Challenges for the Regulatory Affairs Function in Demonstrating Compliance for Existing CE Marked Devices to the New EU Medical Devices Regulation 2017/745

by

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Declaration

Title: Challenges for the Regulatory Affairs function in demonstrating compliance for existing CE marked devices to the new EU Medical Devices Regulation 2017/745.

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Declaration:

I hereby certify that I am the author of this document and I 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 Medical Device industry in Europe, and specifically Ireland, is a critically important manufacturing sector underpinned with strong potential for further growth in the coming years. To place any Medical Device on the European Market, manufacturers must comply with all applicable regulations. The introduction of new EU Medical Device Regulation in Europe, Regulation (EU) 2017/745 of the European Parliament and of the Council 05th April 2017 on medical devices has left the sector struggling to both fully understand the new requirements facing it and, more importantly, ensuring that it can fully comply with same by May 2020.

The aim of this research is to outline the key challenges for the regulatory affairs professionals in implementing the changes introduced by MDR 2017/745, and the impact it is having on industry and regulators alike. At the time of this print there is only one year remaining of the available three-year transition period. Manufacturers have until May 2020 to be fully compliant, leaving many with a significant amount of work still to do given the significantly increased regulatory requirements now facing them under MDR 2017/745.

As well as an in-depth literature review, a mixed-method approach was used to gather information from industry regulatory professionals from both the Medical Device manufacturers themselves and the Regulatory Agencies overseeing them. Interviews were conducted with twelve of these professionals with a survey then created for use with a wider, industry-based audience to ascertain the impact and importance of the various challenges identified during interview.

This research identified the primary challenges the introduction of MDR 2017/745 will bring to the MedTech sector. During the survey phase, challenges identified during interview were ranked by respondents with results used to identify and understand implications of the primary challenges facing regulatory professionals as they move to implementation of MDR2017/745. This research will aid manufacturers understanding of MDR 2017/745 and help with planning and implementation of this new regulation.

Keywords: Medical device, Regulation 2017/745, MDR, challenges, regulatory affairs, CE mark, Europe.

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Chapter 1 Introduction

1.1 Background

Placing a medical device on the European market poses increasing regulatory challenges for medical device manufacturers. A new Medical Device Regulation "Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC" (referred to here after as "MDR 2017/745") was published on April 26th, 2017. The new legislation will become applicable after a three-year transition period for medical devices (May 2020) and a five-year transition period applies for in-vitro diagnostic medical (May 2022) and with it brings a plethora of regulatory changes (Commission 2017a, Commision 2017).

For the last 20 years, medical devices within the EU have been regulated by the following three (3) directives:

- Council Directive 90/385/EEC on Active Implantable Medical Devices (AIMDD) (1990).
- Council Directive 93/42/EEC on Medical Devices (MDD) (1993).
- Council Directive 98/79/EC on In Vitro Diagnostic Medical Devices (IVDMD) (1998)"(Commission 2018).

The new regulatory framework is made up of two new regulations. One deals with medical devices and the other deals with in vitro diagnostic medical devices.

- Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC.
- Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and EU Commission Decision 2010/227/EU.

These were adopted by the Council and the Parliament and entered into force in May 2017.

A CE (Conformité Européenne) mark is a certification mark that indicates a specific product conforms with relevant regulatory requirements allowing it to be sold within the European Economic Area. Before medical device manufacturers can legally CE mark their products in Europe, they must comply with the appropriate medical device regulatory requirements set forth by the EU Commission. (Commission 2017a). Manufacturers can place a CE mark on a medical device once it has demonstrated adequate safety and performance and completed a conformity assessment. Medical devices in the EU must undergo a conformity assessment to demonstrate that they meet the legal requirements to ensure they are safe and perform as intended. (Commission 2017a).

The regulatory environment in the EU is complex with several different bodies involved. The EU Commission has the overall responsibility for the EU regulations and has oversight over the Competent Authorities. A Competent Authority is the regulatory agency in each EU country. Notified Bodies are commercial organisations overseen by the Competent Authorities and they conduct the conformity assessment procedures discussed previously in this section. The conformity assessment usually involves an audit of the manufacturer's quality system, followed by a review of the technical documentation from the manufacturer to demonstrate the safety and performance of the device. On successful completion of a conformity assessment a CE mark may be applied to the device in scope and the product is then available for sale in the EU. Ongoing assessments are completed to ensure that devices continue to meet the regulatory requirements and to ensure state of the art requirements are considered and applied where applicable. Conformity assessment is a feature of both the current and new regulatory framework.

Thesis Purpose

The purpose of this thesis is to understand the challenges faced by regulatory affairs professionals in the medical device technology (MedTech) sector when complying with the specific requirements set out in the new regulation. Compliance with the requirements of the regulations by the defined timelines will enable medical device manufacturers to continue to place safe and effective products on the European market. Figure 1 illustrates the transition timeline to MDR 2017/745. The timelines are discussed in detail in Chapter 2.

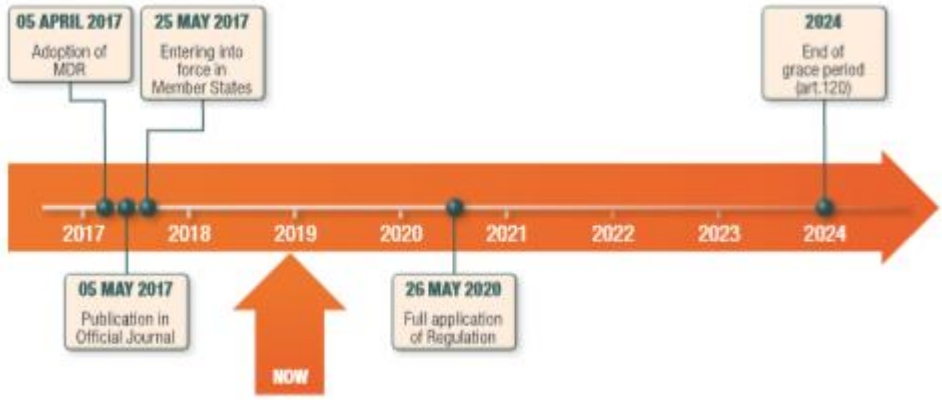


Figure 1: Transition Timelines for Medical Device Regulation 2017/745 (taken from (COCIR 2019b)

Medical devices are products intended to perform a therapeutic or diagnostic action on human beings by physical means. Medical devices are used to save lives or transform the health of individuals suffering from a wide range of conditions. They are used for diagnosing, monitoring and treating virtually every disease or condition that affects us. They range in classification from class I devices to class III devices with class III being the higher risk devices as outlined in Figure 2. Class I devices are self-certifiable devices like wheelchairs, hospital beds, materials like surgical gauze, adhesive bandages, etc. Class IIa devices include devices such as syringes, ultrasound equipment, hearing aids. Class IIb devices includes implantable stents used in the peripheral vasculature, infusion pumps and surgical lasers, and class III devices being ones such as artificial heart valves, drug eluting stents, and implantable prosthetic joints.

Figure 2: Visual Representation of Different Types of Medical Devices

(Troeva 2018)

The Medical Devices Regulation is a complex piece of legislation and detailed interpretation is required. In addition, there are still many unknowns and lack of understanding of these regulations between both the regulators and industry. Some of these unknowns include;

- Timing of when the implementing and delegating acts will be released and what they will look like. The implementing acts are required to help implement the regulation, the delegating acts are required to make changes such as amending, supplementing or deleting elements of the legislation.
- The process whereby expert panels will be utilised to scrutinise the clinical evaluation reports for some higher-class products has not been established yet.
- The use of the Eudamed database with respect to the specific information to be uploaded, the timing, and the process for doing this is still not established.

These are discussed in more detail in chapter 4 under the topic of "lack of clarity" in the additional challenges section.

As manufacturers and regulatory affairs professionals, our aim is to ensure devices continue to be available to patients. Collaboration with European regulatory agencies will be paramount in interpreting the requirements of the regulation and applying them. The regulatory affairs professional is responsible for ensuring all the relevant technical documentation is created and available for each device and this research will explore the challenges and risks associated with this task. It will specifically focus on the challenges associated with ensuring existing devices i.e. those with a CE mark, conform to the new/ revised requirements in the new regulation. It is important that these existing devices transition smoothly under the new regulation to ensure a continued supply of medical devices for the EU population.

1.2 Thesis Scope

This research will focus on medical devices and the requirements of MDR 2017/745. (Commission 2017a), and the new/ revised requirements when compared to the existing MDD. The author works for a multinational medical device company, which manufactures a wide range of medical devices, therefore will have access to information and personnel in this sector, both from industry and regulatory agency perspectives.

The MDR 2017/745 significantly changes the regulatory framework for placing any new medical device on the market, and for applying the new requirements to legacy devices. There is no option to "grandfather" devices into compliance and the effort to create technical documentation to keep devices in the EU market is significant. This thesis will focus on the main challenges associated with existing legacy devices i.e. those devices which are approved for sale in the EU and which need to conform to the new requirements to ensure continued market availability.

This thesis will provide a top-level overview of the impact of the new regulation and the challenges associated with it, specifically the challenges for the regulatory professionals with respect to continuing to place medical devices on the European market with a CE mark.

1.3 Significance of the Study

The medical device industry in Europe, and specifically Ireland, is a key manufacturing sector. "The sector employs over 38,000 people in Ireland and is the second largest employer of MedTech professionals in Europe, per capita. Ireland is one of the largest exporters of medical products in Europe with annual exports of €12.6 billion and companies here directly export to

over 100 countries worldwide. As many as 9 of the world's top 10 medical technology companies have a base in Ireland and 60% of the 450 MedTech companies based here are indigenous" (Irish Medtech Association). It is therefore important that the industry is in a position to recognise and react to the challenges posed by changing regulatory environments.

The medical device industry appears to be extremely promising and ripe with potential. "It has shown strong growth for many years with worldwide revenue consistently on the increase. This can also be seen in the high number of patents filed by MedTech companies, as well as in data with trade trends and employment statistics" (Baldassare 2016). Table 1 shows the top 12 medical device companies which produce a range of products including medical devices, laboratory instruments, reagents, medical supplies, and diagnostic products. These companies are producing products for markets worldwide including the European union hence their understanding and application of the new regulations is of paramount importance. Note the author of this report works for one of the companies listed in Table 1 as a Senior Regulatory Affairs manager, and thus is well positioned to understand the importance of timely conformance with the new regulation. Understanding the challenges for the regulatory affairs personnel will allow plans to be established to overcome these challenges.

Table 1: Global Top 12 Medical Device Manufacturers of 2018

Data is based on sales reported for 2017 fiscal year and shows the trend in comparison to each company's 2016 turnover (Medical Product Outsourcing, 2018)

Rank	Medical Device Manufacturer	2018 Turnover	Trend since 2017
1	Medtronic	29.7B	↑
2	Johnson& Johnson	26.6B	↑
3	GE Healthcare	19.1B	↑
4	Royal Philips	15.2B	↑
5	Siemens Healthineers	16.3B	↑
6	Abbott Laboratories	16.2B	↑
7	Cardinal Health	13.5B	↑
8	Stryker	12.4B	↑
9	Becton Dickinson	12.1B	↑
10	Baxter	10.6B	↑
11	Boston Scientific	9.0B	↑
12	Essilor	9.0B	↑

"The Medical Device Regulation (745/2017, to become applicable in May 2020) is the most impactful legislative change for the medical devices sector since 1993, when the medical devices directive (93/42/EC) was published" (COCIR 2019a). Medical device companies are racing to prepare for this change and are grappling to understand what they need to do by the required timelines. There has been a lack of guidance on how companies will achieve the path to compliance with the revised regulatory system. Both industry and the regulators are struggling to understand the regulation and how to adjust to the heightened requirements. "Industry are questioning the feasibility of the transition timeline" (Bernasconi 2019). The probability of new and existing devices not reaching the market (which also means patients not being treated) due to manufacturers not being able to have new products certified and legacy products recertified is becoming more probable as the transition deadline comes closer. The process of certification/

recertification and associated transition timelines is discussed in more detail in chapter 2, section 2.3.

This research will enable companies to recognise the most common challenges industry faces with the current regulations, from a regulatory perspective, and will help facilitate planning for continued sale of devices in the EU market. Changes in requirements will require manufacturers to change their approach to business over the next number of years. It is expected that there may be less investment in new products and innovation, as resources, time and money will be absorbed by transitioning existing products to comply with MDR 2017/745.

"Europe is now heading in the opposite direction, particularly for innovative products. Due to the uncertainty of MDR implementation and interpretation, increased cost of compliance, fragmented distribution and divergent reimbursement policies, the 40-year old model of 'go to Europe first' will be challenged. Europe may have to wait for innovative medical devices to be proven safe and effective in other markets before European patients will have access to improved technologies" (Ohman 2018).

Recognition of the main challenges facing the regulatory function will facilitate strategic planning by senior management as they endeavour to reduce the risk of the identified challenges and successfully maintain their CE mark.

1.4 Milestones and Success Criteria

There are a number of milestones in this thesis plan:

1. Conducting a literature search on the current thinking of the challenges associated with MDR 2017/745.

2. Conducting semi- structured interviews with identified stakeholders in the regulatory process. These will include regulatory professionals working in the MedTech sector of both large and small companies, Notified Bodies, members of the MedTech organisation, and regulatory consultants working in the industry.

3. Analysis of the quantitative survey data.

4. Discussion of the challenges identified in the research.

Success criteria for each of the milestones will be as follows:

1. Review and analysis of the literature review.
2. A categorised list of challenges from the stakeholders interviewed.
3. Completion of the survey providing quantitative data for the challenges.
4. Data analysis of the survey in conjunction with the output from the interviews resulting in the identification of the main challenges.

1.5 Summary

This chapter introduces the research topic and the purpose of conducting an analysis on same. It outlines the scope of the study and the significance of conducting such a study. It also sets out the design of the study by identifying the milestones and the success criteria for conducting a thorough research.

Chapter 2 The Current Directive Vs the Future Regulation

This chapter explains the history of the regulations in Europe and the reason behind the development of the revised regulations. It also describes, at a top level, the changes introduced by the MDR as compared to the existing requirements today. This chapter also provides a description of the regulatory affair's professional roles and responsibilities.

2.1 Medical Devices Directive - MDD 93/42/EEC

In the European Union, medical devices are tightly regulated by laws that govern the safety and performance both pre- and post-market across the lifetime of a device. EU countries are required to comply with CE marking requirements for medical devices. There are 28 European Union Member States. There are three (3) additional countries (Norway, Iceland and Liechtenstein), although not part of EU, are members of the wider European Economic Area (EEA). Switzerland is not an EU member but is a member of European Free Trade Agreement (EFTA). The countries in the EEA and EFTA have transposed the EU requirements into national law and therefore the requirements apply to products destined for sale in those countries. Turkey has made an application to join the EU; this is not yet complete. However, Turkey follows the principles of the EU Regulations.

The existing regulatory requirements for medical devices in Europe require a manufacturer to demonstrate compliance to the relevant Essential Requirements delineated in Annex I of the Medical Devices Directive 93/42/EEC (MDD). In addition to compliance with the Essential Requirements, an appropriate route to conformity assessment (Annexes II through VII) must be selected. The route is, in part, determined by device classification. The approval of high-risk medical devices requires manufacturers to provide regulatory authorities with detailed technical documentation demonstrating compliance with all applicable regulations and requirements. This technical documentation consists of bench testing, risk assessment, manufacturing information, labelling, packaging, sterilisation validation, biocompatibility testing, clinical data, product specifications etc. The technical documentation is thoroughly reviewed by Notified Bodies. Notified Bodies have technical experts available to support such reviews e.g. biologists, physicians, microbiologists and other subject matter experts, therefore it is essential that the file fully and effectively addresses all the technical and safety issues mandated under the applicable directive.

When the file has been reviewed and any/ all questions have been closed out, the manufacturer can then sign the Declaration of Conformity, the last step in the process, before placing product on the EU market with a CE mark. The declaration of conformity is a legal document which states that the device complies with the appropriate directive.

"Under the current Medical Device Directive (MDD), national medical device laws and ordinances, the scrutiny process to ensure robust evidence on patient safety and performance characteristics prior to market approval is subject to accredited Notified Bodies. However, many Notified Bodies lacked the expertise and experience to adequately evaluate the provided clinical evidence in view of patient safety and clinically relevant risk/benefit ratio" (Buttron 2016).

There has been much greater scrutiny on clinical data since the publication of MEDDEV 2.7.1 Rev 4, June 2016, guidelines for manufacturers and Notified Bodies on clinical evaluation by the Notified Bodies and Competent Authorities in Europe.

"In many cases, clinical data for market approval scrutiny was limited to a critical evaluation of the published relevant scientific literature for similar other (predicate) devices relating to the safety and performance of design characteristics and intended use when compared to the device under evaluation. However, the interpretation and utilization of the term 'equivalence' is left to the device manufacturer and the Notified Bodies to determine" (Buttron 2016).

There were many drawbacks to the approval of medical devices in Europe, one of which was the varying degrees of competency associated with Notified Bodies. Devices were assessed by over 40 privately owned Notified Bodies based in different member states. If a given Notified Body deems that the device conforms to the EU directives and grants the CE mark, this device can be marketed in any other country in Europe without those country member states having any involvement. "In the European Union, reports are not gathered into a single database nor have they ever been made public. Each national regulator collects so-called "incident reports" in individual countries, sharing them with European counterparts, but then only privately, when they spot serious issues" (Bowers 2018).

Directives, by their nature, present a challenge in terms of consistent application. The requirements in directives are transposed into national law which leaves the potential for additional requirements in each member state. "The maze of national laws, decrees and ordinances of Member States led to differences in levels of regulatory pre-market scrutiny; in some cases, to different approaches between EU Member States. As a consequence, a variety of

interpretations could be observed across the European Union for safety and performance requirements" (Buttron 2016).

2.2 Evolution of MDR 2017/745

There were many factors contributing to the new regulations in Europe being developed. It was generally felt that there was a lack of transparency and access to information for patients, healthcare professionals and manufacturers as well as for Notified Bodies and authorities.

The previous directive had numerous weaknesses on interpretation and application of the directive. "All stakeholders agree the current fragmented regulatory system needs a major overhaul" (Buttron 2016). The regulatory framework in Europe had come under much scrutiny and criticism. There was little coordination between Notified Bodies and Competent Authorities. This led to the directives being applied differently across Europe, hence little uniformity in the execution of conformity assessments and severe disparity across EU member states in terms of implementation of the MDD. The lack of consistency encouraged medical device manufacturers to shop for the easiest option to get to market.

In addition to the varying requirements, there were two scandals which occurred in the medical device sector in Europe relating to medical device safety. These scandals were the tipping point outlining the shortcomings of the regulation of medical devices in Europe.

The first scandal within the medical device arena was associated with De Puy Medical. "In 2010 DePuy recalled its metal on metal (MoM) DePuy ASR™ XL acetabular system and DePuy ASR™ hip resurfacing system as a result of high failure rates which resulted in patients requiring follow up surgery" (Cahill 2018).

The second was in relation to a company, Poly Implant Prosthese (PIP), which produced breast implants. They decided to change the material used in the implant from a medical grade silicon to a cheaper, industrial silicone grade which was not approved for medical device use. The use of the cheaper material resulted in the implants rupturing causing inflammation and possible scarring. (Klein *et al.* 2018) discusses how the implants were recalled from the market.

"In the healthcare industry, stories of patient harm can sometimes be the impetus for positive change. This was the case with the PIP breast implant scandal, where cost-cutting decisions that resulted in injuries eventually led to major regulatory updates" (Hegyi 2017). It was unfortunate that such unethical behaviour had gone this far and that so many women suffered as a result of this illegal practice.

These two scandals rocked the medical device industry. Many patients suffered because of these two widely discussed incidents. Thousands of lawsuits and court cases followed, with patients also claiming against other manufacturers on the metal on metal claims. Medical devices are designed and used to improve and save lives. For most people medical devices radically improve health, but the outcome of some of these major scandals put many patients at risk of serious harm it its quest for profit and taking shortcuts. In addition to these two major scandals within the medical device industry there was also concerns raised with regulatory agencies and the inconsistency and level of review performed by some, but not all regulatory agencies. There was a perceived lack of widespread safety issues in general.

In the authors experience, Notified Bodies review of files varied, as well as the level of detail of onsite compliance audits, and the interaction from Competent Authorities. It seems that some of the Competent Authorities are more active in following up on trends than others.

According to an article published in the Guardian newspaper on 25 November, 2018, " data shows there has been a collapse in the proportion of investigations overseen by MHRA at a time when complaints are soaring" (Osborn *et al.* 2018). It went on to state "So far in 2018, one in 100 reports received have prompted it to start a special investigation, compared with one in three in 2008 (Osborn *et al.* 2018).

Instead the majority of the reports have been passed on to the manufacturers and fed into the MHRA's trending database, but not necessarily dealt with. Figure 3: Data reported to MHRA from 2008 – 2016

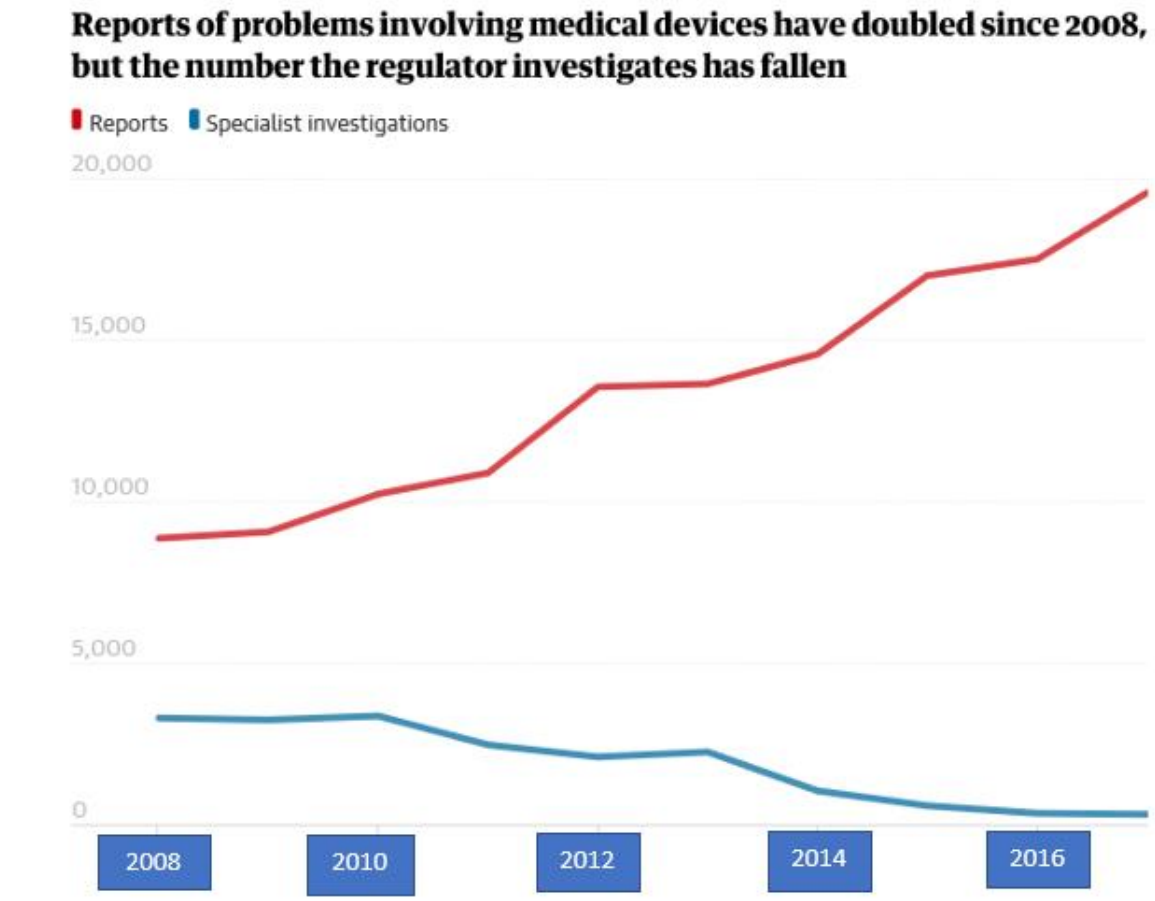


Figure 3: Data reported to MHRA from 2008 – 2016

taken from (Osborn et al. 2018)

These numbers may be an indication of a lacking scrutiny level in the assessment of medical devices including high-risk devices.

The positive from these experiences was that it triggered the most significant change in the EU regulations in years. "The MDR 2017/745 and IVDR represent a significant development and strengthening of the existing regulatory system for medical devices in Europe and will replace the original Directives which have been in place for over 25 years" (HPRA).

"The EU Commission recognised the need to overhaul the regulatory environment associated with medical devices; it was a change needed to restore the public's confidence in the safety and performance of medical devices" (Hegyi 2017). Ensuring safe and effective use of medical devices for both patients and users is a crucial responsibility for all manufacturers. This is not only important in terms of meeting compliance and regulatory requirements but also mitigating risks to public health.

The fact that the new legislation is in the form of a regulation, rather than a directive, means that the EU law is directly applicable at national level and no longer requires transposing into national law. This will prevent additional requirements being introduced in EU countries and drive consistent application of the new requirements. "This should allow for greater legal certainty and prevent variation in the approach taken or in the rules relating to medical devices that are applied across EU Member States" (HPRA).

2.3 Transition Timelines

As May 2020 looms closer, medical device manufacturers are approaching the deadline to adapt their currently approved medical devices to meet the new expectations of 2017/745.

As discussed in chapter 1, regulation 2017/745 was approved and entered into force in May 2017 with a transition period of May 2020. During the transition period the MDR 2017/745 will enter into force gradually. There are some keys dates to be aware of as companies transition through this program, as per Figure 4.

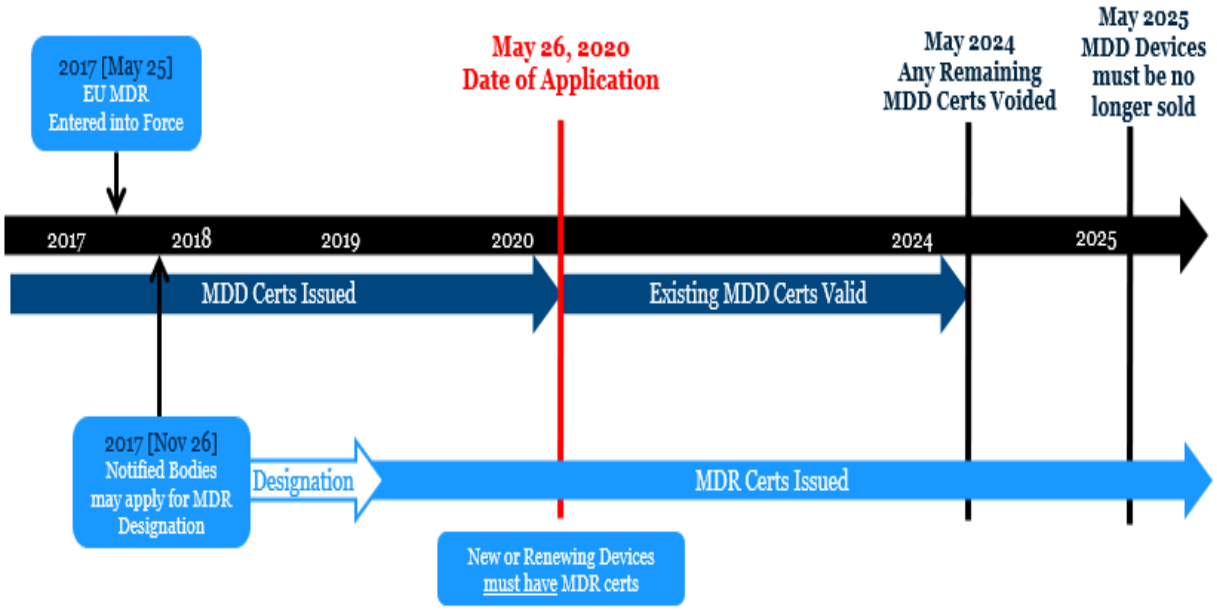


Figure 4: MDR 2017/745 Transition Timelines

(Wolf M 2018)

Items of note:

- For Class I medical devices there is a hard deadline to comply by May 2020.
- MDR post-market, registration and Economic operator requirements apply to all devices.
- MDD certificates are valid after May 26, 2020 until they expire or up to maximum of 4 years, May 26, 2024 (provided there are no significant changes to design or intended purpose).
- A further 1 year of putting these devices into service allows devices to remain on market until May 26, 2025.

There are hard and soft transition timelines associated with this transition. The hard transition timeline is May 26th, 2020; this is the date by which the current directives cease to exist and the MDR comes into effect i.e. the date of application. Any new products being CE marked after this date must comply with the requirements in the regulation. This date also applies for those products which previously did not require Notified Body assessment under the directives but do under the regulations i.e. Class I devices such as surgical reusable instruments. The hard transition date is also applicable for specific requirements introduced in the MDR, such as in the area of post market surveillance.

The soft transition timeline is out until May 26th, 2024; Manufacturers can continue to place products on the market until this point, if they have a valid MDD certificate. There are caveats associated with running business under the soft transition regime. Devices CE marked under the MDD may still be placed on the market after 27 May 2020 providing the certificate is valid.

Certificates issued between 26 May 2017 and 26 May 2020 will remain valid until 26 May 2024. A further 1 year of putting devices into service allows devices to remain on market until May 26, 2025.

After 26 May 2024 only devices complying with the MDR 2017/745 can be placed on the market. Devices holding MDD certifications during this time of May 2020 – May 2024 are restricted to specific changes and manufacturers need to ensure policies and procedures are in place to manage these restrictions during this time. Article 120 (3) outlines the transitional provisions during this time. "By way of derogation from Article 5 of this Regulation, a device with a certificate that was issued in accordance with Directive 90/385/EEC or Directive 93/42/EEC and which is valid by virtue of paragraph 2 of this Article may only be placed on the market or put into service provided that from the date of application of this Regulation it continues to comply with either of those

Directives, and provided there are no significant changes in the design and intended purpose. However, the requirements of this Regulation relating to post-market surveillance, market surveillance, vigilance, registration of economic operators and of devices shall apply in place of the corresponding requirements in those Directives" (Commission 2017a).

To make use of this soft transition date, it is prudent for manufacturers to renew their MDD certificates to give them the extension time and take advantage of gaining more time to be MDR 2017/745 compliant under the soft transition timelines. This process for 'early' renewal is depleting resources at both the Notified Bodies and manufacturers during the run up to the Date of Application.

There are several reasons why manufacturers will not be able to transition to MDR 2017/745 by May 2020. One of the main reasons is that the Notified Bodies has to be ready (designated) to accept files under MDR 2017/745. As of June 2019, there are only two Notified Bodies designated; the first being BSI UK office, and TUV SUD was the second Notified Body to be designated as announced on May 22nd 2019. (ZLG 2019) The majority of Notified Bodies are expected to gain designation in Q3, 2019 timeframe. This leaves a very short window of time to have files reviewed up to May 2020, and with the sheer workload on both Notified Bodies and manufacturers alike, this will be a challenge. This is outlined in great detail by Serge Bernasconi, chief executive officer, MedTech Europe, to the Mr Jykri Katainen, Vice President of the jobs, growth and competitiveness section of the European EU Commission on 15th April 2019. (Bernasconi 2019).

2.4 Summary of the Changes Between MDR 2017/745 and MDD 93/42/EEC

To restore confidence in the European Union regulatory system and to re design the existing regulatory framework, there are several changes being put in place to make the process more robust.

Implementation of MDR 2017/745 is being introduced across several different areas:

First through work with the Notified Bodies to level the playing field by ensuring requirements are being applied consistently across the industry. These requirements include additional oversight of the Notified Bodies, joint assessments conducted with the Competent Authorities, and Notified Bodies will continue to conduct unannounced audits.

There is also going to be increased co-ordination on vigilance among member states and the regulators. There is greater focus on market surveillance in general. This includes strengthened

post market surveillance requirements and the use of traceability through the unique device identifier (UDI). There are also stricter requirements for post market clinical follow up and greater co-ordination between Competent Authorities between the exchange of post market data.

There will be improved communication and transparency regarding device information using the Eudamed database and increased scrutiny of high-risk devices during the CE marking process including the need for more clinical data.

There are always challenges with incorporating safety and risk management across device lifecycles, but manufacturers cannot afford to adopt inadequate measures if their goal is to reduce the risk of post-market problems such as the MOM hip implant and the PIP breast implant incidents. Figure 5 outlines the key changes of MDR 2017/745.

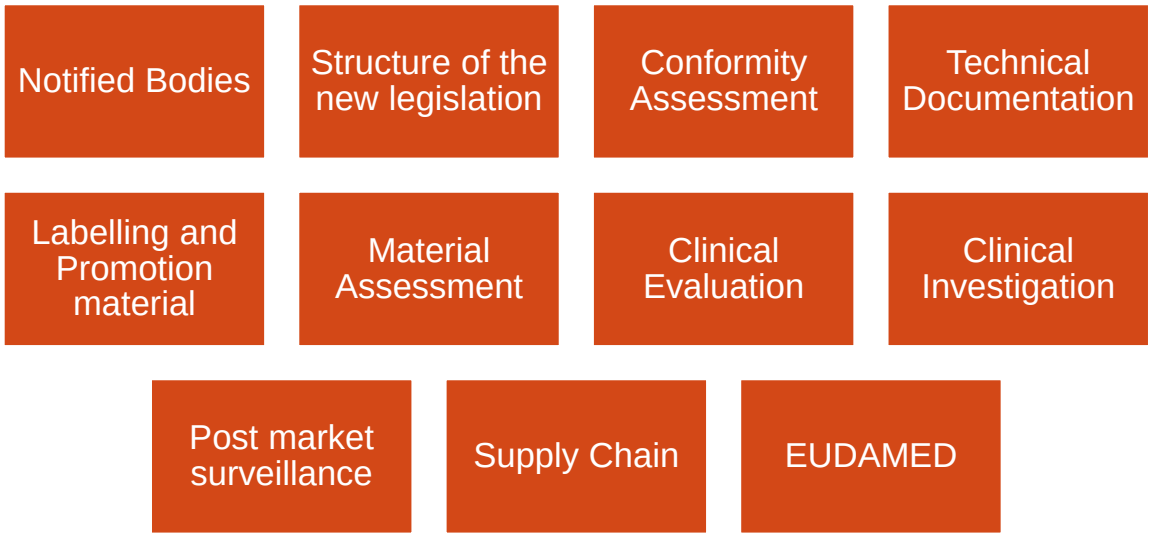


Figure 5: The Key Changes of MDR 2017/745

(as created by the author)

2.4.1 Notified Bodies

All Notified Bodies must apply for MDR 2017/745 designation. As stated on the HPRA website "From 6 months after the enter into force of the new Regulations, i.e. 26th November 2017, Notified Bodies can submit applications to the Competent Authority be designated under the new Regulations" (HPRA 2019).

