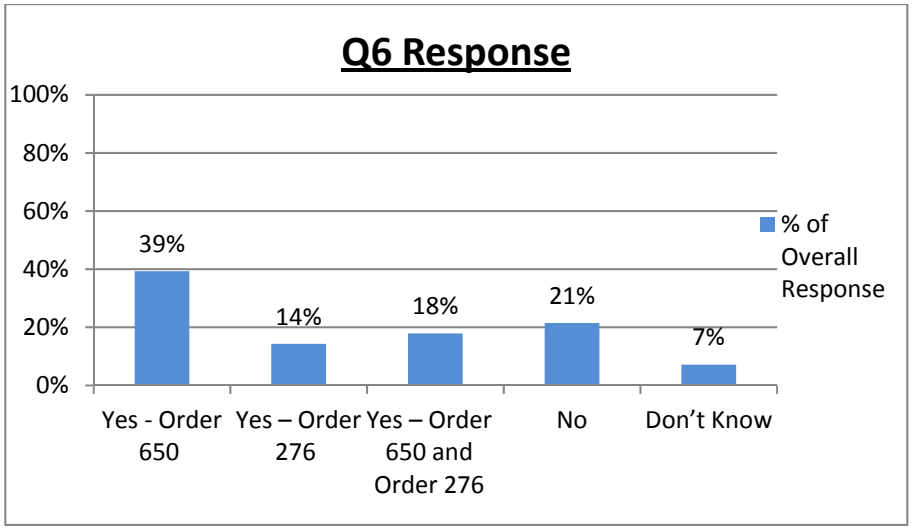

Figure 4-10: Response Percentage Breakdown for Q3 Response

4.4.8 Survey Response Q7

Table 4-10 below outlines the question, response options and number of respondents (n) for Question No.7. The bar chart as per Figure 4-13 presents the percentage of overall responses for each category.

Table 4-10: Q7 – Question, Response and Number of Respondents

No.	Question	Response	n
7	Who is your local agent in China?	- Local Agent - Subsidiary of your company - Consultant - Don't know - Other – Please specify	28

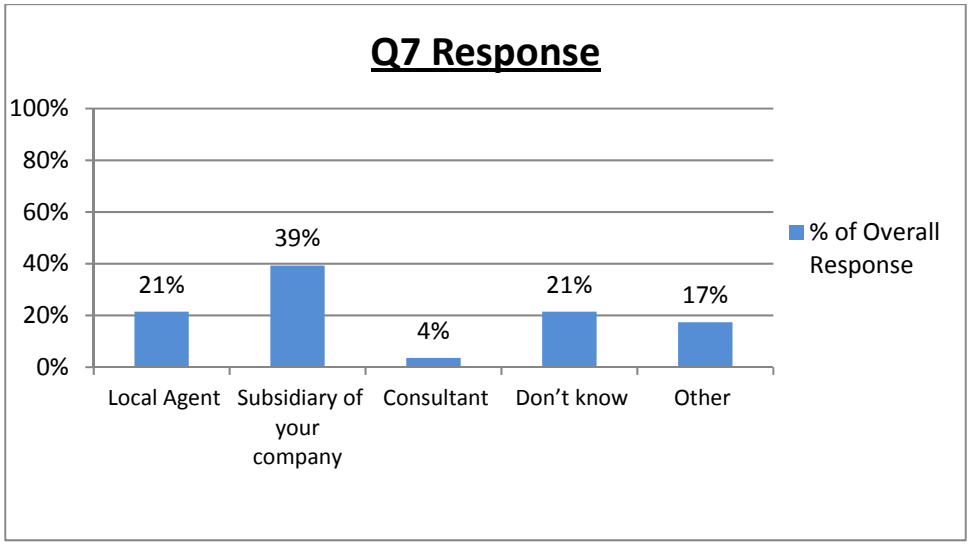

Figure 4-11: Response Percentage Breakdown for Q7 Response

Three responses were included in the 'Other- Please Specify' category. Responses as follows:

- If we were to proceed in China it would likely be via a distributor
- n/a
- Not required for supplier
- Not applicable
- Have an office there

On the basis of these responses and further review of individual responses, the response count for the category 'Subsidiary of your company' was updated by 1 and the 'Other' category was deducted by one.

4.4.9 Survey Response Q8

Table 4-11 below outlines the question, response options and number of respondents (n) for Question No.8. The bar chart as per Figure 4-14 presents the percentage of overall responses for each category. As the respondent was asked to choose 3 categories and/or add verbiage to the 'Other – please specify' category, it was appropriate to present the percentage of respondent chose an individual category.

Table 4-11: Q8 – Question, Response and Number of Respondents

No.	Question	Response	n
8	Can you rate your Top 3 challenges (as applicable)	- Local Clinical Trial Requirements - Compilation of China specific Clinical Evaluation	28

No.	Question	Response	n
	to receiving medical device approval in China?	Report - Submission Process for CFDA Review & Deficiencies - Compliance to China Specific Standards - Country Of Origin Approval Requirement - Understanding the Requirements - Other – Please specify	

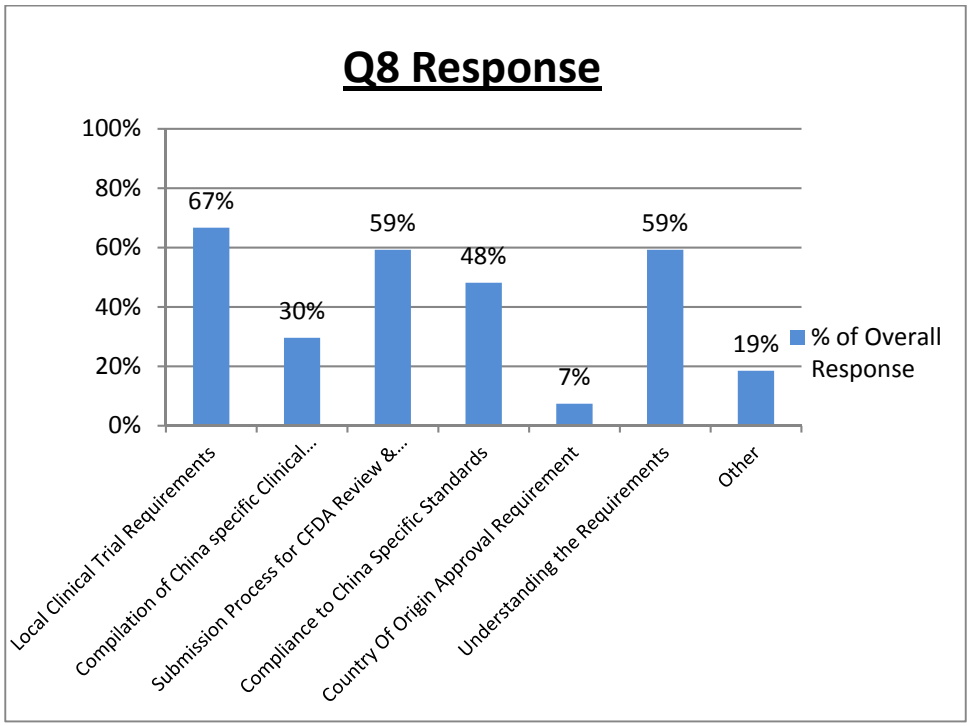

Figure 4-12: Response Percentage Breakdown for Q8 Response

Four responses were included in the 'Other- Please Specify' category. Responses as follows:

- The main challenge we see is the security of data once submitted to authorities
- timelines and frequency of change control of products
- Not applicable
- Don't sell into China

4.4.10 Survey Response Q9

Table 4-12 below outlines the question, response options and number of respondents (n) for Question No.9. The bar chart as per Figure 4-15 presents the percentage of overall responses for each category. As the respondent was asked to choose 3 categories and/or add verbiage to the 'Other – please specify' category, it was appropriate to present the percentage of respondent chose an individual category.

Table 4-12: Q9 – Question, Response and Number of Respondents

No.	Question	Response	n
9	Can you rate your Top 3 challenges (as applicable) to accessing the medical device market in China?	- Cost and Time for Regulatory Approval - Potential for Device 'Copying' - Requirements for a large Marketing & Sales Team - Reimbursement Challenges - Other – Please specify	28

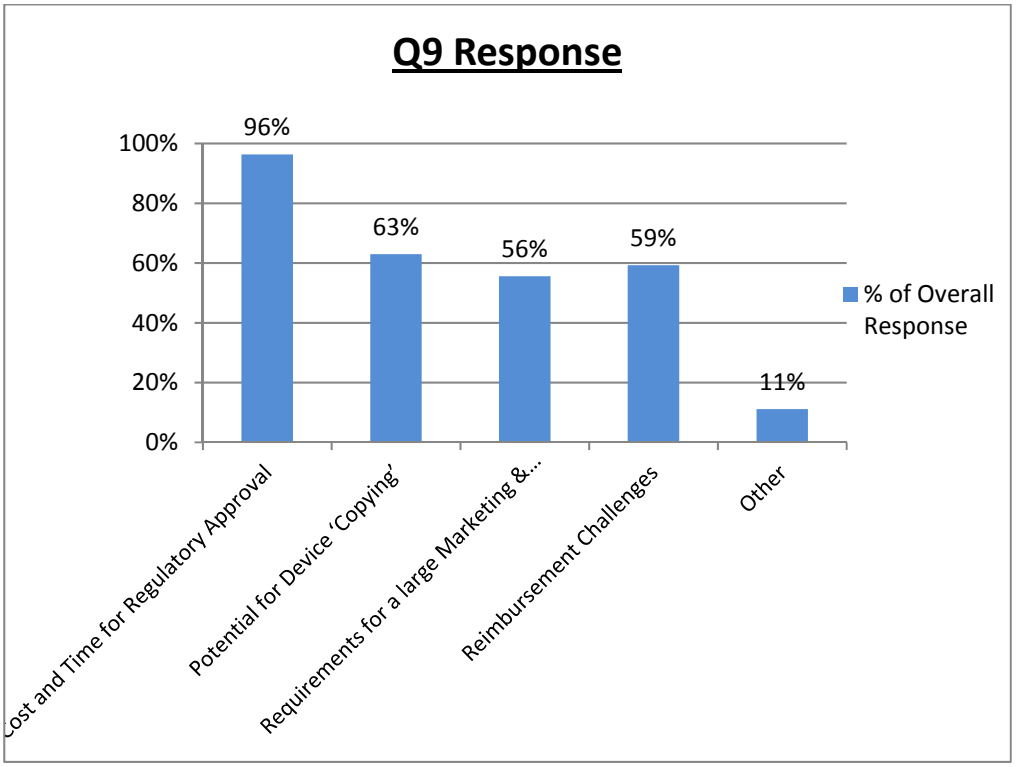

Figure 4-13: Response Percentage Breakdown for Q9 Response

Three responses were included in the 'Other- Please Specify' category. Responses as follows:

- Inventory build associated with an approval timeframe of 18 - 24 months on device changes.
- if replacing existing product (predicate device) reg. requirements for update
- Not applicable

4.4.11 Survey Response Q10

Table 4-13 below outlines the question, response options and number of respondents (n) for Question No.10. Table 4-14 details the individual's response per respondent. 24 out of 28 survey participants completed Q10. The individual survey responses of the 4 respondents that skipped the question were reviewed to understand why they omitted a response. One respondent did not have any device approved in China so may not have found this question applicable. All individual respondents are anonymous therefore no further follow-up was completed.

Table 4-13: Q10 – Question, Response and Number of Respondents

No.	Question	Response	n
10	What is the biggest lesson learned when dealing with the Chinese market?	Open Response	24

Table 4-14: Q10 – Individual Open question responses

	Q10 Responses
1	It's unpredictable
2	expect long timelines
3	The process is very cumbersome, requirements unclear, feedback on deficiencies poor and it takes much longer than anticipated
4	It doesn't stop when you get approval then you have labeling and customs issues to also ensure you understand fully otherwise you will struggle to get your product into China
5	Constant communication is essential
6	Allow sufficient time for submission process (including type testing) - far longer than other jurisdictions
7	Local contacts are key
8	Plan for a long approval time - plan approval of iterative versions of the device appropriately
9	Difficult and long times to register!
10	Use local expertise to manage approvals.
11	A lot of threads to regs and not aligned with other regions.
12	From a manufacturing site perspective, rather than a regulatory perspective (as we do not make the submissions) the planning/ challenges presented regarding a significant inventory build of pre-change product to service the Chinese market while the registration process is underway. Also the chinese interpretation of some standard - sometimes there can be technical issues with associated rationales that are difficult to explain i.e. 'lost in translation' when communicating with our Chinese colleagues
13	Understanding the Chinese device testing requirements
14	Chinese companies experience in Reg requirements can cause projects to proceed or stop
15	Very strong local partner would be crucial

16	hire a local consultant
17	you need good RA people based in China to nagivate on your behalf
18	Be wary of materials being used in the device
19	The biggest lesson learned was to ask multiple questions from local agents before responding to questions/ deficiencies. It was difficult to determine what was being asked and why, the lack of understanding led to simple questions taking a long time to respond to and often providing overly complicated responses. Essentially, clear communication is essential.
20	Ensure the business are aware of submission and approval timelines.It is a slow process to get approval in China but it is possible.
21	Not applicable
22	Have an appropriate agent to cover registration , after slaes and adverse reporting
23	Its take time and detailed local knowledge input
24	Consideration of the Market early in the process and ensuring that test units are available at the earliest possible time (once design is frozen and upon successful completion of DV builds)

5.0 Analysis and Discussion

5.1 Introduction

This dissertation attempts to examine the regulatory pathway and ultimate market access for a medical device in China by answering the following research questions in Table 5-1 with the appropriate research completed:

Table 5-1: Research Questions and Research Methods

Research Question	Research Method Completed
What is the current economic environment for medical devices in China? What are the projections for the future state?	In-depth literature review Peer Survey
What has changed in the medical device regulations in China, with the updated regulations enforced in 2014?	In-depth literature review
What are the challenges to medical device registration and market access in China?	In-depth literature review Case Review Senior Leader Questionnaire Peer Survey
What can the regulatory function do to ensure they create a successful regulatory strategy for Class II and Class III device approval in China that will aid market access?	In-depth literature review Case Review Senior Leader Questionnaire Peer Survey

This chapter presents the analysis and discussion of the findings and results from Chapter 4 and the literature review from Chapter 2. Firstly an analysis and discussion of the results from Chapter 4 are completed individually; this includes the case study, the senior leader consultation and finally the peer survey. Secondly each research question is addressed by the findings and results in Chapter 4 and the literature review in Chapter 2. The data from the different research methods is compared and the key findings/themes are discussed.

5.2 Case Study Analysis & Discussion

5.2.1 Case Review Analysis & Discussion

The results of a sample product case study for medical device registration under the new Chinese regulations were presented in Chapter 4. The key challenges identified are analysed and discussed as follows:

5.2.1.1 Product Technical Requirement

The Product Technical Requirement (PTR) is a test protocol that is used by the China type testing laboratory to test medical device samples. As a foreign manufacturer, we were highly reliant on our Chinese subsidiary to assist in the development of the PTR for our review. The Chinese specific standards are in Chinese and need to be translated. There is a difficulty in understanding what standards to choose and why these standards are appropriate. In this case study the device had a long established predicate in the market in China therefore this made it easier for the PTR to be developed in line with the new regulations. If your device was novel more research would be required to ensure the correct standards were chosen for the PTR. It is also worth noting that the PTR is not once off document for approval, the manufacturer needs to meet these requirements routinely. Any changes to the content in PTR would trigger a product change application so great importance must be given to the development of the PTR.

5.2.1.2 Local Type Testing

For Class II and Class III devices, CFDA requests samples for type testing. The testing centers will use the product technical specifications to determine what tests to conduct. Our type testing units were shipped to China post design verification and pre approval in any other geography. The units sent were held up at customs in China delaying their provision to the type test centre. It is important that a foreign manufacturer has a process in place so that test samples can freely move through customs without any delay.

Type testing for this device took approximately 6 months to complete. During the type testing at the centre a number of minor queries were relayed back via the China contact. It is important

as a foreign manufacturer that you have contact available on the ground in China in order to be able to visit the type test centre and provide the technical expertise.

As per the deficiency letter received during the technical review by CMDE there is an expectation that the tests listed on the PTR and ultimately carried out at the China type test centre should also be carried out by the manufacturer. We had to complete testing to a Chinese standard and its equivalent ISO standard to satisfy the requirements of CFDA. Type testing to this standard alone was not sufficient. In order to avoid repeat testing it is prudent that the manufacturer has completed all testing outlined in the PTR.

5.2.1.3 Clinical Trial Requirements

Our case study device is a Class III device in China. Class II and III medical devices require clinical trials unless they have exact predicates and/or are in the CFDA's clinical trial exemption list. When the device was under development it was not included on the exemption list. The strategy was to complete a robust Clinical Evaluation Report (CER) for China using our predicate device as the comparative device. This was challenging as CFDA's guidance - 'Technical Guidance on Clinical Evaluation of Medical Devices' had not been released. The team spent considerable navigating what content would meet the requirements for CFDA. It was also the first time the company had created a China specific CER. This involved increased planning around the literature searches on Chinese databases, translation Chinese-English, English to Chinese and the clinical review. As a multi-national company with a well-established subsidiary in China we were able to navigate through the process and align the relevant people. This may be challenging to a smaller company who would have to consider ascertaining the people with the relevant expertise.

The CFDA released their guidelines on clinical evaluation post submission of the case study device registration dossier to CMDE. As expected the deficiency letter received during the technical review by CMDE outlined that the China specific CER needed to meet the released guidelines. It took a considerable amount of work to revise the CER to meet guidelines and bridge the literature search gap from the initial release of the CER. It was noted the level of

detail required by CMDE for the comparative with the predicate device. Fortunately our predicate device was our own device therefore we had access to all the data i.e. materials, test methods used, test data and post market surveillance data. If your company did not use its own device as a predicate or have access to the files of the predicate device it seems impossible that the CER route would be feasible to negate a clinical trial.