This involves Notified Bodies being audited by joint assessors such as the EU Commission and the Competent Authority. Once a Notified Body is designated it can commence business under the MDR 2017/745 structure conducting audits, reviewing files and issuing certificates under the MDR 2017/745. There is an enormous additional burden of work for the Notified Bodies. There are many additional "technical documentation" deliverables which will be discussed separately within this section. The certification structure and level of detail displayed on CE certificates becomes more onerous. It is evident already that Notified Bodies are struggling with capacity and with increased demand on their services. The training requirements for individuals working within Notified Bodies has become even more complex.

"The joint assessment process and the burden of the MDR 2017/745 additional requirements could force some Notified Bodies to reduce conformity assessment options offered, reduce product scope for certification, and some Notified Bodies may not pass the assessment" (Clemens 2018). "A reduction in number of notified bodies is expected, with mainly the smaller ones withdrawing." (MedTech 2018c). The EU Commission maintains a list of active Notified Bodies which includes their identification and the tasks for which the Notified Body can perform i.e. which product types they are qualified to review and approve. There are currently 58 Notified Bodies listed against 93/42/EEC. This list can be located on the European EU Commission website and is referred to as the NANDO database. (Commission 2019).

In general, from informal discussion with several Notified Bodies, it is expected that the majority of Notified Bodies will be designated in Quarter 3, 2019. It was not anticipated by anyone in the MedTech sector including the Notified Bodies themselves that it would be this late.

A fuming letter sent by Serge Bernasconi, chief executive officer, MedTech Europe, to the Mr Jykri Katainen, Vice President of the jobs, growth and competitiveness section of the European EU Commission on 15th April 2019 expressed extreme frustration with the status of Notified Body designation. It stated "From the 58 existing Notified Bodies designated to operate under the Directives, only 1 has been designated to the MDR 2017/745 – a UK one. DG GROW expects not more than 12 Notified Bodies will be designated by the end of year, 5 months before the deadline! This is way too late, insufficient and gives no guarantee that Notified Bodies would have enough capacity to ensure continued regulatory approval of devices by May 2020" (Bernasconi 2019).

At the time of print for this thesis two Notified Bodies were designated. These were, "BSI UK and TÜV SÜD). There is no indication that a significant number of Notified Bodies will be

designated in the next months. That is by far not enough to accommodate the demand of medical device manufacturers" (COCIR 2019c).

2.4.2 Structure of MDR 2017/745

There is much more information and requirements within MDR 2017/745 as opposed to MDD 93/42/EEC and thus the structure and content has changed dramatically.

Figure 6: Layout Structure of the Directive Vs the Regulation below shows the different layout/ structure of the MDR 2017/745 versus the MDD.

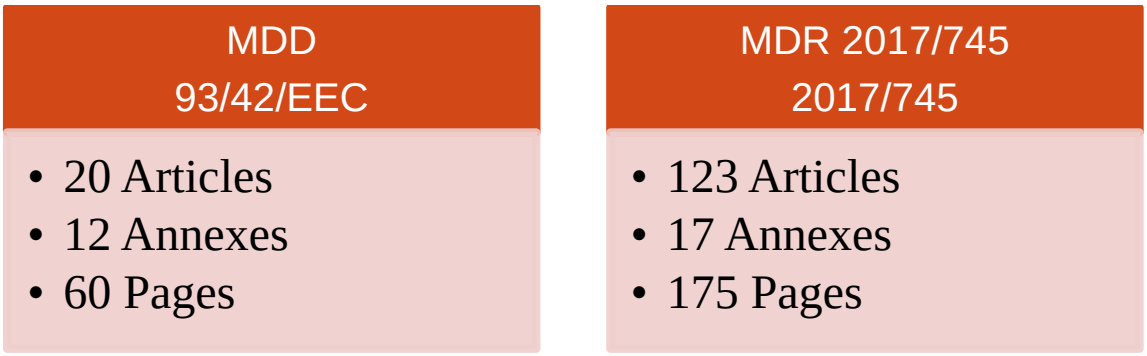


Figure 6: Layout Structure of the Directive Vs the Regulation

(created by the author)

The MDR 2017/745 is organised into chapters, sections, articles and annexes in comparison to the MDD 93/42/EEC which was structured with articles and annexes.

- Why - There are 101 whereas statements, also called "recitals".
- What - There are 10 chapters containing 123 Articles.
- How - There are 17 Annexes that describe this.

These reference/structure changes mean that regulatory affairs professionals need to become familiar with the content of the MDR, and MDD references are no longer valid. All previous references within policies, procedures and existing technical documentation will need to reflect the new MDR.

2.4.3 Conformity Assessment

According to MDR 2017/745 “conformity assessment means the process demonstrating whether the requirements of this regulation relating to a device have been fulfilled” (Commission 2017a) The conformity assessment is dependent on the classification of the device.

In Europe medical devices are classified into five different classes as outlined in Figure 7. These are class I nonsterile/ non-measuring, class I sterile and measuring, IIa, IIb and III, taking into account the intended purpose of the devices and their inherent risks.

Figure 7: Classification of Medical devices

(created by the author)

This following describes the key changes in conformity assessment procedures in the MDR 2017/745 compared to the MDD:

- Full quality assurance system (MDD Annex II – MDR 2017/745 Annex IX) requires increased number of Technical Documentations to be assessed by the Notified Body.
- Some devices will have Notified Body involvement for the first time, per changes in classification rules e.g.

Class IIb implants are equivalent to Class III devices in terms of submission requirements.

- EC type-examination and product verification conformity assessment pathway (MDD Annex III + Annex IV – MDR 2017/745 Annex X + Annex IX, part b.) no longer allows for sampling. Every product needs to be tested.
- EC type-examination and production quality assurance (MDD Annex III + Annex V – MDR 2017/745 Annex X + Annex XI, Part A) conformity assessment option is no longer allowed for class III devices.
- New pre-market scrutiny for some high-risk devices.

For some high-risk devices, specific procedures, including scrutiny by an expert panel, must be applied. This is associated with clinical reviews. The specifics of which devices fall into this "high risk" category is not defined at this time; however, it is expected that devices such as prosthetic implant's – knees or hips, or perhaps combination devices such as drug eluting stents may fall into this category. The expert panel can judge, based on a clinical evaluation assessment report prepared by the Notified Body, whether the clinical evidence provided by the manufacturer is sufficient to provide confidence in the safety and performance of the device and whether an additional scientific opinion is required. This will clearly build in additional time into the review period if these reviews are required.

The following flowchart, in Figure 8, shows the different conformity assessment options that can be used depending on the risk class of the device. This is a complex decision tree and it is very much dependent on device classification to choose the appropriate route to conformity assessment. Some devices have also been up classified as part of MDR 2017/745 including most class I software devices will be up classified to class IIa or higher according to rule 11 in MDR 2017/745.

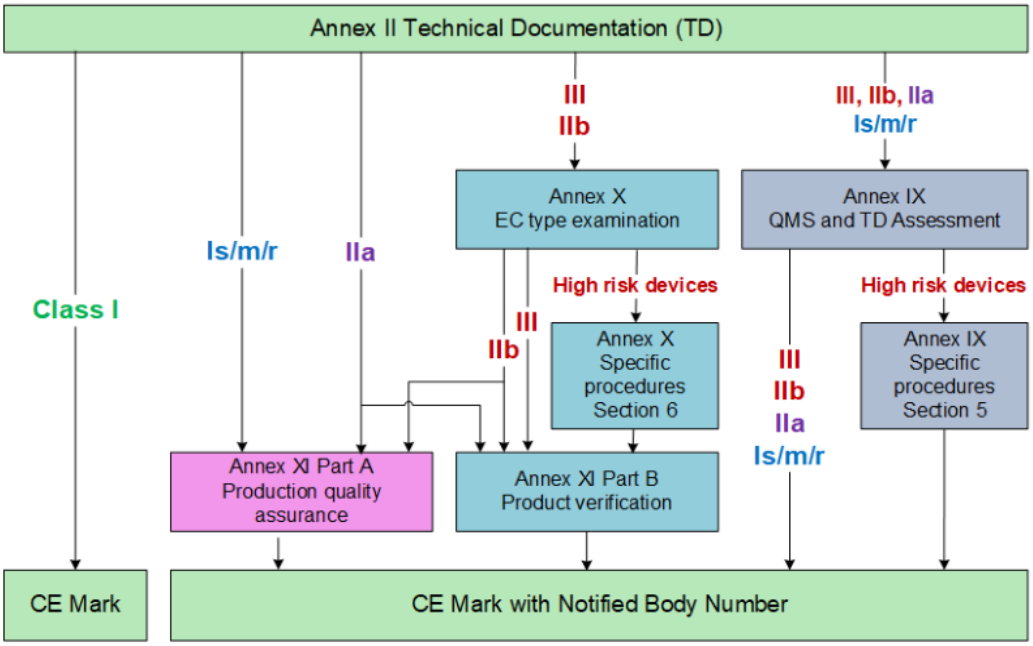


Figure 8: Choice of Conformity Assessment Pathways

(Confinis 2018)

As there is no grandfathering for existing products, all manufacturers need to resubmit their existing product files, under one of the available conformity assessment paths available, for review against the requirements of the regulation. "A grandfather or legacy device is a medical device that was already on the market and pre-dates an applicable standard, directive or regulation. Under the 1993 European Medical Device Directive, for example, some devices were exempt from meeting the new directive and allowed to continue being marketed" (Simons 2019). Since time is running out waiting on all Notified Bodies to be designated, as discussed previously, most manufacturers are recertifying their devices under the MDD to buy themselves more time to have their files certified under the MDR 2017/745 regime.

2.4.4 Technical Documentation

The MDR 2017/745 is much more prescriptive about the required technical documentation to fulfil the requirements of CE marking a device than the MDD. Terminology in the MDD of 'design dossier' and 'technical file' has been replaced by the term "technical documentation". Each submission should be a standalone document and not refer to previous technical file for

evidence of compliance. The flow of the documentation will follow the STED (summary of technical documentation) format. There are additional deliverables such as;

- General Safety and Performance Requirements (GSPRs). These replace the essential requirements (ER) from the MDD. MDR 2017/745 Annex II section, requires the technical documentation to include a demonstration of conformity with the applicable general safety and performance requirements of Annex I. If some GSPRs do not apply to a device this should be pointed out and explained within the documentation.

There are twenty-three (23) GSPRs in the MDR as opposed to there being 13 ERCs in the MDD. In the MDR there so many more elements to be addressed to fulfil all safety and performance aspects of the device. In short, technical documentation should provide suitable objective evidence to show that the device meets the requirements detailed in Annex I of the MDR 2017/745 GSPRs.

While working under the MDD, one method to demonstrate conformance to the requirements contained within was using harmonised standards. Harmonised standards are those listed in the Official Journal of Europe and such standards allow a presumption of conformity i.e. if a manufacturer can demonstrate conformance with harmonised standards then they demonstrate compliance with specific requirements of the directives. Harmonised standards continue to be a concept incorporated in the new MDR only in this case they provide a presumption of conformity with the regulation. The change is the introduction of common specifications. Article 9 of MDR 2017/745 discusses common specifications and their intent to be used where no harmonised standards exist or where relevant harmonised standards are not sufficient, or where there is a need to address public health concerns.

The term “common specifications” is referred to 177 times in the MDR 2017/745 document. They are intended to be used for products without any intended medical purpose. Chapter 1, article 1 of the MDR 2017/745 states “The necessary common specifications shall be adopted by 26 May 2020. They shall apply as from six months after the date of their entry into force or from 26 May 2020, whichever is the latest” (Commission 2017a). As of June 2019, there are no common specifications developed by the commission.

There are also new technical documentation deliverables engrained into the structure and system design of the new regulation. While Periodic Safety Update Report (PSUR) is not part of the technical documentation outlined in Annex II of MDR 2017/745, it is a new technical document which needs to be created. It is essentially an extension of a Post Market Surveillance Report

(PMSR) containing information for higher risk devices. The PSUR requirement is dealt with in article 86 of MDR. They are mainly intended for moderate and high-risk devices (Class IIa, IIb, III, & implantable). A PSUR summarizes the results and conclusions from your Post Market Surveillance (PMS) data. Information within it provides a summary of post market information, vigilance reporting, and the current status of these devices on the market in the EU. The PSUR should include;

- Conclusions of risk-benefit determination.
- Main findings of your Post Market Clinical Follow Up (PMCF).
- Sales volume of the device and estimates of size of other characteristics of audience using the device (plus usage frequency if known).

The frequency for submitting PSUR's for Class IIb both non-implantable and implantable, as well as Class III devices, is at minimum every year, whereas for Class IIa it is at minimum every 2 years and for Class I, when necessary. Manufacturers shall make PSURs available to the Notified Body involved in the conformity assessment and to the Competent Authority upon request.

Oriel 2018 explains the lack of clarity which exists in relation to this topic. The MDR mentions in article 86 and 92 that the document will be submitted electronically however they do not specifically reference the EUDAMED system. "Article 33, Section 2(f) is perhaps less nebulous and specifies that Eudamed shall include "the electronic system on vigilance and post market surveillance mentioned in Article 92." Thus, it is not clear if PSUR reports are part of post market surveillance and will be submitted via Eudamed. "There is no certain information on how this will be handled at this time" (Oriel 2018).

The PSUR requirement will help transparency within the EU system as this information was not previously readily available. This level of information is not available in any other region including in the US from the FDA Maude system.

Process validations (PV) have naturally always existed, however were never required to be provided to Notified Bodies as part of file reviews. Per the revised process, PVs are a new deliverable to be provided within technical files as part of the product approval process. As well as sheer volume of additional documentation to be reviewed as part of this requirement, this has also got implications from a timing perspective. Typically, the creation of new product technical files would occur early in the product lifecycle when design verification data is available and well

before PV (process validation) is complete as illustrated in Figure 9. With this requirement it will have impact on the timing of the submission unless the Notified Body is willing to accept the submission through modular approach, with the process validations in the last submission module. If the manufacturer has to wait for completion of PV prior to submitting the technical documentation to the Notified Body this will delay the CE Mark approval and impact time to market.

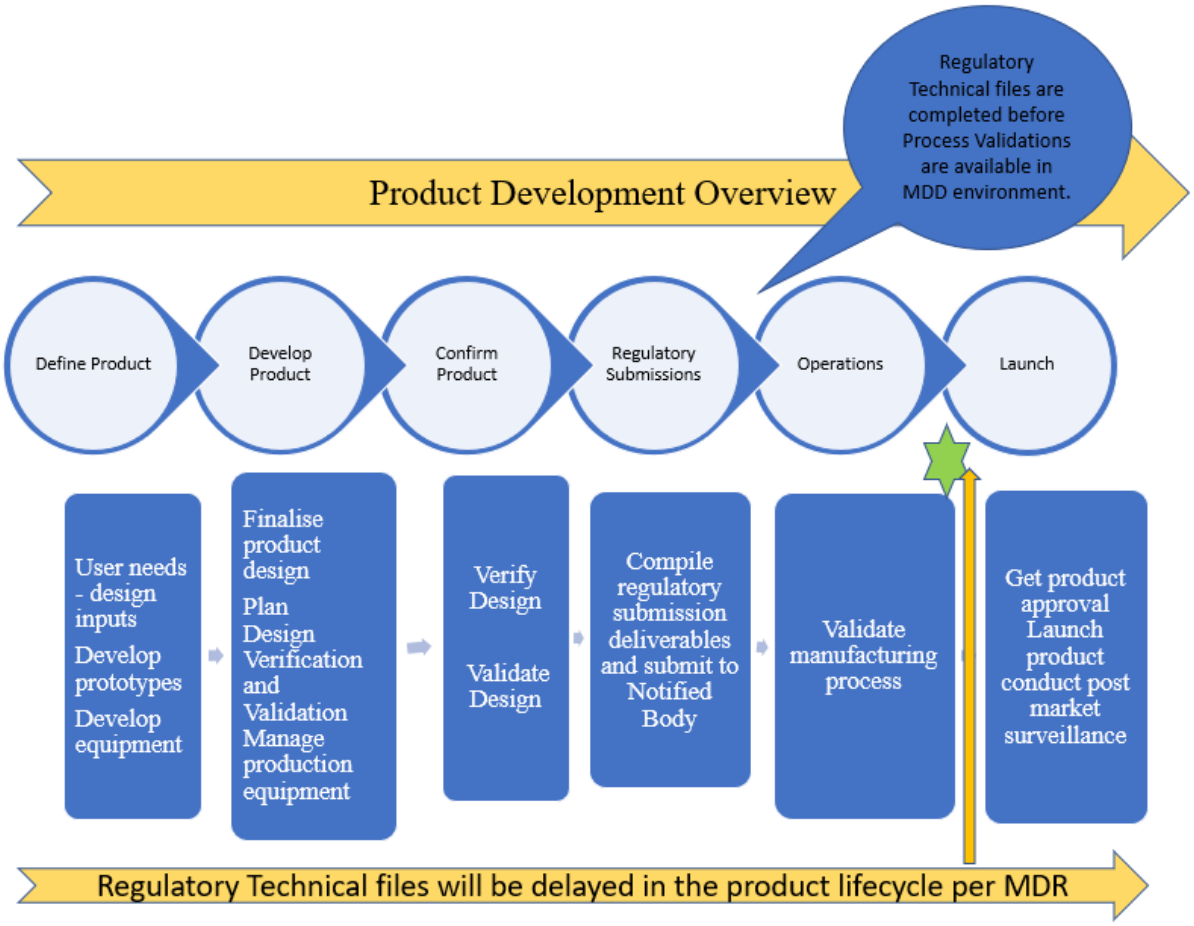


Figure 9: Product Development Overview to Highlight where Manufacturing Process Validations fit in the Product Lifecycle

(Created by the author)

Another new technical documentation deliverable is the Summary of Safety and Clinical Performance (SSCP). It is applicable to implantable devices and class III devices other than custom made or investigational devices. It shall be available on Eudamed. The contents of the SSCP are outlined in article 32 of MDR 2017/745. This document will include information

such as device description and intended purpose, identification through UDI, diagnostic or therapeutic alternatives if applicable, clinical information, warnings / precautions, training information, and the use of harmonised standards or common specifications applied. The SSCP shall ideally be written by the regulatory function with input from the quality, design assurance and the clinical function. The SSCP shall be updated at least once annually and be made available to the public on Eudamed.

The Clinical Evaluation Consultation Procedure (CECP) is applicable to Class III implants and Class IIb active devices intended to administer or remove a medicinal product. An example of a class III implant device is an aortic valve or a coronary stent. The Notified Body will review the clinical evaluation and they will communicate to the Competent Authority and to the EU Commission of whether the consultation is to be applied per article 54 (3) of MDR 2017/745.

During this process the Notified Body documents a report on the clinical assessment. The European Commission forwards this to the expert panel. The panel decides if they will submit their own specific opinion on this review. The Notified Body must take the expert panels viewpoints on board. If no expert opinion is submitted, the certification procedure may continue. This is a new addition to the review process for these types of products. This is discussed in more detail in chapter 5.

The retention of technical documentation has changed. Technical documents must be kept safely for at least ten years and documentation of implantable products must be kept for at least fifteen years. There is an increase of five years to retain technical documentation as MDD 93/42/ EEC stipulated five years to retain technical documentation. The requirement of fifteen years for retention of documentation associated with implants is the same in MDR 2017/745 as in the MDD 93/42/EEC.

2.4.5 Labelling and Promotional Material

All labels and IFU's (information for use) will require revision as part of this program. The MDR introduces a requirement for all labels to include a symbol indicating that the contents are a medical device as per chapter III, 23.1 (h). Figure 10 represents the image of this symbol. At the time of print of this thesis this symbol was not finalised. Upon agreement with the Commission, this symbol will be included in ISO 15223-1: 2016, Medical devices- Symbols to be used with medical device labels, labelling and information to be supplied. (International Organisation for Standardization 2016)

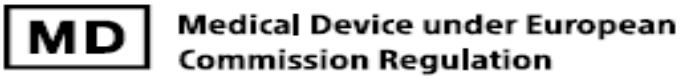


Figure 10: Symbol for a Medical Device

(taken from MedTech Europe guidance on use of symbols for MDR) (MedTech 2019b)

It is a requirement to label all devices with a Unique Device Identifier (UDI). The UDI shall be used for reporting serious incidents and field safety corrective actions in accordance with Article 87. The requirements on UDI are laid out in Annex VI, section 2.1. of MDR 2017/745.

Devices containing substances which are carcinogenic, mutagenic or toxic to reproduction (known as "CMR" substances) and/or endocrine disruptors in a concentration that is above 0,1 % weight by weight (w/w) will have this information included in the IFU. (Commission 2017a).

When one or more of these materials are present, the general "Contains hazardous substances" symbol shall be applied to product labels, and the material(s) shall be listed by name in the device description section of the IFU. Figure 11 illustrates a symbol for hazardous substances.

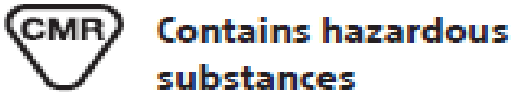


Figure 11: Symbol for Hazardous Substances

(taken from MedTech Europe guidance on use of symbols for MDR) (MedTech 2019b)

In addition, if the device is intended for use on children, pregnant or nursing women, or other populations considered particularly vulnerable to the included materials, the IFU's precautions section shall also include information on residual risks for each patient group, appropriate precautions, and any other relevant information. The instructions for use will also require revision as a notice to the user is to be included to instruct users to report any serious incident to the manufacturer. Specific waste disposal requirements will also be included in the IFU.

The introduction of 'Implant cards, is a new requirement per article 18. This card will contain information relating to the product and will be available to the patient for implantable devices as seen in Figure 12.

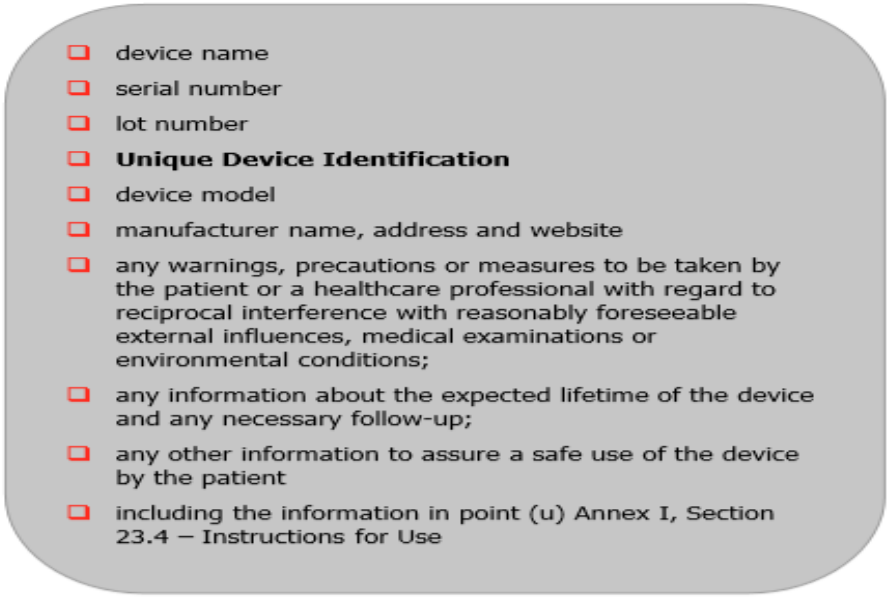


Figure 12: Information to be Provided on an Implant Card

(Taken from (Halliday 2017)

The promotional brochures and material will include the number of the relevant Notified Body involved in the CE marking process. This may mean that Notifies Bodies will require review of the promotional material as part of original submission, this is not something that occurs today. Promotional material is currently reviewed during routine surveillance audits and therefore is not a deliverable for original submission. Manufacturers will need to revise their design processes to ensure that promotional material is available early in the process.

2.4.6 Material Assessment

All materials used within medical devices must be assessed for carcinogens, mutagens and reproductive toxins (CMRs), endocrine disrupting chemicals (EDCs), and nanomaterials. Manufacturers will have to work closely with vendors to supply this information, and if this information is not readily available, testing may need to be performed. This may lead to material changes if exceeding levels of unwanted substances are present.

Chapter II, section 10 of MDR 2017/745 describes materials in detail.

2.4.7 Clinical Evaluation / Clinical Investigation as per Annex XIV of MDR 2017/745.

The clinical aspect of the MDR 2017/745 is probably the most demanding challenge and one that will put many manufacturers to its test. There is much greater emphasis placed on clinical evaluations. It will be much more challenging to demonstrate clinical safety and performance of a device based on predicate devices and equivalence arguments are harder to make. If manufacturers are leveraging clinical evidence they are expected to demonstrate that the device has the same technical, biological, and clinical characteristics as the device they are comparing to, and to demonstrate that sufficient access to the data for that equivalent device is available. In the competitive industry of medical device manufacturing, access to competitor device data is highly unlikely, thus making this option one which few will use. Clearly competitors are not going to share this information which is going to lead to manufacturers being forced to do retrospective post market clinical up (PMCF) studies particularly for implants and Class III devices. This is going to have incredible cost implications for companies which may have had these products on the market for decades without issue. Other scenarios which may occur is that some products may be forced off the market, smaller companies may not have the budget to generate clinical data, or perhaps some of the smaller companies may be bought by the larger companies allowing them access to this information.

Article 61.1 of MDR 2017/745 states "Confirmation of conformity with relevant general safety and performance requirements […] under the normal conditions of the intended use of the device, and the evaluation of the undesirable side-effects and of the acceptability of the benefit / risk ratio […] shall be based on clinical data providing sufficient clinical evidence" (Commission 2017a). MDR 2017/745 is explicit about the expectations on clinical.

One of the leading Notified Bodies sent a communication to their clients in September 2018 to state the following: "It has come to our attention that a minority of manufacturers have not met their PMCF commitments across all their Class III devices for all design variants and indications. Therefore, they do not have sufficient data for certain devices and/or indications at renewal to demonstrate the key requirements for clinical data: safety, performance and benefit-risk in relation to the state of the art" (Smirthwaite 2018).

The Notified Body went on to say, "in such cases where PMCF commitments were not followed up on, these products may need to be removed from the renewed certificates, and/or have certain

indications removed due to a lack of supporting Clinical Evidence directly relating to the devices and their indications" (Smirthwaite 2018). This communication was a clear message that Notified Bodies are taking clinical evidence seriously and was intended as a "heads up" for manufacturers to get their house in order.

2.4.8 Post Market Surveillance

The new MDR 2017/745 takes a step forward in improving post market surveillance as a whole in Europe. There is extensive coverage given to post market surveillance in the content of the regulation. Chapter VII is comprehensive, it is dedicated to post market requirements with Annex III outlining the documentation required to support these requirements. Compared to the post market program in place today, there will be an increase in Post market surveillance (PMS) reports generated, there is a potential for more reportable events submitted and investigated, and there will be closer monitoring of complaint trends and PMS data.

There will be improved mechanisms within the EU system for market surveillance and vigilance. Article 83 of MDR 2017/745 states "Data gathered by the manufacturer's post-market surveillance system shall in particular be used:

> (a) to update the benefit-risk determination and to improve the risk management as referred to in Chapter I of Annex I;
>
> (b) to update the design and manufacturing information, the instructions for use and the labelling;
>
> (c) to update the clinical evaluation;
>
> (d) to update the summary of safety and clinical performance referred to in Article 32;
>
> (e) for the identification of needs for preventive, corrective or field safety corrective action;
>
> (f) for the identification of options to improve the usability, performance and safety of the device;
>
> (g) when relevant, to contribute to the post-market surveillance of other devices; and
>
> (h) to detect and report trends in accordance with Article 88.

The technical documentation shall be updated accordingly" (Commission 2017a)

The Eudamed database will help facilitate much of the information gathered on post market surveillance and will be available with varying access levels to Notified Bodies, Competent Authorities, economic operators, healthcare professionals, and patients which is providing increased patient safety.

Manufacturer's need to understand their role and the requirements around post market surveillance activities. This is not just to meet the regulatory requirements, it is also a measure for the manufacturer that their device continues to operate as it was designed, that it is performing as anticipated, and that it continues to meet "state of the art".

2.4.9 Supply Chain

- MDR 2017/745 introduces many changes to the regulatory obligations of post market importation and distribution of medical devices. This responsibility belongs with various entities collectively described as the "economic operator" and constitutes the manufacturer, the authorized representative, importers and distributors. These entities are defined in article 2 of MDR 2017/745 as follows; 'manufacturer' means a natural or legal person who manufactures or fully refurbishes a device or has a device designed, manufactured or fully refurbished, and markets that device under its name or trademark;
- 'importer' means any natural or legal person established within the Union that places a device from a third country on the Union market;
- 'distributor' means any natural or legal person in the supply chain, other than the manufacturer or the importer, that makes a device available on the market, up until the point of putting into service;
- 'authorised representative' means any natural or legal person established within the Union who has received and accepted a written mandate from a manufacturer, located outside the Union, to act on the manufacturer's behalf in relation to specified tasks regarding the latter's obligations under this Regulation;
- 'economic operator' means a manufacturer, an authorised representative, an importer, a distributor or the person referred to in Article 22(1) and 22(3).

All the above come under the umbrella of supply chain. There are many checks and balances built into the revised system. The roles and responsibility for these operators is clearly defined with increased responsibility and will lead to much change in this area going forward. Each of

these entities must check independently that the device meets the regulatory requirements. As this practice is new and untested, it is difficult to anticipate how this will work out. In many companies, supply and distribution contracts will need to be revised to define these responsibilities and they will be assessed on an ongoing basis as part of the overall quality system accreditation and they will be exposed to unannounced audits.

2.4.10 Eudamed

Eudamed is a European databank which is used to store information relating to medical devices. It was created in 2011 with an aim to strengthening the market surveillance and transparency of medical devices placed on the European market. It provides national Competent Authorities fast access to relevant regulatory information. The database cannot be accessed by the public at present, however as part of MDR 2017/745, it will be open to the public where patients will have open access to product information. This databank will house product information such as product labelling, manufacturer's information including proof of their quality system, registration information, who the legal manufacturer and authorized representative are, clinical investigations, a vigilance and traceability system, post market surveillance and declaration of conformity to name some of the documents which will be openly available.

2.5 Who Are Regulatory Affairs and What is Their Role?

A regulatory professional working in industry is responsible for keeping track of the ever-changing legislation in the regions in which a company wishes to distribute its products, advise on the legal and scientific restraints and requirements, and collect, collate and evaluate scientific data. They are responsible for the presentation of registration documents to regulatory agencies and carry out all the subsequent negotiations necessary to obtain and maintain marketing authorisation for the products concerned.

"A regulatory affairs specialist gives strategic and technical advice at the highest level in their companies, right from the beginning of the development of a product, making an important contribution both commercially and scientifically to the success of a development programme and the company as a whole" (TOPRA 2018).

A regulatory affairs professional is the link between the manufacturer and the regulatory agency.

The role of the regulatory affairs varies greatly between companies; for the purposes of this research the role will be defined by the following tasks / activities in relation to MDR 2017/745 implementation. The regulatory affairs function has responsibility for rewriting all existing design dossiers and technical files to capture the new requirements for technical documentation. They will manage the submission of the new files and work with the Notified Body to resolve any questions during the review process. They will be responsible for creating the GSPR documents, the SSCP and rewriting declarations of conformity. It is assumed that other functional experts will generate other required deliverables and requirements e.g. clinical evaluation reports (CER), labels, IFU (information for use), and periodic safety update report (PSUR's) of which regulatory will be involved in reviewing and approving.

Regulatory affairs role within the regulators

Personnel working for Notified Bodies are also considered regulatory affairs professionals. Their role is to review the technical documentation provided by the manufacturer and perform tasks related to conformity assessment procedures outlined in the applicable legislation, as well as conducting audits, scheduled and unannounced. Manufacturers can choose the Notified Body of their preference, if the Notified Body selected is designated to perform the tasks associated with device(s) they plan to get CE marked.

Notified Bodies are closely aligned with the Competent Authorities. Each country within the EU has a Competent Authority. The role of the Competent Authority is to transpose the

requirements of the medical device directives into law. Their role with medical devices is to protect the public by regulating the safety of medical devices. They will work closely with the other Competent Authorities to ensure consistency with regulation implementation. The Competent Authority in Ireland is the Health Products Regulatory Authority (HPRA) and the Competent Authority in the UK is the Medicines Healthcare Products Regulatory agency (MHRA). The following link provides a list of the Competent Authorities in European Economic Area (EEA).

https://www.ema.europa.eu/en/partners-networks/eu-partners/eu-member-states/national-competent-authorities-human.

The Notified Bodies and Competent Authorities work closely together with manufacturers. They too will be highly impacted by the implementation of regulation 2017/745 as their workload will increase enormously with heightened requirements imposed.

2.6 Summary

This chapter introduces the regulatory framework for which medical devices are regulated. It describes the current Directives versus the Regulation summarising the main changes to be applied as this transition is made. It gives the background as to how the regulation came about and it describes the role of the regulatory affairs function both working for a medical device manufacturer and working in the regulatory affairs function as a regulator.

Chapter 3 Literature Review and Research Methodology

This chapter describes the research strategy to analyse the challenges faced by regulatory affairs personnel in the medical device sector as they implement the new medical device regulations, MDR 2017/745.

Initially, a detailed review of the literature representing the thinking on Regulation 2017/745 was conducted. There were many variations of inclusion criteria associated with the subject used to optimise best results. There were challenges associated with the literature review. The output of the literature search has clearly determined that there is a void in information available on this topic facing the industry. The literature available is very limited in scope and quantity and has not addressed the challenges for regulatory affairs professionals working on MDR 2017/745.

This was followed by a mixed method approach combining both qualitative and quantitative analysis. Finally, a review of the data was conducted to assess the output of each phase. The results of each of these phases is documented in chapter 4, and an analysis conducted in chapter 5 Figure 14 below outlines these stages.

There are many steps involved in any research and Figure 13 describes the different stages in a very generalised model. Selection of the research question is critical. Selecting the research topic can be one of the most challenging parts of the research. The topic for this research was chosen as the author had a keen interest in the topic and wanted to understand how the MedTech sector were responding to the impending regulatory changes.

The research problem needs to be defined clearly as this drives the process of the research to formulate and testing the hypothesis. The hypothesis in this research is to identify the "Challenges for the Regulatory Affairs function in demonstrating compliance for existing CE marked devices to the new EU Medical Devices Regulation 2017/745." The research was designed into four (4) stages incorporating both qualitative and quantitative methods of collecting data. The data was analysed as described in detail in chapter 5 and conclusions drawn as described in chapter 6.

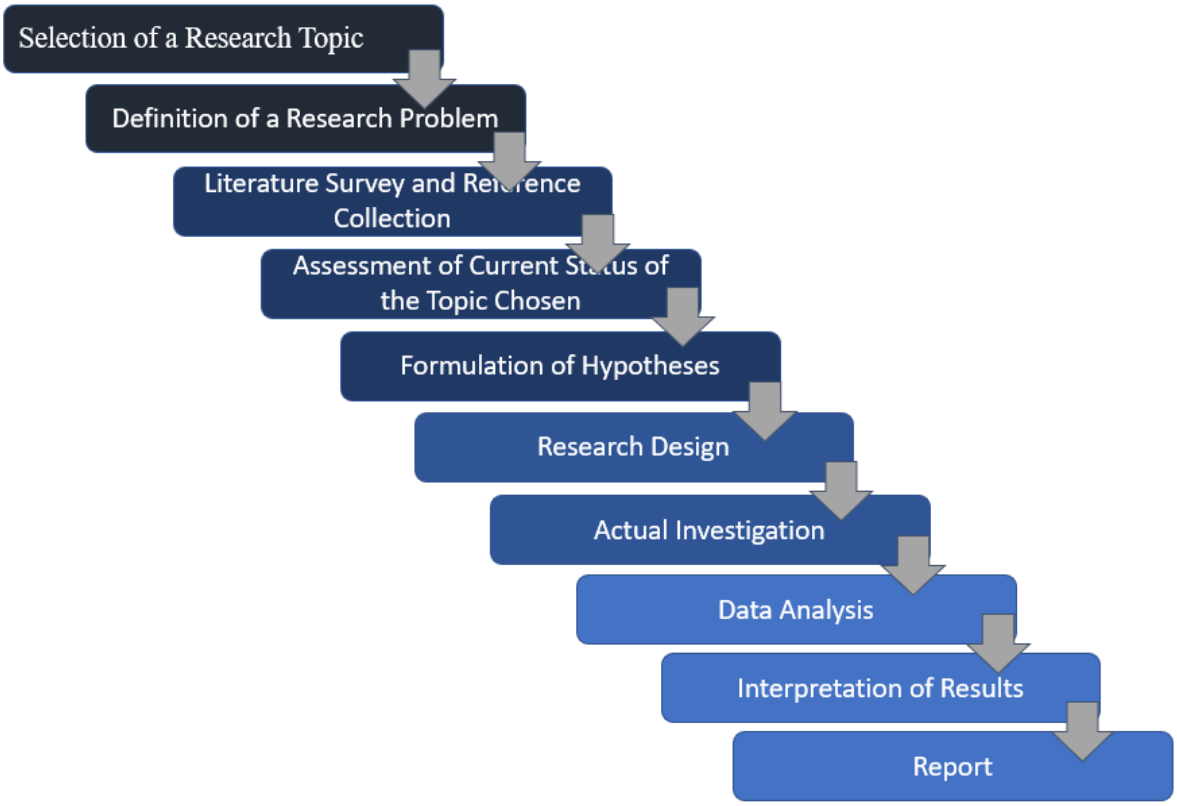


Figure 13: Approaches of Research

(Taken from Bhawna, Gobind June 2015)

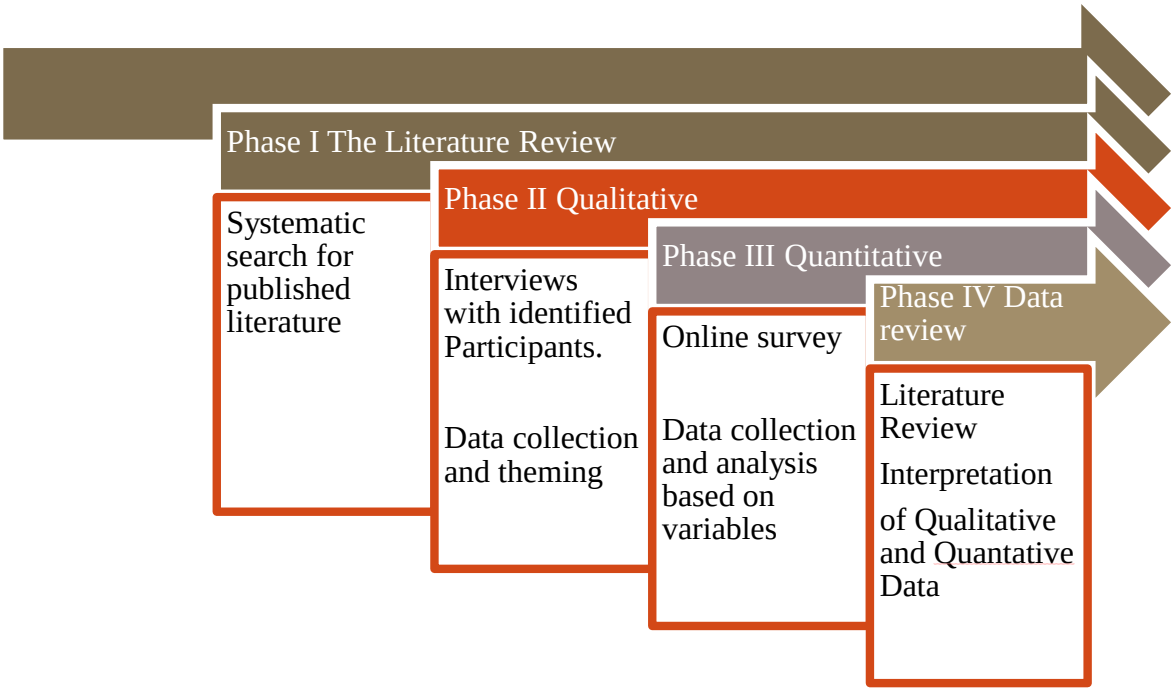


Figure 14: The Stages Involved in this Research

(created by the author)

3.1 Phase I Literature Review

The literature review was the first stage of the research. This was completed to understand if there was work done in this area to date or if the challenges were already identified. The literature review summarises the current research thinking in relation to the challenges associated with implementing MDR 2017/745 and confirms the value of the planned research in this thesis. According to Faryadi, there are many advantages of doing a literature review.

1) To find the latest studies concerning your topic so that you know who the other researchers are and what they have contributed.
2) To make yourself more knowledgeable in your area of specialization.
3) To answer key questions about your topic of study.
4) To see what methods and methodologies are being used by current researchers so that you can apply them in your own research.
5) To collect supporting evidences to justify the investigation of your problem

and hypotheses.
6) To identify any gap in the literature so that your new findings can close or narrow that gap (Faryadi 2018).

One of the main disadvantages is that it is very time consuming.

"A review of the literature is a written summary of journal articles, books and other documents that describes the past and current state of information, organizes the literature into topics and documents a need for a proposed study" (Qais, 2017: p. 34).
The literature search for this research commenced in July 2018 and was revisited through to May 2019 conducting several repeat searches in the interim. The following search terms have been used to establish the availability of literature:

"Medical devices", "EU Regulation 2017/745", "MDR 2017/745", "challenges with regulation 2017/745".

Scientific databases such as PubMed, Google Scholar, Science Direct, and Wiley online library (through Boston Scientific) were used to conduct these literature searches. Articles published from 2010 onwards were included in the analysis. This date was chosen as this was the year the first of the major recalls relating to safety by De Puy as described in chapter 2. It was after this time that scrutiny of the regulatory system began.

The results from the literature review are documented in chapter 4, with further discussion covered in chapter 5.

3.2 Mixed Method Research

"Conducting mixed method research involves one study that employs different methods to answer a specific research question seeking for rich and comprehensive information and results" (Creswell 2013).

The author used a mixed method approach to gain different, multiple perspectives and more complete understanding of the challenges associated with the new regulation. The aim of the approach was to gather data and individual perspectives from people with experience in the research subject.

"A mixed methods research design is a procedure for collecting, analyzing, and "mixing" both quantitative and qualitative research and methods in a single study to understand a research problem. A mixed methods approach is one in which the researcher tends to base knowledge

claims on pragmatic grounds (e.g., consequence-oriented, problem-centered, and pluralistic). It employs strategies of inquiry that involve collecting data either simultaneously or sequentially to best understand research problems" (Bhawna and Gobind 2015).

One of the advantages of using mixed method is that it allowed the author to use several means to research the same phenomenon. The data is more comprehensive because of this method as it includes narrative, words, numbers and statistics. Using both quantitative and qualitative methods complements each other and leads to stronger evidence for a conclusion. Qualitative research is often used to build on a theory and the quantitative portion of the research is to test that theory. One of the disadvantages of mixed method research is that it was very complex, required a large amount of planning and is time consuming, however the author felt it was the right approach for this research to gain useful, comprehensive data providing valuable information for medical device manufacturers.

This research occurred over different stages starting with the literature search, as described in Figure 14. The literature search was followed by a qualitative stage using semi structured interviews. The semi structured interviews were used to learn about the challenges of MDR 2017/74 from experts in both industry and those working for the regulators. This variable data was considered the qualitative analysis.

It was felt that the results from the interview would need to be further explained, hence an additional method supplemented the interviews. The additional method, which was quantitative, consisted of a survey which was developed from the challenges obtained from the output of the interviews Figure 15 is a visual of how we make sense using this approach. (Creswell 2013) describes this as a simple idea of bringing quantitative and qualitative research together to get a more complete understanding of the research question. Sometimes qualitative or quantitative research on its own is insufficient to fully understand the problem. He talks about the use of numbers for numeric data for comparing groups or relating variables for the quantitative data analysis. He discusses personal experiences in the context of theme development and relating themes.

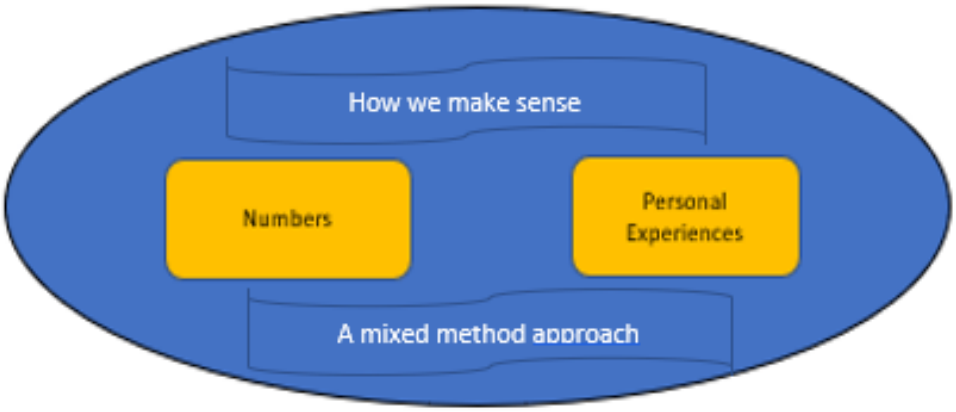


Figure 15: How Do We Make Sense - A mixed Methods Approach

(Creswell 2013)

According to Johnson & Onwuegbuzie, a mixed methods approach to research is an extension of, rather than a replacement for, the quantitative and qualitative approaches to research, as the latter two research approaches will continue to be useful and important. They also believe that the goal for researchers using the mixed methods approach to research is to draw from the strengths and minimize the weaknesses of the quantitative and qualitative research approaches. (Johnson and Onwuegbuzie 2004).

Phase II of the research included a qualitative method of semi structured interviews as part of a phenomenological study. The purpose of this study was to understand the challenges faced by the regulatory affairs professionals working in the medical device industry. The author felt there was a need to investigate the stakeholder views and get a better understanding of the perceived challenges.

The author interviewed stakeholders from the MedTech sector including regulatory professionals from small and large Medical Device Companies, Notified Bodies, Competent Authority, and regulatory consultants working in the industry. The transcripts of the interviews were examined, and challenges identified throughout the discussions were grouped into general themes or categories. From there, a final list of challenges was generated for further analysis.

Using this data, the author executed a quantitative survey to rank the identified challenges (survey results) and discuss the findings. Phase III of the research consisted of a survey. The survey was

completed to rank the challenges facing the sector. This will enable manufacturers to focus on the top challenges with the limited resources available in many companies to deal with MDR 2017/745.

Phase II - Qualitative Research –Interviews

The qualitative method used in this research was conducted by doing semi structured interviews.

3.2.1.1 Semi Structured Interviews

While there are three different types of interview, structured, unstructured and semi structured, it is the semi structured which draws on probing questions to gain a greater understanding of the interviewee's responses within the interview process. This method is the most attractive to researchers in business and management. "Interviewing is a popular way of gathering qualitative research data because it is perceived as "talking" and talking is natural. Interviews do not presuppose any statistical knowledge, and persons to interview, called respondents, might be close at hand and will" (Griffee 2015).

Semi structured interviews are used to collect data to gain knowledge from individuals.

"Most qualitative research projects involve the collection of participants' views, which are transcribed and analysed to reveal a story or conceptual framework that represents the meaning of the experience under investigation. The researcher is directly involved in gathering the data, and their background and assumptions will inform and shape the process" (Bolderston 2012). The interviews in this research was set up as a semi structured interview. Using this method of interview structure allowed the author to have the questions prepared ahead of time by developing the interview guide, however straying from the guide was acceptable too if the conversation permitted.

For interviews to be successful they must be carefully planned with focus on the research question. Interviews can be powerful if conducted and analysed appropriately. To that end, the author determined that an interview guide would be beneficial to ensure the interviews were conducted in a consistent and planned approach. There was one main question asked by the researcher which was, "What do you think are the challenges faced by the regulatory affairs function in bringing our products and files in compliance with regulation 2017/745". From there the interview was allowed move free flow using probing questions to elaborate or explain some of the answers, and to investigate various challenges.

Interviews generate deeply contextual accounts of participants experiences and their interpretation of them (Schultze and Avital 2011). The interviewer in this study was curious, keen to explore this topic and genuinely interested in what she was being told by the participants to understand their thoughts, feelings, views and experiences.

A fundamental principle of conducting interviews is to listen. It was important to hear the meaning of what the participant was saying and understanding where it needed to be explored further. It was also crucial to build trust and establish rapport, because the person needs to be comfortable answering questions honestly. The sequence of steps relating to the interview process is illustrated below in Figure 16.

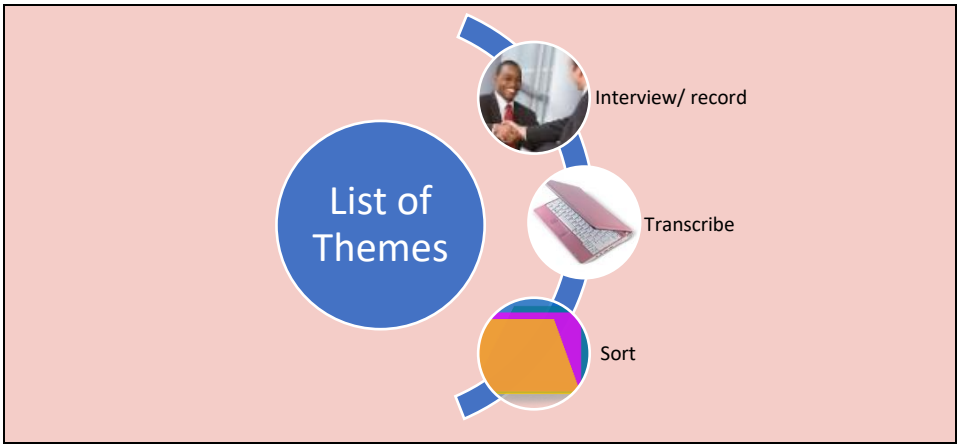


Figure 16: Sequence of Data Review in Phase II

(As created by the author)

3.2.1.2 Interview Design and Execution

When designing the interview there were a few aspects to be considered:

1. Who should be interviewed?
2. Rationale for choice of number of interviewees.
3. Supporting documentation for conducting interviews.
4. Data analysis.

1 Who should be interviewed

"Who is interviewed depends on the intention of the research. In qualitative investigation, sampling is usually purposeful in nature. Purposeful sampling involves the researcher selecting

potential participants who represent the group to be studied with the aim of talking to a reasonable cross-section of people" (Bolderston 2012).

To gain valuable data from the interviews it was important that the chosen candidates had a working knowledge of the medical device industry and specifically the regulatory environment in Europe. The individuals were chosen based on their vast experience in the MedTech sector, be it in industry, or as a regulator.

"Good interviewees are those who are available, willing to be interviewed and have lived experiences and knowledge about the topic of interest" (DeJonckheere and Vaughn 2019).

The selection of participants chosen for this research included regulatory professionals from both small and large Medical Device Companies, Notified Bodies, Competent Authority, and a regulatory professional from a consultancy firm. Personnel working for the regulatory agencies were identified as key respondents for interview. The agencies are at the forefront of dealing with MDR 2017/745 through dealing with multiple manufacturers, with other regulators such as the Competent Authorities and the EU Commission, and so are subjected to a wide variety of challenges from different viewpoints. These agencies have a wealth of knowledge in this area, however, they would also openly state that they too are on the learning curve, and they also have many of their own challenges in applying 2017/745.

Although the author recognised the importance of interviewing regulatory agency personnel, she recognised the difficulty in doing so also. Notified Bodies are extremely busy at present, so it was a challenge to get time scheduled with them. The other factor which had to be considered here is that Notified Bodies are not allowed to provide consultation in any capacity. The author works closely with different Notified Bodies, hence has many connections in this area. Through those connections several professionals in these bodies agreed to participate in the research which was very valuable as it provided a unique insight to challenges for regulatory specialists in all MedTech stakeholders. It can generally be difficult to get regulators such as Competent Authorities and Notified Bodies to participate in research studies. The confidentiality agreement did influence participation as well as the author having built relationships with some of them over the years.

Another great resource that the author identified was a medical device consultant working with several medical companies through their implementation of the regulation. The consultant provided a great spectrum of knowledge and was able to give his perspective on individual topics from both a large and a small manufacturing perspective, and the perspective of some of the

Notified Bodies that deals with through working with these companies. He started out his career in 1990 in quality roles and held various Senior Management positions in companies in Galway, Sligo, and in Holland. On return from Holland he started in a consultancy role over two years ago.

The participants from industry were selected as they were working specifically in regulatory affairs at senior levels within their organisation. It was opportune that the participants were seasoned regulatory affairs professionals who have been working at the forefront of applying the Medical Device Directives and are now actively involved in applying the new regulations into their everyday doings. They were all operating at senior levels within their own respective organisations and had a very good understanding of the EU regulations.

There were no interviews conducted with anyone working in the IVD medical devices area as this is out of scope of this research thesis. Medical device manufacturers making IVD devices will comply with Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices. (Commision 2017). The roles and responsibilities of each of the participants including their involvement with the new regulations to date is detailed in Table 2. A brief description of the type of organisation is also included. For confidentiality reasons neither the participant nor the organization are identified.

2. Rationale for choice of number of interviewees

An appropriate quantity of stakeholders was required to ensure that the data received was valid and sufficient information was extracted for input into the next phase of the research. "Choosing the number of participants to get involved in interview research was analysed and researched. There was one study reviewed where the design consisted of 26 participants. Findings indicated that 84% of symptom concepts emerged by the 10th interview, 92% emerged by the 15th interview, 97% emerged by the 20th interview, and 99% by the 25th interview" (Turner-Bowker *et al.* 2018).

A separate study by Hennenk was reviewed whereby 25 in depth interviews were conducted. This study found that code saturation was reached at nine interviews, whereby the range of thematic issues was identified. (Hennink *et al.* 2017).

"For a typical phenomenological study the number may be around 10 participants" (Bolderston 2012).

For this research 12 interviews were conducted. Based on the analysis above the researcher felt comfortable that this number more than provided an adequate representation of the opinions of key stakeholders in the medical device sector. In addition, this number allowed the author to allocate appropriate time to the process. As mentioned earlier, one of the challenges of semi structured interviews is the time for preparation and execution.

3. Supporting documentation for conducting interviews

As part of the preparation for successful interviews, supporting documentation is key. In this case, two main documents were used to facilitate completion of the interviews; interview consent form and an interview guide. The consent form is the agreement between the researcher and the research participant outlining the roles and responsibilities they are taking on as throughout the research process. It provides the participant with sufficient information for them to make an informed decision and in this case, they were assured that their name and their organisation will be confidential and not made known as part of this interview process. See Appendix A.

An interview guide was developed to manage the interview process and help direct the conversation towards the topics and issues that the researcher wanted to research to a greater degree. It was devised to help the author gather credible evidence that was relevant to the research question. It supported a comfortable interaction with the participant as it was used to set the scene, explain how the interview was structured, explain the purpose and expectation from the interview.

The interview guide also outlined that the topic of clinical was being purposely excluded from the interview discussion. As is well known, among the vast changes occurring with the transition from directive to regulation are the new requirements surrounding clinical evidence. This certainly is a huge challenge for industry and something they are struggling to deal with, however, for the purposes of this research the author is choosing to exclude the topic of clinical to focus specifically on the regulatory affairs function, and their challenges.

See Appendix B for a copy of the interview guide.

4 Data analysis

When the qualitative interviews were complete, they were then transcribed for review. From the transcripts the challenges discussed were identified and then categorised into different themes. An independent review by a regulatory affairs colleague was conducted to ensure that all challenges were recorded appropriately and that agreement on the category was reached. The

output from this was a list of challenge categories. The results of this are outlined in chapter 4 and are discussed in chapter 5.

The following table outlines the roles of the interviewees as well as the type of organisation that they work in. To honour the confidentiality commitment, the name of the interviewee nor their place of work is not disclosed. The interviews were recorded, and transcripts can be found in the appendices referenced below in Table 2.

.

Table 2: Role and place of work of the Interviewees

Interview Reference	Role within their organisation	Organisation	Transcript
C1	Regulatory Specialist part of the core team managing implementation of MDR 2017/745.	Medical Device Manufacturer	Appendix C
C2	Senior Auditor and file reviewer	Notified Body	Appendix D
C3	Regulatory Consultant to several small and large organisations	Regulatory Consultant to Industry	Appendix E
C4	Senior Advisor with a leading Competent Authority	Competent Authority	Appendix F
C5	Regulatory Affairs Director	Medical Device Manufacturer	Appendix G
C6	Senior Regulatory Affairs manager leading MDR implementation in their company	Medical Device Manufacturer	Appendix H
C7	Director of European Regulatory Affairs	Medical Device Manufacturer	Appendix I
C8	Director of Quality & Regulatory Affairs, with global responsibility.	Medical Device Manufacturer	Appendix J
C9	Regulatory Affairs Manager responsible for a portfolio of CE marked devices.	Medical Device Manufacturer	Appendix K
C10	Regulatory Specialists dedicated 100% to working on MDR 2017/745	Medical Device Manufacturer	Appendix L
C11	Lead Auditor and file reviewer	Notified Body	Appendix M
C12	Manager of Business Development	Notified Body	Appendix N

The number of interviewees was twelve in total and included personnel from a Competent Authority, Notified Body reviewers/auditors, a consultant and experienced regulatory professionals from some of the leading medical device manufacturers in the industry. Interviews require careful planning to get the optimum results. The interviews were scheduled at minimum two weeks in advance. Six of these interviews took place face-to-face and the other six were conducted through teleconference.

For the face-to-face interviews, the location was private, quiet and allowed for uninterrupted discussion. The consent forms were arranged in advance of the interviews for any interviews conducted by teleconference, or by signing prior to the interview at the face to face meetings. Each of the interviews lasted approximately 1 hour.

The interviews were recorded, and the resulting audio transcribed. Transcribing is an arduous process, but it is a critical aspect of the process to convert the spoken word to written word. Transcripts from the interviews were typed for review and further analysis. (See Appendix C – Appendix N).

3.2.2 Phase III Quantitative Research – The Survey

Surveys vary in complexity and in the amount of time and money required. The increase in the use of email and intranets has led to new and easier options for gathering information with self-administered questionnaires. Many people use their phones now to complete surveys also which can lead to very quick turnaround on responses. Surveys are used to gather quantifiable data. They are often used in everyday life in places such as industry assessing training effectiveness, they can be used in determining customer satisfaction. The steps involved in conducting a survey are outlined in Figure 17.

The survey in this research ranks the specific challenges identified from the 12 individuals interviewed in phase II, as well as asking additional questions to gain information related to the MDR in general. The output from the survey will help companies learn from each other's experiences of MDR 2017/745 to date, and to plan and execute accordingly. It will facilitate management prioritisation and resource allocation accordingly to work as companies transition to the MDR.

According to Bhawna and Gobind, quantitative research is the systematic empirical investigation of observable phenomena via statistical, mathematical or computational techniques. The objective of quantitative research is to develop and employ mathematical models, theories and/or

hypotheses pertaining to phenomena" (Bhawna and Gobind 2015). The survey was the means for completion of the quantitative aspect of this research.

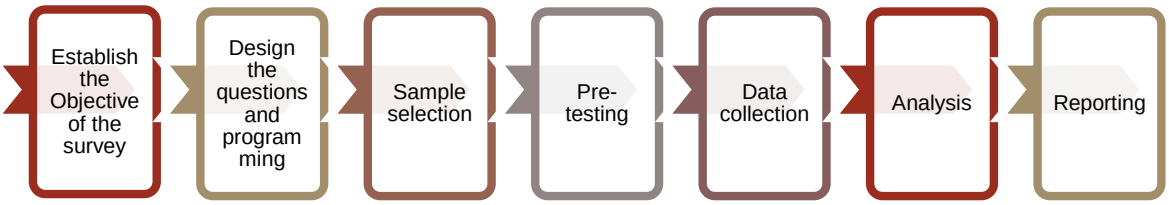


Figure 17: Steps in Conducting a Survey

(Created by the author)

"The term 'survey' is used in a variety of ways, but generally refers to the selection of a relatively large sample of people from a pre-determined population (the 'population of interest'; this is the wider group of people in whom the researcher is interested in a particular study), followed by the collection of a relatively small amount of data from those individuals. The researcher therefore uses information from a sample of individuals to make some inference about the wider population" (Clark *et al.* 2003).

The are many advantages of surveys including the following (Sincero 2012):

- They can collect a large amount of data within a short window of time, and with many software packages available free it is a cost-effective way of collecting data.

  This survey was completed online.

- The data collected is based on real world experience.
- The data can be represented by rich visual tools.
- The anonymity of surveys allows people to answer more freely and give their honest feedback.

Some of the disadvantages include:

- Sending surveys by email is that spam filters may prevent emails from being delivered to the intended participants.

- Sometimes respondents are irritated by having to do “another survey” so the response rates or accuracy may be low, and only those particularly interested in the topic may respond.

The survey worked well for this research in that it collected valuable data in a short space of time, and it did not cost any money. It was able to present the data in visual format with colourful graphs which it made it easy to read. Since the feedback was anonymous it gave respondents the opportunity to give their honest feedback. It is always challenging to get a good response to surveys. The survey was purposely designed to be short and fast to encourage participation. A persuasive email accompanied the survey giving the background and reasons for doing the research to encourage respondents to participate.

The main purpose of the survey was to gain a ranking for the nine (9) challenges identified by the twelve (12) interviewees. In addition, the author used the opportunity to ask additional questions to further explore the respondent’s experiences with the new regulation.

3.2.2.1 Survey Design and Execution

There are two basic structures to questions; they can be open-ended or forced choice. Open-ended questions are those that respondents answer in their own words. The open-ended questions can be insightful but quantifying and analysing the data can be difficult.

The survey questions were carefully planned with the research question at the forefront of the design. Built into that design the layout of the questions was considered, number of questions, and ease of understanding the context of the question. Using the questions correctly is the key to achieving successful survey results. The questions were short, straightforward with various forced choice structures such as yes or no checkboxes, multiple choice or ranking. The wording of the questions was carefully crafted with no bias. The type of questions considered for this research are as follows:

- Checkboxes is a simple closed-ended question type that lets respondents select multiple answers from a defined list of choices.
- Multiple Choice is a simple closed-ended question type that lets respondents select one answer from a defined list of choices.
- A Matrix question is a closed-ended question that asks respondents to evaluate one or more row items using the same set of column choices.

- A Rating Scale question, commonly known as a Likert Scale, is a variation of the Matrix question where you can assign weights to each answer choice. Rating Scales automatically calculate a weighted average for each answer choice in the Analyse Results section.

  The question types included in the survey are documented in Table 3.

How the questions were designed

Question 1: This question was included to understand the type of organisation respondents worked in. This was important as the challenges impact the various organisations in different ways.

Question 2: The purpose of this question was to understand the size of organisation that respondents worked in. This was important as larger companies are more resourced, have bigger budgets, have a larger pool of people to lean on for experience, and typically have a project management team to deal with large assignments such as this. Their challenges may be different to that of a small medical device manufacturer.

Question 3: This survey was conducted in April 2019 timeframe. It was valuable to get a level of understanding of the MDR amongst the participants. The results of this question could have influence on how the main question in the survey is answered, that is question 7. In question 7 respondents are asked to rank the challenges. If the respondents are not knowledgeable on the MDR then that may impact these responses.

Question 4: This question was asked to see if respondents understood what functions are impacted. Often when regulations or standards change, people tend to think that it is just the regulatory function that is impacted. It was worthy to ask this question to see if the respondents understood the impacts on the other functions, which also ties into the challenge of resources and workload.

Question 5 and 6 associated with writing and approving technical files were asked to understand how workload and resources would be impacted by this task.

Question 7 is the most crucial question of the survey as it asks the respondents to rank the challenges. This is important as it helps the author understand what the priority of challenges amongst the regulatory community taking this survey and what should medical device manufacturers and regulators alike get most prepared for.

Question 8 was asked to get opinions on if respondents think this overhaul of the regulations will in fact have any impact on patient safety be it positive or negative.

Table 3: Questions asked in the Thesis Survey

No.	Question	Response Options	Question Type
1	What type of Organisation do you work in?	Please select one option • Medical Device Manufacturer • Notified Body • Competent Authority • Other	Multiple Choice
2	How many people are employed in your organisation worldwide	Please select one option • <50 People • 50-250 People • 250 – 500 People • >500 People	Multiple Choice
3	Rate your level of understanding of MDR 2017/745	Please select one option • No Understanding • Limited Understanding • Moderate Understanding • Good Understanding • Complete Understanding	A rating scale
4	What other departments /functions do you think will be directly impacted by the MDR 2017/745?	Choose all that apply • R&D • Design Assurance	Check boxes

No.	Question	Response Options	Question Type
		• Clinical • Operations • Quality • Sales and Marketing • Distributors • All the functions • Other	
5	If you are responsible for writing and compiling Technical Documentation, how many hours will it take to generate a file compliant with the MDR 2017/745? (assume this is for a file that exists today in MDD and it is being converted to MDR 2017/745)	Please select one option • 0 – 20 hrs • 20-50hrs • 50-100hrs • 100+hrs • NA	Multiple choice
6	If you are responsible for approving Technical Documentation, how many additional hours on average will it take to review the file under MDR 2017/745 compared to MDD? (assume this is for a file that exists today in MDD and it is being converted to MDR 2017/745)	Please select one option • 0 – 10hrs • 10-20hrs • 20-30hrs • 30+hrs • NA	Multiple Choice

No.	Question	Response Options	Question Type
7	The challenges identified below are from interviews conducted with people working in the MedTech sector who are very familiar with the MDR 2017/745. Please rank these challenges from 1 -9 with 1 being the most challenging and 9 being the least challenging.	Please rank from 1 - 9 • Awareness and Training. • Lack of clarity and absence of supporting documentation. • New requirements and reduced reporting timelines for post market surveillance. • Re approval of all products - no grandfathering. • Resources required to manage increased workload. • Management of design changes and changes to intended use post May 2020. • Additional reviews / requirements adding to submission timelines. • Compliance by May 2020. • Cost.	A rating scale
8	Do you think the MDR 2017/745 will have any impact on patient safety?	Please answer one of the following and comment • Yes • No	Multiple choice

The author sent the survey to fifty-two (52) recipients working in regulatory roles within industry and to recipients across four different Notified Bodies and a Competent Authority. In the email, the recipients were also asked to send on to relevant colleagues working in regulatory roles. The group identified to participate in the survey were all regulatory professional either working in the medical device manufacturing, working for a Notified Body or for a Competent Authority. Regulatory affairs only were asked to participate as this research is built around identifying the challenges for the regulatory affairs professionals in complying with the MDR 2017/745.

The survey was piloted with two internal colleagues to get constructive feedback on its design. The piloting process allowed the researcher to identify whether respondents understood the questions and whether the meaning of the question was the same for all respondents.

Each participant received an email including information such as the name and contact details of the researcher, the purpose of the research, details of why the respondent was selected, how the results will be used, and the potential benefits from the study. They were encouraged to participate and were given a deadline for completion. It was only regulatory affairs professionals which were asked to participate in the survey as the research question is exclusively targeting the "challenges for regulatory professionals" in implementing 2017/745. The survey consisted of eight questions and the results on survey monkey indicate that it took approximately six minutes and nineteen seconds to conduct on average.

It can be difficult to predict survey level participation. The author was aiming to receive results from forty (40) participants to satisfy sample size. It was distributed to fifty-two (52) people with a view to it being forwarded on to others. Surprisingly, there were fifty-nine (59) responses in total which exceeded the initial expectation. "What sample size is required for a survey? There is no definitive answer to this question: large samples with rigorous selection are more powerful as they will yield more accurate results, but data collection and analysis will be proportionately more time consuming and expensive. Essentially, the target sample size for a survey depends on three main factors: the resources available, the aim of the study, and the statistical quality needed for the survey" (Clark *et al.* 2003). Fifty-nine (59) respondents provide an adequate response rate for the research question as the data is supplementing the interviews completed.

The survey was sent out on Friday 19 April 2019 and was completed over a six-week period thereafter. See Appendix P for a sample of the email which was sent to participants.

The survey was created and distributed via Survey Monkey ™. SurveyMonkey is an online survey development cloud-based software as a service company. The company provides free, customizable surveys, as well as a suite of paid back-end programs that include data analysis, sample selection, bias elimination, and data representation tools. Survey Monkey is available at www.surveymonkey.com and is used in academia and industry to support research efforts. SurveyMonkey permits the use of a survey link to be emailed to respondents, which in turn allows respondents to forward the link on to suitable people they know thus increasing the response rate.

One of the goals in answering this research question which is "what are the challenges for the regulatory affairs professional as they work to compliance to regulation 2017/745" is to turn data into information, and then turn the information into insights to determine exactly what these challenges are which regulatory affairs professionals are facing and struggling with.

Charts and graphs were used to make the result of each question visible at a glance. The results are included in chamber 4 and an in-depth analysis of those results in chapter 5.

3.3 Summary

This chapter described the design and execution of the literature search and the phases of the mixed method research methodology i.e. qualitative and quantitative. Interviews were conducted with 12 experts from industry and the external regulatory agencies, and a survey circulated to fifty-two (52) regulatory affairs personnel within the medical device sector. Planning and design were two key undertaking factors when completing this section of the research.