5.2.1.4 Country Of Origin

As per Article 13 of Order 4 (2014) Provisions for Medical Device Registration proof of Country Of Origin (COO) is a requirement. The country of origin for the case study device is outside of the EU and US. A pre-requisite for device registration in the COO is EU Approval therefore the timeline for approval in China was exacerbated by the manufacturer's location. As per Figure 5-1 below due to the COO requirement it was 11 months from EU submission until the registration dossier was filed in China. Approval in China was 27 months post completion of verification and validation activities for the case study device.

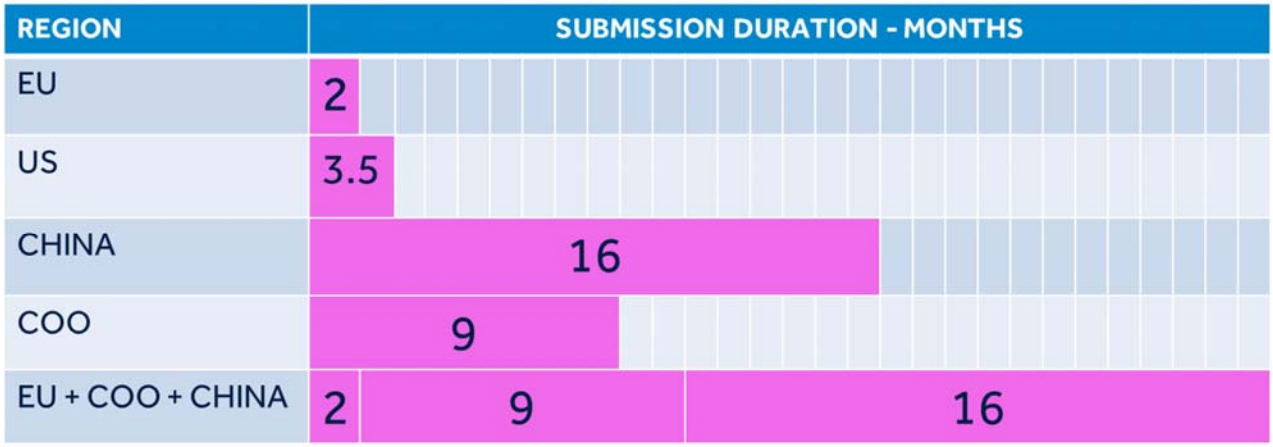

Figure 5-1: Regional Submission Timelines

5.2.1.5 Application Dossier

Once all the pre-requisites to application as outlined above were completed, the application dossier was prepared for submission. A total of 12 document items must be collected and submitted to the CFDA consisting of 9 legal documents, 2 technical documents, and a testing report issued by a CFDA certified testing centre.

As per Article 12 of Order 4 (2014) Provisions for Medical Device Registration the application filing was in Chinese, with the English originals also provided as the deliverables had been translated. The CFDA forwarded the application to CMDE for review where there is an allowance of 90 working days to complete the initial technical review.

5.2.1.6 Application Review with CFDA

The case study initial application to CMDE was a substantial compilation of documents. The documentation needs to be signed by the legal manufacturer prior to being forwarded to China for translation. We needed to understand the China specific references therefore this requires close collaboration with the Chinese subsidiary and increased time to completion. It is important that the manufacturer understands their responsibilities and the content of any letters required for signing on behalf of the legal manufacturer. A considerable amount of time is required in formatting, signing, notarisation and the translation of documentation prior to submission. It is advised that a portion of time is allocated for these activities. Due to the volume of documentation this can pose a challenge in itself.

The deficiency letter for the case study arrived approximately 5 months post submission. There is an allowance of 12 months for the provision of responses. This does sound generous but in reality this timeline can be challenging depending on the deficiencies received. A cross functional team was assembled to work on the case study responses, this included Clinical, Design Assurance, R&D, Biocompatibility, China Regulatory and Business Unit Regulatory. The functions required to address the deficiency letter show the depth of review and the challenges with interpreting the requirements of the new regulations. It is important that the different functions are available to work on the deficiency letter responses immediately. There may be long lead times should repeat testing or if a clinical study is required. There is an increased criticality of this process due to the fact that one deficiency letter only will be issued by CMDE. If the response is rejected or you fail to respond within 12 months you are back to the start of the submission process delaying market access to China.

For the case study a number of the questions were unclear on their intent so the reviewer was consulted on the requirement for these particular questions. This consultation was required to ensure we were answering the questions adequately It is important that your China local agent is aware of this process and can ascertain the information required for successful responses. The challenge of access to the reviewer has increased since the case study application with CMDE removing the weekly open day where your local agent could consult with the reviewer.

A large quantity of information was required to be compiled to respond to the deficiency letter. It was noted that we are now providing more information as per the new regulations than what we would have previously provided under the old regulations. Similar to the initial submission it is important not to underestimate the time required for the compilation of responses.

5.2.2 Senior Regulatory Leadership Questionnaire Analysis and Discussion

The results of collated feedback from Senior Regulatory Leaders form a multinational company were presented in Chapter 4. From the collated feedback, potential counter measures including internal procedures and advocacy are in progress, see Section 5.4.3.1 for further discussion. The key challenges identified are summarized, analysed and discussed as follows:

5.2.2.1 Local Clinical Trials

Upon analysing the feedback two key challenges were apparent, the timelines for when a clinical trial and the lack of clarity in navigating the pathways for clinical trial exemption. If there is a requirement for local clinical trials this in turn extends the time-to-market and delays access of medical technology within China. A Clinical Trial Application (CTA) must be approved before the trial can begin in China for high risk devices. The CTA requires Country of Origin approval.

Many of our products are not exemption list therefore we must look to the “substantial equivalence” route or complete a clinical trial. The “substantial equivalence” route requirements are vague due to the new regulations but as a company we are learning more via the products being routed for approval via the new regulations.

5.2.2.2 Clinical Evaluation Reports (CER's)

Previously we did not have to complete China specific CER's or CER's for Class 1 products. The CER's used to support CE mark do not meet Chinese requirements. Creating CER's specifically for China is burdensome in the management of the preparation, the Chinese literature search is translated from Chinese to English and then back to Chinese for CER submission.

5.2.2.3 Unique Device Identifier (UDI)

China CFDA plans to require UDI. If UDI is not consistent with the US requirements this may be quite burdensome for the burdensome for the business to implement.

5.2.2.4 County of Origin Approval (COO)

COO approval is now needed before the local CTA commences or the initial device submission. The COO requirement and pre-requisite events extends time-to-market and delays access of medical technology.

5.2.2.5 China Specific Standards

As per the revised regulation, CFDA requires compliance with specific Chinese standards for the both products under initial application and products under renewal. This creates challenges in interpreting the China National Standards and ensuring conformance for product approval and renewal. Any additional testing required to be completed will extend approval/renewal timelines.

5.2.2.6 Type Testing

It has been observed that the tests chosen for type testing to comply with China specific standards are not appropriate for the device being evaluated. During type testing on-site technical support is required from the company which is burdensome.

5.2.2.7 Submission Process

The submission process is lengthy and does not benefit getting new technology to Chinese patients. When a device is under review with CMDE there is no ability to implement changes.

This is very restrictive on the business as the submission cycle in China is lengthy. A new iteration of the same product will have to wait for approval of the current iteration before starting the submission process.

There is a challenge in accessing the reviewer as there is no formal consultation or pre-submission process. The informal feedback solicited via the weekly open day at CMDE which is useful but not binding.

5.2.2.8 Submission Process - Deficiency Letter

The 'one strike you're out'/"one chance only" rule for the deficiency process is restrictive. It's impossible to get an original application through the review process without any questions.

5.3 Peer Survey Analysis & Discussion

5.3.1 Question 1

What type company do you work? What is the size of your Regulatory Affairs (RA) Department?

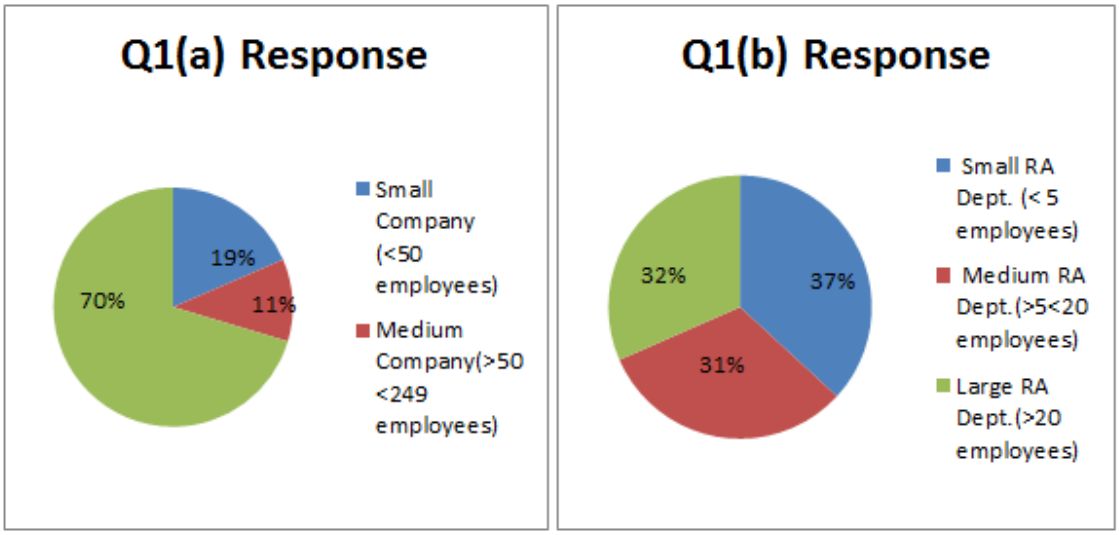

Figure 5-2: Response Percentage Breakdown for Q1a Response and Q1b Response

Figure 5-2 shows that the majority of respondents to the survey are working in Multi-National companies, with 70% choosing this category. There was an even spread across the size of the Regulatory Departments within the respondents individual company. This may be down to organisational structures where regulatory is located in another global location.

5.3.2 Question 2

What is your perception of the importance to your business of accessing the Chinese market?

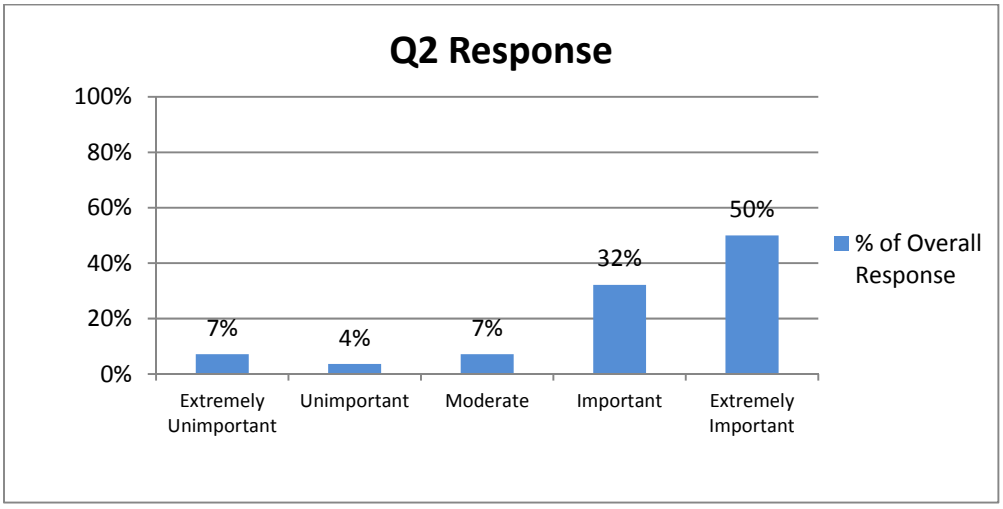

Figure 5-3: Response Percentage Breakdown for Q2 Response

Figure 5-3 shows that the majority of respondents to the survey categorised the importance of the Chinese market as 'Important or Extremely Important'. A total of 82% chose either of these categories. The individual responses were reviewed individually to understand if there was a trend to the responses. All respondents that chose the 'Extremely Unimportant' and 'Unimportant' category were part of Multi-National companies. We may consider that the importance of the Chinese market is subjective to a particular business and their products.

5.3.3 Question 3

What is your perception of the level of difficulty in gaining market access for a medical device in China?

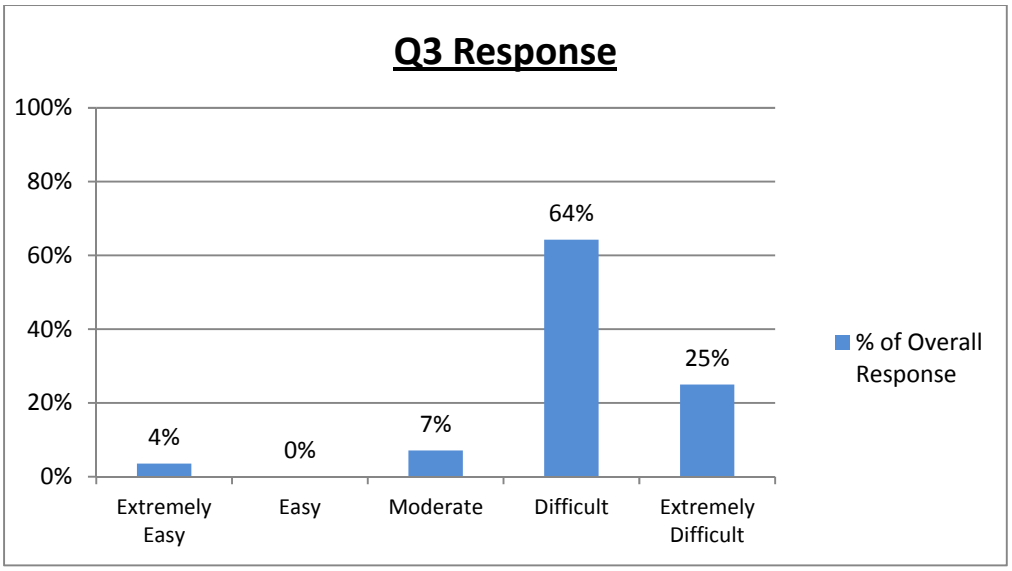

Figure 5-4: Response Percentage Breakdown for Q3 Response

Figure 5-4 shows that the majority of respondents to the survey categorised the level of difficulty of accessing the Chinese market as 'Difficult'. A total of 67% chose the category 'Difficult' and 25% chose the category 'Extremely Difficult'. The individual responses were reviewed individually to understand if there was a trend to the responses. Only one respondent chose the 'Extremely Easy' category. Upon review of the individual's survey this response is inconsistent with the other responses within the survey, this response should be considered as an outlier and potentially an error on behalf of the respondent.

5.3.4 Question 4

What is your perception of the level of difficulty in gaining Regulatory Approval of a medical device in China?

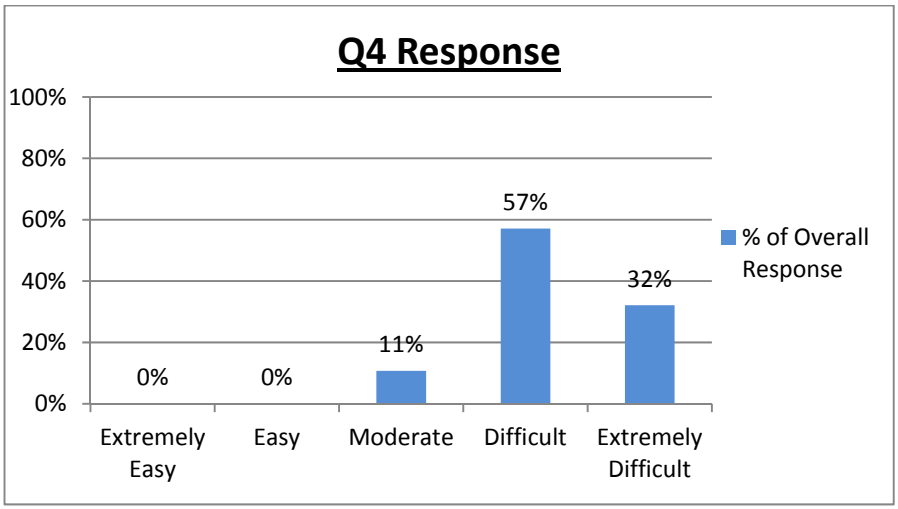

Figure 5-5: Response Percentage Breakdown for Q4 Response

Figure 5-5 shows that the majority of respondents to the survey categorised the level of difficulty of gaining regulatory approval in China as 'Difficult' or 'Extremely Difficult'. A total of 57% chose the category 'Difficult' and 32% chose the category 'Extremely Difficult'. The individual responses were reviewed individually to understand if there was a trend to the responses. The majority of respondents (68%) were aligned with their response in Q3 by assigning the same category response for market access and regulatory approval.

5.3.5 Question 5

Does your company have a local manufacturing facility within China?