Chapter 4 will discuss the results of the survey and the subsequent prioritisation of the challenges.

Chapter 4 Results - Phase IV Data Review

This section of the thesis reviews the literature review from phase I, the qualitative data from the interviews in phase II, and the quantitative data from the survey results in phase III. More than one method of data collection was chosen to give a better picture of what the challenges are for the regulatory professionals as they work towards compliance of Regulation 2017/745. The data obtained from interviews and the survey provided a robust mechanism for determining these challenges.

4.1 Literature Review Results

As stated in chapter 1, the objective of this thesis is to understand the challenges faced by the regulatory affairs professionals in the medical device technology (MedTech) sector when complying with the specific requirements set out in the new regulation. The literature review documented in this section of the report summarises the current knowledge and research on MDR 2017/745 to date and confirms the value of the research in this thesis.

Recognising that the US regulations are not within the scope of this thesis, but with the limitations of the number of articles available to review, the author decided to include those articles to understand what was being said in the US versus EU in terms of regulation of medical devices. There was a trend across the literature available on medical devices with respect to the regulations is comparisons between the EU and the US regulatory system, with many criticisms directed towards the EU.

From the thirteen (13) articles listed in table 4, six (6) of those, namely Mishra, Richwine, Sorenson & Drummond, Maak, Campillo and Hwang are comparing the European and US regulatory systems in different ways, each of them eluding to Europe having an inferior system. There was some information documented in journals such as "New European Regulation for Medical Devices: What Is Changing?" (Martelli *et al.* 2019) and "On the new regulation of medical devices in Europe', *Expert Review of Medical Devices"* (Migliore 2017), however many of the articles reviewed were in the form of white papers which were not peer reviewed.

The article written by Marteli was the most relevant article of all with respect to this research as it was specifically about MDR 2017/745. This is discussed in detail in chapter 5. The other articles touch on aspects of the impact of the regulation but are limited in detail.

The literature review documented in this section summarises the current status of literature published to date and confirms the values in this thesis as there is very little relevant literature available in the public domain currently.

The MDR 2017/745 was released in April 2017, therefore there has not been much research conducted in this area yet. This lack of research points to the importance of this study to provide information to the medical device industry. The literature review in chapter 4 confirms the value of the research in this thesis. There is however useful and explanatory information available from regulatory agencies and industry advocacy groups. Where any of these non-published documents have been used for this research they have been referenced accordingly.

Table 4 below lists the articles which were reviewed in detail. Each of these articles are discussed in chapter 5.

Table 4: Relevant articles obtained from literature search.

Article #	Ttle of the Articles
1	New European Regulation for Medical Devices: What Is Changing?" (Martelli *et al.* 2019)
2	New regulation of medical devices in Europe', *Expert Review of Medical Devices"* (Migliore 2017)
3	"FDA, CE mark or something else? – Thinking fast and slow", published by (Mishra 2017)
4	'Devices and desires: industry fights toughening of medical device regulation in Europe' (Cohen, D). (2013)
5	'Regulation of medical devices in the United States and European Union. Kramer, D. B., Xu, S. and Kesselheim, A. S. (2012)
6	*"Guinea pig" remark spurs US, EU device spat.* [Online]. Available: Richwine, L. (2011)
7	Improving medical device regulation: The United States and Europe in perspective" (Sorenson and Drummond 2014)
8	'The EU commission's risky choice for a non-risk-based strategy on assessment of medical devices', Quinn, P. (2017)
9	'A full-fledged overhaul is needed for a risk and value-based regulation of medical devices in Europe' Campillo-Artero, C. (2013)
10	'Comparison of rates of safety issues and reporting of trial outcomes for medical devices approved in the European Union and United States: cohort study', *Bmj*, 353 p. i3323. Hwang, T. J., Sokolov, E., Franklin, J. M. and Kesselheim, A. S. (2016)
11	Medical Device Regulation: A comparison of the United States and the European Union. Maak TG[1], Wylie JD. 2016
12	New regulations on medical devices in Europe: what to expect? Alice Fouretier, Delphine Bertram 2014;11(4):351-359
13	How a fake hip showed up failings in European device regulation, Deborah Cohen, (2012)

4.2 Interview Results

Transcripts from the interviews were reviewed line by line by the author and challenges identified. To ensure an accurate reflection of the interviewee position, an independent regulatory affairs colleague also reviewed the transcripts. The output of both reviews captured the list of challenges. There was a total of one hundred and thirty-three (133) challenges identified. See Appendix O for a list of the challenges extracted from the transcripts. The challenges were categorised into nine (9) different themes. These themes established the challenge statement for the survey. These challenges were used to support the survey design. The output of the challenge themes is shown in Table 5 below.

Table 5: Themes from the Interviews

#	Challenge Statement	Frequency
1	Lack of clarity and supporting documentation in the regulatory framework	40
2	Training/ Awareness/ knowledge of new requirements	27
3	Resources/ workload –Additional work burden	20
4	Change management – How can product changes be handled during the transition period.	10
5	Additional reviews built into the process, e.g.; for higher risk devices, CECP etc.	9
6	Time Restrictions – Time is running out- May 2020 is approaching fast	8
7	No grandfathering / complete file reviews	7
8	Post market surveillance additional requirements	5
9	Cost associated with implementation of the new regulation.	4

While the interview purposely set out to avoid discussing one of the biggest challenges of MDR 2017/745, the clinical requirements, this topic unavoidably came up in several of the interviews as can be seen from the transcripts.

Interviews are one method used to collect data and gain knowledge from individuals. The group of people selected for this analysis were all personnel in senior roles within each of their organisations who are extremely knowledgeable in the subject matter of the upcoming new regulations 2017/745. A rapport was established in each of the interviews with the participants

which is clear from the recordings. The relaxed environment allowed the participants to speak freely of their views and experiences to date with the regulations. The author believes reassurances of confidentiality through signing a consent form enhanced this open atmosphere.

There were similar challenges raised across all the interviews which can be seen from the coding / theming exercise which strengthens the validity of the interpretation and fulfils the research objective. Further analysis of the results of the interviews is included in chapter 5.

All the participants were genuinely interested in the topic as the research topic is prevalent in our everyday working lives at present, so everyone was curious as to how other companies were reacting to certain challenges. Several of the interviewees expressed an interest in receiving a copy of this research as they are interested in the combined opinion of the other interviewees and the survey respondents.

The words of an interview constitute raw data, somewhat like the numbers resulting from a test. Raw data does not in itself reveal its meaning; rather it must be interpreted. Hitchcock and Hughes (1995) describe two main strategies to analyse interview data. "The first strategy is to become very familiar with the data; the second strategy is to create meaning using analytical categories" (Hitchcock and Hughes 1995).

Using the first strategy the author transcribed the notes from the interview and went over the transcripts many times. This helped to categorise the themes of the different challenges coming through from the interview discussions thus analysing the data.
"Theming refers to the drawing together of codes from one or more transcripts to present the findings of qualitative research in a coherent and meaningful way" (Sutton and Austin 2015)

As stated earlier, the number of ten participants is typical for a phenomenological study. For this study the author contacted in excess of twenty possible candidates. This number was chosen to ensure that at least ten participants were available. Twelve interviews were conducted.

As per listed in Table 5 in chapter 3, different challenges emerged from the twelve (12) interview analysis. The raw data (transcripts) for this can be found in Appendix C – Appendix N. A summary of the interview challenges can be found in Appendix O. The pie chart in Figure 18 illustrates the number of times these challenges came up during the discussions. This can be reviewed further from the interview transcripts also.

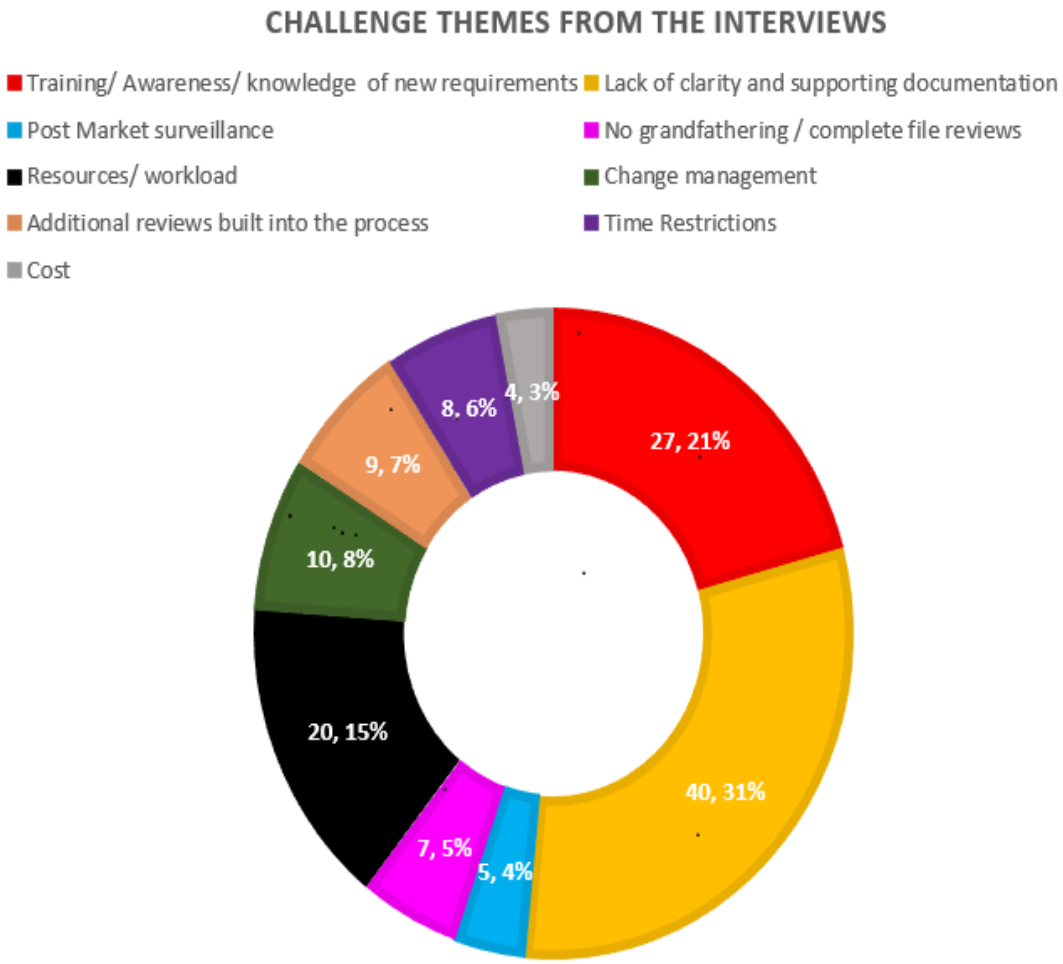


Figure 18: Qualitative Data from the Interviews

(Taken from SurveyMonkey)

4.3 Survey Results

The survey was completed by 59 participants in full; 62 people initiated the survey, but 3 respondents skipped some questions. The aim of the survey was to gain quantitative data by getting responses from regulatory professionals working for regulators and industry alike.

As this research is exploring the challenges for the regulatory professionals working for the regulators as well as those working in industry, it was sent to four different Notified Bodies involved in the regulatory framework in Europe and seven (7) individuals from same completed it. Competent Authorities were also contacted, and one respondent completed the survey. It was an achievement to get people working for Notified Bodies and a Competent Authority to participate in both the interviews and the survey, albeit the numbers are much lower than those in industry, and naturally so.

The Notified Bodies taking part in this survey are considered key Notified Bodies working in the industry today who have applied for designation of MDR 2017/745 and are used by many of the respondents participating in the survey. The Competent Authority was also one of the leading ones and one which Irish manufacturers interacts with regularly.

The following sections present the results from each of the questions asked in the survey. A graphical representation is provided with a subsequent written explanation of the output.

4.3.1 Survey Response Question 1; Type of Organisation.

ANSWER CHOICES		RESPONSES	
Medical Device Manufacturer (1)		87.10%	54
Notified Body (2)		11.29%	7
Competent Authority (3)		1.61%	1
Other (4)		0.00%	0
Other (please specify) (5)	Responses	0.00%	0
Total Respondents: 62			

Figure 19: Types of Organisations Respondents Work In

(Taken from SurveyMonkey)

As can be seen from Figure 19, the majority of respondents, fifty-four (54) / 87%, taking part in the survey were from medical device manufacturers, seven (7) participants were from Notified Bodies, and one (1) from a Competent Authority.

Note that a second "other" appears in the bottom legend of the above graph. This is not intentional and was an error in designing the question layout.

4.3.2 Survey Response Question 2; Size of Organisation.

ANSWER CHOICES	RESPONSES	
<50	1.61%	1
50 - 250	32.26%	20
250 - 500	14.52%	9
>500	51.61%	32
Total Respondents: 62		

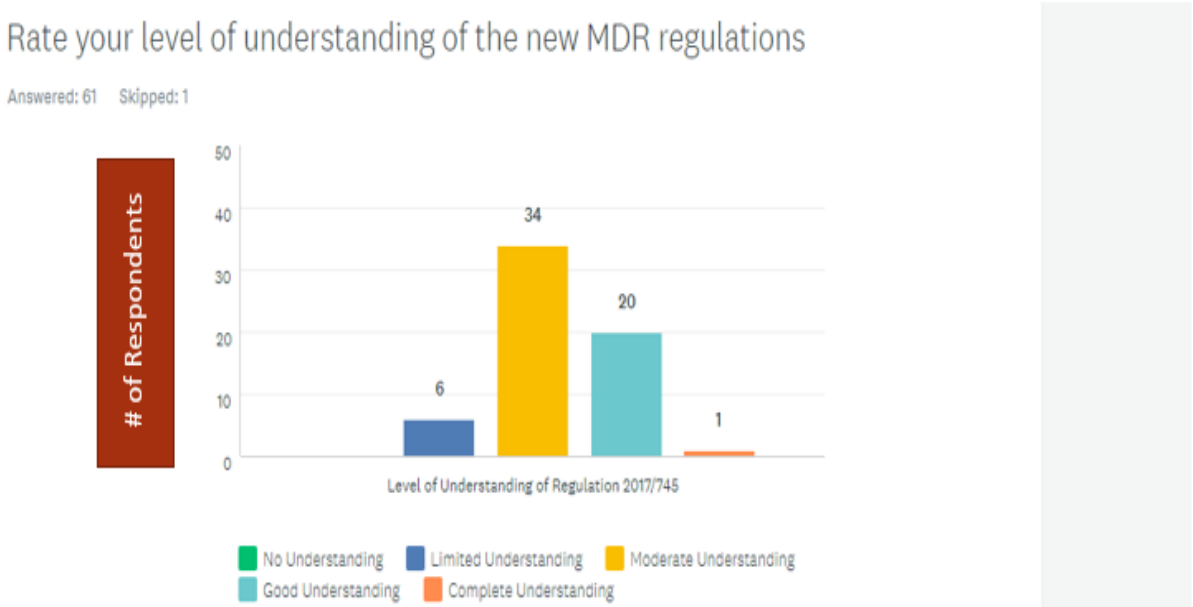
Figure 20: Size of Organisations Respondents Work In

(Taken from SurveyMonkey)

The majority of respondents, thirty-two (32) respondents which equates to 52%, were from large organizations of >500 employees. There were twenty (20) 32% from organisations of size between 50- 250 employees. There were nine (9) 14% from organizations sized between 250 – 500 employees, and one person who participated works in an organization of <50 people.

While there is no traceability from each of the individuals completing the survey to their own discrete results, it is expected that one person working in an organisation <50 is that of the consultant.

4.3.3 Survey Response Question 3; Level of Understanding of MDR 2017/745.



	NO UNDERSTANDING (1)	LIMITED UNDERSTANDING (2)	MODERATE UNDERSTANDING (3)	GOOD UNDERSTANDING (4)	COMPLETE UNDERSTANDING (5)	TOTAL	WEIGHTED AVERAGE
Level of Understanding of Regulation 2017/745	0.00% 0	9.84% 6	55.74% 34	32.79% 20	1.64% 1	61	3.26

Figure 21: Level of Understanding of 2017/745

(Taken from SurveyMonkey)

This survey was completed in April 2019. The aim of this question was to understand the level of understanding amongst that respondents in respect to Regulation 2017/745. The results of this were positive in that thirty-four (34) / 56% indicated that they had a moderate level of understanding, twenty (20) 33%, indicated that they had a good understanding, six (6) participants indicated that they had limited understanding, and one (1) brave person indicated that they had complete understanding.

Fortunately, nobody indicated that they had no understanding, as this would have been worrying considering it was regulatory professionals completing the survey. The results are discussed in detail in chapter 5.

4.3.4 Survey Response Question 4; Other Functions Impacted by MDR 2017/745.

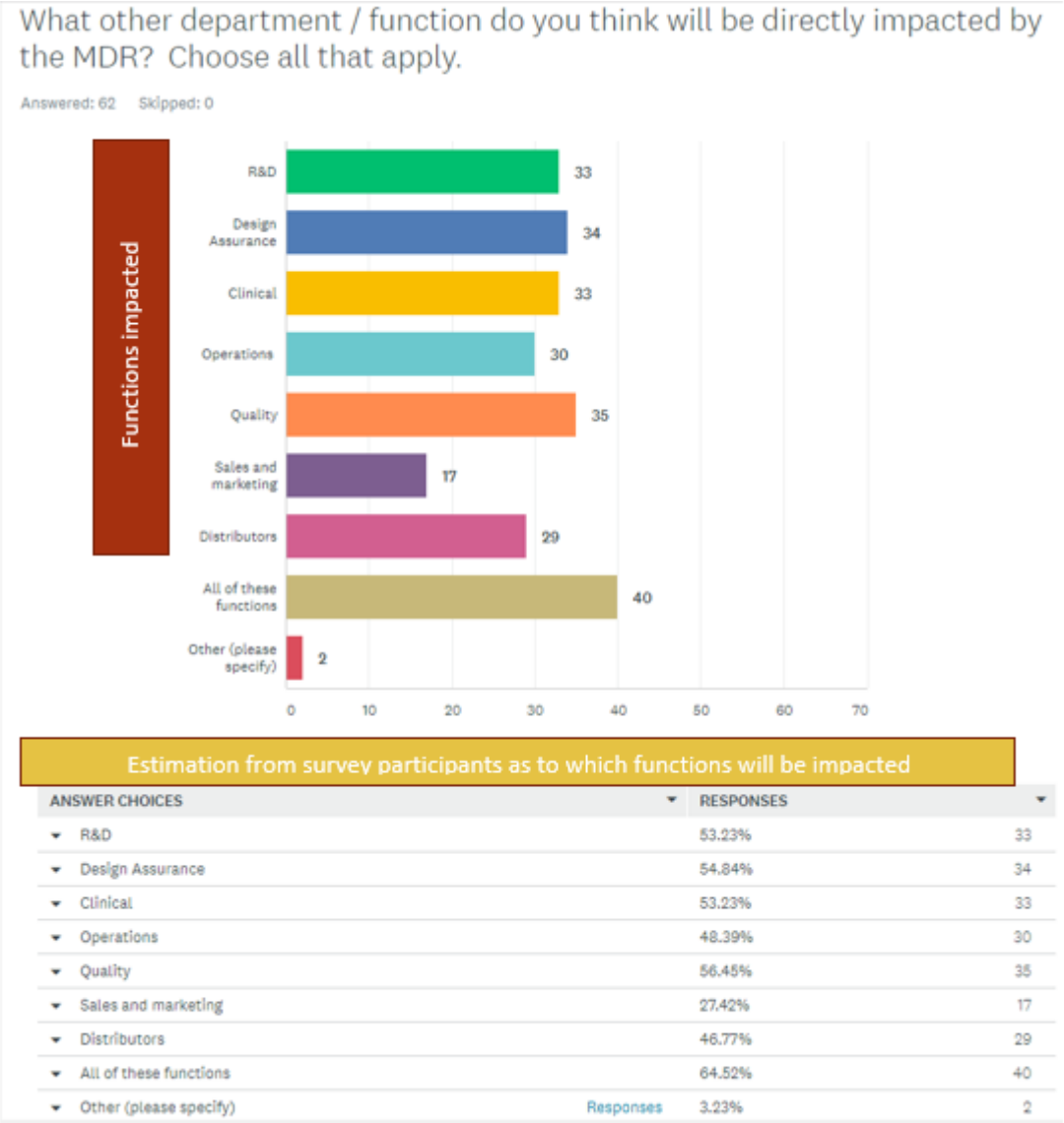


Figure 22: Impact of MDR 2017/745 on Other Functions

(Taken from SurveyMonkey)

It is well known that regulatory is not the only function impacted by MDR 2017/745 and the purpose of this question was to establish the other impacted functions. There are so many deliverables, new requirements, changes that also impact other functions. 64.5% of the respondents felt that all functions would be impacted. The two (2) responses to the "other" category were 1) the labelling department, and 2) the packaging department. These were valid to point out as every device label and IFU will need to be revised as part of the MDR project.

4.3.5 Survey Response Question 5; Time to Write Technical Files.

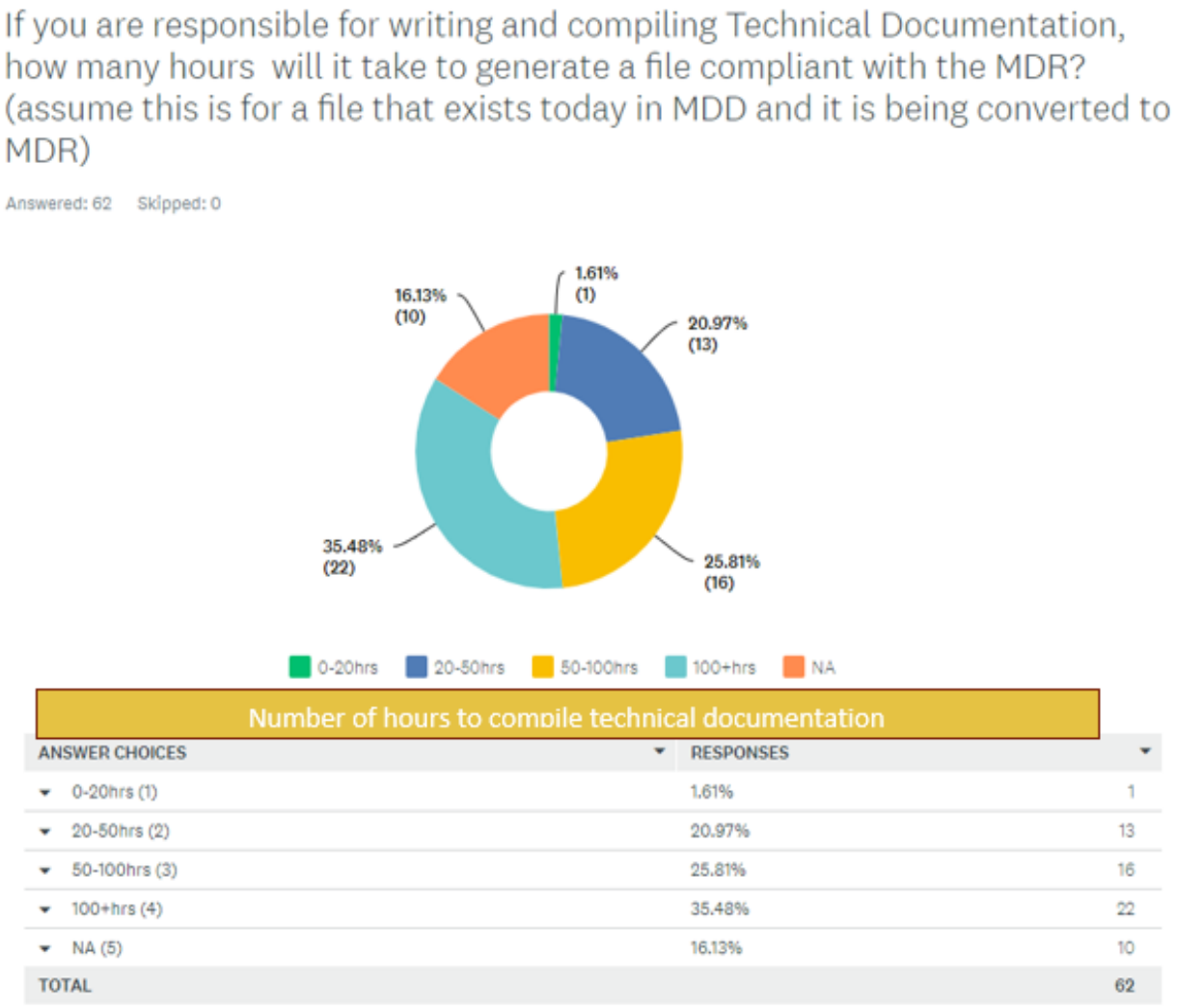


Figure 23: Estimated # of Hours to Compile Technical Documentation

(Taken from SurveyMonkey)

The results from this question indicate that twenty-two respondents, (22) 35%, thought it will take 100 + hours to compile technical documentation to meet the new requirements in the MDR. Sixteen (16) 26% thought it will take 50-100 hours, thirteen (13) 21% thought it will take 20-50 hours, ten (10) 16% answered as NA, and one (1) person thought it will take 0-20 hours.

The collection of people who answered NA was most likely those from Notified Bodies who would not be writing technical files as part of their role. That is the responsibility of the manufacturers. These results are discussed in detail in chapter 5.

4.3.6 Survey Response Question 6; Time to Review Technical files.

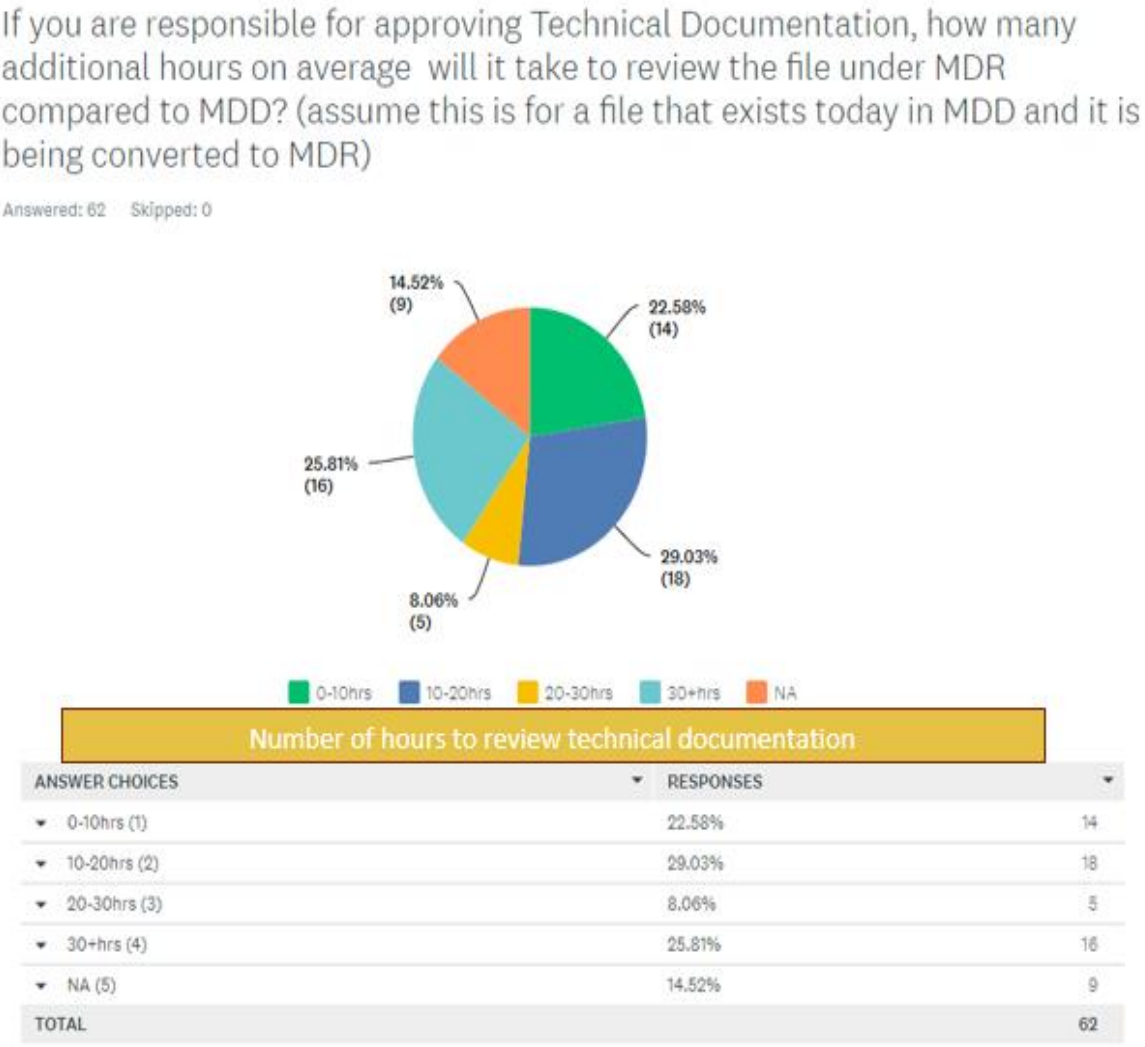


Figure 24: Estimated # of Hours to Review a Technical file

(Taken from SurveyMonkey)

The results from this question indicate that eighteen (18) / 29% respondents felt it would take 10 – 20 hours to review a technical file. Sixteen (16) / 26% thought it would take 30 + hours. Fourteen (14) / 22% said it would take 0-10 hours. Five (5) / 8% thought it would take 20-30 hours and Nine (9) /14% of respondents said this was not applicable to them. It is typically Regulatory Management that reviews technical files so the nine (9) respondents that said it was not applicable to them may have been regulatory specialists who writes technical files.

4.3.7 Survey Response Question 7; Ranking MDR Challenges 1-9.

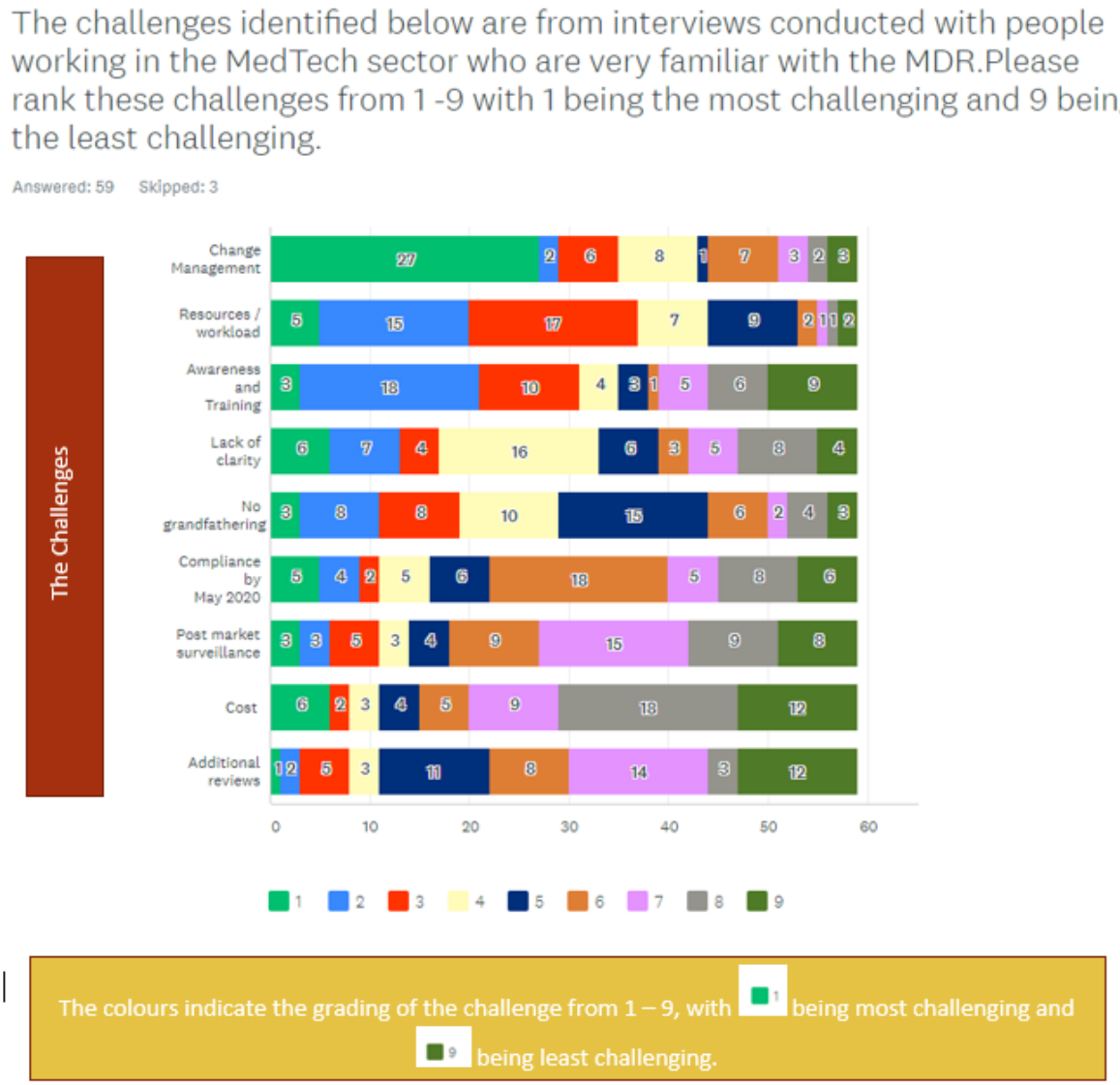


Figure 25: Ranking of the Challenges

(Taken from SurveyMonkey)

Weighted average refers to the mathematical practice of adjusting the components of an average to reflect the importance of certain characteristics. (Primus).

To present the survey data, the weighted averages has been used to convey the information. A weighted average is an average of factors when certain factors count more than others or are of varying degrees of importance. The factors have been ranked 1 to 9 with 1 being the most

challenging and 9 being the least challenging. All of these factors have been combined to create a final grade by question asked, which is expressed as the weighted average.

The raw data from question 7 and Figure 25 can be found in Figure 26 As can be seen from the results the top 3 challenges are Change Management, Resources and workload, and Training and awareness.

	1 (1)	2 (2)	3 (3)	4 (4)	5 (5)	6 (6)	7 (7)	8 (8)	9 (9)	TOTAL	WEIGHTED AVERAGE
Change Management	45.8% 27	3.4% 2	10.2% 6	13.6% 8	1.7% 1	11.9% 7	5.1% 3	3.4% 2	5.1% 3	59	2.98
Resources / workload	8.5% 5	25.4% 15	28.8% 17	11.9% 7	15.3% 9	3.4% 2	1.7% 1	1.7% 1	3.4% 2	59	3.31
Awareness and Training	5.1% 3	30.5% 18	16.9% 10	6.8% 4	5.1% 3	1.7% 1	8.5% 5	10.2% 6	15.3% 9	59	3.83
Lack of clarity	10.2% 6	11.9% 7	6.8% 4	27.1% 16	10.2% 6	5.1% 3	8.5% 5	13.6% 8	6.8% 4	59	4.17
No grandfathering	5.1% 3	13.6% 8	13.6% 8	16.9% 10	25.4% 15	10.2% 6	3.4% 2	6.8% 4	5.1% 3	59	4.20
Compliance by May 2020	8.5% 5	6.8% 4	3.4% 2	8.5% 5	10.2% 6	30.5% 18	8.5% 5	13.6% 8	10.2% 6	59	4.93
Post market surveillance	5.1% 3	5.1% 3	8.5% 5	5.1% 3	6.8% 4	15.3% 9	25.4% 15	15.3% 9	13.6% 8	59	5.12
Cost	10.2% 6	0.0% 0	3.4% 2	5.1% 3	6.8% 4	8.5% 5	15.3% 9	30.5% 18	20.3% 12	59	5.22
Additional reviews	1.7% 1	3.4% 2	8.5% 5	5.1% 3	18.6% 11	13.6% 8	23.7% 14	5.1% 3	20.3% 12	59	5.24

Figure 26: Raw Data Associated with Question 7 and Figure 25

(Taken from SurveyMonkey)

Question 7 is the crux of the survey as it establishes the respondent's thoughts on the challenges identified in the interview process. As discussed in chapter 3, these challenges were derived from the interviews conducted with regulatory stakeholders. There are many challenges associated with MDR 2017/745 and many which have not been reported in this research as this research is focussing on the challenges specific to the regulatory function. Since 59 people responded to this survey this can be considered a representative sample, and the survey results are meaningful. Figure 25 outlines how the respondents voted on ranking their challenges.

Twenty-seven (27) respondents which equates almost 46% ranked change management as their #1 challenge. This is not surprising as imposing restrictions on making changes to existing products will have a massive impact on manufacturers, especially large manufacturers who tend to make changes routinely as part of innovation. Section 5.3.1 analyses change management further. For the challenge of resources and workload fifteen (15) respondents ranked this to be their second biggest challenge, and seventeen (17) respondents ranked it to be their third biggest challenge. This is not surprising considering the amount of additional work which is forthcoming. The implications of this is discussed in section 5.3.2.

Awareness and training are other challenges which stands out as a concern at the top end of the challenges, with eighteen (18) ranking this as their second highest challenge, and ten (10) ranking it as their third highest challenge. This challenge is interlinked with the challenge of, lack of clarity, which indicates sixteen (16) respondents ranking lack of clarity as their fourth biggest challenge. There is great frustration as there is lack of clarity in so many areas as discussed in section 5.3.4. It is difficult to deliver the right training when such lack of clarity exists.
Surprisingly, the challenge of cost was veering towards one of least concern with eighteen (18) respondents ranking it as their eight challenge of concern, and twelve (12) respondents ranked it as their least challenge of concern. More details on drivers of spend is discussed in section 5.3.8.

4.3.8 Survey Response Question 8; MDR Impact on Patient Safety.

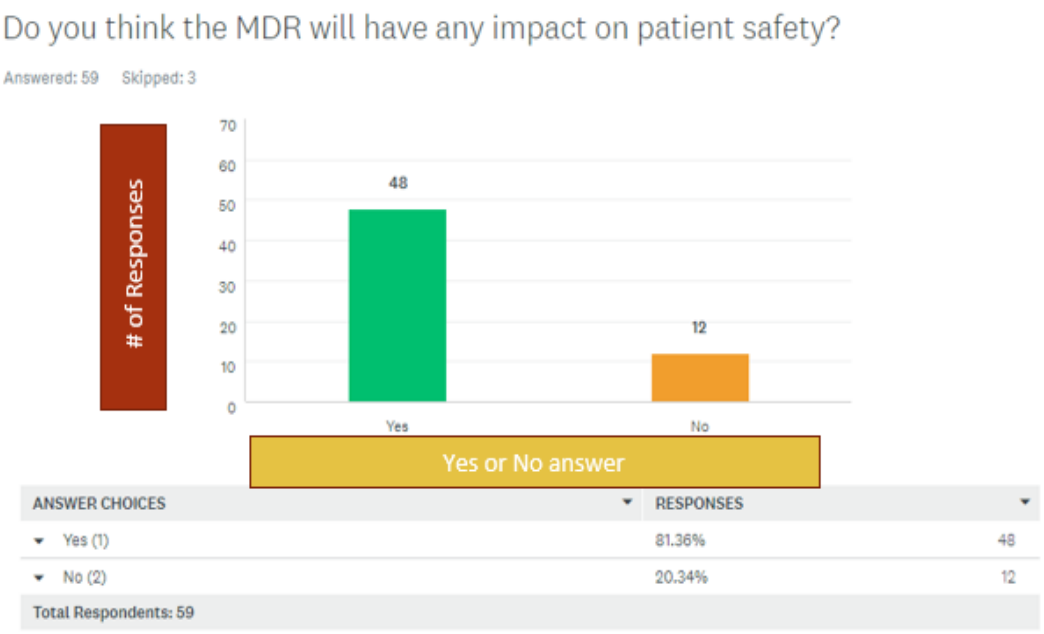


Figure 27: Respondents Opinion on Whether MDR 2017/745 will have any Impact (Taken from SurveyMonkey)

In response to this question forty-eight (48) respondents, which equates to 80%, felt that the MDR would have a positive impact on patient safety, whereas twelve respondents which equates to 20% felt that it would not have any impact on patient safety. There was an optional section with this question for respondents to leave comments to substantiate their yes or no answer. These comments can be found in Appendix Q.

4.4 Summary

This chapter identified the results from phase I, the literature review. It also included a summary of the themes of the challenges that were resulting from the interviews. Interviews were conducted with twelve (12) regulatory affairs professionals from a mix of industry and the regulators. This captured the qualitative research. The quantitative research was obtained by completing a survey. This chapter presented the results from the eight (8) questions asked in the survey.

Chapter 5 Discussion and Analysis

5.1 Literature Review

A literature review was conducted as part of this research however the available relevant literature was minimal. Addressing the research hypothesis of identifying the challenges for the regulatory affairs professionals on becoming compliant with MDR 2017/745 would not be answered with the limited literature available.

The available literature was assessed and is discussed in this section. While this research is focussed on the European regulations, a few articles comparing the European regulatory system to the US regulatory system emerged from the literature search which was worth exploring to understand some of the frustrations from medical professionals working with both regions.

According to Martelli, he believes "this regulation significantly tightens controls to ensure that devices are safe and effective" and he also states, "these new requirements will probably lead to a dramatic increase in the number of clinical investigations and to a delay in the availability of certain devices on the market" (Martelli *et al.* 2019) The author agrees with Martelli's analysis on both accounts. There are so many areas where controls are tightened, and requirements heightened from more detailed technical documentation requirements, more detailed reviews performed by Notified Bodies, better structure with systems and procedures to increase transparency, and a more robust post market surveillance program. This article discusses clinical requirements in detail and it gives a thorough description of the roles and responsibility of the expert panels. In the authors opinion, this was the best article as it was specifically about regulation 2017/745. There were many similarities in Martelli article to those outlined in this research such as increased clinical requirements, the challenges with Eudamed, additional reviews performed by expert panels, reclassification of devices, and many others also.

One of the articles reviewed during this phase called "FDA, CE mark or something else? – Thinking fast and slow", published by (Mishra 2017) was interesting as he was comparing regulatory processes against different regions. He stated "there is a robust debate going on among the Medical Device stake-holders whether FDA is better or CE mark or something else. Currently the process of obtaining an FDA approval is bogged down by ever-increasing unpredictability, inconsistency, prolonged time, and huge expense but CE mark has its own problems". He also brought Japan regulatory process into the mix and concluded by stating a

general comment intended at all regions "the actual approval process can also be very tardy, inconsistent and expensive" (Mishra 2017). This was interesting as it is a very topical discussion at conferences and open forums at present. The primary focus of medical device regulation is to facilitate rapid movement of innovative technologies and devices through the approval process while maintaining a high standard of safety and efficacy. Up to now reports have suggested that patients in the EU gain access to higher risk devices such as coronary stents faster than their US counterparts. As a result, the European system has been praised for benefitting the care of patients. The time it takes for a device to progress from concept to market is a frequent point of comparison between the US and EU regulatory systems.

Differences in the evidence which must be supplied to obtain a CE mark in comparison to the evidence required for the PMA pathway mean that devices tend to be approved faster in the EU. A study conducted in 2013 reported a three year 'lag time' between approvals in the US and Europe, (Cohen 2013). "Devices in the US must demonstrate efficacy and safety prior to approval" (Kramer *et al.* 2012). In Europe it was sufficient for a device to demonstrate that it performs as designed, is safe and that the potential benefits are greater than the potential risks.

In 2011 there was an article written in a US paper by the FDA's Director of Centre for Devices and Radiological health Jeffrey Shuren. He responded to a plastic surgeon's description of what happens in the EU. He said, "We don't use our people as guinea pigs in the US" inferring that the EU regulatory system is faster at a price. (Richwine 2011). The EU regulatory system may make innovative technology available to people faster, but patients may suffer as the necessary clinical data may not exist to demonstrate its safety.

There seems to be a paradigm shift in this philosophy now and it is MDR 2017/745 and its many facets that is changing this regime. EU seems to be losing its credibility and FDA seems to be gaining it. FDA have defined timelines set out for each of their submission types which it makes it easier for companies to plan regulatory timelines and estimate approval timelines better. One could argue that the single authority system of the US is more advantageous than the complex system of government agencies and regulatory bodies in the EU. The approval of devices by one authority, the FDA, could be attributed with the ability to enforce and coordinate in a more streamlined manner.

From a clinical perspective FDA seem to be better on giving guidance with respect to clinical requirements comparing to that in the EU where the requirements are less clear. The EU

regulatory system is the subject of scrutiny as the overall process has been criticised as being unclear, expensive, time consuming and inflexible with respect to implementing 2017/745.

A similar article written by Sorenson. “Improving medical device regulation: The United States and Europe in perspective” also compares the US system against the EU system. “Recent debates and events have brought into question the effectiveness of existing regulatory frameworks for medical devices in the United States and Europe to ensure their performance, safety, and quality” (Sorenson and Drummond 2014). The article provides a comparative analysis of medical device regulation in the two jurisdictions, explores current reforms to improve the existing systems, and discusses additional actions that should be considered to fully meet this aim.

He goes on to state “Medical device regulation must be improved to safeguard public health and ensure that high-quality and effective technologies reach patients”, and concludes by saying “although the current reforms address some of the outstanding challenges in device regulation, additional steps are needed to improve existing policy” (Sorenson and Drummond 2014).

Travis Maak and James Wylie also infer that it is easier to get a medical device on the European market versus the US. They state, “Many physicians and innovators in the United States cite a restrictive US FDA regulatory process as the reason for earlier and more rapid clinical advances in Europe” (Maak and Wylie 2016). They compare the two region approvals processes by saying, “The FDA approval process mandates that a device be proved efficacious compared with a control or be substantially equivalent to a predicate device, whereas the European Union approval process mandates that the device perform its intended function. Stringent, peer-reviewed safety data have not been reported” (Maak and Wylie 2016). This article was written in 2016 and they recognise that substantial reforms of the European process in the next few years will result in a more stringent approach.

An article written by Fouretier and Bertram in the early days, back in 2014, recognised the need for the changes in the regulations. They stated, “the existing regulatory framework for medical devices has been in place for 20 years and needed a revision” (Fouretier and Bertram 2014). They discussed how the regulation needed to increase transparency and guarantee a high level of health protection. This article also analyzed what they thought would change in the regulation, and to give them credit, they did touch on many of the changes which was incorporated into the publication of Regulation 2017/745.

In 2010, discussions began and there was a lot of unsettlement where people were beginning to speak publicly about the flaws in the regulatory system. In 2012, Cohen wrote an article about a scenario where a fictitious company was set up to test an EU regulatory authority to seek approval for a hip implant. This fictitious company called Changi submitted a file to a regulatory agency and got approval based on very little data to support its safety and performance. Cohen stated, "even though the dossier we created said that tests had shown that our hip prosthesis produced potentially toxic levels of metal ions in the body, the implant was passed as having an acceptable design for use in patients across Europe" (Cohen 2012). This is a perfect example of the negligent controls in place and the inadequacy of the review that the Notified Body performed in this instance.

Paul Quinn authored a good article on medical device software and the use of apps ranging from those that can be described as concerned with 'well-being' to those that perform roles classically associated with medical devices (e.g. the monitoring of symptoms, the diagnosis of disease and the administration of medicines). Examples range from apps that may be used to plan a healthy lifestyle, considering dietary and exercise factors, to apps that may play a role in the management of chronic illnesses such as diabetes.

The wide spectrum of mHealth apps that are now available has presented major challenges for the regulation of medical devices, particularly in terms of deciding which of these should be submitted to the requirements of the EU Medical Device Framework and which should not. This article discusses, the EU's current approach (and its proposed new approach in the form of a new regulation). Quinn criticise the EU approach by saying " the EU Commission has opted to maintain its current approach in the newly proposed regulation, choosing not to employ other approaches as the FDA has for example done in opting to use a 'risk based case-by-case approach" (Quinn 2017).

An article written by Campillo, "A full -fledged overhaul is needed for a risk and value based regulation of medical devices in Europe" states "the unacceptably high incidence of clinical adverse events caused by medical devices (MDs), their high recall rates, and the frequent phase out of some of the devices that pose a greater risk to health have triggered alarm concerning the long-standing weaknesses of their regulatory processes. It has long been known that regulation is not strongly associated with the existence of market failures". He goes on to discuss the deficient approval process and post marketing surveillance of MDs in the United States and Europe, as well as the causes and effects of their very serious failings, that put patient safety at serious risk, are critically reviewed. (Campillo-Artero 2013). It is clear from reading through this article that

he also is very frustrated by the European legislation system governing medical devices. He discusses examples of products where FDA denied approval in the US, yet these products are marketed in the EU. Another quote includes "All such partial changes could be useful references for any improvements that are undertaken in Europe, where such studies barely exist, transparency is lacking, preapproval trials are not accessible, ambiguous standards are applied willy-nilly, and the scientific evidence presented is weak" (Campillo-Artero 2013).

He claims the review, approval and surveillance systems, which are no guarantee of safety (the number of recalls of Class III devices has risen sharply in the UK without a parallel rise in the number of alerts issued by the Competent Authorities) and have been associated with preventable morbidity and mortality.

A cohort study documented by (Hwang) on comparison of safety issues reporting of trial outcomes for medical devices approved in the European Union and the United States. The objective of the study was to evaluate safety alerts and recalls. It analyses delay in market access and safety issues related to a set of medical devices approved in Europe and the US.

The study identified high profile new medical devices approved in the EU between 2005 and 2010 and evaluated safety issues related to these devices and publication of the key outcomes of trials. The study focussed on cardiovascular, neurologic, and orthopaedic devices, which account for most high-risk devices used in clinical practice.

It concluded that evidence on the safety and performance of the EU's approach to the regulation of devices is limited. It stated "Devices approved first in the EU are associated with an increased risk of post-marketing safety alerts and recalls. Poor trial publication rates mean that patients and clinicians need greater regulatory transparency to make informed decisions about treatment" (Hwang *et al.* 2016). This article did make it clear that European citizens had earlier access to the most important new treatments compared to the US.

Migliore, in his article is hopeful that shortcuts to faster market access will be used less frequently and supported by proper documentation. "An improved designation of the notified bodies and further monitoring actions by national authorities should guarantee a scandal-proof system and balance those aspects of the human nature, which sometimes address profit before anything else" (Migliore 2017). He feels that the medical device sector is populated by many small to medium enterprises which may not have the budgets, resources or skills to fulfil the new requirements.

"However, the changes have been introduced to address real problems, gaps, and critical issues mainly related to safety. Achievements in this direction have to come with a price" (Migliore 2017).

The literature review clearly indicated the need to review the EU regulatory framework which had been in place for over 20 years. There were weaknesses in the MDD that needed to be addressed to ensure safe medical devices are put on the European market. The improvements to the EU regulatory framework resulted in the publication of the new regulation 2017/745.

Aside from the limited information which was available through the various searches, considerable knowledge in this research to date has been obtained through networking with colleagues both internal and external to Boston Scientific, working closely with Notified Bodies, attending conferences, and attending various training forums both internal and external to my company. The author sourced a course specifically related to the MDR 2017/745 which was titled "MDR 2017/745 – how to write a technical file". This course was held on 14th February 2019 in Munich and was run by a consultancy group called Qserve.

5.2 Interview and Survey

This section analyses the results of the survey questions and evaluates the interview discussions further.

5.2.1 Survey Question 1 combined with Interview Analysis.

Question 1: What type of organisation do you work in?

The mix of people taking part in the interviews resulted in seven (7) from medical device manufacturers, one (1) from a regulatory consultancy firm, three (3) from Notified Bodies, and one (1) from a Competent Authority. As can be seen from the results of question 1, Figure 19 the majority of respondents, fifty four (54), 87% taking part in the survey are from medical device manufacturers, seven (7) participants are from Notified Bodies, and one (1) from a Competent Authority.

There is a good combination of experience from both industry and regulators for input to this research. Their experience working in regulatory adds great value as they are working to ensure medical devices are designed, developed, tested, manufactured, and distributed in compliance with the relevant regulations. It was apparent from the interviews that these regulatory professionals working in industry interacts with Notified Bodies and is very familiar with requirements for placing product on the European market.

5.2.2 Survey Question 2 combined with Interview Analysis

Question 2: How many people are employed in your organisation worldwide?

As can be seen from Figure 20, many of the respondents were from large multinational medical device manufacturers. This should be kept in mind when reviewing the analysis of the other questions in the survey. Large medical device companies are better resourced to deal with big assignments such as this from a budget, resource, knowledge, and training perspective. In general, large medical device companies have dedicated teams project managing MDR with a full dedicated team dedicated to working on the deliverables. It is more difficult for smaller companies to fit an assignment such as MDR 2017/745 into their current structures.

As can be seen from Figure 20, there were respondents from very small companies right up to the large multinational companies and those in between. It was important to get input from the different size companies to gain the overall spectrum of how the MDR 2017/745 challenges affect each of them. The general perception, and this is stated based on the interviews conducted, is that the bigger companies typically feel more prepared, leaving some of the smaller companies in a more vulnerable position. It is likely that investment and / or divestment opportunities may arise as a result with bigger companies taking the market share of smaller companies.

With MDR affecting so many critical processes it is imperative that manufacturers, but especially small manufacturers should be proactive. Early engagement and frequent updates and discussion with the Notified Body is paramount to align expectations. This will help manufacturers with their planning, it will also give the Notified Bodies a good sense of where the manufactures are with respect to knowledge and status. Pragmatic strategies are advised. Pursuing these new challenges in an isolated and siloed approach will not work. It needs members from various functions within the business to take responsibility and own some of these specific processes and deliverables. "A cross – functional team is indispensable when it comes to reviewing and discussing dependencies and impacts of the regulation across functions" (Misra R 2018).

It was also obvious during the interviews that the smaller companies are waiting on the larger companies to take the lead in many areas of moving forward with MDR, as they appear to be in a "wait and see mode".

This is also a good time for manufacturers to evaluate their product portfolio to establish if the return on investment for new or existing products can be substantiated against the cost of MDR

implementation and maintenance thereafter. In the authors experience working with a large manufacturer, the number of products discontinued was minimal which was surprising. It is always a challenge to convince marketing to forgo products from the portfolio even if the numbers are low. There may be some physicians that are attached to some of these legacy products and do not want to remove them.

It also might be an opportune time for manufacturers to upgrade their tools and systems to deal with MDR. Examples of this include the documentation system, complaints system, the system for following up on clinical data et cetera.

5.2.3 Survey Question 3 combined with Interview Analysis

Question 3: Rate your level of understanding of the new MDR Regulations

The MDR 2017/745 regulation document is a very complex piece of legislation with a huge number of additional information and requirements comparing to the MDD. While this regulation is published since May 2017, not everyone has taken the opportunity to read it yet in its entirety. It was apparent from the interview discussions that some companies had dedicated personnel working to the MDR 2017/745, while other companies were just trying to fit it in as part of their day job. It is more difficult for these individuals to get to grips with it on that basis. It was important for this research to understand the level of knowledge across the sector at this point in time. It was encouraging that nobody said they have no understanding, and courageous for one person to say they have complete understanding. That is a first when it comes to this topic! 34 respondents said they had a moderate understanding and 20 had a good understanding. Considering the individuals who were chosen to partake in the survey, this is no surprise that both ratings are on the mid to upper end of the scaling. Some of these individuals are working on the MDR 2017/745 in full capacity as part of their jobs so are in a position to have such a wealth of knowledge. In the authors experience of workplace there is a dedicated team working on MDR 2017/745. The rest of the organisation benefits greatly from this too from their passing on of knowledge through training, newsletters, and various communications.

The other factor to consider here for the mid to higher end rating is in relation to individuals from Notified Bodies and one respondent from a Competent Authority. One would expect their

knowledge levels to be strong. The data representing the knowledge levels is outlined in Figure 21.

In June 2018 a survey was conducted by KPMG and Regulatory Affairs Professional Society (RAPS). KPMG is a global network of professional firms providing audit, tax and advisory services, with an industry focus. (KPMG 2019) Their survey represented companies spanned across geographies such as Africa, Asia, Europe, the Americas, the middle East, with 91% of participants from the EU and North America. The respondents from these companies were either Regulatory Affairs Directors or Quality Assurance Directors. This report outlined that "78% of medical device companies stated that they do not have a sufficient understanding of the EU MDR legislation" (Misra R 2018). This statistic is quite alarming especially as it is representative of 220 Senior Regulatory Affairs and Quality Directors.

The results from data of this study compared to that of the KPMG study are much more positive with 55% of the participants saying they had a moderate understanding and 32% saying they had a good understanding of MDR 2017/745. Only 9% said they had no understanding and one person claimed they had complete understanding. One thing to bear in mind here is the time difference as to when the surveys were conducted. KPMG's survey was completed in June 2018, whereas this research survey was conducted in April 2019. As each month passes people are learning more about MDR. More training is being provided by companies, people are generally getting to understand the content of the regulation through discussions with their Notified Bodies and attending conferences.

Developing the right training materials and instigating an appropriate training program as early as possible will support getting knowledge levels raised on this complex legislation. It will give employees more confidence when talking to the regulators if they are well versed in the subject, and it will help them present their case better if there are any discussions of dispute or difference of opinion.

5.2.4 Survey Question 4 combined with Interview Analysis

Question 4: What other departments / function do you think will be impacted by MDR?

This section discusses the different functions impacted by the MDR and the workload implications of same.

- R&D and Design Assurance will have additional roles in implementing a strategy for addressing post market surveillance, in combination with creation of PSUR's. A proactive and systematic process for collecting information, building in indicators and threshold values for the continuous reassessment of benefits Vs risk analysis is constant throughout the lifecycle of the device. Any risk that arises in a clinical setting must be addressed by post market clinical follow up and evaluation. R&D will likely be less impacted than Design Assurance. Thirty- three (33) of the respondents, (53%), thought that R&D would be impacted, while thirty- four (34) of the respondents, (55%) thought design assurance would be impacted. Forty participants who took this survey felt that all functions would be impacted which would also have impact on these results.
- Clinical evidence is not a new requirement, however the MDR has increased the clinical investigation requirements. In addition to Clinical Evaluation Reports, a public summary of safety and clinical performance (Article 32) is now required for certain types and classes of devices. This summary is expected to consider diagnostic or therapeutic options addressed in the CER and diagnostic/therapeutic alternatives. Class III and implantable devices are required to have clinical investigations as outlined in the standard ISO 14155: 2011, Clinical investigations of medical devise for human subjects – good clinical practice. Clinical investigations will become mandatory for class III or implantable medical device applications upon implementation of this regulation. These heightened requirements are certainly going to add to the workload within the clinical function.

  Clinical is one of the most impacted functions of this regulation, yet only thirty-three (33), 53% of the respondents thought that clinical would be impacted. This is concerning as the expectation on the results of this part of this question should be 100%. Companies are already experiencing the bar being raised in clinical reviews with the MDR expectations being embedded through existing reviews. This also ties back to level of knowledge and the importance in training. One thing to note to counteract this result is that forty (40) 64% of respondents did feel that ALL functions listed in the survey question would be impacted.
- Operations is going to be impacted by the implementation of new labels and IFU's on all products. This will involve changes to be processed, lines to be purged, bill of materials to be updated as well as all the other checks and documentation required to implement

such updates. Process validations are a new deliverable required for technical files, therefore operations will be under more pressure to have these process validations completed per schedule and ensure that the technical reports supporting these validations are written with high quality. Again, only thirty (30) 50% of the respondents assumed that operations will be impacted. Since this survey was completed by regulatory professionals they should be aware of the crossover of deliverables to the operations function.

- Quality will need to have their quality system ready. Quality manuals will need to be re written, and many of the procedures of the quality system elements will need to make reference to the new regulation. They will also need to document the chosen conformity assessment path for their products. Any companies who have EN ISO 13485 2016, Quality Management Systems and have the MDSAP program initiated are well underway to having the system ready for MDR. Quality will feed into many of the other functions review and deliverables, therefore will also be impacted by MDR 2017/745. Remarkably only thirty-five (35) 56% of participants thought that quality would be impacted. It would be expected that this result should also be higher, however, (40) 64% of respondents did feel that ALL functions listed in the survey question would be impacted.
- Sales and marketing will also be impacted. For those companies deciding to retire some of the older legacy products, marketing will have to find the right replacement for their existing clients. The information in promotional materials will change and the information in the IFU and labels will change. Sales and marketing will need to very familiar with these changes and be able to explain them to physicians when out in the field. Only seventeen (17), 27% of respondents felt that sales and marketing will be impacted. This is low and perhaps understandably so. While all the promotional materials will need to be updated, it is generally the packaging and labelling function that do this activity. Nothing about the physical device will change, it is really for sales and marketing to be aware if any special warnings or precautions are added to the IFU.
- The role of supply chain, including distributors, has increased their role to have traceability requirements, post market obligations and will have to provide inputs to the Eudamed database.

  Many adjustments will be required by all parties involved in manufacturing and distributing medical device products in Europe (Articles 10-15). (Clemens 2018). It is

clear from the results of this question that not everyone is aware of the additional burden for distributors and supply chain in general. This is validated by only twenty-nine (29), 47% of the respondents listing distributors as being a function impacted.

All combined, the number of cross functional resources and man hours invested in MDR efforts is colossal. It was important to point out the enormity of the changes the MDR 2017/745 is bringing and how they will impact other functions. The main changes of the MDR was discussed in depth in chapter 2.

The results from this question do not align with the results from question 3 on the level of understanding of the regulation where fifty-four (54) respondents answered in the categories of "moderate" and "good understanding", which encompassed 85% of responses. It makes me question; do they really understand MDR 2017/745? as they should know that all these functions are indeed impacted. Often when people are unsure how to respond in surveys they choose the middle option, which for question 3 was moderate to good understanding? Perhaps they over rated themselves from a knowledge perspective. This ties back to the importance of training in this area. It is paramount for companies to design and develop a robust training program which is rolled out frequently over the next two years and beyond.

5.2.5 Survey Question 5 combined with Interview Analysis

Question 5: If you are responsible for compiling a Technical file, how many hours do you think it will take to create a file to be compliant with MDR?

Regardless if a device has been on the market for decades, and pre-dates MDR 2017/745, these legacy devices will require their technical files to be rewritten to adopt all the new requirements. The MDR 2017/745 introduces a new view on technical documentation that is broader than the current view. It differentiates between data needed prior to market access (MDR 2017/745 annex II technical documentation) and post market data (annex III). As with most legal documents, the devil is in the detail.

The files will have a different format and structure and contain much more information. This question was asked to help build on resource requirements to try and plan and factor in

accordingly. Some people have had to guess the answer as they may not be at that stage of re writing their technical file just yet.

The figures speak for themselves as depicted in Figure 23 in that 22 respondents thought it would take 100hours +, and 16 respondents anticipate it will take between 50 and 100 hours to write a technical file. This will depend on how ready the company is with respect to what tools, templates, and procedures etc they have in place to assist the regulatory professionals carry out this task.

The author would agree on the estimate of it taking 100+ hours based on experience to date. The company she is working in is currently preparing technical files to be submitted to the Notified Body and there is a significant amount of time being dedicated to this task.

One would expect, after writing a few files, that this task would become easier, and faster as regulatory professionals will become more familiar with the format and deliverables required. The other factor which may influence the time taken to complete technical files is Notified Body feedback. As there are learnings from the first file reviews and feedback from Notified Bodies on specific requirements or changes, this can be built into file writing going forward. As you might expect, this will be a learning curve for all involved but with the right training and guidance technical documentation will be generated in line with the requirements of the MDR.

5.2.6 Survey Question 6 combined with Interview Analysis

Question 6 If *you are responsible for reviewing Technical files, how many hours do you think it will take to review a file that is compliant with MDR?*

As part of good submission practices, technical files are reviewed by regulatory management to ensure content is accurate and that there is no conflict of information anywhere within. This task involves cross checking data and potentially reaching out to other function to verify information or data. Documentation to demonstrate safety and performance of the device is included in a file with emphasis on fulfilling all the GSPRs.

There is a spread on the opinion in the response to this question which is quite interesting. This could be due to a number of reasons:

- the style of reviewer and the depth they get into during the review.
- experiences with different Notified Bodies.
- complexity and classification of the medical devices being reviewed.

It is worth noting again that Notified Body regulatory professionals have answered this question and obviously their review of the file will be an in depth one which will take a considerable amount of time.

5.2.7 Survey Question 7 combined with Interview Analysis

Question 7: The challenges identified below are from interviews conducted with people working in the MedTech sector who are familiar with the MDR. Please rank these challenges from 1-9 with 1 being the most challenging and 9 being the least challenging.

As stated earlier, question 7 is the crux of the survey. This question was designed from the output of the results of the interviews. The interview results revealed that there were nine (9) distinct themes coming from the interview discussions. These nine themes were built into question seven (7) by asking the respondents to rank these challenges in priority as to how they would impact them, with 1 being the most challenging and 9 being the least challenging. It was interesting to see that the four (4) top dominant themes from the interviews were also the four (4) top challenges from the survey, albeit they were in a different order as can be seen in Figure 28.

These nine challenges are discussed individually in chapter 5, section 5.3.

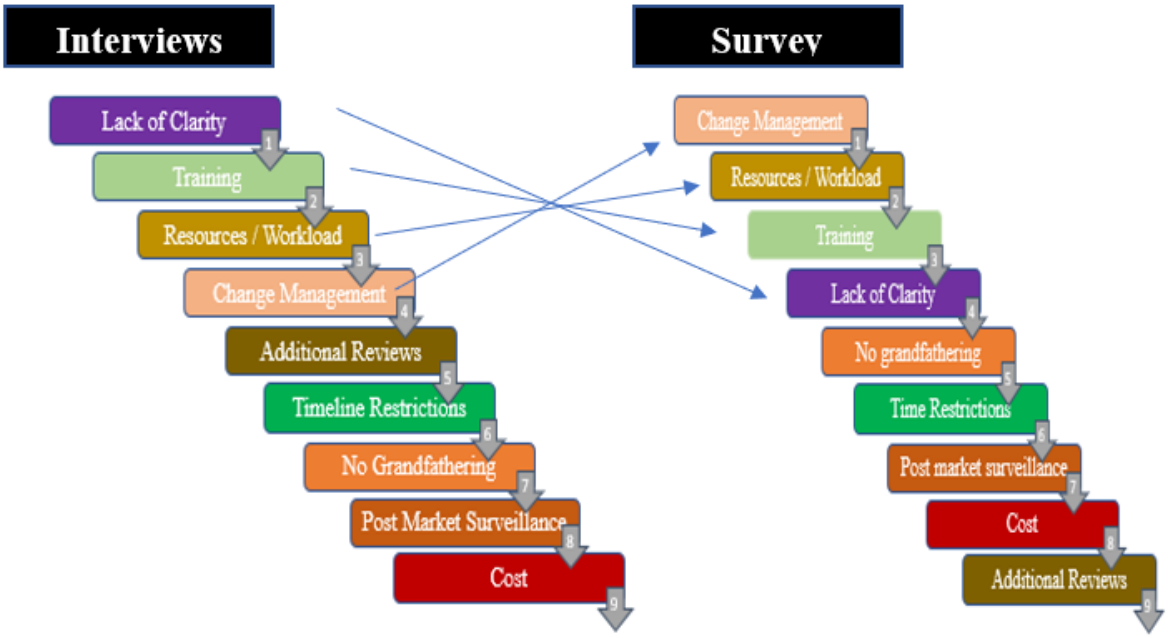


Figure 28: Comparison of the Ranking of the Challenges from the Interviews Vs the Survey

(Created by the author)

5.2.8 Survey Question 8 combined with Interview Analysis

Question 8: Do you think MDR will have any impact on patient safety?

Question 8 was a mix of a closed and an open question as it was a yes/ no answer with an option to leave a comment to support their yes or no answer. As can be seen from the response, the majority voted yes with 48 and only 12 voting no. As the author worked through this research it was interesting hearing different opinions on this thinking. Was the birth of MDR 2017/745 a good thing? Or, is it just introducing unnecessary burden?

One of the interviews, interview C5 relayed a great argument on this and argued that if the current directive 93/42/EEC was applied correctly in the first place, this chaos would not be here today. The chaos being the need to apply over burdensome procedures and systems to respond to a political disarray in response to some of the leading scandals within the MedTech sector, such as the PIP, and MOM described in chapter 2. Past experience has shown that maltreatment to

patients can teach regulators and policy-makers a ruthless lesson and it is a powerful trigger for change.

Migliore wrote a curious article on the new regulations stating "Some could argue that the changes introduced will delay market access and reduce innovation and investments, considering that the medical devices sector is populated by a relevant number of small and medium enterprises, which often have no resources or skills to fulfil the new requirements. However, the changes have been introduced to address real problems, gaps, and critical issues mainly related to safety. Achievements in this direction have to come with a price" (Migliore 2017). He also goes on to state, "delays introduced by a more stringent regulation could cause late access to new technologies and would be linked to a 'human cost".

MedTech Europe conducted a survey towards the latter end of 2018 and the results of that were more negative than this research. The report titled, "Medical Devices Regulation Impact Assessment Survey and Interview Report", stated, "Depending on the company, some see the implementation of the new Regulation as positive and others as negative. The general trend of the participants is towards the latter, with over 50% of the respondents answering either "slightly negative", "negative", "strongly negative" or "close business" (MedTech 2018c). The survey results from that survey also go on to say;

a) It is understood that there is a high documentation burden for companies, with little to no benefit for the patient.

b) The perceived impact is not influenced by the size of the company.