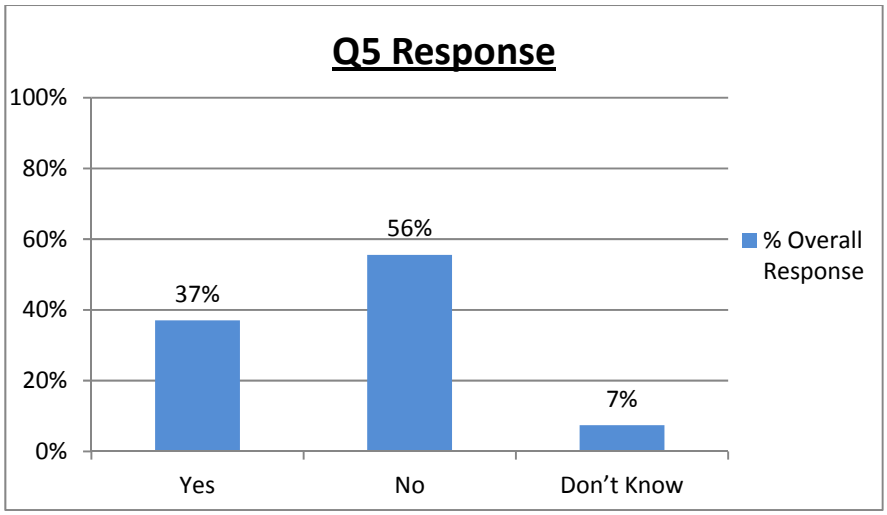

Figure 5-6: Response Percentage Breakdown for Q5 Response

Figure 5-6 shows that the majority of respondents to the survey have a manufacturing facility within China. A total of 37% have a manufacturing facility within and 56% do not have a facility within China. This shows that there is a useful spread across respondents that do and do not have a facility within China. The responses to other questions will not be overly skewed by a population that manufactures within China. The individual responses were reviewed individually to understand if there was a trend to the responses. It is worth noting that the two respondents that chose the category 'Moderate' in Q3 for market access also have manufacturing facilities within China.

5.3.6 Question 6

Has your company received approval for a device in China?

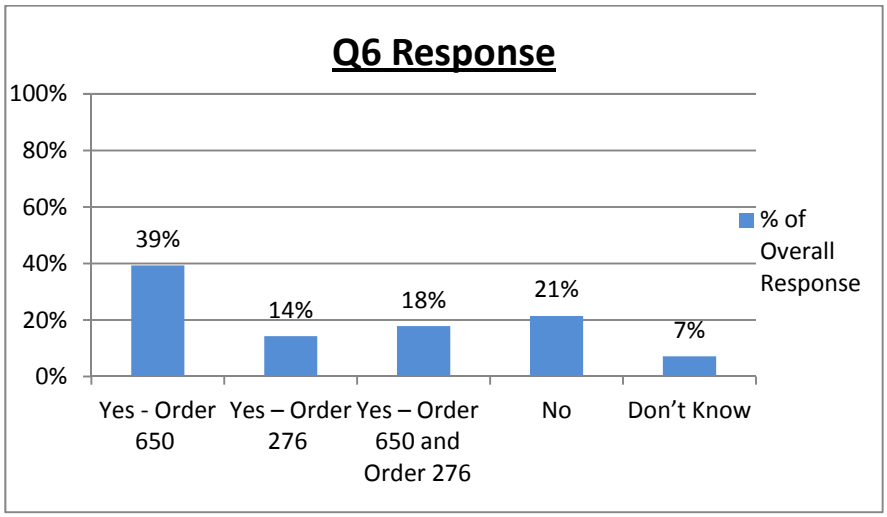

Figure 5-7: Response Percentage Breakdown for Q6 Response

Figure 5-7 shows that the majority of respondents companies have gained approval of a medical device in China. A total of 57% have also received approval under the new regulations which were implemented in 2014. The individual responses were reviewed individually to understand if there was a trend to the responses. For the respondents that chose 'No' (n =6) or 'Don't Know' (n=2) category their responses to Q2 was reviewed. Four of the respondents had chosen 'Important' or 'Extremely Important' for the importance of the accessing the Chinese market and four of the respondents had chosen 'Moderate', 'Unimportant' or 'Extremely Unimportant'. It can be considered that there are two subsets – an individual's company does not see the Chinese market as important therefore has not proceeded for regulatory approval and an individual's company that does see the Chinese market as important but has yet been successful in gaining regulatory approval.

5.3.7 Question 7

Who is your local agent in China?

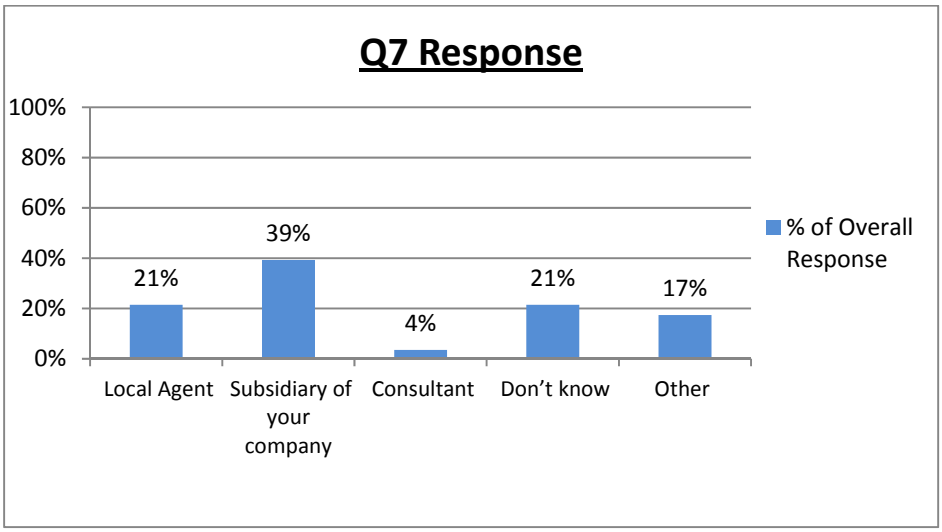

Figure 5-8: Response Percentage Breakdown for Q7 Response

Figure 5-8 shows that the majority of respondents companies have a local agent or subsidiary of their company in China. A total of 21% chose the category 'Local Agent' and 39% chose the category 'Subsidiary of your company'. An important contribution was included via the text response to the category 'Other – please specify'. One respondent suggested a distributor as a potential local agent for their company.

5.3.8 Question 8

Can you rate your Top 3 challenges (as applicable) to receiving medical device approval in China?

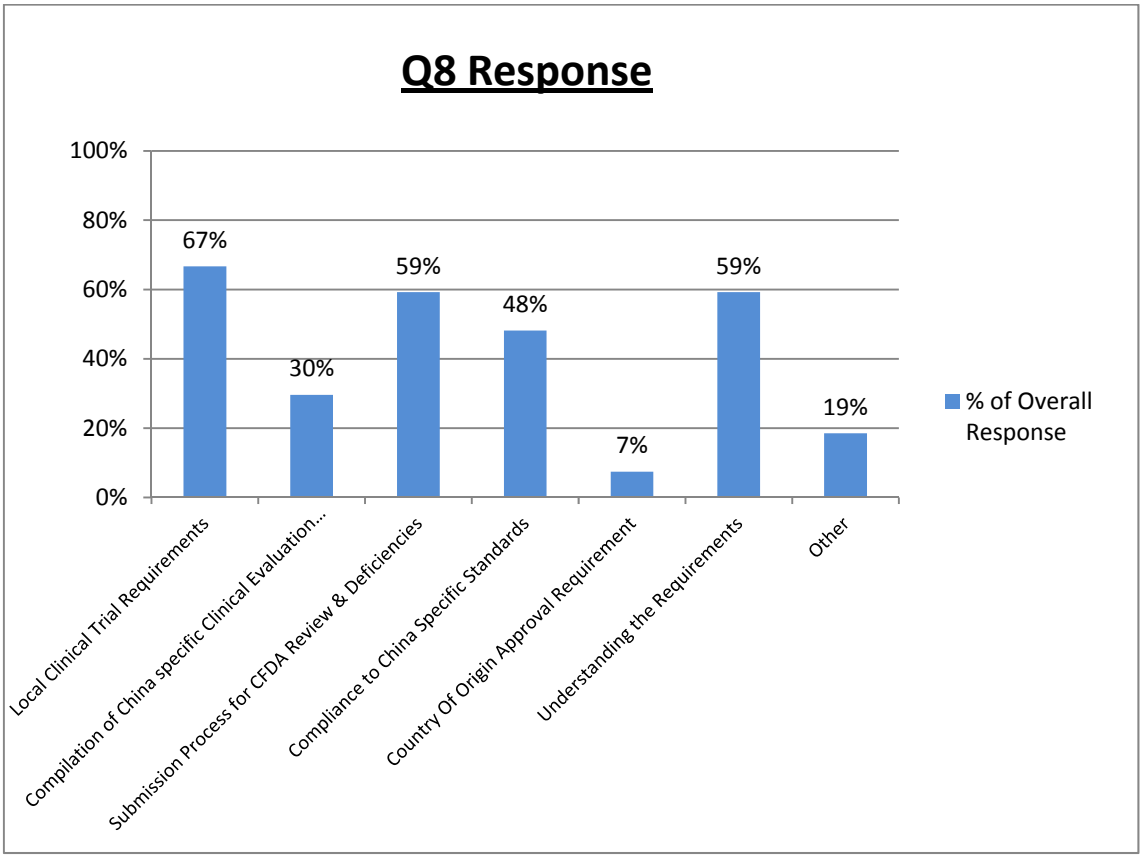

Figure 5-9: Response Percentage Breakdown for Q8 Response

Figure 5-9 shows the spread of challenges respondents companies chose for medical device approval in China. The top three challenges are as follows - a total of 67% chose the category 'Local clinical trial requirements', 59% chose the category 'Understanding the requirements' and 59% chose 'Submission Process for CFDA Review & Deficiencies'. Some important contributions were included via the text response to the category 'Other – please specify'. One respondent recognised a challenge over the loss of security of data when it is supplied to the authorities. Another respondent added the challenge of change control. This can be seen as a

challenge both pre-and post market. Whilst the regulatory review process is under way companies are constrained on making any modifications to their device. For Post market device changes may require entry into the lengthy regulatory review process.

5.3.9 Question 9

Can you rate your Top 3 challenges (as applicable) to accessing the medical device market in China?

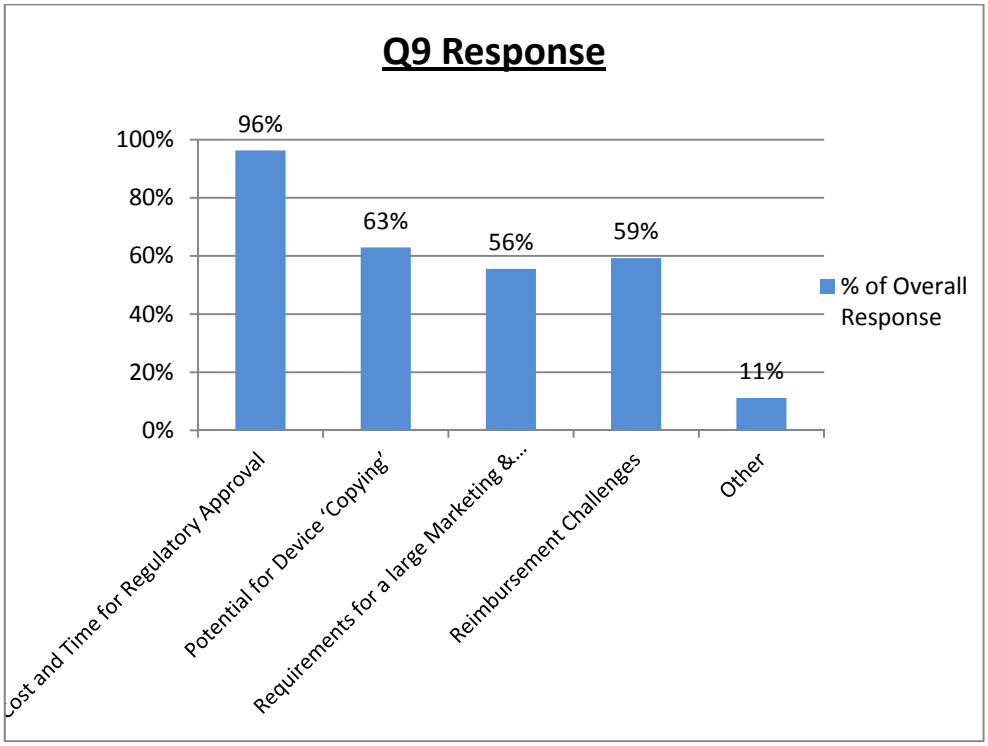

Figure 5-10: Response Percentage Breakdown for Q9 Response

Figure 5-10 shows the spread of challenges respondents companies chose for medical device approval in China. The top three challenges are as follows - a total of 96% chose the category 'Cost and Time for Regulatory Approval', 63% chose the category 'Potential for Device Copying' and 59% chose 'Reimbursement'. Some important contributions was included via the

text response to the category 'Other – please specify'. One respondent recognised a challenge to the business of building inventory for device changes in China. Product distributed in China must have a manufacturing date post approval of any device changes; therefore inventory for the Chinese market cannot be built ahead of approval. Another respondent added the challenge of regulatory requirements for replacing predicate product.

5.3.10 Question 10

What is the biggest lesson learned when dealing with the Chinese market?

Upon review of the responses to Question 10, themes were easily identified. Some of the responses were found to be applicable to several themes. These themes included:

- Importance of Local Agent
- Long Regulatory Timelines
- Understanding the Requirements
- Communication

Importance of Local Agent

Seven out of the twenty three responses for lessons learned spoke to the importance local agent (See Table 5-2 for specific response details). This stresses that having a good in-country contact with local knowledge to manage registrations and post market activities is a requisite for success in China.

Table 5-2: Responses to Theme 'Importance of Local Agent'

	Q10 Responses
1	Local contacts are key
2	Use local expertise to manage approvals.
3	Very strong local partner would be crucial
4	Hire a local consultant
5	You need good RA people based in China to nagivate on your behalf
6	Have an appropriate agent to cover registration , after sales and adverse reporting
7	Its take time and detailed local knowledge input

Long Regulatory Timelines

Eight out of the twenty three responses for lessons learned spoke to the lengthy regulatory timelines (See Table 5-3 for specific response details). This shows the importance of the business understanding the challenges of long lead times for regulatory approval and market access in China. This also poses challenges for when a business wants to introduce iterative versions of its products. Timelines in China are longer relative to other regions including the EU and US.

Table 5-3: Responses to Theme 'Long Regulatory Timelines'

	Q10 Responses
1	It's unpredictable
2	Expect long timelines
3	The process is very cumbersome, requirements unclear, feedback on deficiencies poor and it takes much longer than anticipated
4	Allow sufficient time for submission process (including type testing) - far longer than other jurisdictions
5	Plan for a long approval time - plan approval of iterative versions of the device appropriately
6	Difficult and long times to register!
7	From a manufacturing site perspective, rather than a regulatory perspective (as we do not make the submissions) the planning/ challenges presented regarding a significant inventory build of pre-change product to service the Chinese market while the registration process is underway. Also the chinese interpretation of some standard - sometimes there can be technical issues with associated rationales that are difficult to explain i.e. 'lost in translation' when communicating with our Chinese colleagues
8	Ensure the business are aware of submission and approval timelines.It is a slow process to get approval in China but it is possible.
9	Consideration of the Market early in the process and ensuring that test units are available at the earliest possible time (once design is frozen and upon successful completion of DV builds)

Understanding the Requirements

Nine out of the twenty three responses for lessons learned spoke to the clarity of the requirements (See Table 5-4 for specific response details). Understanding the requirements is difficult; this includes the test requirements, the standard requirements, the deficiency process and the requirements post approval. All these obstacles identified add to the long lead time for approval of a medical device and market access.

Table 5-4: Responses to Theme 'Understanding the Requirements'

	Q10 Responses
1	It's unpredictable
2	The process is very cumbersome, requirements unclear, feedback on deficiencies poor and it takes much longer than anticipated
3	It doesn't stop when you get approval then you have labeling and customs issues to also ensure you understand fully otherwise you will struggle to get your product into China
4	A lot of threads to regs and not aligned with other regions.
5	From a manufacturing site perspective, rather than a regulatory perspective (as we do not make the submissions) the planning/ challenges presented regarding a significant inventory build of pre-change product to service the Chinese market while the registration process is underway. Also the chinese interpretation of some standard - sometimes there can be technical issues with associated rationales that are difficult to explain i.e. 'lost in translation' when communicating with our Chinese colleagues
6	Understanding the Chinese device testing requirements
7	Chinese companies experience in Reg requirements can cause projects to proceed or stop
8	Be wary of materials being used in the device
9	The biggest lesson learned was to ask multiple questions from local agents before responding to questions/ deficiencies. It was difficult to determine what was being asked and why, the lack of understanding led to simple questions taking a long time to respond to and often providing overly complicated responses. Essentially, clear communication is essential.

Communication

Four out of the twenty three responses touched on communication (See Table 5-5 for specific response details). This can be the communication with your local China agent or the communication by your local China agent with CFDA. There are challenges in both aspects. It is important that the communication is open and frequent with your local agent so that the correct deliverables are provided. A strong local agent must gain access to and communicate with CFDA in order to understand and clarify requirements.

Table 5-5: Responses to Theme 'Communication'

	Q10 Responses
1	The process is very cumbersome, requirements unclear, feedback on deficiencies poor and it takes much longer than anticipated
2	Constant communication is essential
3	From a manufacturing site perspective, rather than a regulatory perspective (as we do not make the submissions) the planning/ challenges presented regarding a significant inventory build of pre-change product to service the Chinese market while the registration process is underway. Also the chinese interpretation of some standard - sometimes there can be technical issues with associated rationales that are difficult to explain i.e. 'lost in translation' when communicating with our Chinese colleagues
4	The biggest lesson learned was to ask multiple questions from local agents before responding to questions/ deficiencies. It was difficult to determine what was being asked and why, the lack of understanding led to simple questions taking a long time to respond to and often providing overly complicated responses. Essentially, clear communication is essential.