In response to question 8 of this survey, 45 respondents left comments of which the raw data can be found in Appendix Q. The main arguments coming from the positive slant of answering yes was along the lines of feeling that product safety will be improved by means such as;

1. Creating greater transparency within the regulatory framework.
2. Patients having more access to device and manufacturers information.
3. More clinical evidence will improve patient safety and seen as a positive initiative.
4. The Eudamed database was viewed as being a positive tool that will facilitate product information storage.
5. More scrutiny being applied on the Notified Bodies.

Some of the negative tones from respondents who answered "no" include;

1. There was a sense that small manufacturers may be forced off the market.

2. Product innovation is likely to be impacted negatively.
3. More scrutiny on device approvals.
4. Notified Bodies do not have enough capacity.
5. There may be a reduced selection of devices available.

Not everyone is convinced that the MDR is going to improve the regulatory framework around medical devices. Some people feel it is just bringing more work for the same product that is being used in the field.

"This new EU regulation for medical devices (MDR) makes many changes to the previous directives and fully come into force on May 26th, 2020. However, does it solve the structural problems with past regulations, does it protect patients and improve safety, or, does it provide more work for manufacturers, more work for notified bodies and false reassurance – is the MDR a smokescreen?" (Heneghan C 2018).

5.3 Analysis of the nine (9) Challenges Identified

This section explores the challenges identified in the interviews and rated in the survey. It studies the challenge in detail and details the context behind each one to evaluate its ranking.

5.3.1 Management of Change Control – Design Changes.

As can be seen from the data gathered during phase II, the qualitative phase, the topic of change management came up as a concern during 10 of the 12 interviews conducted and was ranked the fourth highest in the ranking of the themes from the interviews. In February 2019 when these interviews were conducted, manufacturers were already feeling the restrictions on capacity working with their Notified Bodies.

The survey revealed an overwhelming result of 27 respondents stating this to be their # 1 challenge as they work through MDR 2017/745. The author can relate to such an outcry as she is experiencing this same challenge in the organisation she works in. For a manufacturer to be restricted in making design changes or changes to the intended use for their devices during this transition time is a significant impediment. Business will deteriorate, and innovation will decline. As stated in Chapter 1 for a manufacturer to legally place a medical device on the European market, they must meet the requirements of Directive 93/42/EEC and must have a CE mark applied. The Medical Devices Directive 93/42/ EEC which companies are working under today require certain changes of the device or quality system to be notified to the Notified Body. Changes which "could affect the conformity with the essential requirements" are considered substantial changes. In these circumstances, review and approval by the Notified Body is required. The same rules will apply for MDR.

The pathway to deciding whether a change is substantial and requires Notified Body approval is not always straight forward and can be difficult to make the decision in some cases. No definitive list exists which will guide a manufacturer to that decision, it is made on sound regulatory experience and judgement. It is very much dependent on the classification of the device, and as expected the requirements for the higher risk, class III devices are greater than the lower-class devices.

At a top level there are 2 types of changes allowed today under MDD which will continue with MDR

1. These are changes which can be implemented without receiving prior approval from the Notified Body before implementing.

2. Changes requiring prior approval from the Notified Body. These are significant changes.

However, during the transition period there is a restriction on changes for products under MDD. This restriction is in place until the product transitions to the MDR and is detailed in article 120 (3) "By way of derogation from Article 5 of this Regulation, a device with a certificate that was issued in accordance with Directive 90/385/EEC or Directive 93/42/EEC and which is valid by virtue of paragraph 2 of this Article may only be placed on the market or put into service provided that from the date of application of this Regulation it continues to comply with either of those Directives, and provided there are no significant changes in the design and intended purpose" (Commission 2017a). The difficulty for industry is determining which changes fall under the restrictions specifically which changes are design changes. A pictorial representation of the current and future state is illustrated in Figure 29 below.

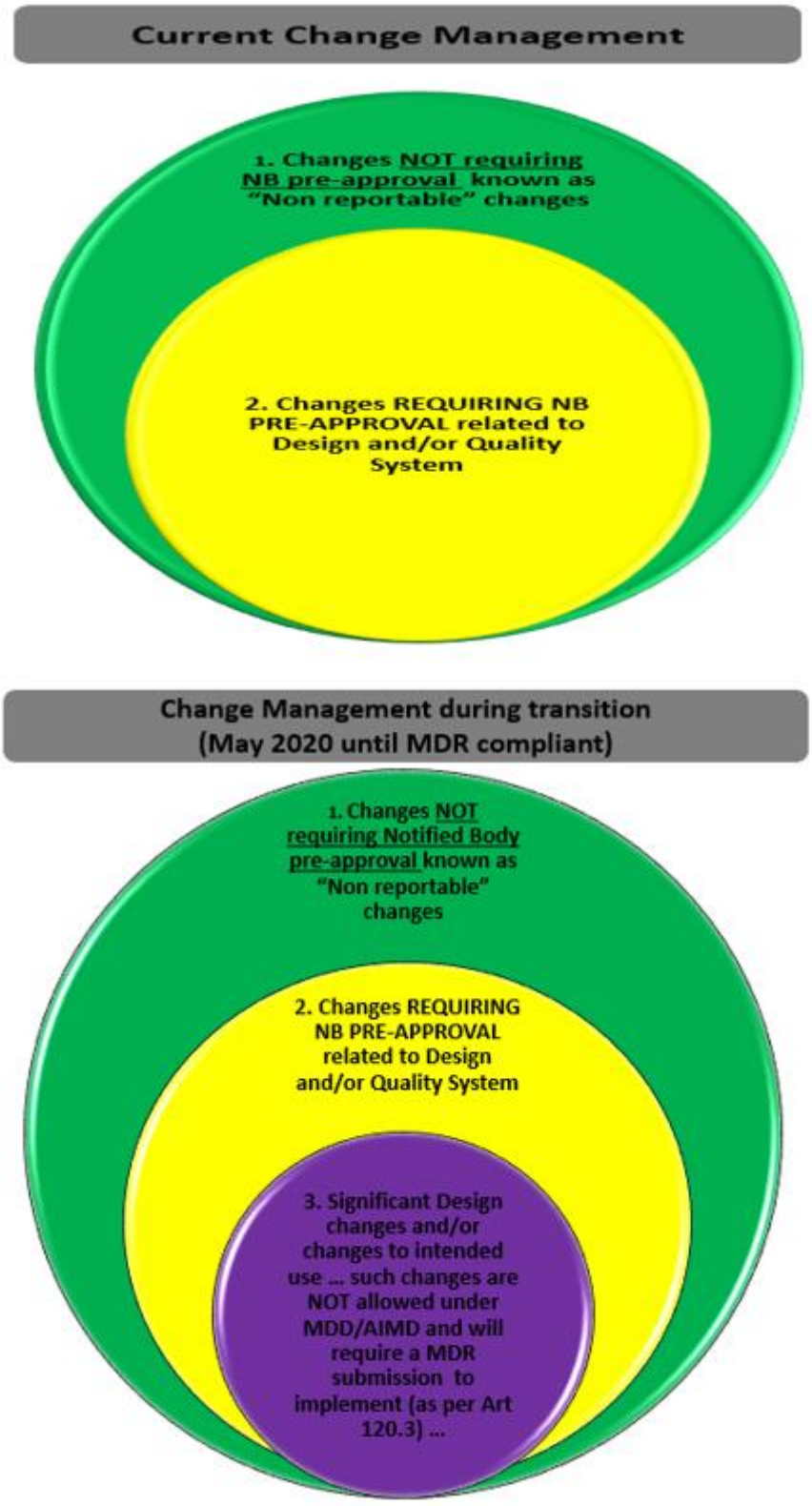


Figure 29: Categories of Changes & Associated Regulatory Assessment

(Created by the author)

There are two guidance documents which manufacturer's use when making the decision on whether the change is a substantial change and if it requires Notified Body approval. These guidance documents are;

1) NB-MED/2.5.2/Rec 2, Reporting of design changes and changes of the quality system, rev 8, 2008. (NB-MED 2008).
2) NBOG Best practices guide for manufacturers and Notified Bodies on reporting of design changes and changes of the quality system, 2014-3. (NBOG 2014).

These guidance documents will also be used when assessing product changes under MDR 2017/745. MedTech Europe issued a position paper in October 2018 on "Assessing significant changes in the design and intended purpose of a medical device to address article 120 (3) of the medical device regulation 2017/745/ EU" (MedTech 2018a). This position paper is written using various flowcharts to determine the decision-making process and is written based of "NBOG Best practices guide for manufacturers and Notified Bodies on reporting of design changes and changes of the quality system, 2014-3" (NBOG 2014). Unofficially industry have heard that this position paper is not being accepted by the European Commission and they have plans to issue their own guidance. At time of print this guidance is not available.

NBOG 2014-3, Best practices guide for manufacturers and Notified Bodies on reporting of design changes and changes of the quality system, describes design changes as "Changes in design span the full spectrum from minor engineering changes to major changes in operating principles. All design changes must be evaluated, verified and validated according to the documented procedures accepted by the Notified Body" (NBOG 2014).

It describes "changes to design specifications" as Changes to the design specifications (including but not limited to change in expiration date, primary packaging or energy type), physical, dimensional, environmental specifications, ergonomics of patient user interface, may be substantial if they affect the indications for use or the performances of the device or raise new safety and performance issues.

Some examples of n changes which will be restricted during the transition period.

1. A change to the indications for use.
2. Material changes
3. Some sterilization changes, examples include modality change (i.e. EO to Radiation, Steam to EO)
4. If new technology was applied when manufacturing the device

5. Change in critical suppliers

There are many different reasons why a manufacturer would want to make changes to their products. The lifecycle of any medical device can be divided into various stages from concept, through planning, design, validation, launch and post market. In the post market phase medical devices undergo changes as part of their product life cycle. "Medical technology is characterised by a constant flow of innovations, which are the results of a high level of research and development within the industry, and of close co-operation with the users. Products typically have a lifecycle of only 18-24 months before an improved product becomes available" (MedTech 2019a).

Product change is inevitable for many different reasons. These reasons may include;

- Post market surveillance activity including adverse events and complaint trending.
- Feedback from the users in the field to enhance usability to improve product performance. Designs changes often occur in response to industry pressure for increased customer satisfaction and device safety, better manufacturability, maximized performance, cost efficiencies, and innovation in general.
- Design changes required from a recall corrective action.
- Supplier issues, be it suppliers closing or perhaps running out of specific raw materials.

The context behind the root of the problem and the major concern for manufacturer's during this transition period is that ***(Manufacturers are not permitted to make significant changes to a device design or intended purpose under an MDD certificate post May 2020, unless they move their file to MDR 2017/745*)**. This has huge implications for all manufacturers and may result in products coming off the market in some instances.

Within the new regulations, significant design changes that impact product performance and changes to intended purpose as per Article 120 (3) or change to MDD certification will trigger a need for the product to convert to MDR 2017/745 prior to the implementation of those changes or put the planned change on hold until the product is MDR 2017/745 compliant. In such a scenario, the MDR 2017/745 conversion cadence for products may take priority over the plant activity such as VIP's, (value improvement projects) vendor changes, etc. This could lead to wasted time and effort and a delay in realizing planned savings.

One of the other areas where there is lots of changes is with material changes. A typical example here is where a supplier can no longer supply a resin and the same resin is not readily available

from an alternative supplier. This leads to enforcing a material change which is considered a design change. The two options a manufacturer has with this is to 1) make the change under MDR 2017/745, or 2) take the product off the market.

These restrictions of no design changes which may impact product intended use or product performance has significant impact to medical device manufacturing business. The challenge here is for functions outside of regulatory to understand and plan for these restrictions. Operations, and R&D are two of the main functions impacted by these restrictions as they are often the drivers in seeking changes to existing products on the market.

Extra due diligence must be applied upfront to all planned changes to existing (MDD) products with the goal of determining whether such a change can be pursued without impacting the MDR 2017/745 conversion cadence.

This restriction will have impact on larger companies which are involved in investing in acquisitions. Where there is legal manufacturer or Notified Body, changes involved in such acquisitions it will not be possible to make these changes under the MDD certificates, therefore again companies will be forced into MDR 2017/745 technical files to continue business.

5.3.2 Resources and Workload

The third theme simmering under the surface of these interviews was resources and workload. The reality of the volume of work required to be completed is overwhelming and with each month passing it gives the manufacturer less time against the clock. With less than a year to go, the workload is fast increasing. It was clear from the interviews that there was a strong sense of unease around this area.

The challenge here is that many medical device manufacturers have not hired staff specifically to deal with MDR. They are using existing workforce capacity. This is especially true for the small manufacturers and in many for the large manufacturers also. Some companies had hired a regulatory professional to understand the new laws and work in a Project Management capacity and help with training materials. None of the companies which the author had talked to had hired staff to do the hands-on work at the time of interviews, however they did envisage that hiring staff for this purpose was imminent.

The Notified Bodies on the other hand knowing they were being stretched beyond their limit already were further along with hiring new staff. The training program within the Notified Body structure is very demanding and it can take anything from 6 months to up to 1 year to have the

appropriate training conducted. This depends on the persons background from an academic work experience perspective. There are lots of people interested in working Regulatory, however, finding experienced staff is the challenge.

Results from the question 7 of the survey showed that resources and workload are unsurprisingly a huge concern within the sector. While only 5 people ranked it as their # 1 challenge, 15 people ranked it as #2 and 17 people ranked it as their # 3 challenge. These numbers are a definite signal of what to expect from a workload perspective.

Market access to place medical devices on the European market will change significantly post May 2020. Manufacturers of medical devices will face many new challenges for their products in the future. They need to have a clear understanding of the scope and plan of implementation as this is a huge challenge. As discussed in chapter 2 there are many new deliverables embedded in this regulation as well as a life cycle approach to ongoing CE marking compliance. There are deadlines to be meet hence planning and execution will be paramount.

Larger companies with many products to get through this process are managing waves of technical documentation updates using a staggered approach. This will help get through the workload in a more streamlined approach. With companies realising the mammoth workload ahead, many have begun recruiting. Both medical device manufacturers and Notified Bodies alike have invested heavily in the recruitment of regulatory professionals and will continue to add to this investment over time to ensure that their teams continue to grow to support the needs of the business.

As mentioned previously it is difficult to find the right people to hire. While Notified Bodies and medical device manufacturers may have approval from their management to recruit staff, this is proving to be challenging. Everyone is trying to recruit from the same pool of people, and with regulatory being a specialized area, it is difficult to get the right candidates. "To meet requirements many companies, need to increase their quality and regulatory staff. It will take lots of time to review all specifications of all products to verify their conformity" (Vila Wagner and Schanze 2018).

There are ways to manage the resource challenge to a degree. A gap assessment between the new regulation and existing MDD is a useful tool and helps to generate a task list so that companies can figure out what they need to do and when they need to do it by. It also helps identify required resources, financial and otherwise. There are lots of generic gap assessments available through consultancy companies which is a good starting point to get kick started.

Another tool is a portfolio assessment which is generated to weigh up the financial costs of bringing a product file through MDR 2017/745. Maybe it's time to retire some older products if the transition cost outweighs future profit.

All Notified Bodies are currently under immense pressure to meet the resource needs to conduct conformity assessment under the increased regulatory requirements. They are working through the designation process, continuing to review ongoing technical files for legacy devices and new files being born under the MDD system, recertifying product files under the MDD, getting ready to review MDR 2017/745 files, conducting regular audits, unannounced audits, preparing for all the additional reviews which will occur with MDR 2017/745. They must hire, train and develop additional new resources which cost time and effort that are not available.

According to Sergi Bernasconi, chief executive officer of MedTech Europe, in an article written 04th December 2017 states "Not only will Notified Bodies need more people, they will need a huge influx of expertise and time to train new staff. Our concern is that Notified Bodies may not be available early enough in the transition period and that it may take too long to ramp up the needed capacity and experts to review the many products out there.

National Competent Authorities, designating authorities and agencies also need to invest in people, IT systems and infrastructure to match their expanded role. The EU Commission itself has only eight core people actively working on this major regulatory revamp" (Bernasconi 2017).

Another reason that resources is a concern is that there are less Notified Bodies available. The number of Notified Bodies has dropped from 83 to 58, which again puts more pressure on them, and more pressure on industry as all manufacturers are craving their time and resources. These numbers were noted in the one-year application document written by Team NB. (Team NB 2018). This will also lead to longer review times which in turn slows down business.

On 02 July 2018, Notified Body X, as referred to previously, sent a communication to their clients titled "An urgent notice of the timelines for all MDD and AIMD certificate renewals and reviews" (Slack 2018). Within that communication they outline their expectations as they undertake the anticipated increase in workload required for renews and renewals throughout the transition period. They believe that many of their clients face the possibility of not completing the transition in time and therefore placing themselves or rea risk of not holding a valid MDR 2017/745 certificate by the May 2020 deadline for all products on the market. They urge manufacturers to submit MDD certificates for renewal before March 31st, 2019, and if it occurs after this date they cannot guarantee to review it. They put this responsibility on the manufacturer and state "it is

the manufacturer's responsibility to ensure the validity of its certificates" (Slack 2018). This communication went on to state "In the absence of CE certificates under MDD with validity beyond the transition period, one can no longer to place affected devices on the EU market until they have been certified under the MDR 2017/745" (Slack 2018).

A communication of this nature from one of leading Notified Bodies in the industry, demonstrates that they too were nervous about the avalanche of work that needs to be completed within a specific window of time.

An additional concern is over Notified Bodies being able to certify class I devices before May 2020. Notified Bodies are required to review class I and some software devices as part of the MDR 2017/745 implementation. This is a new requirement which has been brought in by MDR. Notified Bodies do not know the volume that is coming at them for this category of devices. The time remaining to assess these products is getting less every day as only two Notified Bodies are designated to date. This additional workload will lead to capacity, resource, and workload also. There is no allowance for extra time for these categories of devices.

The graph in Figure 30 below is Notified Body predictions of their future workload titled "big waves are coming". It is not only the initial audits according to the new regulations that will place burden on the shoulders of the Notified Bodies. There are more waves of work coming, e.g. SSCP and PSUR,. (Team NB 2018).

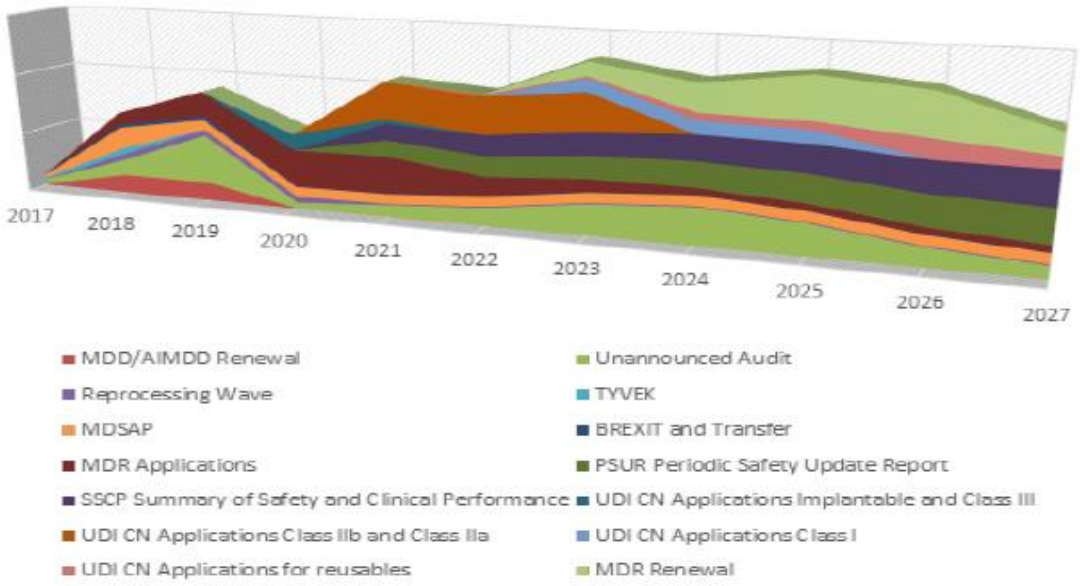


Figure 30: Notified Bodies Perspective - Big Waves are Coming

Taken from (Team NB 2018)

5.3.3 Awareness and Training

Lack of training, awareness and knowledge was mentioned 27 times during the interviews. In question 7 of the survey, 3 people identified awareness and training as a # 1 challenge. However, 18 people listed this as their # 2 challenge and 10 people listed it as their #3 challenge. This challenge is linked to the additional challenged of lack of clarity which is discussed in the next section. It is difficult for training to be designed, developed, and delivered if there is a lack of clarity in the requirements and expectations of the regulations and what the new system will look like. Medical device manufactures are hesitant to provide detailed training if the message in this training changes as further clarification and information is received from the Commission. There is a certain level of training which can and must be rolled out in all sectors such as manufacturers, Notified Bodies and Competent Authorities. The next layer of training down which contains the "how to" and "when to" is where the challenge lies. Mistakes can often prove to be expensive, resource and time constraining which is leaving many challenged with this task.

The individuals interviewed for this research were all at management level and above within their organisations, so they had a good level of understanding of Regulation 2017/745. However, during our discussions it became apparent that while they were knowledgeable with the content of the regulations, there are some specific areas where they felt was still unclear. Examples of this was discussed in the previous section under "lack of clarity". The respondents of the survey also demonstrated a good knowledge of the regulations as per question 3, where twenty (20) said they had a good understanding of the regulation.

Moving from MDD 93/42/EEC to MDR 2017/745 is a huge change for everyone with new information to become familiar with. As with anything in life change can be difficult, and with the magnitude of new requirements introduced with MDR 2017/745, it is daunting. This long-awaited text has brought with it many nuances and more scrutiny of technical documentation.

Understanding the legislation is important to manufacturers to place a medical device on the market in the European union.

As illustrated in the feedback from question 4 there are many functions within a medical device manufacturer that is impacted by this change. These include quality, operations, clinical, design assurance, research & development, sales and marketing, and distributors. It is important that each of these functions understand how they are impacted and understand what they need to do to be compliant. Knowledge of these changes is a crucial foundation to ensure a smooth and compliant transition. The regulatory professionals must be able to translate regulations into

language that resonates with the various functions and audiences to help them understand their role in achieving this goal. Appropriate resources and tools are required to enable them to this.

It is fundamental that senior leaders in organisations buy into the importance of training and promote this as being an opportunity for growth and people development. The MDR is a learning curve and some parts of this legislation is to easier weave through than others.

According to weaver "Background Evaluation and measurement are the building blocks of effective skill development, transfer of training, maintenance and sustainment of effective team performance, and continuous improvement. Evaluation efforts have varied in their methods, time frame, measures, and design" (Weaver *et al.* 2011).

It is good practice to organise training around three phases, planning, implementation and follow up to check on the effectiveness Figure 31 depicts the sequence of steps in this process.

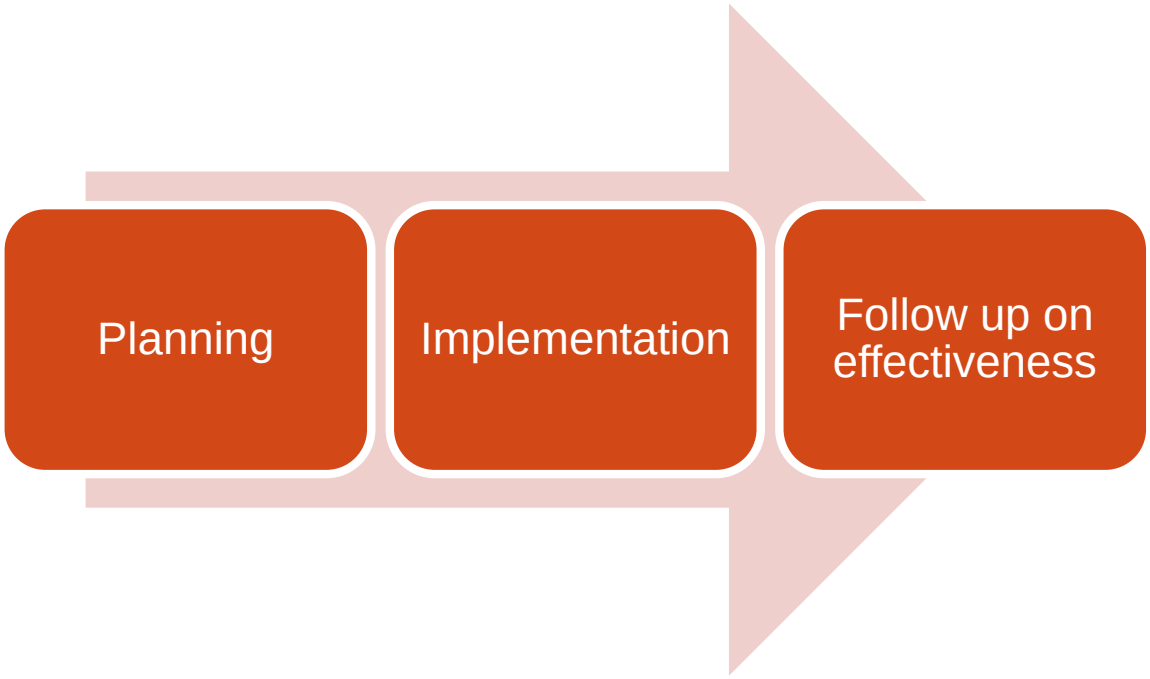


Figure 31: Stages in Development of Training

(Created by the author)

As part of the planning phase it is important to consider the training needs. Different levels of training were required for the various functions. Some needed to understand sections of the legislation more than others, therefore training was tailored to different audiences. It was important picking the right individuals to be involved in the MDR 2017/745 project. Implementation requires not only leaders but also technically competent employees.

"Key factors to creating a motivated team to deliver new training material include selecting the correct team members, outlining an education plan, identifying resources, and creating a safe learning environment" (Sudarshan and Blackmon 2018).

The general feeling in companies and in the MedTech sector in general is that people want to be involved in the MDR 2017/745. While its burdensome, and brings on more work, it is new, it is different, it is challenging, it will grow employee's knowledge and skillset, and it will provide new opportunities for people in the future.

"Key factors to creating a motivated team to deliver new training material include selecting the correct team members, outlining an education plan, identifying resources, and creating a safe learning environment" (Sudarshan and Blackmon 2018).

Timelines are important, and it is key to applying the initial training swiftly since there is so much to do with such little time to do it. Over the transition training is ongoing with employees receiving different iterations of the same topic. This is important as new information is constantly becoming available from the Notified Bodies.

Training was provided by several different methods as shown below in Figure 32.

Figure 32: Different Methods how Training can be Achieved

(Created by the author)

Training is a key element of a Quality System. As per the international standard for quality systems, ISO 13485 2016 Medical Devices Quality Management Systems- Requirements for Regulatory Purposes, personnel performing work affecting product quality shall be competent based on appropriate, education, training, skills and experience. The organization shall document the process(es) for establishing competence, providing needed training, and ensuring awareness of personnel. (International Standards Organisation 2016).

There are different mechanisms being used to create awareness and provide training in the various organisations.

- Procedures were written to interpret the regulations and provide clarity when completing a task or an activity.
- Newsletter – These are used a tool to keep employees informed on information at a top level. They are typically issued monthly or quarterly.
- Brainshark – These are essentially PowerPoint presentations with a voiceover.
- Conferences – There are many conferences dedicated to the popular topic of MDR 2017/745. MedTech Europe have dedicated many of its national and some of its global

conferences to this topic. These have speakers from industry, Notified Bodies, Competent Authorities, FDA, and regulators from some of the International countries. There are great debates and information sharing and therefore. are a great method of networking and making connections within the global regulatory community. It empowers professionals to share the knowledge and ideas with one another.

- Classroom training- "Instructor-led classroom training remains the most popular training method. Training's annual survey shows that instructor-led classroom training accounts for 41% of the total training hours delivered by organizations compared to 30% for online training and less than 5% for social learning and mobile learning" (Training Industry Report, 2016).

With MDR 2017/745 being so complex classroom training is a valid method of learning. The legislation is very intense, and it was hard to keep attentive throughout, therefore it was worthy to have an interesting slide deck, and to bring in some light humour. People need to be released from their day job to give them adequate time to attend training sessions. They need to be in the right frame of mind to focus on the training. "The brain is more receptive to learning when relaxed, unthreatened and stimulated" (Green 2019).

All medical device companies are competing to get through this mission of placing their medical devices on the market under MDR 2017/745. Training and awareness of what needs to be done and by when is key. Companies thrive on their sense of investment in training and being ahead of the game. They can use it as a marketing strategy.

The effectiveness classroom training should also be measured. This can be done through conducting a test or can be completed more informally through a questions and answer session at the end of the training module.

"After training, positive transfer to the job seems to be highest when three conditions are met. One, allow trainees to use their newly acquired skills on the job as soon as possible. Two, provide tangible organizational support from supervisors and peers, as well as positive reinforcement for the successful application of the new skills. Three, hold trainees accountable for positive transfer of their newly acquired skills to the job" (Kraiger 2014).

- Intercompany information sharing

Local companies are open to helping each other by sharing feedback from their Notified Bodies and Competent Authority. While this information sharing is minimal, every bit of additional intelligence sharing is welcomed.

Conclusion:

Training is extremely important in this area to provide all personnel with the knowledge they need to perform the various tasks associated with MDR 2017/745. Training will be an ongoing activity as companies transition their products from MDD to MDR.

5.3.4 Lack of Clarity

The data from the interviews indicate lack of clarity in the regulation in addition to insufficient supporting documentation is the most repeated challenge. This challenge came up 40 times throughout the 12 interviews and was widespread across medical device manufacturers, Notified Bodies and the Competent Authority. Regulatory professionals in industry feel they do not have a clear plan to move forward with implementation of the new regulation. They are asking questions of Notified Bodies, who in turn do not know the answers and are pointing the manufacturers to the Competent Authorities. The Competent Authorities do not have all the answers either and they are ultimately depending on the EU Commission to make the final call in many of these areas. It feels like all the stakeholders are going around in circles.

Some of the interviewees made the point that there is language used throughout the regulation which is vague and open to interpretation. Language such as “sufficient”, “as a general rule”, “adequate data”, “sound procedure”, and many more which is wide open to varied understanding and application.

The results of the survey further indicated lack of clarity as a prevalent concern with it ranked as the fourth main challenge.

As mentioned there are numerous examples of ambiguity in the text. An example in case is in MDR 2017/745, Recital 56, “For class III implantable devices and class IIb active devices intended to administer and/or remove a medicinal product, notified bodies should, except in certain cases, be obliged to request expert panels to scrutinise their clinical evaluation assessment report.” (Commission 2017a). It is not clear what the term “in certain cases” means. These expert panels have not been established yet so more information on this matter cannot be obtained at this time.

Since the approval of MDR2017/745 by the EU Commission on April 5th, 2017, the lack of substantive guidance has hindered manufacturer's preparation in addressing new regulatory requirements by the mandatory conformity dates of May 2020. It is now two years after publication of the regulation and no formal guidance has been issued by the EU Commission. Industry are waiting on documents such as implementing acts, delegating acts and common specifications, as well as more information on expert panels.

The MDCG (medical device coordination group) is a group which was created to enforce the new medical device regulations and its representatives comes from all the EU member states. This group wrote to the EU Commission on Friday 25th March 2019, urging clarification of the meaning of "device already on the market". The group said it believes the expression is not intended to mean devices marketed uniquely under the MDR 2017/745. The communication to the EU Commission stated "As we are about to launch the procedures for the establishment of expert panels, clarification of this issue is extremely urgent, notably due to its impact on the future workload of panels and hence on relevant budget and workload estimations" (MDCG 2019). No formal response has been issued by the Commission.

There is an unease in the sector. Everyone is trying to do their best yet without formal guidance this is very challenging. With so much to do and so many questions unanswered this is certainly one of the most challenging times in the regulatory community. Prolonged ambiguity is not helping and could have serious consequences for manufacturers.

In December 2017, Serge Bernasconi, Chief Executive Officer of MedTech Europe, listed three reasons why manufactures are concerned: the challenges facing Notified Bodies that approve new products, the lack of clarity over governance, and tight transition times. He stated "For the system to work, authorities need to dedicate experts who can support implementation of each regulation - the IVDR as well as the MDR 2017/745. Clarity over who will draft the guidance documents is needed. We believe the EU Commission is best placed to publish guidance, as they have done in the past under the medical devices directives" (Bernasconi 2017).

Manufacturers face unique constraints particularly when there is lack of guidance. Manufacturers and government stake holders need to resolve outstanding unanswered questions and work together closely. "Although planning for the unknown, navigating gray areas and adjusting regulatory strategy along the way are essential elements of regulatory affairs, those whose scope of work includes products developed or marketed in Europe are really being stretched right now" (Brooks P 2019).

Bernasconi turns to the political associates in the parliament looking for help by saying "MEPs can help by raising awareness of these challenges at national level and encourage the EU Commission to put in place the resources needed to make these new regulations work. With political will, a healthcare crisis can be averted" (Bernasconi 2017).

The Eudamed database came up during a few different conversations in relation to lack of clarity. The requirements are unclear. The functional specifications of the database must be developed and an implementation plan to be agreed. This is a big task to deliver on. The functioning on the Eudamed is crucial to the success of implementation of regulation 2017/745, so the sooner this becomes operational, the better.

The absence of implementing acts, delegating acts, and official guidance documents from the EU Commission makes it very difficult for everyone to feel comfortable that they are interpreting the regulations correctly and that they are doing the right thing to gain compliance. On June 6th 2019, a communication from the Irish and German delegates was sent to the council of the European Union. The subject of this communication was titled "Employment, Social Policy, Health and Consumer Affairs Council session on 14 June 2019 Medical devices: Implementation of Regulation (EU) 2017/745 on medical devices (MDR) - Information from the Irish and German delegations". This letter was sent as a request to be discussed at a meeting to be held with the Commission on June 14th. The letter documented many concerns around the lack of clarity and on the status of preparedness and readiness to implement these new requirements both at Member State and European level. It stated " Fundamentally however there is currently a lack of clarity and available guidance on many requirements of the regulation and what the expectations of the regulatory system will be" (General Secretariat of the Council 2019). The document suggested the following next steps.

1. Member States should immediately consider their state of preparedness for implementation of the new Regulations both at each national level and, along with the European Commission, at European level.
2. Specific and particular challenges should be identified and discussed along with options for solutions to these challenges.
3. Further discussion of this topic should take place between Member States, the European Commission and, if necessary, the European Parliament before the end of 2019. (General Secretariat of the Council 2019).

In the meeting held in Brussels on June 14th, 2019, Germany's Health Minister Jens Spahn asked for the regulation to be postponed due to lack of readiness. He said "We don't want bottlenecks in the provision of medical devices for patients in May" (Bowers 2019). He called for an existing grandfathering clause in the legislation, which effectively allows many existing medical devices to stay outside the new rules until 2024.

The German Health Minister was backed up by the Irish Health Minister Simon Harris when he echoed the concerns raised by Spahn about the readiness of Notified Bodies. "It's important that we are honest with each other and assess the state of readiness," he told his EU counterparts. "Almost as big a public safety risk as a lack of regulation is the ineffective implementation of regulations, where you could end up actually creating an impression that something is effectively operationalized only to find out later that it is not" (Bowers 2019). In this same meeting Vytenis Andriukaitis, European Commissioner for Health, rejected claims that regulators would not be ready by May and replied with "May 2020 is a realistic and achievable deadline," he insisted. (Bowers 2019). The theme of "lack of clarity" was one that kept appearing and reappearing during these conversations. It clearly is one that is taking place with all stakeholders at local, national and EU level and includes discussions on system requirements, infrastructure and secondary legislation.

5.3.5 No Grandfathering

This topic came up seven (7) times across the twelve (12) interviews. The results of the question 7 from the survey indicates that only three respondents ranked it as their biggest challenge, eight (8) respondents as their second, and eight (8) respondents ranked this as their third challenge. This ranking may be due the fact the issues associated with no grandfathering are captured in other challenge categories, e.g. No grandfathering increases the workload and resources, as well as increasing cost. Legacy devices currently on the market today, and CE marked under existing directives, are required to meet the new requirements as outlined in the MDR. For these products there will be an additional transitional period up to four years after full application of the new regulation, but with certain restrictions. No design changes or changes to the intended purpose of those devices are allowed during this transition. The implications of this restriction were described in detail earlier in this chapter.

"The MDR requires existing ('legacy') medical devices to undergo conformity assessment to the MDR and to be CE marked anew, even if they have been on the market previously under the MDD (no 'grandfathering')" (Bobela 2017). Medical devices will have to address any gaps in

data between the MDD and the MDR and files will need to be submitted to the Notified Bodies for review and approval for all class IIb and class III products. The same amount of work will need to be completed for technical files for the lower-class devices, however, files for these devices will only be submitted to Notified Bodies on a sample basis.

One of the dominant gaps for many manufacturers is having sufficient clinical evidence. The aim of creating elevated clinical evidence requirements is to ensure greater health and safety for patients through transparency and traceability. The clinical evidence documents will face heavy scrutiny during the review process. Regulatory bodies are aiming to close any previous loopholes that may have allowed devices to enter or stay on the market without sufficient clinical evidence. Many legacy products have been CE marked and on the EU market for many years based on the market history of the product and on equivalence to other similar products. One of the challenges today is determining what constitutes sufficient clinical evidence.

5.3.6 Compliance by May 2020

Compliance by May 2020 came up eight (8) times during the interviews. The interviews for this research were conducted in February / March timeframe in 2019. With over a year to go it was clear that people were getting nervous with a compliance date of May 2020 approaching very soon. Designation of Notified Bodies, or lack thereof was the main concern of the manufacturers, Notified Bodies, and the Competent Authority. This is slowing down progress as manufacturer's cannot submit files to be under the new regulation until the Notified Body get designation. The longer this is delayed, the less time it leaves for the file review process. The Notified Bodies were also frustrated by this but assured us that their team was working very hard in the background on getting through the designation process. Surprisingly, only five (5) respondents answered this as being their biggest challenge in question seven (7) of the survey, four (4) ranked it as their second, and two respondents ranked it as their third biggest challenge.

It will not be possible to have all devices reviewed and approved by the Notified Bodies between the time they are designated and May 26, 2020. Therefore, most companies were submitting their products to be recertified under MDD to obtain an additional 5 years onto the expiry of their certificates. This will allow manufacturers to place products on the market up to May 2024 under MDD certificates. This strategy is really impacting Notified Bodies workload during the same time as they are trying to get designated.

MDR compliance is entangled with other required certifications such as ISO 13485 2016, and MDSAP. MDR certification is easier to obtain with certain aspects of ISO 13485 2016.

Similarly, for MDSAP, there are overlapping requirements across these programs from business procedures and process modifications. Many of the large companies seem to be far along in this compliance effort, whereas some of the smaller companies were only at the initial stages of this process.

The rapidly diminishing time-frame within which MDR compliance is to be in place is one of the primary challenges now facing manufacturers. The first-time certification of such a large number of products across the sector will significantly increase the workload facing Notified Bodies, potentially leading to severe capacity constraints in same and inevitable delays for those seeking re-certification for products under MDD. These certification constraints may also be exacerbated by mounting evidence of the reduction in Notified Bodies available for business and limiting their range of services.

The possibility of significant tensions arising between the Notified Bodies and the manufacturers is of concern, leading to potential outcomes that may not be in the best interests of current customers nor indeed the market at large e.g. the withdrawal of uncertified product from market without adequate substitutional product being in place.

A document was written by "Team NB" called the "One Year Application". (Team NB 2018) This document was written one year after the Notified Bodies had made their application for designation. The document outlines concern from the manufacturer's perspective and from the Notified Body perspective. It states, "Many manufacturers, healthcare professionals and other stakeholders fear that insufficient number of Notified Bodies will be designated on time enabling them to start managing the waves of technical files for initial certification according to the new legislative framework. There are also doubts about the capacities of already designated Notified Bodies under the current system " (Team NB 2018). Those doubts about insignificant capacities are also based on the fact that the expectations of the Joint Assessment Teams on resource qualification is dramatically increased compared to the requirements laid down by previous directives.

This same paper outlines the concerns of the Notified Bodies to be

1. Implementation period, May 2017 until May 2020, is too short for all stakeholders, taking into account that many details for both, manufacturers and Notified Bodies, are still under discussion.
2. Capacity shortage for some medical device codes.

3. Workload for two legislative frameworks running in parallel for a period, from May 2020 until May 2024.

In July 2018 MedTech Europe wrote to its members with an assessment of progress and next steps on the "State of Play". This was a very detailed report that lay out many concerns and much of it was of the theme of all that had to be done with not enough time to do it. The lack of sufficient MDR 2017/745 readiness and the limitations of the grace period mechanism to May 2024 were the two key problems.

The key messages from this report were

1. Industry invests heavily to comply with the new medical device and in vitro diagnostic regulations;
2. Industry sees slow progress in putting the necessary essential elements of the new regulatory systems in place, e.g., Notified Bodies, implementing acts, expert panels, reference laboratories and common technical specifications;
3. Industry stresses that the mechanism to provide existing products with a grace period, which exists in both regulations and ends for both on 26 May 2024, does not provide a system-wide solution;
4. Industry calls for an urgent discussion of solutions, including the following three options, which could be pursued either separately or in combination: a. A 'stop the clock' mechanism, that freezes the remaining transition time for both regulations until full readiness of the system has been achieved;
5. Industry certainly welcome the principle of a 'grace period' but not the way it is proposed as currently it is set up. (MedTech 2018b).

Despite the European Commission's confidence that the current certification system is sufficiently robust to deliver MDR certification in a timely manner it remains very difficult to accurately predict the actual readiness of all the affected stakeholders from Manufacturers, Notified Bodies, member countries and even the European Commission itself. Will the essential elements of the Eudamed database really be ready in time?

Any manufacturer failing to receive their MDR certification in time and who hasn't planned for same by way of either securing a temporary extension of their existing MDD certificate, or, by front-loading their supply chain stocks to bridge delays in the introduction of new product onto the market, are exposed to several risks.

- Reduced revenues and cash-flow generation leading to loss of profitably and restricted financial flexibility;
- Sectoral competitors will replace missing manufacturers, rapidly building market share (often hard-won in the first place) which can be difficult to regain even when a manufacturer returns to market; and,
- The lack of a valid CE mark (even temporarily) could disrupt extra-EU markets where they rely on CE as a passport for access to their markets.

Certification delays will inevitably mean that many companies aren't permitted to continue selling affected devices after May 2020 because they lack valid MDR certification. With any extended period of restricted access to the EU market it is feared that innovation in the sector will falter with manufacturers instead attracted to markets with lower compliance requirements such as the United States, where it becomes easier to achieve reliable market clearance.

This is a really important time for industry, Notified Bodies, Competent Authorities and the European Commission and everyone will have to work very closely together to get through this crucial time within the medical device sector.

5.3.7 Post Market Surveillance

Post-market surveillance only came up 5 times over the course of the 12 interviews and was not ranked high in the survey results with only three (3) respondents ranking this as their # 1 challenge, three (3) ranking it as their # 2, and five (5) ranking it as third biggest challenge. Manufacturers are required to actively gather information from post-marketing experience and update their technical documentation accordingly. This is possibly down the priority list as it is one of the last tasks to complete, albeit an ongoing task thereafter. Manufacturers may well be concentrating on the getting the product onto the market and this may feature as a more prominent challenge at a later point in time. There are new deliverables to be completed as part of this stage in the product lifecycle, such as PSUR. The interviews would suggest that many companies had not yet developed a plan for this process of data collection nor have they procedures developed to describe the strategy for post market activities.

In general, larger companies seem to be better prepared than smaller companies. Most of them had dedicated teams working specifically on MDR, as opposed to the smaller ones building it into existing workforce capacity.

One of the new major changes is the increased focus on post market surveillance. Post market surveillance will be used as a tool to distinguish flawed devices on the market from those that are safe and effective. The requirements are in chapter VII, article 85 of MDR 2017/745. The post market surveillance plan is developed based on the risk plan and classification of the device. The MDR significantly increases the role of PMS, requiring a 'post-market surveillance system' to be an 'integral' part of a company's quality management system.

There is a section within the technical documentation file dedicated to PMS. The details of what is required is outlined in Annex III. This will consist of the post market surveillance plan, the PSUR (periodic safety update report) and the PMS report. The PMSR is intended for low risk Class I devices. It will summarise the results and conclusions of Post Market Surveillance (PMS) data along with a rationale and description of any corrective actions taken for products on the market and forms part of the technical file. It is updated as necessary and sent to Competent Authorities when requested. The PSUR is a similar document only for higher classification devices, class IIa, IIb, & III. This document will include results and conclusions from PMS data including vigilance reporting, and current status of these devices on the market in the EU. It will also include a rationale and description of any corrective actions taken for product on the market, if applicable.

"The words 'post-market surveillance' (PMS) appear 129 times in the new European Medical Devices Regulation (MDR). This repetition is not accidental. The requirements for manufacturers to 'actively and systematically' gather, record and analyse relevant data for the lifetime of each device they market is work most companies had not been conducting effectively – and the European Commission wants that to change" (Ward 2019).

While this initiative brings additional workload and cost, it is a very positive initiative and may mitigate costs in the long run. Slow reaction to post market data can be costly in more ways than one, and this can be seen through some of the examples of incidents in the field referred to earlier such as the PIP and MOM stories. Speedy reaction to the possibility of adverse incidents will ensure any potential risk to public health is minimised.

5.3.8 Cost

It was interesting that cost was ranked as one of the lesser challenges, even though it is well known the enormous cost MDR2017/745 will impinge on manufacturers. If individuals working in finance took this survey, perhaps this result would look different. Sometimes

regulatory, and particularly those working in large medical device companies are detached from the financial aspects of the business, hence the author was not surprised with this data. While cost is an important factor, compliance with the regulation is mandatory, therefore cost is somewhat irrelevant.

The costs associated with achieving full certification under MDR are having a significant economic impact on affected manufacturers. Not only is MDR a requirement for all new products brought to market but all legacy products must also comply, and this is significantly increasing the cost factors to be considered as there is no grandfathering from the current EU MDD permitted.

Costs are being incurred right across the product lifecycle from R&D to Testing, Production, Marketing and Sales, Economic Operators. These costs are substantial and include multiple aspects as illustrated in Figure 33 including;

- labour costs;
- the enhancing of all affected technical files;
- the updating labels and IFU;
- the development of clinical evidence and additional post-market surveillance activities;
- the implementation of comprehensive product tracking through UDI & Eudamed;
- the enhancement of required IT & software development programmes; and,
- Notified Body submission fees.

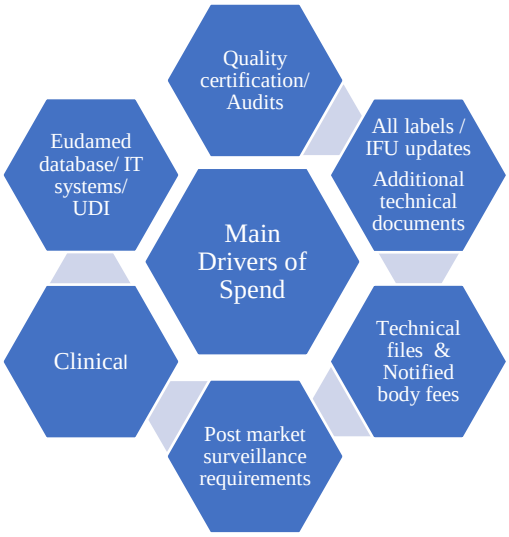


Figure 33: Drivers of Spend

(Created by the Author)

The associated expense factors with MDR compliance bring into sharp focus for manufacturers the cost versus return on investment (ROI) impact of securing the necessary certification for affected products. A thorough analysis is needed to determine whether the potential ROI will exceed the expected costs of compliance, particularly for lower revenue, older generation, legacy devices.

Manufacturers are being driven towards critically reviewing their current device portfolios and ultimately into decisions to retire early some older legacy products (particularly where more advanced versions are already on the market or are in development). Next generation product versions tend to offer better ROI and be considered as superior to older devices.

MedTech Intelligence has developed a detailed survey to gauge what industry believes will be the effect on costs of the entire compliance effort related to MDR. (Fontanazza 2018). One of the questions asked in this survey as outlined in Figure 34 is -what % of company EU revenue do you expect the compliance effort will take? The results are stark with over 50% of respondents indicating that they expected a cost factor of over 5% of annual revenue as a direct consequence of securing MDR Compliance. This kind of cost burden is onerous for any business and without careful management could undermine profitability significantly.

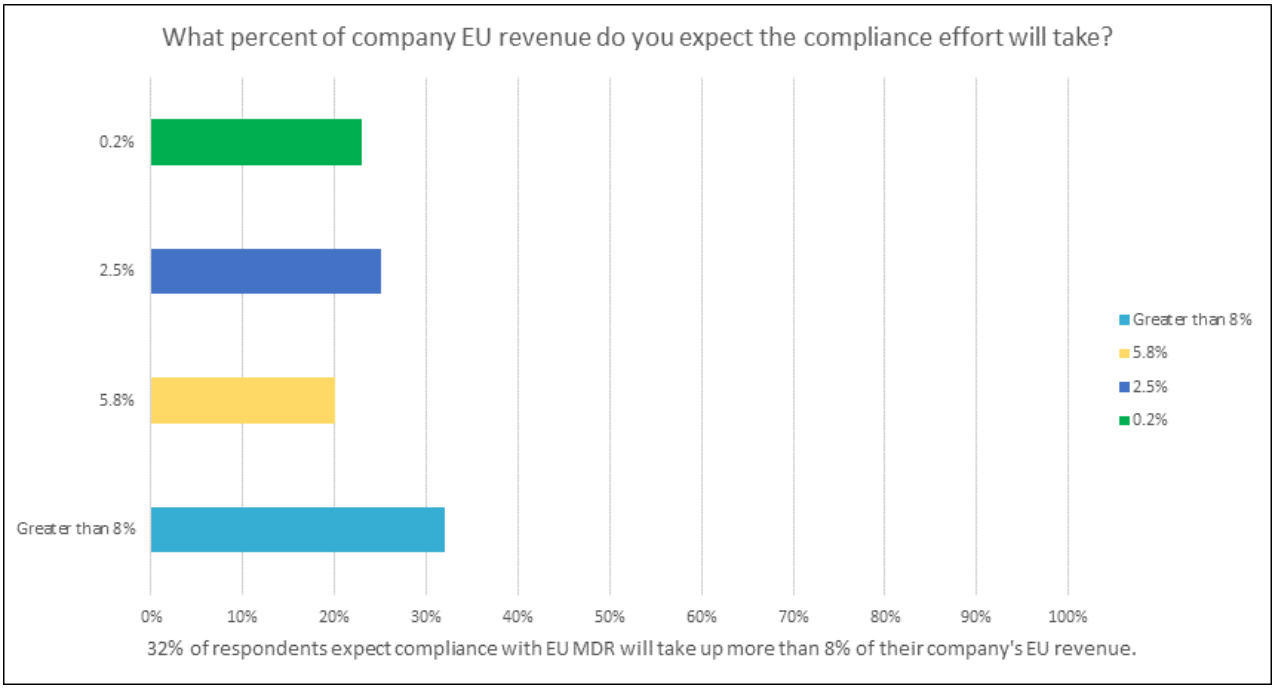


Figure 34: EU MDR Cost of Compliance- The Results are in.

Taken from (Fontanazza 2018)

With the first MDR deadline less than 12mths away (May 2020), manufacturers need to be assessing (and prioritising accordingly) their existing and pipeline product suites, with a view to removing products that are no longer financially viable, focussing on those with the highest potential.

Meeting the new MDR requirements for clinical evidence, device tracking and quality and risk management will necessitate significant alterations to existing operational, financial and marketing strategies. These changes will span the organisation and will require significant resource allocations with the impact of MDR going well beyond the traditional regulatory compliance function.

The complexity of the new MDR regulations will challenge many manufacturers and given the company wide impacts outlined above, those organisations that have incorporated adequate budgets are best placed to secure an effective transition. The magnitude of the financial and operational implications of MDR compliance suggest that the financial officer and the operations officer should take lead roles with an assessment of costs globally and allocated by product

resulting in the allocation of significant, adequate and ultimately necessary funding required to support the certification efforts.

5.3.9 Additional Reviews

The challenge of additional reviews came up nine (9) times during the interviews. It ranked low in question seven (7) of the survey, with only one (1) person identifying this as their biggest challenge, two (2) ranking this as their second challenge and five (5) it as their third challenge. Under MDR, class III implants and active class IIb products which are intended to administer and/or remove medicinal products from the body are subject to a double safety mechanism. A process called the "scrutiny procedure" will be applied to some medical devices that the Notified Bodies deems to have a higher risk of application. This will add on time to the review process and potentially delay product approvals. During this process the Notified Body documents a report on the clinical assessment. The European Commission forwards this to the expert panel. The panel decides if they will submit their own specific opinion on this review. The Notified Body must take the expert panels viewpoints on board. If no expert opinion is submitted, the certification procedure may continue.

"For certain high-risk devices, the new Regulations require the Notified Bodies to consult with an expert panel before placing the device on the market. According to this procedure, an expert panel could provide a scientific opinion to the Notified Body on its assessment of the manufacturer's clinical file. While the Notified Body would not be bound by the opinion, it would have to provide a justification for not following it. All relevant documents regarding the opinion and the final decision of the Notified Body would be publicly available in EUDAMED" (Commission 2017b).

Fortunately, the scrutiny process is only applied for devices which are new at the time of the conformity assessment application for the MDR.

5.4 Summary

This chapter analysed the results of the literature which was identified as part of phase I. This was followed by a review and analysis of the results of the interviews and the survey. The challenges were ranked per question seven (7) of the survey. Each of these challenges were then discussed individually to outline the impact each would have on the regulatory affairs professionals, and industry in general.

Chapter 6 Conclusion

This chapter outlines the conclusions of the completed research and documents the possible next steps for future research. The aim of the research was to identify the challenges faced by regulatory affairs professionals in implementing impending regulation 2017/745 and to use the research findings to help companies plan existing and future sales strategies for devices in the EU market.

Several research methods were employed to understand the key challenges introduced by MDR 2017/745 through conducting a literature review, qualitative interviews and a quantitative survey. The analysis of the literature discovered the lack of published documents on this topic which underlines the value and importance of this research. This research will provide data to help manufacturers plan for the challenges ahead.

In -depth interviews were conducted with twelve (12) industry stakeholders including regulatory personnel working in small and large Medical Device companies, industry experts employed in the Notified Bodies and Competent Authorities. The output of the interviews was examined and stratified into nine (9) challenge themes which were then further analysed using a broader web survey tool. Multiple respondents, fifty-nine (59), were asked to rate the identified challenges from 1 – 9 with one (1) being the most challenging and nine (9) being the least.

Results are outlined below in Figure 35.

Figure 35: Ranking of Challenges Highest (1) to Lowest (9) from the Output of the Survey (Created by the Author)

Summary of the findings

1) Change Management: As per outlined in section 5.3.1, manufacturers have significant concerns regarding the management of changes to existing products post MDR implementation date of May 2020, with design changes or changes to intended use on existing products restricted. The restriction on changes will hinder further innovation on existing products and may lead to supply issues if business critical design changes are required for any of the products prior to their conversion to MDR.

2) Resources and Workload: Resources requirements and workload increase were also cited as a major concern, particularly in terms of the capacity within Notified Bodies. There is a reduction in the number of Notified Bodies (a drop from 83 to 58 at the time of print of this thesis) in Europe yet their workload has increased significantly. This concern is discussed in detail in section 5.3.2.

3) Awareness and Training: Serious concerns over the level of training and MDR awareness were repeated frequently during the research underlining an over-riding sense confusion

over the implications and scope of MDR. It is difficult for suitable training to be designed, developed, and delivered if there is a lack of clarity on the precise requirements and expectations of the regulations.

The completed research indicates that Medical Device manufacturers and Notified Bodies are investing time, resources and effort on MDR training but are having to update it constantly as further information becomes available – See Section 5.3.3. Having the right training and knowledge is critical and will be the key to success for companies seeking MDR compliance.

4) Lack of Clarity: The research revealed a significant lack of clarity within the MDR with one interviewee putting the situation as like "moving into a house as the house itself is still being built. We don't have a system; the system is not ready" (Interviewee #6). It appears the EU Commission are pushing to introduce MDR even whilst still framing its intended final shape. Section 5.3.4 details respondents concerns on the lack of clarity around MDR certification which was one of the most repeated challenges raised by interviewees. Industry is leaning on the regulators for direction whilst the Notified Bodies themselves cannot provide sufficient guidance to industry as they themselves are seeking direction from the Competent Authorities. Everyone is depending on the Commission for guidance much of which remains absent and which is creating a ripple and growing frustration effect in moving forward.

5) No Grandfathering: As discussed in section 5.3.5, legacy devices currently on the market (and CE marked under existing directives) will also need to meet the new requirements as outlined in MDR. There is no grandfathering allowed which will bring substantial challenges, particularly in the area of clinical trials as many of these legacy products do not have had clinical trials to support them, (thereby presenting potential issues in convincing the Notified Bodies that this is acceptable).

6) Compliance by May 2020: Respondents also believe that an adequate sense of urgency is not being evidenced by the EU Commission which is supported by MedTech Europe's' own July 2018 guidance to members in which it stated –

"However, the medical device manufacturers' ability to place the majority of products on the market by 26 May 2020 is jeopardized by the slow regulatory progress, and lack of transparency thereof. Considering that the (re-) certification period from file submission to approval by a Notified Body is estimated to take six (6) to twelve (12) months, it

becomes evident that – if no solutions are put forward – health systems across Europe might face a 'perfect storm'" (MedTech 2018b). During interviews, the expected final implementation date of the 26th May 2020 was of particular concern for respondents and considered wholly inadequate. This is discussed in further details in Section 5.3.6. Not only is it difficult to predict when manufacturers will be able to submit files (as they are waiting on the Notified Bodies to get designated) but it is also evident that clearer implementation guidelines are necessary to achieve a successful and timely adoption of the new regulations.

This timeline challenge was highlighted in a letter by Serge Bernasconi, chief executive officer, MedTech Europe, to Mr Jykri Katainen, Vice President of the Jobs, Growth and Competitiveness section of the European EU Commission on 15th April 2019,

"The Medical Device industry in Europe confirms that without immediate action by the European EU Commission, the new regulatory system will not be ready on time to ensure continued access of patients and healthcare systems to life-saving and life-transforming devices" (Bernasconi 2019). He goes on to state, "This situation is clearly untenable, and time has run out to build a functioning regulatory system. This set of circumstances will profoundly disrupt the medical technology internal market and create yet another significant 'Cliff Edge' putting patient safety, healthcare services and EU healthcare environment in major disarray" (Bernasconi 2019).

7) Post Market Surveillance: In the MDR there is a much greater emphasis on manufacturers actively gathering information from post market surveillance activities with a view to updating their technical documentation accordingly. These new requirements, whilst adding to the work burden facing manufacturers, are a positive initiative and will improve transparency if there are negative trends in the field. This is discussed in detail in section 5.3.7, and, whilst not at the forefront of respondent's concerns will become more of a challenge in the long term when manufacturers are actively completing this activity.

8) Cost: The financial burden of achieving full MDR certification is having a significant impact on affected manufacturers. MDR certification is a requirement for all new and legacy products and with no grandfathering of certification permitted the cost profile of the achieving MDR is onerous. In fact, many smaller companies cannot afford this burden and may well end up getting bought out by bigger companies or closing their business. See section 5.3.8 for an analysis of the MDR cost drivers.

9) Additional Reviews: The additional review built into the process for some class III implants and active class IIb products which are intended to administer and/or remove medicinal products will potentially slow down the approval process even further and will add cost. This review is known as the scrutiny process. The new process will bring its own challenges with new decision makers and different expectations on evaluating patient safety.

The new Regulations will create a robust, transparent and sustainable regulatory framework, recognised internationally, that improves clinical safety and creates fair market access conditions for manufacturers." (EU Commission 2019).

It is clear from the survey that respondents are taken aback by the magnitude of change involved in implementing 2017/745, further hampered by a significant lack of clarity on some aspects of the regulation. Other areas of concern identified included; clinical evidence, post market surveillance, vigilance, labelling, UDI, and Eudamed. Even as these highlighted concerns are getting intense focus at the highest levels in the affected organizations the reality is that there is no simple fix. There are so many strands to the challenges that arise with significant complications involved in most. Even the US raised serious concerns in a statement to the World Trade Organization (WTO) 24th July 2019. "Our industry is worried about their continued access to the EU's USD 125 billion medical device market, USD 20 billion of which is supplied by US products" (Mulero 2019).

The technical complexity, cost, time and resources involved in implementing MDR are reshaping how companies are choosing their markets. If companies are forced to conduct clinical trials, this will lead to significant additional costs and Europe may not feature on the sales map for some of these products going forward. Medical Device manufacturers will need to focus on their business pipeline, removing products that are no longer viable and focusing on those with the highest potential.

Overall Conclusion from the research:

I believe my thesis demonstrates my ability to contribute original work to an already heavily debated topic in the Medical Device industry at present. Introduction of this regulation will dominate the thinking and actions of the Medical Device sector in Europe for the next few years. As discussed in section 4.1, this research provides valuable information where existing literature is scarce. It will provide support to industry as companies can use the data provided to focus their resources on the main areas of concern. They can also use it to sanity check their current progress with compliance and ensure they are working on the right areas which regulators and other companies feel are important.

The challenges identified in this research are real challenges and ones that are going to take time, resources, effort and money to resolve.

Future work:

The research presented in this report offers opportunity for future research projects. The likelihood is that the challenges faced by regulatory professionals today will change as more experience is gained. Analysing the challenges in a years' time may prove to be different types of challenges. The impact on the healthcare markets may be different. It would be expected that there will be much more literature published at a future point in time also which would help support further analysis.

This research excluded the challenge of "clinical evidence" which is one of the biggest challenges of MDR 2017/745. Future research could explore this and review how current clinical evidence is being accepted by the regulators, or if companies are being mandated to conduct clinical trials.

It would be interesting to do a deeper dive on the results of the survey to analyse individual results of each respondent in more detail. That would allow separation of the results of the regulators from the medical device manufacturer respondents thus providing a clearer picture of the challenges from the different organisations. While this thesis only focussed on medical devices under regulation MDR 2017/745, the scope in future research could include devices under regulation 2017/746, which is on *in vitro diagnostic* medical devices.

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Appendix A Interview Consent Form

Challenges for the Regulatory Affairs function in demonstrating compliance for existing CE marked devices to the new EU Medical Devices Regulation 2017/745

Consent to take part in Research

I _____ voluntarily agree to participate in this research study.

I have had the purpose and nature of the study explained to me and I have had the opportunity to ask questions about the study.

I understand that I can withdraw permission to use data from my interview at any time after the interview, in which case the material will be deleted.

I agree to my interview being audio-recorded.

I understand that signed consent forms and original audio recordings will be retained by the researcher until the exam board confirms the results of their dissertation.

I understand that all information I provide for this study will be treated confidentially. Neither my own identity, nor the identification of my organisation will be revealed.

I understand that under freedom of information legalisation I am entitled to access the information I have provided at any time while it is in storage as specified above.

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Signature of the participant Date

I believe the participant is giving informed consent to participate in this study

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Signature of the researcher Date

Appendix B Interview Guide

Introduction: 10 minutes.

Hello. My name is Noeleen Mc Devitt. I work in Boston Scientific medical device company as a Senior Regulatory Affairs Manager. I am currently studying a MSc in Medical Technology Regulatory Affairs. As part of that course I am writing a thesis. The particular topic that I choose to research is on **"The Challenges for the Regulatory Affairs Function in demonstrating compliance for existing CE marked devices to the new EU Medical Devices Regulation 2017/745":** otherwise known as the MDR and referred to hereafter as same.

As is well known, among the vast changes occurring with the transition from directive to regulation are the new requirements surrounding clinical evidence. This certainly is a huge challenge for industry and something we could talk about all day, however, for the purposes of this research I am choosing to exclude the topic of clinical to focus specifically on the regulatory affairs function, and their challenges.

I would like to thank you for taking time out of your busy schedule to accommodate this interview and I look forward to getting your opinion in this area. There are no right or wrong answers here, the purpose of the interview is to hear your experience to date in this area. This will allow me to identify the challenges.

NMD: We have all been talking about this new regulation for many years, and now as it is upon us I would like to discuss this further with you to seek your opinion on the challenges we face.

Setting the scene:

- The interview is set up as a semi structured interview where I will ask you some specific questions, but I would like it to be flexible and let us explore issues that arise spontaneously.
- I would like to point out that everything you say in this interview will be confidential and will only be used for the purposes of research for this thesis. You will not be identified by name or organisation.
- I will be recording the interview so that I can transcribe from it later.
- I expect the interview to be completed in approximately 45 minutes.
- If I ask a question that you are not comfortable answering, you can just ask me to move on.

Do you have any questions for me before we commence the interview?

Background of the participant: 5 minutes

Can you tell me a little bit about your background, your current role and how you are involved in the MDR regulations?

Interview: 30 minutes

What do you foresee as the "**challenges for the Regulatory Affairs function**" in bringing existing medical device products in line with the new MDR requirements.

Probing questions if these 5 topics do not come up as part of the free flow of the interview

- Change Management
- Resources
- Time
- Lack of clarity
- Training

1. Is the introduction of MDR impacting change management in your organisation and if so could you please explain how this is happening?

   When interviewing Notified Bodies this question was switched around as per below.

In Industry we are starting to feel the restrictions of change management in leading up to the May 2020 date in that we are limited with the number of submissions that the Notified body can get to review. What is your position on this?

2. Has your organisation made any changes with respect to resources or set up any specific roles to deal specifically with MDR.

3. Do you feel that we will have enough time to implement our files by May 2020? If not, how will you work around that?

4. Do you feel there is an understanding of the requirements of the MDR and how has your organisation approached training for this topic?

Interview wrap up:

Is there anything else you would like to cover?

I would like to thank you for taking the time to talk to me today. I have enjoyed hearing your perspective on what you perceive to be the challenges for the regulatory affairs function. I appreciate your comments and experience you have shared. I will take your feedback and extract some of the challenges identified. I would like to re assure you that the interview is confidential and will not be directly traceable back to you.

I will be working on this thesis over the summer of 2019 and would be happy to share the final research when it is complete.

My contact details are, mcdevitn@bsci.com or 087 9808218, should you wish to contact me at any time. I will provide these details to you by email.

Appendix C Transcripts from Interview C1

Interview with Noeleen Mc Devitt (NMD) and C1.

Hello [redacted]

Hello Noeleen

NMD: My name is Noeleen McDevitt and I work in Boston scientific it is a Regulatory affairs manager I am currently studying the master's degree in medical technology regulatory affairs and as part of that course I am writing a thesis the topic that I chose for my thesis is the challenges for the regulatory affairs function in writing technical documentation to comply with the new regulations. we will refer to these new regulations as the MDR from here on. I would like to thank you for taking time to talk to me this morning and to do this interview. There is no right or no wrong answers. I'd like the Interview to be open and flexible if I ask you any questions that you are not comfortable with you can just say that and we will move on. The purpose is for me to hear your experience and your involvement in the regulations to date. This will allow me to identify the challenges.

So just before we start I would like to go through a few things with you. The interview is set up as a semi structured interview. I would like the interview to be flexible and for us to explore issues that arise spontaneously. I would like to point out to you that everything that we discussed today will be confidential and will only be used for the purposes of this research thesis. You will not be identified by name nor by organisation. I would also just like to let you know that I am recording this interview so that I can transcribe it later to read in detail. I expect interview to go on for about 40 minutes. I would also like to let you know [redacted] that if I ask you any questions during this interview that you are not comfortable with or don't want to answer we can just move on.

Do you have any questions now for me before we start the interview?

C.1: So, let me just clarify you are asking about challenges for the regulatory affairs professionals in in line with the MDR

NMD: Correct.

Also, before we start I would just like to point out one thing. As we know that we all been talking about this regulation now for many years and it is now upon us there are lots of changes happening with this new regulation and we know that clinical is a huge focus of the changes to the MDR.

We know the that clinical is a huge challenge that we as manufacturers will be dealing with, but purely for the purposes of this research we are going to exclude the topic of Clinical. The clinical functions within industry will be primarily dealing with this challenge. As you and I know that clinical is a huge challenge but we're not going to talk about that today during this interview.

C.1: Ok

NMD: So, my main ask of you Susan is really, as a regulatory affair professional in the medical device industry what do you see as the main challenges as we worked through bringing our files in compliance with MDR. And maybe before you start if you could give me a little bit of background on your role within industry and how you are involved with the regulations.

C.1: I have been working in regulatory for far too long or approximately "laugh" 20 years at this stage. I mainly work with notified bodies, so I am European focused somewhat and deal a lot with sterilisation. I am involved in standards as well. Standards development and that is an area we are keeping an eye on in terms of MDR. I am part of the core team within [redacted] that is tasked with looking at this and I guess we've been looking at this for a long time.

I have been involved doing some training with regulatory- affairs function so I would say I am somewhat not knowledgeable on the MDR.

NMD: great, that's great. You have great experience so.

C.1: Well, yeah. "Being modest" There are a lot of changes so i don't know if everyone knows everything, but yes, we have been preparing for a while.

NMD: How long would you say [redacted] you are preparing for it?