5.4 Comparative Analysis & Discussion

5.4.1 Research Question 1

What is the current economic environment for medical devices in China? What are the projections for the future state?

The literature review included an overview of the current economic environment for medical devices in China and the projected future state Figure 5-11 below presents the key summary points from each research method used.

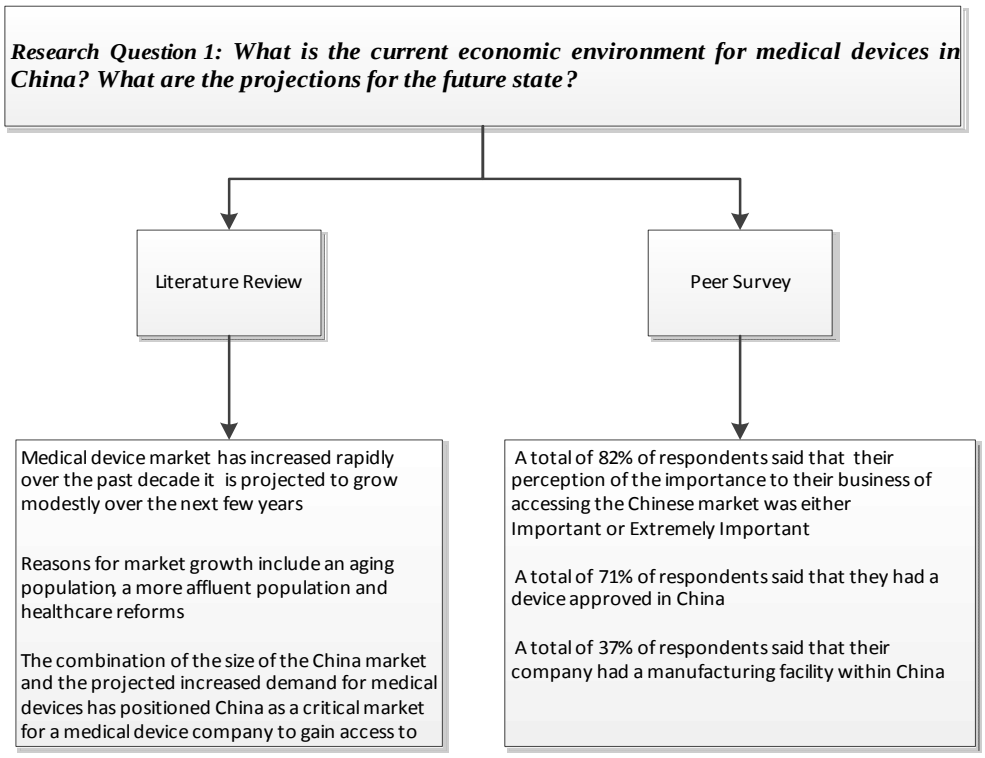

Figure 5-11: Research Question 1 Summary

China's medical device market is ranked second largest in the world at this time. Driven by both an increase in discretionary income and a population that is aging faster than any other nation's population. The combination of the size of the China market and the projected increased demand for medical devices has positioned China as a critical market for a medical

device company to gain access to. The faster a company can gain approval for their medical device product in China, the faster it can reap the awards of the revenue the China market will bring. China's economic growth may be slowing down but the medical device industry is still on the rise (EMERGO 2017a).

The peer survey reflected the opportunities there is for the medical device business in China. A total of 82% of respondents to the survey said their perception of the importance to their business of accessing the Chinese market was important or extremely important. This shows that the respondents within their individual companies are aware of the market size in China and the revenue it can bring to the business. A total of 71% of respondents companies already had a device approved in China and a further 37% demonstrating their commitment to China by having a manufacturing facility within China. The future state is promising for China and the medical device industry is fully aware of this by getting their products to the market

5.4.2 Research Question 2

What has changed in the medical device regulations in China, with the updated regulations enforced in 2014?

Chapter 2 Literature dealt with an overview of changes in the medical device regulations in China as per Order 650. Upon further analysis of the changes Table 5-6 below provides a summary of the new regulation Order 650, what was new, what was amended and what was reduced in comparison to the old regulations Order 276.

Table 5-6: Updates to Chinese Medical Device Regulations

What is amended?	What is new?	What is reduced?
Definition of medical device	Requirement of medical device standard management	Class I: Registration to Notification Filing
Principle of medical device classification	For foreign companies, may conduct on-site QMS inspection during tech review	Non-substantial changes made to Class II and III: Notification Filing only
Encouraging innovation of medical device	Policy for specifying medical devices exempted from clinical trial	Sales of Class II: Notification only
Regulatory requirement of one time use device	Requirement posed on clinical trials and facilities where clinical trials are carried out	Approval requirement removed for clinical trial of Class II
Reinforce industry's self-discipline	Self-QMS-Inspection system applied on medical device manufacturers	Scope reduced for clinical trial approval of Class III
Requirement of dossier for medical device registration application	Requirement of standardized administration of medical device manufacturing, quality, sales	Approval removed for medical device invented by medical institution
Replacing registration with notification for Class I	For domestic company that manufacturer/sell on-site inspection will be conducted	Mandatory CCC certification removed for some Class III
Requirements for clinical trial management (GCP)	Requirements posed on type testing centers	
Medical device license now valid for 5 years	Supervision/Administration information disclosure	
Condition requirement of application for medical device manufacturing	Requirement of adverse event handling and product recall	
Switching order between product registration application and manufacturing permit application	Medical device for exportation must comply with the requirement of the importing country	
Re-registration/Renewal of Manufacturing Permit of medical device is changed to Registration Extension/ Manufacturing Permit Extension	Supervision/Administration system of the quality of medical device in use	
Enterprises selling Class I no longer require approval or notification filing	.Provision of fee charging for medical device registration	
Enterprises selling Class II only require notification filing with city level CFDA	Restricting policy applied on personnel's who are in charge of supervision/administration and technical evaluation	
Increased penalties for illegal enterprises	Policy of joint work required among government agencies	

The new regulations have now been implemented for three years. A medical device manufacturer already operating within China should by now have adjusted to the changes and a manufacturer planning to access the Chinese market should be well aware of the requirements. With the new regulations has come new guidance's either published or announced for comment by CFDA. With the new guidance's and procedures comes opportunity for the medical device manufacturer to gain approval in China in a streamlined manner. Instead of the normal registration approval route the manufacturer could avail of the 'priority review' or 'green-channel' approval process.

Based on CFDA Order No. 13, in February 2014 the China Food and Drug Administration released Trial Procedures for the Special Examination of Innovative Medical Devices (CFDA 2014a) also known as the Green Channel process. To be eligible for the Green Channel process the following must be met:

- Patent registration in China - Patent technology should be consistent with the core technology of product. Novelty Search Report and supporting patent applications filed in China.
- Innovative product, internationally advanced - new working mechanism, internationally advanced technology
- Significant clinical application value
- Prototype - A sample model/machine should be finished
- Reality, control & traceability - Cover letter, test report, pre-clinical data, animal test data, internal literature

The 'Green Channel' has been in effect since 2014. Several devices have been granted "priority" status including 'Micra' Medtronic's leadless pacing system in 2015. The benefits include:

- High priority review status, CFDA will appoint one contact person for pre-assessment consultation and subsequent application review; this person will liaise with the applicant to provide technical guidance.
- Testing center provides preliminary technical feedback during the in-China type testing process.

- Prioritized CTA, technical evaluation and quality system inspection. (6 – 9 months saved).
- Official device classification category can be decided in parallel with the registration application assessment (no separate classification application required even if no existing classification code is suitable).
- Contract manufacturing is permitted (For local manufacturing in China only).

(Partners 2017)

The Priority Review and Approval Procedure for medical devices came into force from January 1, 2017. In this draft document, CFDA announced they would open up a Priority Review channel to the below categories of device:

- The device is listed on the "Scientific and Technology Major Projects" or "Key Research & Development Plans" (i.e., two nationwide initiatives that China launched in recent years to promote innovation and technological advancement);
- The device has oncology-related indications, and offers a significant advantage over existing technologies;
- The device is used in the diagnosis/treatment of rare diseases, and offers a a significant advantage over existing technologies;
- The device is used in the diagnosis/treatment of diseases affecting children and the elderly, for which no approved alternative exists;
- The device answers an unmet clinical need, for which no approved alternative exists;
- CFDA otherwise determines that the device should be granted a priority review status.

(Partners 2017)

To apply for such Priority Review, in addition to the regular product registration dossier, the applicant is also required to file the "Priority Review" application form. If the qualification gets confirmed (which involves both CFDA and a panel for assessment and also must pass the public notice window), the following benefits will be guaranteed:

- Prioritized technical review (a specific “cue” will be formed, separate from the Regular Channel or Green Channel)
- Prioritized QMS audit scheduling (currently applied to local products 100%, is also being extended to imported products gradually)
- Prioritized administrative review
- More frequent and active communications between the reviewer and the applicant

Priority Review channel option appears to be simpler in comparison to the Green Channel pathway with no lengthy pre-qualification and less potential risks pertaining to Intellectual Property.

5.4.3 Research Question 3

What are the challenges to medical device registration and market access in China?

There have been a number of recurrent themes in the research findings for the impact and challenges of the new regulations to product registration in China. Ultimately all challenges within the regulatory approval process create burden and impact time to market/market access in China. Historically China has consistently set out the longer approval timelines in comparison to other geographies with its complex submission process. This has not improved with the onset of the new regulations; timelines for approval are increasing. The combined challenges across the research data are compared and commonalities discussed. Figure 5-12 below presents the key summary points from each research method used.

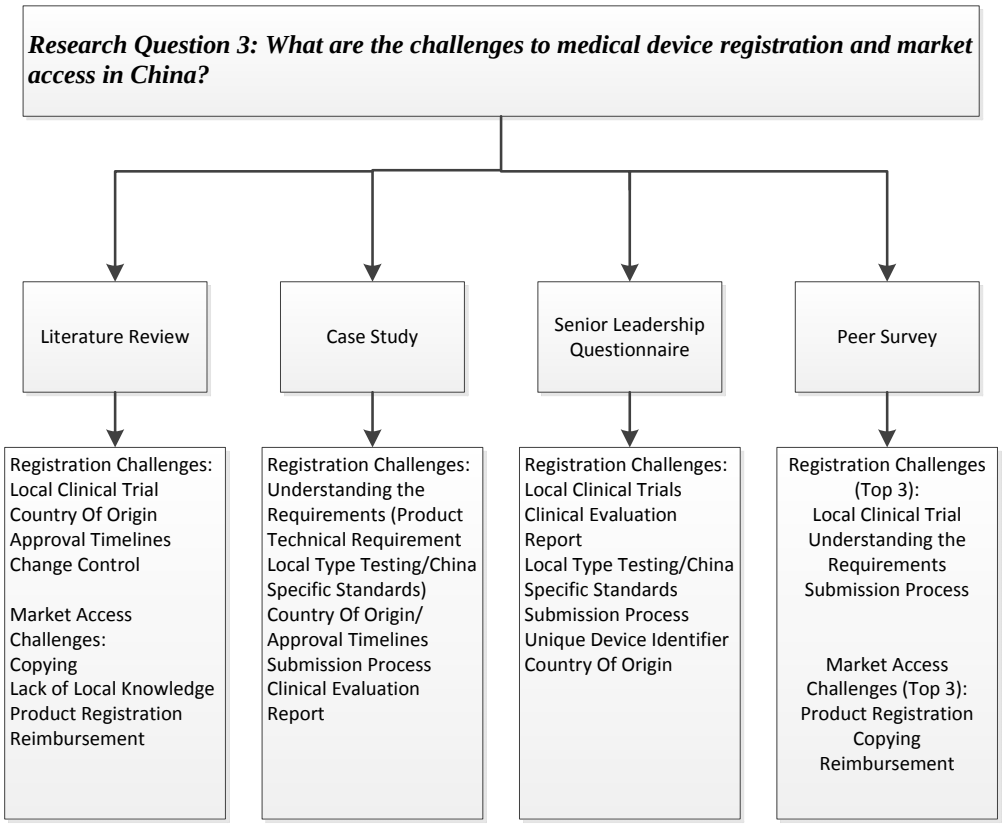

Figure 5-12: Research Question 3 Summary

For registration challenges there is one main common challenge theme across the data collated from all research methods. This is the requirement for Local Clinical Trials and the Clinical Evaluation process to negate a local clinical study. In the peer survey 67% of respondents selected the local clinical trial as one of their top 3 challenges. Senior regulatory leaders from the multinational questioned voiced their concerns around the lack of clarity on what devices are clinically exempt and the requirements for using substantial equivalence for the CER route. The case review also addressed the complexity of the CER route and the uncertainty is brought throughout the submission process until finally the case device was published in the clinical trial exemption list. If a clinical trial is required it will bring increased timelines, cost and resourcing to access the market in China. Figure 5-13 below shows a simple comparative below of the

steps involved for a China submission process without a clinical study required and a China submission process with a clinical study required.

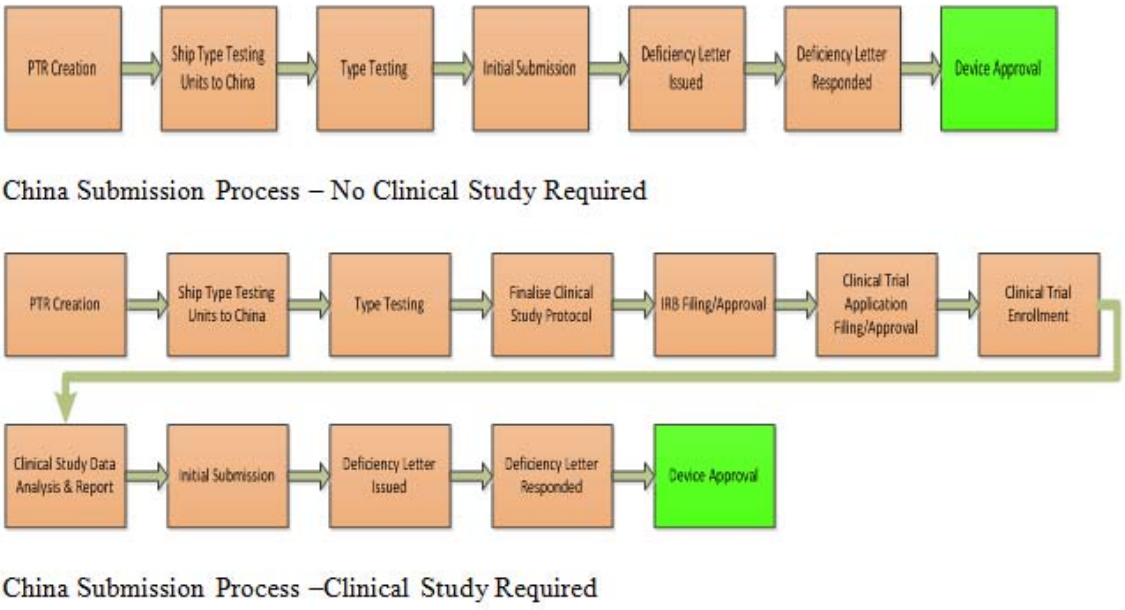

Figure 5-13: Submission Steps Comparative

Understanding the Requirements was also found to be a common theme, be it for the Product Technical Requirements, Local Type Testing, China Specific Standards or Clinical Evaluation. Whilst these weren't specifically called out in the literature review, the case review, senior leadership questionnaire and peer survey have all found the complex requirements a challenge to registration. In the peer survey 59% of respondents selected the understanding the requirements as one of their top 3 challenges.

The Submission Process poses challenges, in particular around the one deficiency letter policy. If the response is rejected or you fail to respond within 12 months you are back to the start of the submission process delaying market access to China. This unnerving possibility was expressed in the case review, senior leadership questionnaire and peer survey. In the peer survey 59% of respondents selected the submission process for CFDA review and deficiency process as one of their top 3 challenges.

Post Market there is also the challenge of Change Control to device registration. This was discussed in the literature review but also echoed by one respondent in the peer survey with regard to device registration and by another respondent with regard to market access. Device changes may require a new registration for you device and therefore incorporating all the challenges of initial approval. The business will be tasked with inventory management prior to implementation of device changes as per the lengthy approval lead times.

The challenges to market access as per the literature review completed in Chapter 2 were echoed in the Peer Survey results. This included Product Registration, Copying and Reimbursement. The top three challenges are as follows - a total of 96% chose the category 'Cost and Time for Regulatory Approval', 63% chose the category 'Potential for Device Copying' and 59% chose 'Reimbursement'.

5.4.3.1 Research Question 4

What can a regulatory function do to ensure they create a successful regulatory strategy for approval in China that will aid market access?

Each research method has presented the challenges to registration in China from what is available in the literature, what was experienced by one regulatory professional, the experiences of senior regulatory leaders in one multinational company and the experiences of multiple regulatory/quality professionals from different organisations. With all these challenges there is plenty of opportunity for the regulatory function within a business to influence success. Figure 5-14 below presents the key summary recommendations for regulatory and ultimately business success from each research method used. The combined challenges across the research data are compared and commonalities discussed.

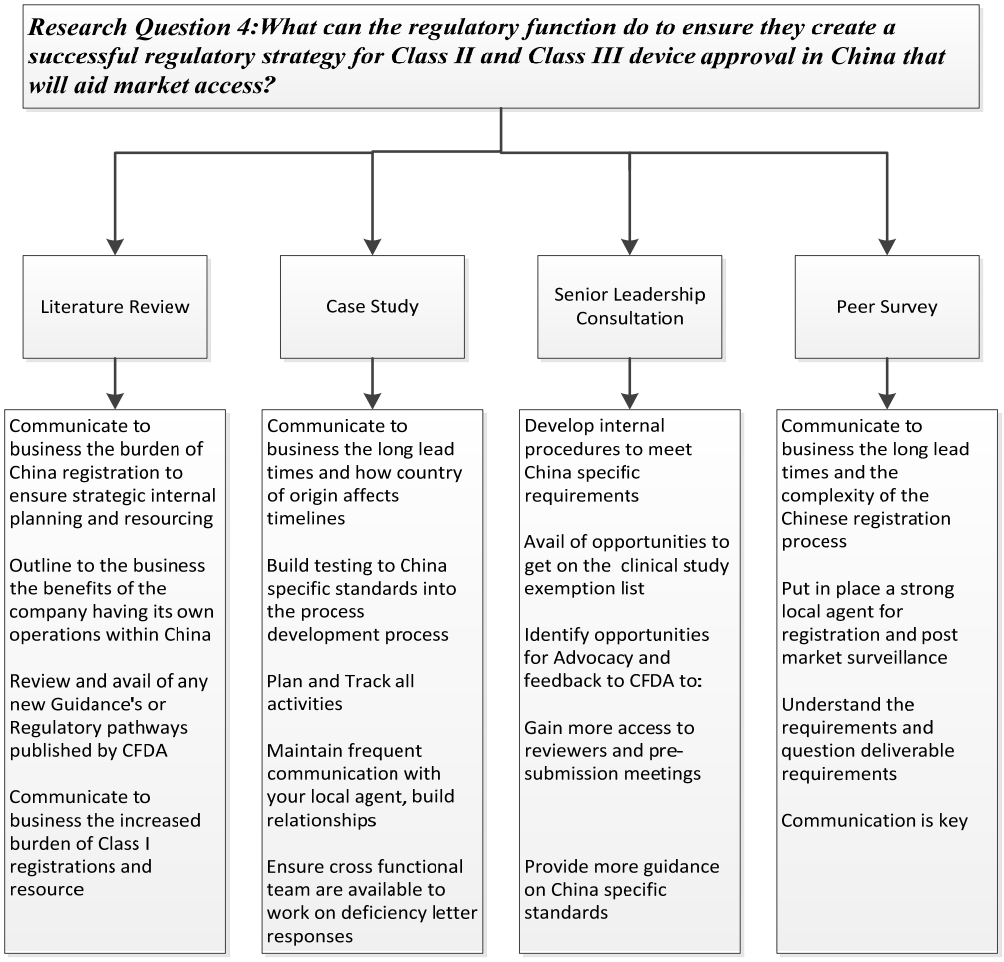

Figure 5-14: Research Question 4 Summary

There are several proactive suggestions a Regulatory function can facilitate to aid a medical device businesses success in China. This included communication and influencing that can be supported heavily by the Regulatory function. Communication is a clear theme across all research methods be it internally or externally. When asked in the Peer Survey what was their biggest lesson learned with China, eight responses were categorised as understanding the long lead-times and nine responses were categorised as understanding the requirements. It is important that your business understand the requirements for China, the lead times and the complexity of the approval process. This will help with internal strategic planning and ensure that the business is aware of the burden required to access the market in China. If you are

dealing with medium to high risk devices the real possibility of a clinical trial must also be communicated to ensure accessing China is a worthwhile investment.

As an individual working on a registration for China, frequent communication with your local China agent cannot be underestimated. The Case Review and Peer Survey highlighted communication with your Chinese colleagues. When asked in the Peer Survey what was their biggest lesson learned with China, four responses were around communication, its challenges and the importance of constant and clear communication and seven responses spoke to the importance of the local agent. There is the 'lost in translation' element that one respondent eluded to. It is recommended that you have frequent communication with your local agent, ask multiple questions to understand the requirements and challenge requests as appropriate. The regulatory professional can also influence the business by stressing the importance of the local agent and that due diligence should be completed when selecting a local agent or the business should consider setting up a local office in China. As per the literature review it may be worthwhile for a business to consider setting up manufacturing within China, a regulatory professional can work with the business to outline the advantages to registration by pursuing such an investment.

The Literature review and Senior Leadership Questionnaire recommended some additional recommendations for the Regulatory function. The regulatory function should constantly review new guidance's from CFDA to ensure the optimum regulatory strategy is outlined for any device. New processes offered by CFDA need to be utilised to a company's advantage. It is recommended that a regulatory function create its own internal procedures for China. It is a complex pathway that needs to be formalised rather than relying on an individual's experience with China. It is also recommended that your company looks for opportunities for advocacy in China. There are numerous challenges as previously discussed. Industry should use the appropriate mechanisms to influence CFDA.

6.0 Conclusion

6.1 Introduction

This research has conducted an analysis of medical device registration and market access in China. Several research methods were employed to understand the process of registration as per the new regulations, the challenges to registration and market access and if this is a worthwhile market for a medical device company to pursue. By utilizing various research methods each research objective was met. A comparison of data from the various research methods as outlined in the Methodology section was completed. This identified key challenges and recommendations for device registration and market access in China. Each research objective conclusion will be summarized further in the following section.

6.2 Research Objectives: Summary of Findings and Conclusions

6.2.1 Research Objective 1: What is the current economic environment for medical devices in China? What are the projections for the future state?

The literature identified the current economic environment in China and its future state. The combination of the size of the China market and the projected increased demand for medical devices has positioned China as a critical market for a medical device company to gain access to. The faster a company can gain approval for their medical device product in China, the faster it can reap the awards of the revenue the China market will bring. The peer survey reflected the opportunities there is for the medical device business in China. The majority of respondents to the survey said their perception of the importance to their business of accessing the Chinese market was either important or extremely important. This shows that the respondents within their individual companies are aware of the market size in China and the revenue it can bring to the business.

6.2.2 Research Objective 2: What has changed in the medical device regulations in China, with the updated regulations enforced in 2014?

The literature review identified what has changed in the medical device regulations in China with the introduction of the new regulations as per Order 650 in 2014. A further analysis was completed in Chapter 5 to summarise the changes, what is amended, what is new and what has

been reduced in comparison with Order 276. What has been reduced with the introduction of Order 650 is minimal but there are benefits to the manufacturer. In particular a Class I manufacturer no longer requires device registration only notification. Additional pathways for device registration are also available for innovative devices, this includes the 'green channel' registration pathway established in 2014 and the more recent 'priority review' in affect since 2017. The 'green channel' to date has been seen to benefit domestic companies for the majority. The 'priority review' is relatively new so it is to be determined what type devices and manufacturers have had success in accessing this pathway.

The new regulations have now been implemented for three years. CFDA's Order 650 issued in 2014 was intended to improve and standardize registration of medical devices. The research completed as per Research Objective 3 detail the ongoing challenges for medical device registration as per Order 650.

6.2.3 Research Objective 3: What is the impact and challenges to product registration and market access in China?

The literature identified the main challenges to product registration in a pre-market setting as Local Clinical Trials, Country of Origin and Approval Timelines. In a post market setting Change Control were also identified as a challenge. Upon comparative with the further research methods employed one key challenge to registration is echoed repeatedly, this is the requirement for Local Clinical Trials. If a clinical trial is required it will bring increased timelines, cost and resourcing to access the market in China. As per the research results this is a well-recognized challenge when pursuing registration approval in China. Understanding the Requirements, Submission & Deficiency Process, Country of Origin, Approval Timelines, Clinical Evaluation, China Specific Standards and Change Control were all also identified as key challenges to product registration. All these factors accumulate in long lead times for product approval and ultimate market access. Figure 6-1 schematically outlines all the challenges that were identified as part of the literature review and/or reiterated within the practical research completed.

Figure 6-1: Key Challenges to Product Registration

The challenges to market access as per the literature review completed were also substantiated by the Peer Survey results. The literature identified the main challenges to market access as Copying, Lack of Local Knowledge, Product Registration and Reimbursement. The peer survey identified Product Registration, Copying and Reimbursement as the top 3 challenges. A total of 96% chose the category 'Cost and Time for Regulatory Approval' for challenges to market access. We can conclude that it is understood within industry that the product registration is a highly ranked obstacle to market access in China. The peer survey also identified Change Control as a challenge to market access due to the potential long lead times and implication to inventory management. Figure 6-2 schematically outlines all the challenges that were identified as part of the literature review and/or reiterated within the practical research completed.

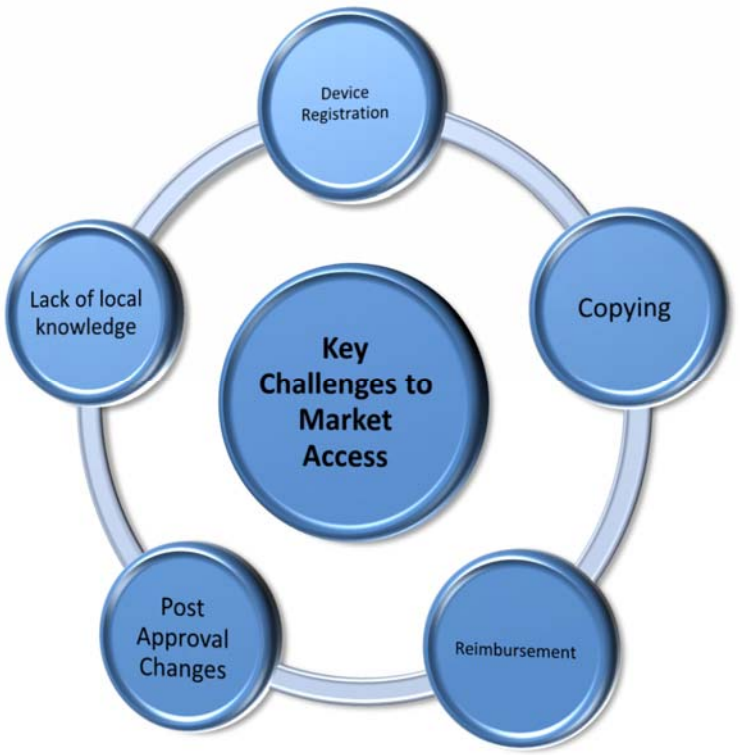

Figure 6-2: Key Challenges to Market Access

6.2.4 Research Objective 4: What can the regulatory function do to ensure they create a successful regulatory strategy for Class II and Class III device approval in China that will aid market access?

The literature review identified several strategies for a business to aid market access in China. There are several proactive suggestions a Regulatory function can facilitate to aid a medical device businesses success in China. Upon comparative with the other research methods one key recommendation is substantiated, this being 'Communication'. Communication is a clear theme across all research methods be it internally or externally. The Case Review and Peer Survey highlighted communication with your Chinese colleagues. It is recommended that you have frequent communication with your local agent, ask multiple questions to understand the requirements and challenge requests as appropriate. The regulatory professional can also influence the business by stressing the importance of the local agent and that due diligence should be completed when selecting a local agent or the business should consider setting up a

local office in China. As per the literature review it may be worthwhile for a business to consider setting up manufacturing within China, a regulatory professional can work with the business to outline the advantages to registration by pursuing such an investment. It is important that your business understand the requirements for China, the lead times and the complexity of the approval process. This will help with internal strategic planning and ensure that the business is aware of the burden required to access the market in China.

The Literature review and Senior Leadership Questionnaire also brought up some additional recommendations for the Regulatory function. The regulatory function should constantly review new guidance's from CFDA to ensure the optimum regulatory strategy is outlined for any device. New processes offered by CFDA need to be utilised to a company's advantage. It is recommended that a regulatory function create its own internal procedures for China. It is a complex pathway that needs to be formalised rather than relying on an individual's experience with China. It is also recommended that your company looks for opportunities for advocacy in China. There are numerous challenges as previously discussed. Industry should use the appropriate mechanisms to influence CFDA.

Figure 6-3: Key Recommendations

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APPENDIX A Literature Review Protocol & Report

Literature Protocol & Report

THESIS –LITERATURE REVIEW

Contents

Purpose

The purpose of this protocol is to define the criteria which will be utilized to perform a literature search and report for the Thesis – 'An analysis of medical device registration and market access in China'

Scope

The scope of the literature search includes a query of scientific databases Embase and PubMed for a five/ten year time period. It is expected that this will provide sufficient coverage of any literature that might have arose during the time period.

Methods

Period covered by Search: 5 years - 10 years

Literature Sources used to identify data:

- Embase
- Pubmed
- Google Scholar
- Internal Company and External Presentations
- Conferences
- Google
- RAPs membership site

Keyword Search:

- China AND Medical Device
- China AND Healthcare
- China AND Regulatory

Database search details: Details for Embase and Pubmed databases are covered in Appendix A, Literature Search Report. All searches will be performed through online databases.

Selection criteria The following criteria will be used to assess the suitability of material (articles, reports, etc.) for

	inclusion/exclusion in the analysis stage of this report:
Inclusion Criteria:	Journals Books Reports Web Articles Conference Proceedings Web Pages
Exclusion Criteria:	Material specific to Pharmaceutical's or other Industries Full text is available only in a language for which an English translation is not readily available Subject Matter not applicable upon review
	Outputs All literature citations selected for inclusion will be listed in Appendix B: References of the Literature Report. Where the same paper or article appears repeatedly in database searches it will be noted and flagged in the report if the data in the original paper is being used to inform subsequent author's analysis. Otherwise the paper/ article will be treated as though it appeared in only one search and evaluated on its own merits
Data selection process:	A flowchart describing how data were assessed for suitability for inclusion in the clinical evaluation is included overleaf – Figure 1: Citation Assessment Flowchart. • The outputs of the Literature Search will be summarized and any deviations from the Search protocol will be noted. Following this method a summary identifying all

	outputs of the database search will be created. • The screening and selection of the published literature will be conducted as detailed in Figure 1 and recorded in a report. • Those data which were identified and subsequently excluded following closer review will be recorded and the rationale for exclusion noted.
Date of Search:	The dates of the respective searches will be listed in the report
Name of person conducting search:	The search will be conducted by Elaine Gullane

The flowchart in Figure 1 below visually outlines the process used in assessing citations retrieved from queries of online databases for suitability for inclusion in the literature review.

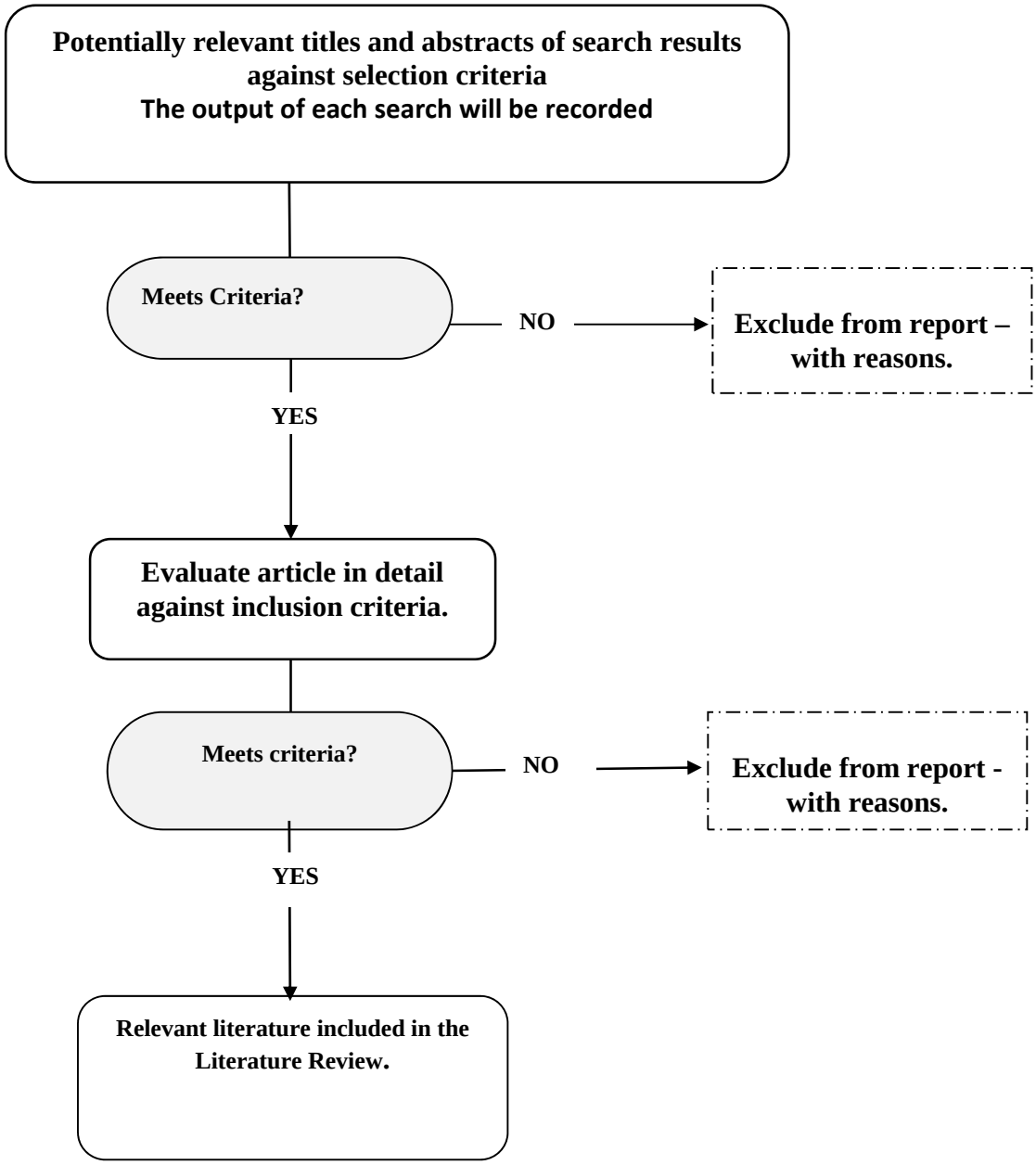


Figure 37 Citation Assessment Flowchart

Results

Search completed on the 18/December/2016 by Elaine Gullane

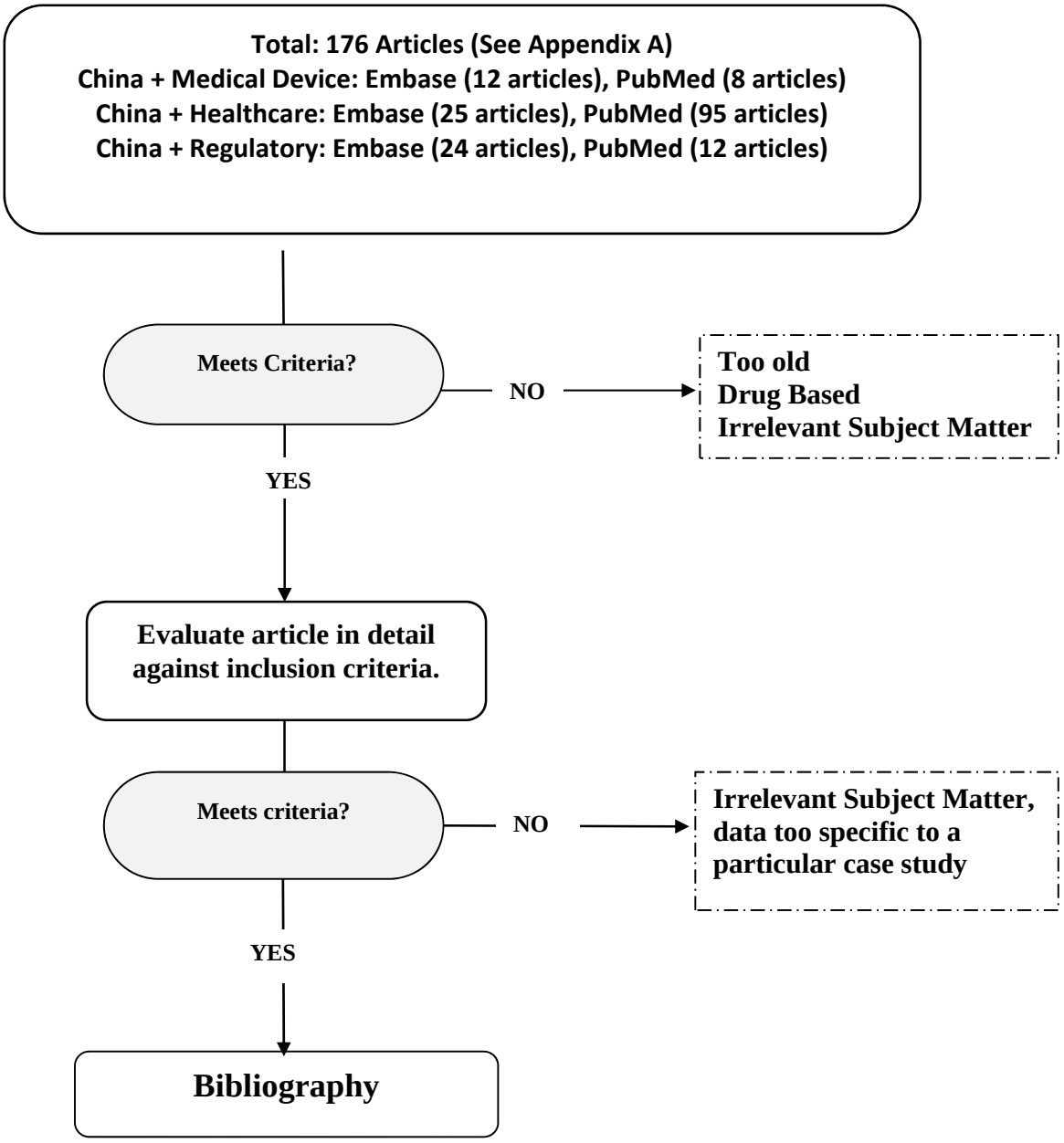


Figure 1: Citation Assessment Flowchart with Results

Conclusion

The majority of articles from the search results in Embase and PubMed were excluded from the literature review. Due to the new regulations only being in force since 2014 there hasn't been many journals published on this subject matter for medical devices. On review of the journals the data was found either to be outdated, specific to the pharmaceutical industry or specific to case studies in healthcare. Other sources of data were used to complete the literature review, these included internal company and external presentations from SME's, web articles, professional reports and articles published on the RAPs membership site.

Appendix A

Embase Search 1: China + Medical Device

1	The Preliminary Study on the Construction of Medical Device Naming System in China
2	Medical Device Market in China
3	Accessing the medical device market in the people's republic of china-policy changes since the restructuring of the china fda
4	The current situation and consideration on the quality of medical device standards in China
5	Comparative study of medical device classification between China and USA
6	Analysis on current laws and regulations of medical device clinical trial in China
7	Study on situations of review and pre-evaluation for medical device product specification in China
8	Study on the reform and improvement of the medical device registration system in China
9	China healthcare reform and opportunities for medical device industry
10	A survey on publication standards of medical drug and device advertisements published in core medical journals in China
11	Discussions on the regulatory requirements for medical device risk management in China
12	Medical device registration system comparison between China and U.S.A

Embase Search 2: China + Healthcare

1	Expanding public health in China: an empirical analysis of healthcare inputs and outputs
2	The attitudes of primary healthcare providers towards web-based training on public health services in rural China: a cross-sectional study
3	Assessing spatial access to public and private hospitals in Sichuan, China: The influence of the private sector on the healthcare geography in China
4	Direct medical cost and healthcare resource utilization in elderly patients with type 2 diabetes mellitus among insured urban population in china
5	Cost-effectiveness of rivaroxaban versus warfarin for stroke prevention in nonvalvular atrial fibrillation in the Guangdong healthcare setting in China
6	Adherence, healthcare resource utilization and direct medical costs among patients with alzheimer's disease in Tianjin, China
7	Administrative claims analysis of all-cause healthcare resource utilization for T2DM with chronic comorbidities patients in China

8	Retrospective survey of the efficacy of mandatory implementation of the Essential Medicine Policy in the primary healthcare setting in China: failure to promote the rational use of antibiotics in clinics
9	Sexual and reproductive healthcare utilization among women aged 40 to 49 in rural China
10	From a finger on the pulse to modern technology—the transformation of healthcare in China
11	Improving hand hygiene compliance among healthcare workers: an intervention study in a Hospital in Guizhou Province, China
12	Effectiveness and impact of the cross-border healthcare model as implemented by non-governmental organizations: Case study of the malaria control programs by health poverty action on the China-Myanmar border
13	The effect of herd formation among healthcare investors on health sector growth in China
14	Job satisfaction and associated factors among healthcare staff: A cross-sectional study in Guangdong Province, China
15	Point-prevalence survey of healthcare-associated infections in Beijing, China: A survey and analysis in 2014
16	Annual surveys for point-prevalence of healthcare-associated infection in a tertiary hospital in Beijing, China, 2012-2014
17	Knowledge, attitudes, and practices survey of drug allergy among healthcare practitioners in central China: A multicenter study
18	The impact of a bundled policy intervention on improving the performance of rural healthcare in China
19	Nursing education in China: Meeting the global demand for quality healthcare
20	Job satisfaction of urban community health workers after the 2009 healthcare reform in China: A systematic review
21	Impacts of a new insurance benefit with capitated provider payment on healthcare utilization, expenditure and quality of medication prescribing in China
22	International publication trends and collaboration performance of China in healthcare science and services research
23	Access to and affordability of healthcare for TB patients in China: Issues and challenges
24	Measles Outbreak among Previously Immunized Adult Healthcare Workers, China, 2015
25	Hypertension prevalence, awareness, treatment, and control following China's healthcare reform

Embase Search 3: China + Regulatory

1	China's new environmental protection regulatory regime: Effects and gaps
2	Challenges in orphan drug development and regulatory policy in China
3	Regulatory watch: Innovative drug availability in China
4	Overview of China’s pediatric drug situation and regulatory policy
5	A review of the common technical document (CTD) regulatory dossier for generic drugs in china
6	Major regulatory changes in China to impact western drug developers
7	Regulatory guidelines for approval of biosimilars in India, Europe, Brazil and China: A comprehensive overview
8	The Contrasting Medicines Regulatory Environments of China and the Western World
9	Regulatory development of narcotic drugs in China and extraterritorial revelation
10	Investigation of gene regulatory networks associated with autism spectrum disorder based on MiRNA expression in China
11	Enterprise-Level Motivations, Regulatory Pressures, and Corporate Environmental Management in Guangzhou, China
12	From Regulatory Approval to Subsidized Patient Access in the Asia-Pacific Region: A Comparison of Systems Across Australia, China, Japan, Korea, New Zealand, Taiwan, and Thailand
13	Current issues with the regulatory framework for managing soil contamination in China
14	A Legislative Reform for the Food Safety System of China: A Regulatory Paradigm Shift and Collaborative Governance
15	Regulatory system reform of occupational health and safety in China
16	From regulatory approval to subsidised patient access in the Asia-pacific region: A comparison of systems across Australia, China, Japan, Korea, New Zealand, Taiwan and Thailand
17	The historical evolution of china's drug regulatory system
18	Assessing new developments in the pre-market regulatory process of medical devices in the People's Republic of China
19	Navigating the regulatory CMC landscape in China
20	What happened to outsourcing in Asia?: The industry may not be ready for India and China as regulatory issues emerge

21	Frequency of Regulatory T-Cells in the Peripheral Blood of Patients with Pulmonary Tuberculosis from Shanxi Province, China
22	Regulatory and policy control on food safety in China.
23	Exploring Best Practices on Development Regulatory Affairs and Clinical Development Related to Multiregional Clinical Trials (MRCTs) in China, Korea, and Taiwan
24	MRNA expression levels among cell regulatory and DNA damage genes in benzene-exposed workers in China

PubMed Search 1: China + Medical Device

Search: (China[Title]) AND Medical Device[Title] Filters: 5 years

PubMed Results

Items 1 - 8 of 8

1	The Preliminary Study on the Construction of Medical Device Naming System in China
2	Medical device market in China
3	The current situation and consideration on the quality of medical device standards in China
4	Accessing the Medical Device Market in the People's Republic of China--Policy Changes Since the Restructuring of the China Fda
5	Comparative study of medical device classification between China and USA
6	Analysis on current laws and regulations of medical device clinical trial in China
7	Study on situations of review and pre-evaluation for medical device product specification in China
8	Study on the reform and improvement of the medical device registration system in China

PubMed Search 2: China + Healthcare

PubMed Results

Items 1 - 95 of 95

1	The attitudes of primary healthcare providers towards web-based training on public health services in rural China: a cross-sectional study
2	Assessing spatial access to public and private hospitals in Sichuan, China: The influence of the private sector on the healthcare geography in China
3	Understanding the rise of Yinao in China: A commentary on the little known phenomenon of healthcare violence.
4	Shortage of healthcare professionals in China.
5	From a finger on the pulse to modern technology-the transformation of healthcare in

	China
6	Effectiveness and impact of the cross-border healthcare model as implemented by non-governmental organizations: case study of the malaria control programs by health poverty action on the China-Myanmar border.
7	Sexual and reproductive healthcare utilization among women aged 40 to 49 in rural China.
8	Doctor Competence and the Demand for Healthcare: Evidence from Rural China.
9	Retrospective survey of the efficacy of mandatory implementation of the Essential Medicine Policy in the primary healthcare setting in China: failure to promote the rational use of antibiotics in clinics
10	The role of family physicians contracted healthcare in China: A "Cardiotonic" or a "Band-Aid" for healthcare reform?
11	Job satisfaction and associated factors among healthcare staff: a cross-sectional study in Guangdong Province, China.
12	The effect of herd formation among healthcare investors on health sector growth in China.
13	Measles Outbreak among Previously Immunized Adult Healthcare Workers, China, 2015.
14	Improving hand hygiene compliance among healthcare workers: an intervention study in a Hospital in Guizhou Province, China.
15	Inequity in level of healthcare utilization before and after universal health coverage reforms in China: evidence from household surveys in Sichuan Province.
16	Assessment of diabetes care and the healthcare system in economically and transport underdeveloped rural mountain areas of western China: A cross-sectional survey.
17	Knowledge, attitudes, and practices survey of drug allergy among healthcare practitioners in central China: a multicenter study.
18	Point-prevalence survey of healthcare-associated infections in Beijing, China: a survey and analysis in 2014.
19	Healthcare reform in China: making sense of a policy experiment?
20	Annual surveys for point-prevalence of healthcare-associated infection in a tertiary hospital in Beijing, China, 2012-2014.
21	Prevalence and factors associated with occupational burnout among HIV/AIDS healthcare workers in China: a cross-sectional study.
22	The impact of a bundled policy intervention on improving the performance of rural healthcare in China.
23	Job satisfaction of village doctors during the new healthcare reforms in China.
24	Attitudes towards Advance Care Planning and Healthcare Autonomy among Community-Dwelling Older Adults in Beijing, China.
25	International publication trends and collaboration performance of China in healthcare science and services research.
26	Access to and affordability of healthcare for TB patients in China: issues and challenges.
27	Job satisfaction of urban community health workers after the 2009 healthcare reform in China: a systematic review
28	China takes an active role in combating an Ebola outbreak: On-site observations and reflections from a Chinese healthcare provider.
29	Evolving Healthcare Quality in Top Tertiary General Hospitals in China during the China Healthcare Reform (2010-2012) from the Perspective of Inpatient Mortality.

30	Truth-telling to the patient, family, and the sexual partner: a rights approach to the role of healthcare providers in adult HIV disclosure in China.
31	Workplace Violence and Job Performance among Community Healthcare Workers in China: The Mediator Role of Quality of Life.
32	Integrating traditional Chinese medicine into mainstream healthcare system in Hong Kong, China-A model of integrative medicine in the HKU-SZ Hospital.
33	Impacts of a new insurance benefit with capitated provider payment on healthcare utilization, expenditure and quality of medication prescribing in China.
34	Characteristics and Healthcare Resource use of Patients with Major Depressive Disorder Initiated on Snri Compared to Ssri In Beijing China.
35	[Investigation of current cognition of occupational exposure to HIV in healthcare workers in Liuzhou, China].
36	Alarming and increasing prevalence of multidrug-resistant Pseudomonas aeruginosa among healthcare-associated infections in China: A meta-analysis of cross-sectional studies.
37	HIV prevention among street-based sex workers (SSWs) in Chongqing, China: interviews with SSWs, clients and healthcare providers.
38	Tuberculosis prevention in healthcare workers in China 10 years after the severe acute respiratory syndrome pandemic.
39	Spatial inequity in access to healthcare facilities at a county level in a developing country: a case study of Deqing County, Zhejiang, China.
40	Epidemiology and the prognosis of healthcare-associated infective endocarditis in China: the significance of non-nosocomial acquisition.
41	Differences in Staphylococcus aureus nasal carriage and molecular characteristics among community residents and healthcare workers at Sun Yat-Sen University, Guangzhou, Southern China.
42	Use of appropriate healthcare technologies: a cross-sectional study in rural Zhejiang of China.
43	Self-reported hand hygiene practices, and feasibility and acceptability of alcohol-based hand rubs among village healthcare workers in Inner Mongolia, China.
44	Web-based training for primary healthcare workers in rural China: a qualitative exploration of stakeholders' perceptions.
45	China lays out bold plan to improve healthcare.
46	Who benefits from government healthcare subsidies? An assessment of the equity of healthcare benefits distribution in China.
47	The development of intelligent healthcare in China.
48	Determinants of initial utilization of community healthcare services among patients with major non-communicable chronic diseases in South China.
49	Introduce fair competition mechanism in China healthcare system.
50	Tuberculosis among healthcare workers in southeastern China: A retrospective study of 7-year surveillance data.
51	Evaluation of outbreak detection performance using multi-stream syndromic surveillance for influenza-like illness in rural Hubei Province, China: a temporal simulation model based on healthcare-seeking behaviors.
52	Factors influencing the quality of preconception healthcare in China: applying a preconceptional instrument to assess healthcare needs.

53	Epidemiology of multimorbidity in China and implications for the healthcare system: cross-sectional survey among 162,464 community household residents in southern China.
54	The healthcare costs of secondhand smoke exposure in rural China.
55	Point-prevalence of healthcare-associated infection in china in 2010: a large multicenter epidemiological survey.
56	A Changing Healthcare System Model: The Effectiveness of Knowledge, Attitude, and Skill of Nursing Assistants Who Attend Senile Dementia Patients in Nursing Homes in Xi'an, China - A Questionnaire Survey.
57	The mediating effects of burnout on the relationship between anxiety symptoms and occupational stress among community healthcare workers in China: a cross-sectional study.
58	Healthcare reform in the United States and China: pharmaceutical market implications.
59	Low back pain beliefs are associated to age, location of work, education and pain-related disability in Chinese healthcare professionals working in China: a cross sectional survey.
60	Equity in access to healthcare among the urban elderly in China: does health insurance matter?
61	Factors associated with utilization of reproductive healthcare services among migrant women workers in Chong Qing, China.
62	Suggestions to ameliorate the inequity in urban/rural allocation of healthcare resources in China.
63	Evaluation of a systematic cardiovascular disease risk reduction strategy in primary healthcare: an exploratory study from Zhejiang, China.
64	Integration of rural and urban healthcare insurance schemes in China: an empirical research.
65	Healthcare provider intervention on smoking and quit attempts among HIV-positive versus HIV-negative MSM smokers in Chengdu, China.
66	Acquired immunodeficiency syndrome/human immunodeficiency virus knowledge, attitudes, and practices, and use of healthcare services among rural migrants: a cross-sectional study in China.
67	China launched a pilot project to improve its rare disease healthcare levels.
68	A comparison of outpatient healthcare expenditures between public and private medical institutions in urban China: an instrumental variable approach.
69	Empowering village doctors and enhancing rural healthcare using cloud computing in a rural area of mainland China.
70	The impact of clinical pharmacy services in China on the quality use of medicines: a systematic review in context of China's current healthcare reform.
71	The political economy of healthcare reform in China: negotiating public and private.
72	Annual point-prevalence of healthcare-associated infection surveys in a university hospital in China, 2007-2011.
73	Influence of gender equity awareness on women's reproductive healthcare in rural areas of mid-west China.
74	Advancing universal coverage of healthcare in China: translating political will into policy and practice.
75	Prevalence of latent tuberculosis infection among healthcare workers in China as detected by two interferon-gamma release assays.
76	Building a professionalism framework for healthcare providers in China: a nominal group

	technique study.
77	Serological investigation of subclinical influenza A(H7H9) infection among healthcare and non-healthcare workers in Zhejiang Province, China.
78	Theory and best practices of medical professionalism as well as the policy recommendations for healthcare reform in China].
79	Access to healthcare and medical expenditure for the middle-aged and elderly: observations from China.
80	Assessing equity of healthcare utilization in rural China: results from nationally representative surveys from 1993 to 2008.
81	Experiences with primary healthcare in Fuzhou, urban China, in the context of health sector reform: a mixed methods study.
82	Analysis of government investment in primary healthcare institutions to promote equity during the three-year health reform program in China.
83	Some reflections on China, US-Chinese relations, and healthcare in China.
84	Health governance and healthcare reforms in China.
85	Consumer choice among Mutual Healthcare Purchasers: a feasible option for China?
86	Health insurance benefit design and healthcare utilization in northern rural China.
87	Listeriosis at a tertiary care hospital in beijing, china: high prevalence of nonclustered healthcare-associated cases among adult patients.
88	Effects and cost-effectiveness of a guideline-oriented primary healthcare hypertension management program in Beijing, China: results from a 1-year controlled trial.
89	Factors associated with the transmission of pandemic (H1N1) 2009 among hospital healthcare workers in Beijing, China.
90	A review of healthcare service and education provision of Autism Spectrum Condition in mainland China.
91	Performance comparison among the major healthcare financing systems in six cities of the Pearl River Delta region, mainland China.
92	Antibiotic resistance amongst healthcare-associated pathogens in China.
93	Controlling cost escalation of healthcare: making universal health coverage sustainable in China.
94	Healthcare sector reform and its influence on public hospitals in mainland China.
95	Application of case classification in healthcare quality assessment in China.

PubMed Search 3: China + Regulatory

Search: (China [Title]) AND Regulatory[Title] Filters: 5 years

PubMed Results

Items 1 - 12 of 12

1	Regulatory watch: Innovative drug availability in China.
2	A Legislative Reform for the Food Safety System of China: A Regulatory Paradigm Shift and Collaborative Governance.
3	Investigation of Gene Regulatory Networks Associated with Autism Spectrum Disorder Based on MiRNA Expression in China.

4	Regulatory Considerations for Approval of Generic Inhalation Drug Products in the US, EU, Brazil, China, and India.
5	Enterprise-Level Motivations, Regulatory Pressures, and Corporate Environmental Management in Guangzhou, China.
6	Regulatory system reform of occupational health and safety in China.
7	From Regulatory Approval to Subsidised Patient Access in the Asia-Pacific Region: A Comparison of Systems Across Australia, China, Japan, Korea, New Zealand, Taiwan And Thailand.
8	Assessing new developments in the pre-market regulatory process of medical devices in the People's Republic of China.
9	Frequency of regulatory T-cells in the peripheral blood of patients with pulmonary tuberculosis from shanxi province, china.
10	Regulatory and policy control on food safety in China.
11	mRNA expression levels among cell regulatory and DNA damage genes in benzene-exposed workers in China.
12	Organic trace pollutants in the aquatic environment--regulatory and technical problem-solving approaches in Germany and China.

APPENDIX B SurveyMonkey™ Questionnaire

MSc in Medical Technology Regulatory Affairs - Thesis Survey to collect data on the perception and experiences of the Chinese Medical Device Regulations and Market

+ Add Page Title

1. What type company do you work for and what is the size of your Regulatory Affairs (RA) Department? (Please select one option for the company size and one option for the RA Dept size)

- [ ] Small Company(< 50 employees)
- [ ] Medium Company (>50 <249 employees)
- [ ] Multi National Company
- [ ] Small RA Dept (<5 employees)
- [ ] Medium RA Dept (>5<20 employees)
- [ ] Large RA Dept (>20 employees)
- [ ] Other (please specify)

2. What is your perception of the importance to your company of accessing the Chinese market?

- ◯ Extremely Unimportant
- ◯ Unimportant
- ◯ Moderate
- ◯ Important
- ◯ Extremely Important

3. What is your perception of the level of difficulty in gaining market access for a medical device in China?

- ◯ Extremely Easy
- ◯ Easy
- ◯ Moderate
- ◯ Difficult
- ◯ Extremely Difficult

4. What is your perception of the level of difficulty in gaining Regulatory Approval of a medical device in China?

- ◯ Extremely Easy
- ◯ Easy
- ◯ Moderate
- ◯ Difficult
- ◯ Extremely Difficult

5. Does your company have a local manufacturing facility within China?

- ◯ Yes
- ◯ No
- ◯ Dont know

6. Has your company received approval for a device in China?

- ◯ Yes (as per new regulations in China - Order 650 in effect since 2014)
- ◯ Yes (as per old regulations in China - Order 276 prior to 2014)
- ◯ Yes (as per new and old regulations in China - Order 650 and Order 276 respectively)
- ◯ No
- ◯ Dont know

7. Who is your local agent in China?

- ◯ Local Agent
- ◯ Subsidiary of your company
- ◯ Consultant
- ◯ Dont know
- ◯ Other (please specify)

[ ]

8. Can you select your Top 3 challenges (as applicable) to receiving medical device approval in China?

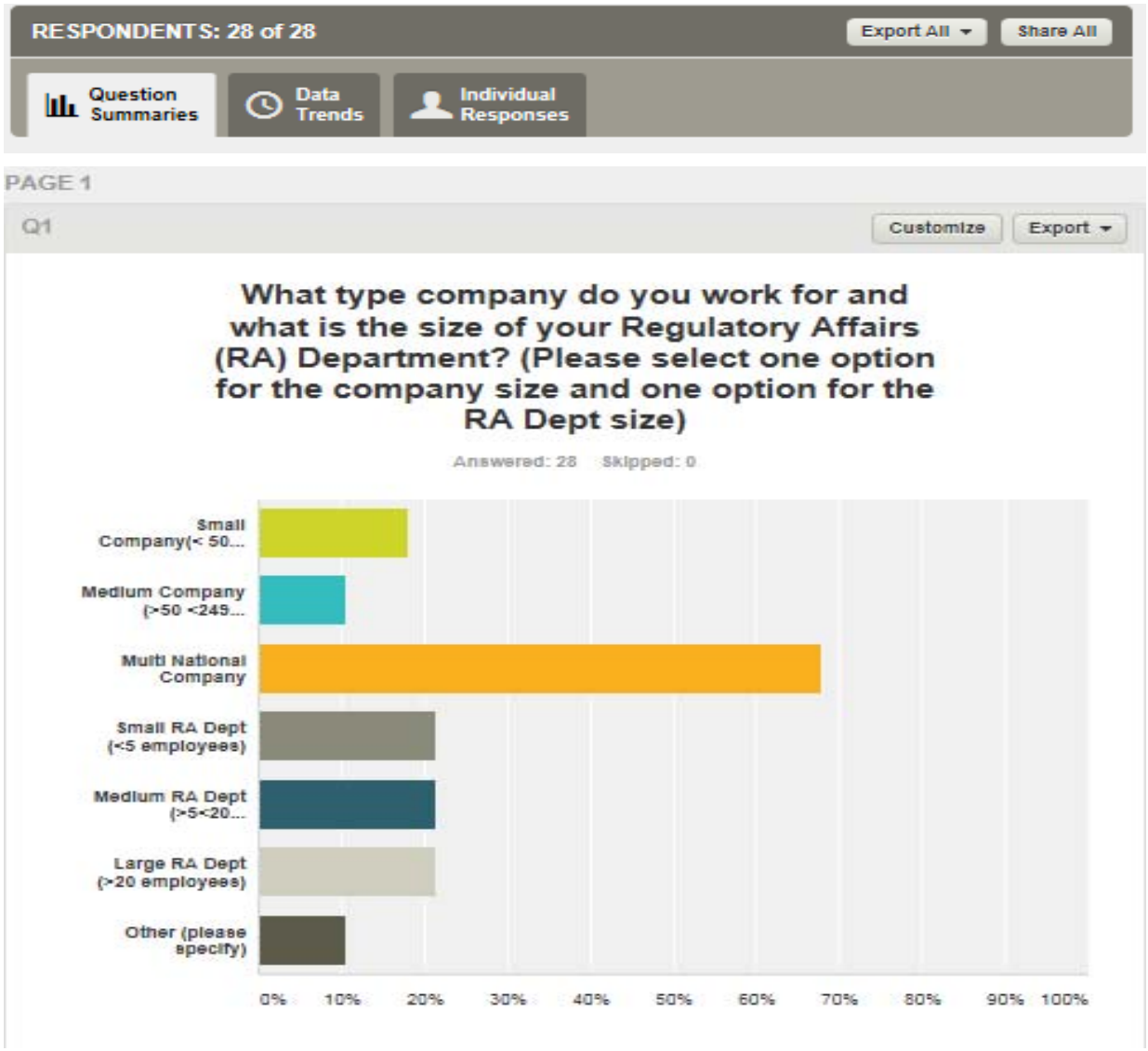
- [ ] Local Clinical Trial Requirements
- [ ] Compilation of China specific Clinical Evaluation Report
- [ ] Submission Process for CFDA Review & Deficiencies
- [ ] Compliance to China Specific Standards
- [ ] Country Of Origin Approval Requirement
- [ ] Understanding the Requirements
- [ ] Other (please specify)

9. Can you select your Top 3 challenges (as applicable) to accessing the medical device market in China?

- [ ] Cost and Time for Regulatory Approval
- [ ] Potential for Device 'Copying'
- [ ] Requirements for a large Marketing & Sales Team
- [ ] Reimbursement Challenges
- [ ] Other (please specify)

10. What is the biggest lesson learned when dealing with the Chinese market?

APPENDIX C SurveyMonkey™ Raw Data

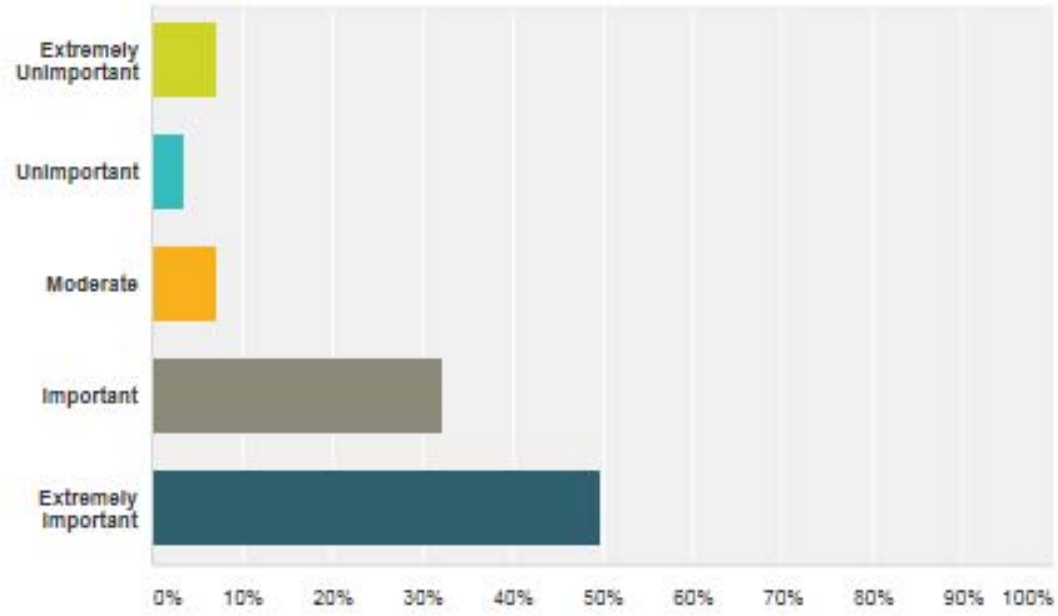


Answer Choices		Responses	
Small Company(< 50 employees)		17.86%	5
Medium Company (>50 <249 employees)		10.71%	3
Multi National Company		67.86%	19
Small RA Dept (<5 employees)		21.43%	6
Medium RA Dept (>5<20 employees)		21.43%	6
Large RA Dept (>20 employees)		21.43%	6
Other (please specify)	Responses	10.71%	3
Total Respondents: 28			

Q2 Customize Export

What is your perception of the importance to your company of accessing the Chinese market?

Answered: 28 Skipped: 0

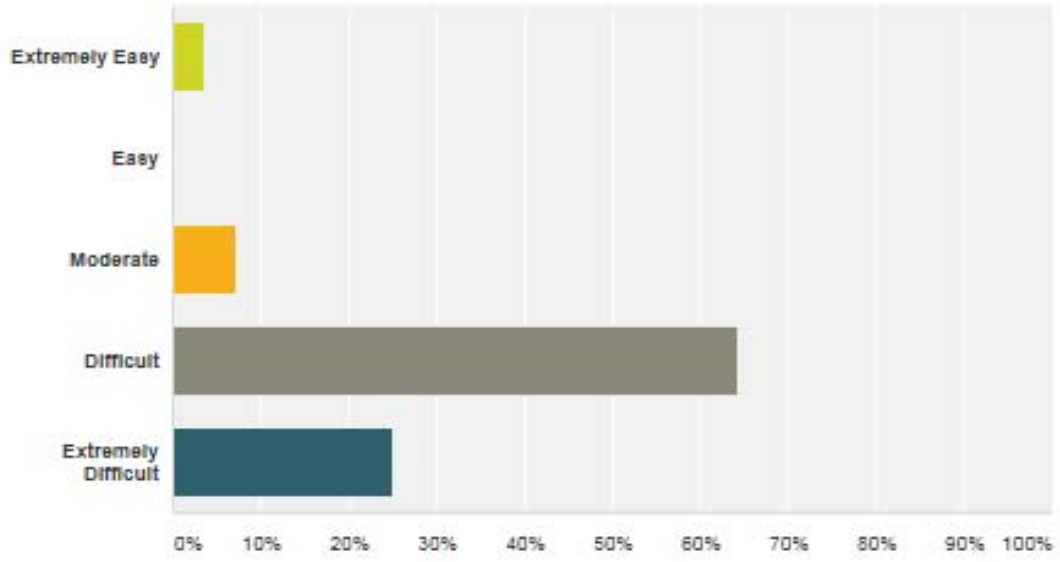


Answer Choices	Responses	
Extremely Unimportant	7.14%	2
Unimportant	3.57%	1
Moderate	7.14%	2
Important	32.14%	9
Extremely Important	50.00%	14
Total		28

Q3 Customize Export

What is your perception of the level of difficulty in gaining market access for a medical device in China?

Answered: 28 Skipped: 0

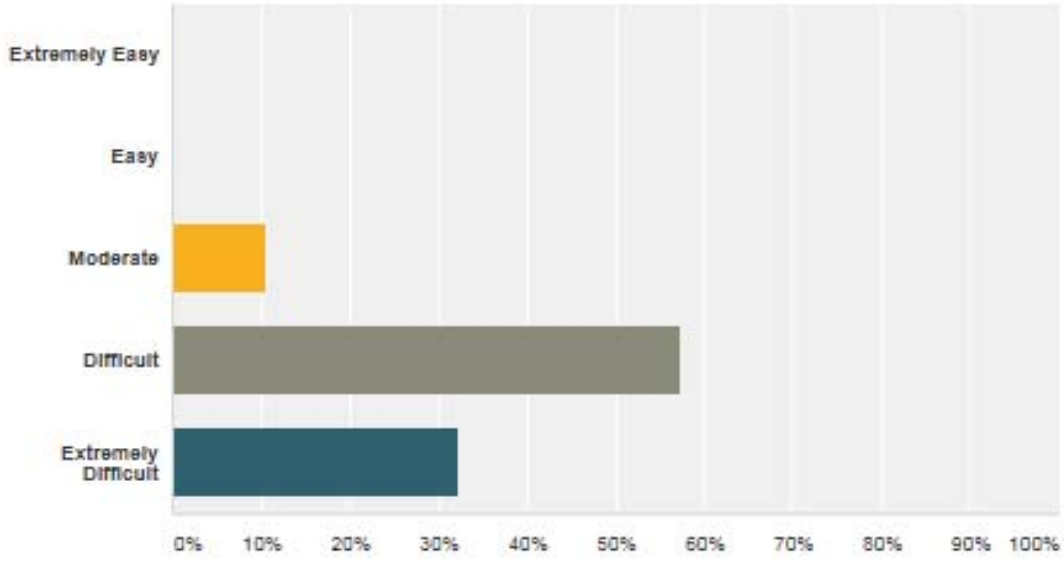


Answer Choices	Responses	
Extremely Easy	3.57%	1
Easy	0.00%	0
Moderate	7.14%	2
Difficult	64.29%	18
Extremely Difficult	25.00%	7
Total		28

Q4 Customize Export

What is your perception of the level of difficulty in gaining Regulatory Approval of a medical device in China?

Answered: 28 Skipped: 0

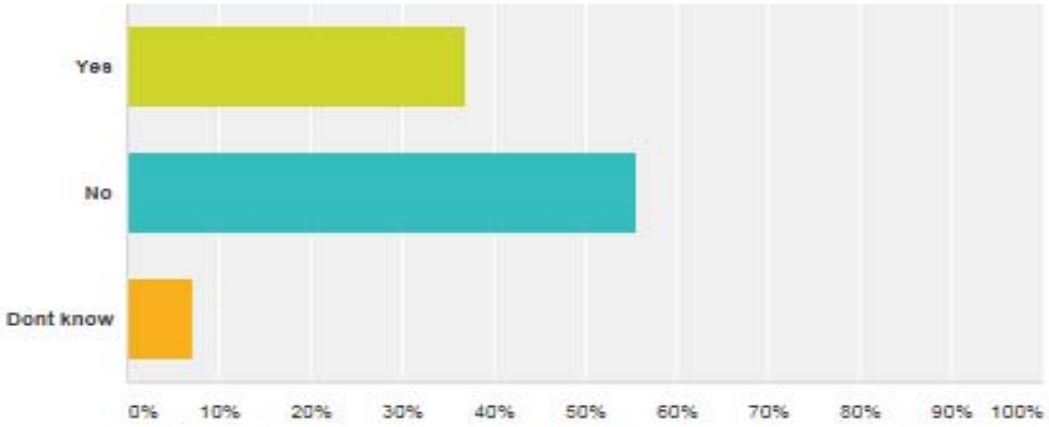


Answer Choices	Responses	
Extremely Easy	0.00%	0
Easy	0.00%	0
Moderate	10.71%	3
Difficult	57.14%	16
Extremely Difficult	32.14%	9
Total		28

Q5 Customize Export

Does your company have a local manufacturing facility within China?

Answered: 27 Skipped: 1

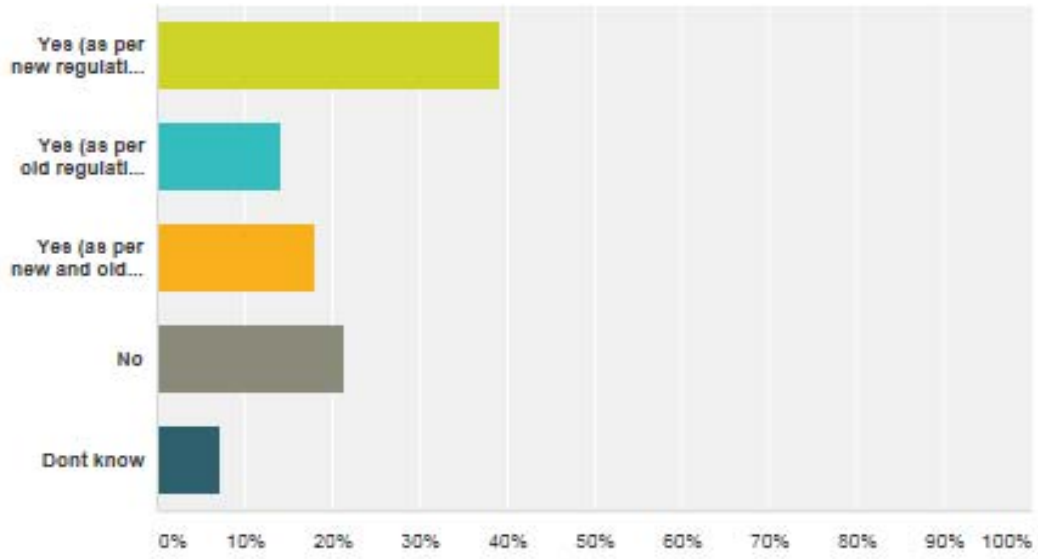


Answer Choices	Responses	
Yes	37.04%	10
No	55.56%	15
Dont know	7.41%	2
Total		27

Q6 Customize Export

Has your company received approval for a device in China?

Answered: 28 Skipped: 0

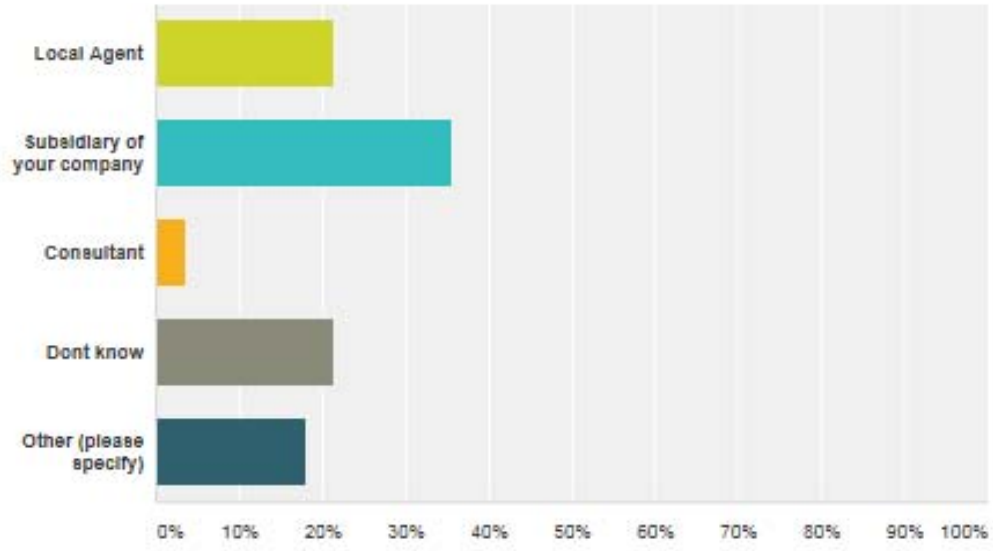


Answer Choices	Responses	
Yes (as per new regulations in China - Order 650 in effect since 2014)	39.29%	11
Yes (as per old regulations in China - Order 276 prior to 2014)	14.29%	4
Yes (as per new and old regulations in China - Order 650 and Order 276 respectively)	17.86%	5
No	21.43%	6
Dont know	7.14%	2
Total		28

Q7 Customize Export

Who is your local agent in China?

Answered: 28 Skipped: 0

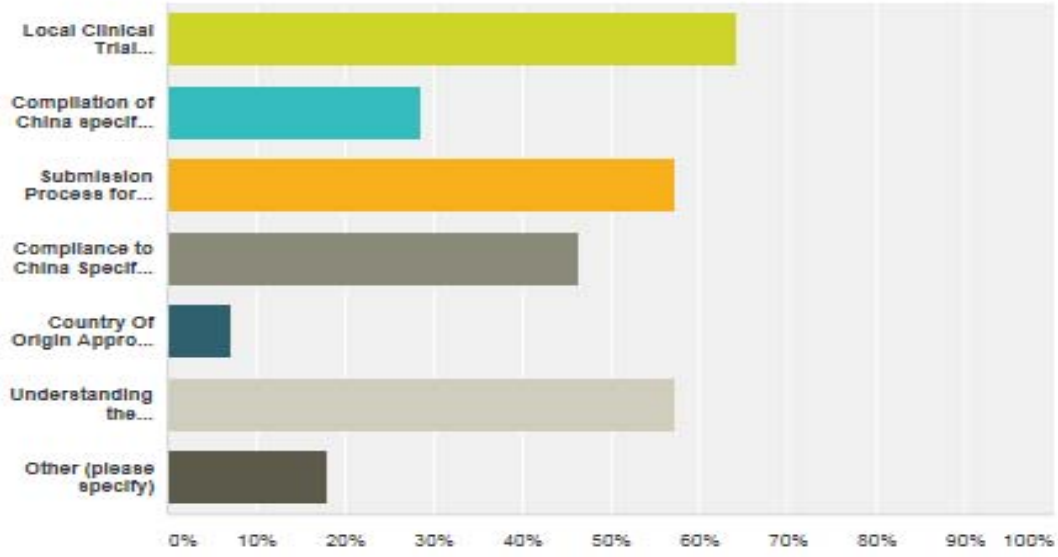


Answer Choices		Responses	
Local Agent		21.43%	6
Subsidiary of your company		35.71%	10
Consultant		3.57%	1
Dont know		21.43%	6
Other (please specify)	Responses	17.86%	5
Total			28

Q8 Customize Export

Can you select your Top 3 challenges (as applicable) to receiving medical device approval in China?

Answered: 28 Skipped: 0

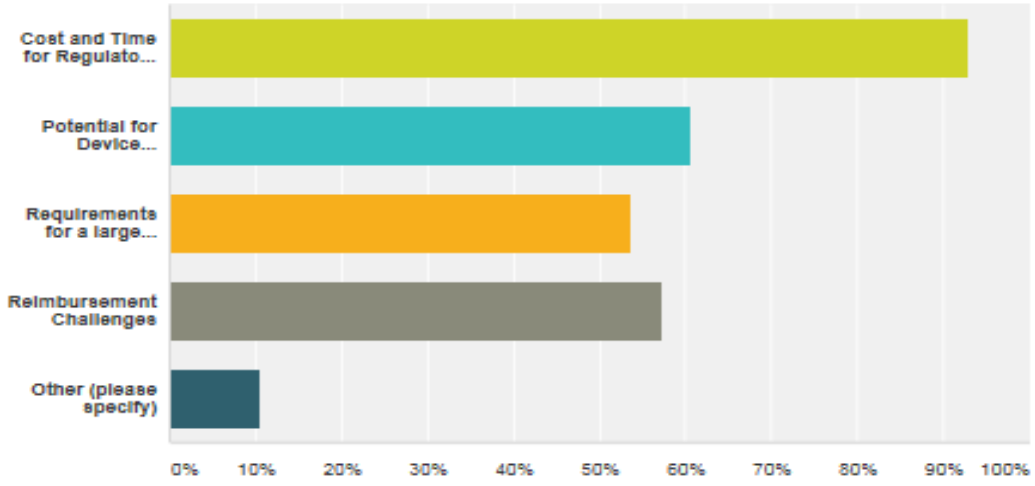


Answer Choices		Responses	
Local Clinical Trial Requirements		64.29%	18
Compilation of China specific Clinical Evaluation Report		28.57%	8
Submission Process for CFDA Review & Deficiencies		57.14%	16
Compliance to China Specific Standards		46.43%	13
Country Of Origin Approval Requirement		7.14%	2
Understanding the Requirements		57.14%	16
Other (please specify)	Responses	17.86%	5
Total Respondents: 28			

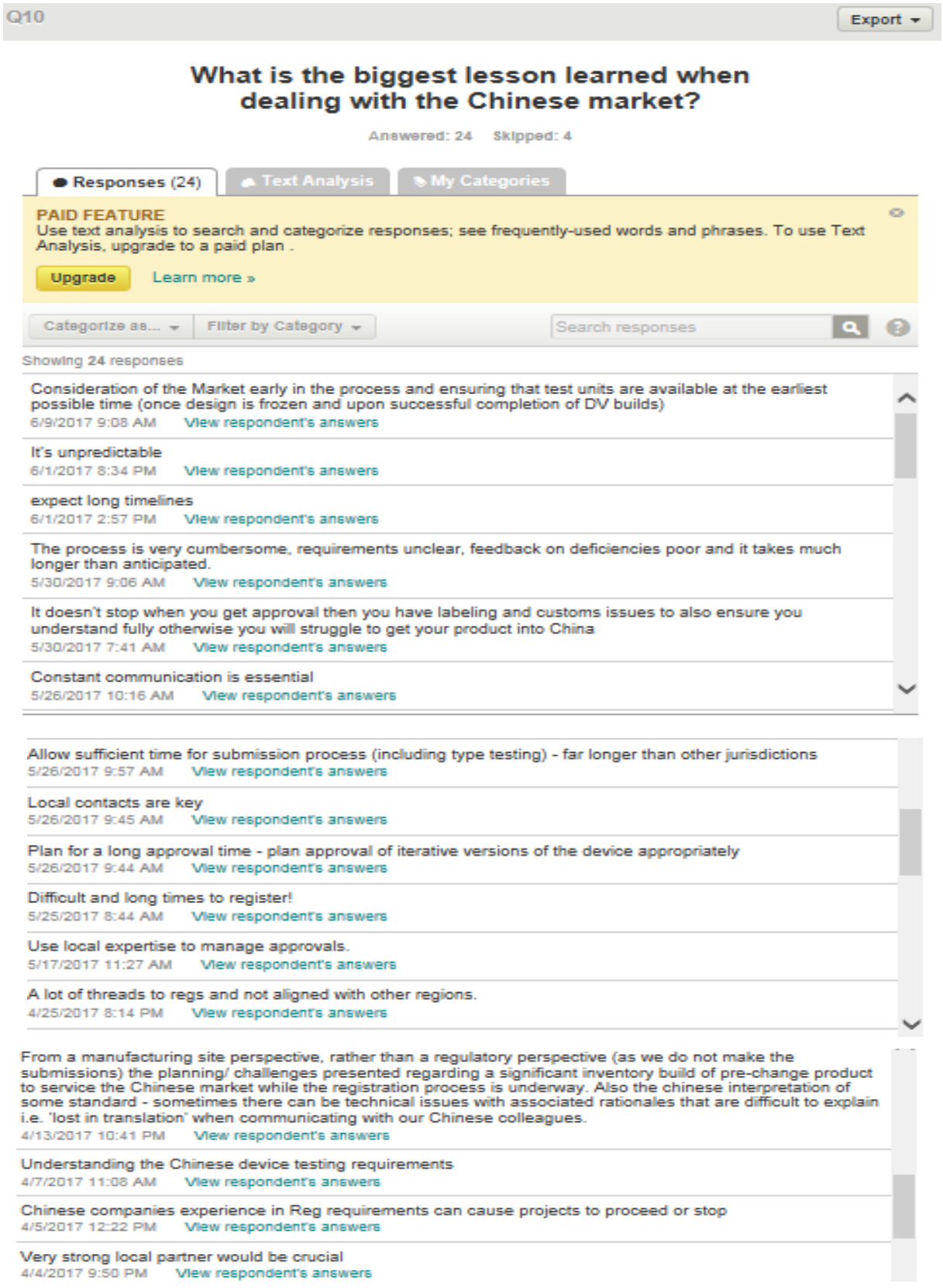
Q9 Customize Export

Can you select your Top 3 challenges (as applicable) to accessing the medical device market in China?

Answered: 28 Skipped: 0



Answer Choices		Responses	
Cost and Time for Regulatory Approval		92.86%	26
Potential for Device 'Copying'		60.71%	17
Requirements for a large Marketing & Sales Team		53.57%	15
Reimbursement Challenges		57.14%	16
Other (please specify)	Responses	10.71%	3
Total Respondents: 28			


Q10
Export
What is the biggest lesson learned when dealing with the Chinese market?
Answered: 24 Skipped: 4
Responses (24)
Text Analysis
My Categories
PAID FEATURE
Use text analysis to search and categorize responses; see frequently-used words and phrases. To use Text Analysis, upgrade to a paid plan .
Upgrade
Learn more »
Categorize as...
Filter by Category
Search responses
Showing 24 responses
Consideration of the Market early in the process and ensuring that test units are available at the earliest possible time (once design is frozen and upon successful completion of DV builds)
6/9/2017 9:08 AM View respondent's answers
It's unpredictable
6/1/2017 8:34 PM View respondent's answers
expect long timelines
6/1/2017 2:57 PM View respondent's answers
The process is very cumbersome, requirements unclear, feedback on deficiencies poor and it takes much longer than anticipated.
5/30/2017 9:06 AM View respondent's answers
It doesn't stop when you get approval then you have labeling and customs issues to also ensure you understand fully otherwise you will struggle to get your product into China
5/30/2017 7:41 AM View respondent's answers
Constant communication is essential
5/26/2017 10:16 AM View respondent's answers
Allow sufficient time for submission process (including type testing) - far longer than other jurisdictions
5/26/2017 9:57 AM View respondent's answers
Local contacts are key
5/26/2017 9:45 AM View respondent's answers
Plan for a long approval time - plan approval of iterative versions of the device appropriately
5/26/2017 9:44 AM View respondent's answers
Difficult and long times to register!
5/25/2017 8:44 AM View respondent's answers
Use local expertise to manage approvals.
5/17/2017 11:27 AM View respondent's answers
A lot of threads to regs and not aligned with other regions.
4/25/2017 8:14 PM View respondent's answers
From a manufacturing site perspective, rather than a regulatory perspective (as we do not make the submissions) the planning/ challenges presented regarding a significant inventory build of pre-change product to service the Chinese market while the registration process is underway. Also the chinese interpretation of some standard - sometimes there can be technical issues with associated rationales that are difficult to explain i.e. 'lost in translation' when communicating with our Chinese colleagues.
4/13/2017 10:41 PM View respondent's answers
Understanding the Chinese device testing requirements
4/7/2017 11:08 AM View respondent's answers
Chinese companies experience in Reg requirements can cause projects to proceed or stop
4/5/2017 12:22 PM View respondent's answers
Very strong local partner would be crucial
4/4/2017 9:50 PM View respondent's answers

Very strong local partner would be crucial
4/4/2017 9:50 PM View respondent's answers

hire a local consultant
4/4/2017 3:38 PM View respondent's answers

you need good RA people based in China to nagivate on your behalf
4/3/2017 6:51 PM View respondent's answers

Be wary of materials being used in the device
4/3/2017 5:35 PM View respondent's answers

The biggest lesson learned was to ask multiple questions from local agents before responding to questions/ deficiencies. It was difficult to determine what was being asked and why, the lack of understanding led to simple questions taking a long time to respond to and often providing overly complicated responses. Essentially, clear communication is essential.
4/3/2017 5:30 PM View respondent's answers

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Ensure the business are aware of submission and approval timelines.It is a slow process to get approval in China but it is possible.
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Not applicable
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Have an appropriate agent to cover registration , after slaes and adverse reporting
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Its take time and detailed local knowledge input
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