C.1: Well, since the draft was issued and that was always a challenge. We didn't know how much they changed or not, so we have been looking at those and doing draft gap assessments against the existing requirements for years. 3 years maybe.

NMD: Right, that's a long time so.

C.1: Yeah, it's a long time.

C.1: Am I ok to jump into challenges?

NMD: Yeah that would be great.

C.1: well I think my first one is that tied to that is it's been on the go for such a long time and it's a huge change to industry in Europe and one of the challenges for reg affairs is just understanding all the changes that have happened? How it relates to the existing MDD, and AIMD. EM, I think there is a lack of clarity. I mean we have the text but so much has changed and there's talk of supporting documents and guidance and help that will help facilitate the transition, but a lot of those documents are not available yet. So, and I am going to talk now about standards as that is

an area that I am involved in, e.g. they talk about harmonised standards, and the fact that they are, you know, the standards will now be harmonised against the new regulation. em. And they won't be done until 2024, which is no use when we have a time crunch. So, there's 5 standards that is going to be harmonised this year in 2019, but they haven't even at the stage yet when we can stand over the fact that they will be done in 2019. So, I think guidance and support and having that not available it makes things difficult.

I talked about the fact that we have done training within [redacted] for our reg affairs personnel, that was basically a training session and even at that there is so much that has changed.

NMD: Would that training have touched on everything or was it just on specific aspects of the MDR. Did it focus on anything in particular?

C.1:: Well we focused a lot of it on the Notified bodies, everyone deals a lot with the different Notified Bodies so we talked a lot about that aspect of it and how we were going to manage that piece of it, and then we were going to focus on our technical documentation, so we focussed on what was previously technical files and design dossiers, what was new ? what to look out for? Big things that would jump out, that there are new material assessments required, you mentioned clinical that you did not want to focus on clinical, just eve the new documents that are required such as the post market documentation, there is now a new section in the MDR for post market documentation and that is something the reg will own. At least the collation of that data will be reg owned, so that will be brand new. Material assessments I mentioned there are new requirements to test for material composition, that is all new area that reg affairs need to get their heads around. The fact that we cannot grandfather any existing products, we basically have to write new submissions for them all which is a huge burden on reg affairs. We now have to manage all those products, especially in a large organisation where you have multiple products, and some products which have existed for years, we have to transition them and bring them up to date with this new regulation. So even just the workload involved with the fact that we need to update all our documentation and potentially test for some of these material aspects, so a lot of work, a lot of products in our case and just to understand how it all ties together.

Apart from that then there is change management, how do we manage the business when this is going on, how do we keep our business ticking over and make changes that we need to make while we are considering MDR, there are two aspects to this. The MDR has brought certain restrictions, you know, once 2020 comes for your existing CE marked products then you can't make significant design changes or changes to intended use. Em, so how do you manage that, how do we as reg affairs professionals do not allow those changes to happen, or that we got them

early in the process so that teams do not spend a lot of time working on those changes and then we tell them that they can't do them in Europe.

NMD: Just on that, would you say other functions are aware of that time crunch, and that freeze that is going to happen with change. Do you think operations are familiar with what is going on there?

C.1: I would say it has been a challenge, I don't know if everyone is aware or that they understand what it means. I think they understand that MDR is coming, and that there will be restrictions, but when we get down to the day to day application of that I think people struggle with it. I can talk to the sterilization experience, that we need to be able to sterilise our products to get them on the market and we have loads of projects in the pipeline you know to increase capacity, just develop our cycles, approve, just because thankfully our business is going well, and we are going to have more volumes , then we really need to have more sterilisation capacity. For some of them, I am telling teams you can't do this after May 2020 until your product transitions and some of our products are not transitioning until 3 years after that date, so its understanding how you manage that piece of it, and, prioritising appropriately. So, having some method to prioritise across the organisation, because the other piece that comes into change management is notified body resources.

So, all changes that are significant and have to be approved prior to implementation, they need to go into our notified bodies. They are struggling already. They have put restrictions in place because of the workload. They understand that we are going to basically you know transition everything to MDR. They are getting designated, they are doing all this good stuff. The workload on them is huge. They have said to us that we are going to have to slow down and stop in some cases. So, some of our notified bodies have restricted us from doing submissions from next month. So, they are saying from March 2019 you need to stop guys. We have other dates from other notified bodies from august 2019. But we need to keep the business going so it is managing their resource issues with the fact that we still need to make change. So those e two aspects, notified body resources and how they manage it and the fact that there are restrictions under the MDR for changes and in an organisation like ours where you have various divisions, various priorities, conflicting priorities, it is managing the overall picture for [redacted] with our notified bodies is a huge challenge, prioritising it appropriately , So I guess that patients get the products that they need .

NMD: Yeah, I hear you, but I suppose we are not the only company in this boat. I am sure all other medical device companies are going through the same thing and I am sure the notified

bodies are hearing about this too from other companies', so they are under pressure too other companies as well.

C.1: Yeah:

NMD: Just in saying that do you think it may come to a standstill in industry where you, or the commission may be forced to extend the date. Do you think that is a possibility?

C.1: I think it is a possibility in that there has been more discussion about it recently, but it not is something that we can guarantee, so from our point of view we have been working towards that date of May 2020 presuming that is the date. If we get longer time or there are extensions, then happy days, but we just have to work with this date and work with our notified bodies to make this date. They are struggling also because there is a reduction in notified body numbers. So, you know, a lot of these products have to go somewhere so they are going to the notified bodies that exist today. So, there is just more workload across the whole of Europe.

NMD: Yeah, the whole of Europe.

Can you tell me how has your company hired many people for the MDR project and if so what area would they have hired them in?

C.1: It's a very good question and I am not even sure if I know the answer. I know that they created positions internally for this and changed people's roles to accommodate this but as from hiring from external, yet I am not sure. I don't think we have hired in regulatory affair and that might be because that up till this point we have not been heavily involved. As in, until all these other functions get their documentation together, and until we get the Notified bodies designated we can't submit any of the technical files, we can't transition any of the products, so I feel like the reg affairs part of it probably hasn't sunk in yet for reg affairs. There may be a chance of more people in reg affairs, but not ye.

NMD: I agree this is inevitable. This is coming down the tracks. I think in 6 months' time even, we will see a lot more traction when the notified bodies are designated, and we are in a position to start submitting our files.

C.1: Yes, it's still very early yet.

NMD: What is your thoughts [redacted] on the possibility of the drug agencies having to re review the files even though technically nothing has changed with the device.

C.1: Yes, that is a challenge for BSC as we do have products that have both drug and animal tissue. There are no new requirements in the MDR for those areas, however, there is the requirement that you must have your product transitioned like a new submission, therefore there is that requirement or perceived requirement that you must go through that again. There are areas with the MDR where the practicalities were not though through. Down to the nitty gritty, that the

politicians writing these documents understood the practical applications of it, so that we now must live with that. The only hope is the notified bodies and these agencies will have some common sense and if we do have to do a review, that it is a minor review and that they are practical.

NMD: That will slow things down for sure if we have to go through those full reviews again.

C.1: The other area that we are concerned about is that we do not have enough knowledge on the clinical evaluation consultation process. (CECP) You may not want to talk about it as you are excluding clinical, but it is a consultation process that calls out for certain classes of devices, and we would have devices in those categories and that process is not in place yet, and so how do you plan for something where there is no panel. It is very unclear and very difficult to plan appropriately when those are not in place

NMD: Yes, I absolutely agree that is going to be a challenge.

C.1: The other challenge is also in line with classification. There have been products up classified and brings its challenges. Lower class products which are now considered class III products, will create a bolus of work associated with that. This is more related to resource workload point of view.

The other one, which is gone out of my head!!

NMD: Was it the class IIb implantable being treated like class III.

C.1: Oh yeah, it was. So that is a big change. We would have had changes before that we would never have considered for the lower-class devices and now we have to treat them same as class III. That's a big shift in our thought process and increases the amount of submissions required and all that good stuff, so that is going to be a challenge for us as well.

NMD: There certainly is a lot of challenges for us there [redacted],

It's great to hear that everyone is having the same challenges

If you were to pick 3 challenges of everything you talked through, what ones would you pick as ones that is going to be a burden.

C.1: The first one I would pick is change management, just resource piece of it, and the notified body and managing that together is a big concern, and the fact that we are restricted at what changes we can make.

The next is that we can't move anything, and time is ticking fast. We have one notified body who is designated but it is of no use to us as they are UK based and with Brexit they are of no use to us. At the minute we can't transition, we can't start doing anything and if they don't transition to the end of the year, it's very late when we have a May 2020 deadline.

It is very difficult to co-ordinate all this.

NMD: I think when this all started out we thought the notified bodies would be designated a lot sooner and we would have more time on our hands to work towards to May 2020.

Well [redacted] that has been great talking to you today and I would like to thank you for that. I have enjoyed hearing your perspective on what you perceive to be the challenges for the regulatory function. I appreciate your comments and experience you have shared with me. I will take this feedback and extract the challenges from it. I would like to assure you again that this interview is confidential.

I will be working on this thesis over the summer and I would be happy to share it with you when I am finished. So, thanks again.

C.1: Not at all, your welcome, thanks Bye.

Appendix D Transcripts from Interview C2

Interview with Noeleen Mc Devitt (NMD) and C2.

Hi [redacted]. How are you. This is Noeleen Mc Devitt from Boston Scientific, working in Regulatory affairs. I am currently studying an MSc and as part of that course I am writing a thesis. The particular topic that I have chosen to write on is in relation to the challenges faced by the regulatory affairs function in the medical device sector in bringing our files in line with MDR. As we know there are many challenges associated with MDR, and one of the biggest challenges is around clinical evidence. So purely for the purposes of this research I am going to exclude that topic as I think we could talk about it all day, for many days, and a few thesis on this subject alone could be written, however I am not in an expert in this area, and for that reason I am excluding it from this thesis.

I'd like to thank [redacted] for taking time out of your busy schedule. This is going to be a semi structured interview where I am going to ask one leading question and we will see where that takes us. I would like us to be flexible and explore issues that arise spontaneously. I will be recording the interview to transcribe it. Everything as I said will be confidential. If its ok, we might just start off if that is ok with you [redacted]

C2. Oh yes that is ok and its lovely to talk to you Noeleen and delighted that I can help in any way.

NMD: Excellent. So, [redacted] would you be able to tell be about how you are involved in the MDR as part of your role to date.

C2. Sure, so I work for a NB, and as part of that we are obviously aware of the MDR requirements. We have requested for designation to the Dutch Competent Authority. I am part of an organisation where we are going to be looking at the implementation of the medical device directive in companies that uses a Notified Body. This is my involvement in MDR so far.

NMD: So, you are very involved so.

C2. Yes, indeed it would.

NMD: Ok that's great.

What do you are the challenges for Regulatory working in industry in implementing this new regulation.

C2. Well I think the first challenge is getting a handle on it and reading it. It is much longer that the Medical Device Directive. I am sure you can find word counts and things like that to do the comparison but even just looking at the sheer volume of it putting them side by side as printed copies you can see that there is a huge increase which obviously means that there is more information that is in there that needs to be read, digested and see what applies. So that to me is the first challenge to read all the requirements.

NMD: Yes, exactly and understanding them, and as we know they are not straight forward in all cases and a lot of it is up to interpretation. I presume you are finding that as well.

C2. The second big thing is that we as a Notified Body are not allowed interpret anything. This is good in one way as hopefully it will lead to a more level set of expectations, however, the ISO's that are supposed to being issued to cover these interpretations such as the Implementing Acts and the Delegating Acts, these have not yet been done. This makes it difficult for a Notified Body to answer questions.

Companies will often ask questions such as "what do you expect from a particular section, and we have to say we really don't know, and we have our own ideas but until everything has been sorted out and our designation has been approved we really don't know if this is the way it is going to be". We may not know if it is going to be acceptable. We may know from a big picture point of view, but we have to read the text in the regulation, but we are not allowed interpret. This is a huge difficulty for us to be able to know what it is and to be able to reassure our clients that it will be ok.

NMD: Where will all that end up though? Down the line how will you interpret it, as obviously you will have to be able to interpret it to do business with clients. Is it the Competent Authority, or the Commission, who is going to be that body giving you direction on how to make these interpretations.

C2. We believe it will be coming from the commission. That is the information we have been given. They seem to want it to be a certain way and that was the purpose of the Implementing Act and the Delegating Acts. The problem is that they have not yet been written. However, the clock is still ticking, and they have indicated that there will be no change to the transition date, and that timetable is staying as is. It is difficult to figure out what is going to happen. Notified Body X is going to be having their own get together in April. At that stage we are going to be agreeing our own internal approach and even at that I think it will still be dependent on when we get our designation and anything else that may be coming out from the Commission.

It is not an easy time for anybody.

NMD: That is absolutely very true and anything you have described there is basically lack of clarity from so many different angles.

C2. There is a lot of information in the regulations which is good. There were things which were in guidance documents such as the vigilance system has been brought into this system. So, there is more clarity in something that is in a regulation as opposed to a guidance document. However, we all know what is written down in words is good, but when you come to the practical end of things you need to decide does this apply or does this not apply. This is often times when you need clarification. More clarifications on the logistics to be handled. the practicality of the application of the regulations. I think that's what missing. They have covered quite a lot in the regulation and they have added a lot to it. I think sometimes what is missing is when scenarios that occur in real life, how will they be handled.

NMD: Can I ask you [redacted] how do you feel that change management is being handled, and just from an industry perspective we are starting to feel the restrictions in change management leading up to the May 2020 date. What is your position on this?

C2. Again, I would say this is an area where there is clarity in some cases, but it has not been fully defined. An example of this would be where it talks about you continue to place product on the market under MDD unless there is a significant change, but they really have not defined what is a significant change? and it doesn't restrict the change to just class III devices. Historically companies with an Annex II certificate, if it was a lower-class device, not a class III there was situations because you had Annex II capability, so as long as it was within the scope you could go ahead and make changes.

With the new regulation it does not make any distinction with the class of device. With a significant change, so potentially that could mean a change to any device and in additionally, significant change has not been adequately defined. That is certainly an area where there is some potential for discussion, or clarity and get some more information. It has huge implications to companies. Does it mean that you cannot make any changes to devices until you go MDR route? This is an area to be worried about. It is also worrying for a Notified Body as we would have to review more information as well. This puts constraints upon the Notified Body with respect to resources.

We are actively recruiting but there is only a limited pool of people. If there is a lot more work to be done it just puts a strain on the whole system.

NMD: Yes, that is what we are seeing at the minute. Separate teams and projects want to make changes to their products and we are limited with some of the Notified Bodies we are working with, purely because of the number of changes they will accept. Their resources and time are getting filled up. May 2020 is creeping up on us, so it is coming faster than we thought it would.

C2. Yes, we understand that.

NMD: Do you think you will have to tell companies that there are changes you will not have resources to review. Do you think it will impact business to that extent?

C2. It is difficult to say. We are actively recruiting but it does take time to get people trained up. I know our Notified Body did communicate to their clients that there are certain things we will not be able to review after certain dates.

We have already tried to set expectations. Obviously, the higher risk devices are earlier than the lower risk devices are earlier than the lower risk devices as they take more time. These are the kind of things we are trying to manage expectations with our clients, and if you don't get them in before a particular date, then we can't guarantee that it will be reviewed. The implications of that from a manufactures point of view is not something that I can answer.

I do know that there will be implications. Our deadlines we are talking about this year. The chances are if changes are not in by July 2020, then there's every chance that it is not going to happen. It is really cutting it fine as really, we are talking about a few months as opposed to a year. I think that must be a big concern.

NMD: It is a big concern, and I think the regulatory function gets it, sometimes it hard to get that point across to operations where is no limit to what they want to do. So, we are struggling with messaging that to the operations world.

C2. Yes, and I think the other big concern from our end is that there is no grandfathering.

NMD: Yes, so all Class IIb implantable will be reviewed again and treated like a new product.

C2. Yes, and that is going to take some time, and with any new system it is going to take time as it will be new to everyone. I expect the reviews will take longer, particularly in beginning as everyone will be finding their feet. Once people get in the swing of it and people understand the expectation. When we are doing something new like this we need to figure out how to settle down, what do we need to review, what evidence do we need? So, we are all learning and obviously that is going to take longer. So, this timing issue is going to play into it.

Time is money, so it is obviously going to cost more. While we may not increase our hourly rates, the n number of hours that we will have to do will increase. So, there will be an extra cost, and obviously that cost will be on the manufacturer. That will be another concern, especially for small companies, or for the companies with a large portfolio. It may economically prohibitive for them.

It may end up that they do not transition all devices, which may have an impact to the market too.

NMD: You mentioned resources there earlier. Can you tell me a little bit about that from your organisation's perspective?

C2. We have been trying to recruit. The recruiting process itself is difficult to get people on board. The qualifications are very exacting, and it is quite difficult. It is not just a case of you bring someone in and they are qualified. It could take up to a year to qualify somebody and with the MDR the qualifications of the individual are under more scrutiny too. so, it is becoming harder and harder to get people and training up on the various codes. It is more difficult to select team for auditors and file reviews purely because of matching up their qualifications Vs the codes of products that needs to get covered.

Demonstrating the competence of the reviewer is more onerous for the Notified Body now.

NMD: Yes, that seems to be a restriction hiring for you folks alright.

C2. Yes, qualification paperwork has expanded, and which also has impacted on resources. While yes, we may have auditors, but they may not all be able to audit a particular product code. The qualifications paperwork has expanded, and the demonstration of competence is a lot more. That is a resource problem for all the Notified Bodies and something we need to be mindful of.

NMD: How is your organisation dealing with training. You mentioned there training on the particular codes, but in general how is your Notified Body educating your staff on the requirements of the MDR in general, content and interpretation of it as much you can.

C2. We get together every year as a group for an annual meeting. We use that meeting to figure out hot topics. That is in April this year, so it is only around the corner now. As part of that harmonisation meeting we will discuss this topic. We have already been informed that this will be one of our main topics at the meeting. In advance of that meeting we were instructed to have read the MDR to be prepared and at least have some knowledge of it before we come to the meeting. So that it will make the training more effective. The training will include what our Notified body will be doing. We also have a system within our Notified Body called

[redacted] which is like knowledge modules. In these we have the Notified Body thinking on certain topics.

We would go through any standards that apply, what sort of things to look for during an audit, what sort of things to look for during a technical documentation review, any questions that routinely come with answers to those. We have a system that covers things like clinical investigations, packaging, labelling, all sorts of things. As part of preparation for MDR we are updating those knowledge modules to take into account the requirements of the MDR. So, we are trying to put it into tools that we use during the audit. We would use it as a common support structure with documented procedures and that would be rolled out during the harmonization meeting in April.

Given that it is still draft as we have not yet been designated. While our processes have been audited, they have to be in line with the joint assessment process teams. We cannot really finalise anything until that has been done. That is generally how we are approaching it. We are doing our harmonisation, we are doing our training on the MDR and we are updating our procedures.

NMD: That sounds very structured in your approach and well organised, and it sounds like a great plan that you have in place.

C2. I think we have to be organised. We can't just walk in and say it will work out. We have to make some preparations, even if there are some gaps or holes from information that we don't know, at least we have to be organised for the information that we do know.

NMD: I have one last question for you. When you will be reviewing files in MDR mode, for example a class III file. Do you envisage that it will take more man hours to review these new files when they go back in, and the same goes for a class IIb, do you think there will be more questions? Asked as part of those file reviews.

C2. I would say yes, and I don't even have to hesitate on that. I don't bet but if I was a betting person I would bet money on it. First of all, it's a new regulation, it's a much longer regulation, so without a shadow of a doubt it is going to take more man hours.

More questions, yes, I would say probably yes. There are going to questions because I think everyone needs to understand each other. Under MDD, we all have a good sense of what is required for a technical file or a design dossier. I don't think that is going to be the case under MDR. I think both sides are going to learning which means there are going to be questions asked. Particularly in the early days I would be pretty confident that there are going to be more questions.

NMD: Yes, that's what I was thinking too, and I asked because I wanted you to re affirm this for me. Again, it will be more challenging for us in our day jobs to get file reviews completed and over the line.

C2. Yes, time is money and the more hours we spend reviewing the more it will cost. I can see this as being a significant cost to companies to implement this whole thing. It is going to be quite expensive.

NMD: Yes, I agree. Totally agree.

I am going to finish up this interview now. Do you have any questions for me before I wrap it up?

C2. No, I don't think so. Hopefully I have been able to help. Hopefully I have not been too off from what other people are saying.

NMD: The same theme is coming through in most of these interviews, and that being resources, time, lack of clarity, change management, training and cost. These seem to be the main trends of the interviews I have conducted to date.

I would agree with all of them. There are many other challenges as well as we know. It is an endless list at this point, but the same theme has come across in most of the interviews.

C2. That's good.

NMD: I have thoroughly enjoyed listening to you and hearing your perspective on it all and I would like to thank you again for taking time out of your busy schedule.

I am going to writing this thesis now over the summer, I can share my outcome of it at the end of the summer if you wish to see it and thank you once again.

C2. It was a pleasure to talk to you too and if there is anything else I can do to help please let me know. Feel free to give me a call.

Appendix E Transcripts from Interview C3

Interview with Noeleen Mc Devitt (NMD) and C3.

NMD: Good afternoon [redacted] my name is Noeleen McDevitt. I work at Boston Scientific, medical device company as the senior reg. affairs manager. As I think I have mentioned to you before, I am doing the master's degree in Regulatory and as part of that course I am writing a thesis. The thesis that I chose to write about is on the challenges for the regulatory affairs function as we work through being compliant with the new regulation. As we both know [redacted], there are many challenges associated with the MDR and there is one in particular that we are seeing as a huge challenge, and that is the whole topic around clinical and having clinical evidence where some of our old products that have been on the market for twenty years. Now we could talk about clinical for a long time, and I could write a thesis alone on that but purely for the purpose of this thesis, I am going to exclude the topic of clinical and because I need to narrow my thesis and focus on a few challenges. Just so you know, I would rather we don't talk about clinical today.

I would like to thank you for taking time out of your busy schedule because I know you are busy, very busy. This is going to be a semi- structured interview where I am going to ask you a leading question on your perspective of the MDR. I would like you to be flexible and explore the issues as we talk through and if things arise spontaneously, that is great. I am just dying to hear your viewpoint on it. I will be recording the interview, as I have explained and transcribing that, but confidentiality will be not be named by name, or by organisation. If I ask you a question that you are not comfortable with [redacted] or don't want to answer, that is fine too, you can just ask me to move on. Do you have any questions before I start into the questions piece of it, [redacted]

C3 Not this time Noeleen, no.

NMD: Okay great. [redacted]l, can you tell me a little about your background and your current role, and how you are involved in the new regulations to date.

C3: Okay, I have been a quality manager most of my working life, started in electronics and subcontracting manufacturing and then in 1990, I joined a medical device company in Galway, followed by several others who I would probably say since 1990 with few little breaks, I have been involved exclusively as quality manager, senior quality manager level with medical device companies in Ireland, in Galway and abroad, in Holland with two companies. On returning from working in Holland, I ended up joining a consultancy company, around two years ago. In the

meantime, obviously the whole introduction of MDR as we call it has come up. It was announced, it was released and there is the whole transition period who were in the unique position that we are offering advice, or consultancy services to companies around the world to help them implement MDR requirements successfully, but we probably specialise in project management and subject matter experts and there is some areas where companies are looking for a lot of help on, and others where they seem to be driving it themselves. That's my initial comments Noeleen.

NMD: Excellent. You have a wealth of experience behind you [redacted] You have the beauty of working with I suppose, with small and large medical device organisations at the moment. Would that be true to say?

C3: That is true yea. We are going from small indigenous Irish companies who are looking at the new regulation with trepidation, to bigger companies that, some need reports, some don't, some are driving their own path throughout this. I worked with big US multinational companies and small Irish companies, and in between, ranging from thirty people offices to four or five hundred on site in Galway so I have a wealth of experience, mainly with US and a few European manufactures

NMD: Excellent. [redacted] what do you see as a regulatory consultant in your day job at the minute, what do you see as the challenges for the regulatory affairs function in dealing with the MDR and bringing our files and our systems and our companies in compliance with this new regulation?

C3: There are numerous hoping's to come out in some type of order

NMD: No, that is fair enough. I think that's a great point because we all know there is a lot of challenges. It doesn't have to be in any particular order. I am just curious, from your perspective, what do you think is the biggest challenges.

C3: I think the first thing is the initial trying to grapple with the legislation itself and trying to understand it and trying to decipher for it and making it into what we call working man's talents and that leads you to our developing an as in status, or here's where we are, here's what we got. Now we need to do a gap analysis to find out what bits are missing. The other thing that is very important that people do, we are not helping companies that much, do it because it is more a financial analysis is to just figure out what products are going to go down the MDR path, which ones are going to stay on MDD, and be phased out over time. The whole portfolio analysis is an area the companies need help on, gap analysis and the whole breaking down the project into teams, charters, deliverables, something that people can work to, that they can understand, the

deliverables and where they are needed and what sequence they are needed, the development of work streams. I know a lot of companies that tried to break the MDR into challenges.

The other key one that comes to mind is the availability of resources and whether people are going to be asked to take on extra work or whether they are looking for additional resources, whether it is to implement the MDR or else to bring in new people to implement the MDR and leave the current people on their current projects. This is always the dilemma, but I think the resources are very scarce at the moment. We are all pulling out of the same pot, whether it comes to notified bodies, comes to authorities, the expertise which they are looking for, that is there based on people getting experience of the MDD. That, I think is the major challenge at the moment. I am certainly aware some companies around Ireland, they are nine, ten, twelve months at this stage and longer looking for resources.

The most fundamental one is getting to understanding, getting very comfortable moving from article to article. I would love to say that there are only certain ones that affect reg. affairs but being the nature of the beast, reg. affairs are involved in almost everything. There is probably not just one article or one annex that they are not going to have an impact on. I think that is, I won't say a concern but there is no expertise of such, nobody has got through it all yet, so it is very much try it and see what happens. I think there is a lot of discussion about implementation and about are we going to get this done on time and if this date is going to change. Brexit has affected things, so it is a period of great uncertainty and I think one of the roles of regulatory affairs is to bring clarity to the other stakeholders on what is going on and when things have to be done by and what they are supposed to be looking for.

NMD: Yea, I absolutely agree with you [redacted] on the lack of clarity. Do you find that there is a lack of clarity across the regulatory framework right from the commission, through to the competent authorities, notified bodies? Are you finding that as you deal with customers that they don't really understand what they need to be doing at this point?

C3: Well, it comes down to things like I'll give you a few examples. What does a post market surveillance plan look like? What does a PMCF study look like. They are mentioned quite often, but people have no clue what should be in them and I mean, until the commission produce all these guidelines with examples and clarity of this is what you need to have, and this is how you do it. People are making best faith efforts and the advice that we have got at all the conferences and seminars that we have attended over the last two years is just try and see. The adequate is better the none so we are the whole time, there is that lack of clarity like it is a huge document, it

is full of you shall, you shall, you shall but at the end of the day there is several places where people are scratching their heads. They are looking for advice from the commission, or from the notified bodies or competent authorities but it is not coming. It is nearly you have to move forward without having the advice and in some cases, it is a wasted effort going down a road saying this is our interpretation and then next thing you find out, it is completely the opposite to what you should have done. That can be very frustrating. What we try and do is break all the and articles and all the requirements down into bite size junks if you want to use that word and around that and give advice on what does that mean and what do they have to do

NMD: That's great. That leads me to, you touched on time there. Do you think [redacted] we have time on our side or what's your expectation of how we are going to deal with this by May 2020?

C3: I think when they released it there was time but I think what has happened, in the meantime, there has been a lot of pontification, and discussions about what's needed, and some companies have basically stuck their heads in the sand a bit, you know, said we are not doing anything, and we are not going to be the first. There are companies working away, the bigger companies, I would say without possibly, I won't say revealing but they are not sharing where they are too much. I think it is around a year away now and most people are have taken the decision to extend their MDD search and rather than trying to be in compliance with the MDR. Now, I know that has a finished date of 2024 but that's the more realistic approach I think people are using at the moment. I think to try and be compliant with the MDR in totality with all the articles of sections by next year is a huge challenge for most companies, but I am very concerned about the effect it will have on the smaller companies that don't have the manpower and resources to deal with it a big project like this. Even if it is, there are only one or two projects or products that they have, I still think the amount of work they have to do to prove compliance at the end of the MDD for even one or two projects is going to be severely challenging. It is nearly like they should give up doing everything else and just concentrate on this and I don't think that is the case so very onerous, I don't think the date is going to change and it wouldn't look good if they backed off on it. The only date that could probably change now is Brexit. I think people are really concerned at this stage about how could we get to compliance by May 2020, which I think for a lot of cases is just not going to happen. I think they are all going down MDD research potation and that in itself brings its own challenges because there are certain parts of the MDR that need to be implemented for even if you stick with MDD so the clock is ticking, there is a certain amount of anxiety that is beginning to come into play and a lot of companies still don't know if their notified bodies is going to be around or not for the MDR. I think the message we are giving to people is decide

fairly quickly what you are trying to do and what you are going doing in the transition period and be ready to speak about it. I think a lot of companies won't have the information or the processes in place at the moment to be compliant with the MDR and trying to get them all done in the next year is a big project, a very big project.

NMD: Well it is absolutely, and especially that the notified are not designated and looks like most of them won't be designated to at least to Q2 if not Q3. Purely from working in a large multinational, we are also taking that approach of recertifying our files under MDD because we are not in a position to be able convert anything to MDD at this point. Going back to the position of the notified bodies, they are not ready for us.

C3: From talking to the Irish notified bodies, not to mention names, they are still being put through the process, they are hopeful, but they can't tell when they are going to be certified. They haven't got the resources and I think, another thing with the Brexit thing there is more uncertainty now if people decide they have to try register with an EU 27 notified body, that is going to bring more uncertainty and more pressure to bear on the notified bodies that I don't think they are set up to handle. Most of them, are quite small apart from the four or five big ones that are making all the headlines. For the rest of them, I think it is going to be like war trying to get slots with them going forward for either MDD or MDR.

NMD: I can vouch for that as well. We are in the middle of that with both our notified bodies but there is one in particular that we are struggling with change. That actually leads me on to another question, I wanted to ask you [redacted]. Do you find that companies are struggling with change management at this time and for the foreseeable next say year or so, from making substantial changes within the workplace?

C3: Are you talking about change management in the change order sense?

NMD: Yes, yes, making changes to products, making substantial changes to products and getting them approved.

C3: Well first, they are not allowed make substantial changes after a certain date, next year anyways even if they stick with the MDD, so they either start taking shortcuts which is not the preferred way to go on their current process or else they just say we are not going making the changes. The safety related one, I think the mandatory ones fine they have to do it but getting a change to a product, through the process including the notified bodies I wouldn't see this as being easy just at the moment because even though they are technically applying a MDD ticket to everything, I think MDR is being factored into all the discussions because you don't want

something to change before the deadline to impact on you after the deadline. I think there is a reluctance to make changes at the moment even though some of them may be needed. I'm not sure am I answering the question?

NMD: No I think you are, spot on [redacted] and what we are finding is operations want to make changes, to continue making changes to products and it is just trying to make changes that middle ground where number one the notified bodies doesn't have the time to deal with it purely with the number of changes that is going through at the moment and I suppose we are struggling a small bit with that change management piece at our end and trying to manage that portion of it. Can I ask you [redacted], about training, from the various different companies that you deal with, how do you think they are dealing with the MDR to educate themselves I suppose on the regulatory function and then pass on that knowledge to the various different functions. How are you seeing that be handled within the different manufacturers?

C3: Not too many are drawing up lists of people that need training on the MDR, whose impacted by it but its selective and its very budget driven type of training so I think there are various options of training, bringing in consultants, doing online training etc., etc. They have to do it, but I still think the simplest one is read this, read that and then come back to us with any questions you have because I think it's almost impossible to cover every change in a formalized training. It would be an in-week course rather than most people have a one or two days, so it is basically executive management get a top-level overview or the main changes and then as it come down I think either companies have to develop in house training modules for the different articles or different work streams or else they bring in someone from outside. Now there are companies who claim they can train you in on the MDR in two days, but I think you'd have more questions than answers, but I think it is the fundamental part of it how do you introduce it, what are the major changes, how does it affect you, what do we ask to fix. Training of such doesn't give you think, you have to go out and do your gap analysis, ask the tough questions and after that you'll end up developing a plan. I think it's important that people get it but I'm wondering is it worth spending five grand per person on someone coming in to train you, versus taking the whole training/ communication process as one of your big workstreams and coming up with a plan people that people get educated as needed. You don't have to train everyone, but in the long run you should, but they are using various approaches. I think the bigger companies have the budget for either external training or internal programmes whereas smaller companies like everything else money is tight. They are probably trying to figure out do we have to do it, do we not have to do it, can we get it off somebody if somebody has done it already. There are a few guys around Ireland that

are doing it. I'm sure they would love to get a contract from a big multinational to train all our people on MDR.

NMD: There is a lot of money to be made at the moment in that area, isn't there?

C3 It was one that we said when we were setting up first, we just said we are not doing training but what we are finding people as part of consulting with them are looking for training as part of the services. If specialists be spoke on in house training, certain aspects. I don't know what other companies like, the big companies are doing but I think a lot of them are basically trying to educate themselves and then if there are things they don't understand or need further clarification on, they'll go find that advice whether it is free or otherwise.

NMD: That is the approach we are taking too, there are not dedicated to the MDR project, so they are doing a mixed approach of training themselves through reading, through talking to notified bodies, through going to conferences, through working with other people in industry so we are using a mix bag. Those experts in-house are enrolling the training to the other functions and the people who need to be aware of what the MDR is about. That has been great [redacted] you have covered a lot of the challenges and in fairness, you brought up many of the main challenges that I would see, that we face as we work through this, so it was great listening to your conversation and gearing your perspective on it. [redacted] I don't have any more questions on this, at this point. Do you have any other questions that you would like to share? One last question, from dealing with small companies and large companies, do you envisage, and I think we know the answer to this, do you envisage that there will be a lot of costs associated with this project?

C3: Absolutely, but I think as well as costs, I think there is a big danger that we will lose some of the smaller players. To go to MDR even on their current projects or currents products, that number that they will have to end up spending if they want to do it properly is a lot of money. I heard different numbers, eight, ten, twelve percent of revenue, which is okay if you got the resources or if you are bigger or if you can absorb it somehow and you are a big part of the market, but eight or ten percent of a small company's revenue is taking over. That would include hiring a lot of people and getting a lot of additional resources. They just may not have the budget or the resources or funding to do that and I subscribe a lot to industry news and MedTech insight and I think that's one of the big concerns that is being looked at the moment, whether smaller companies will survive and how the MDR will affect innovation. We can do it under MDD again, but I think there is more requirements across all areas, including clinical which you don't want to talk about, across PMS that I think people are going to ask is this worth it by the time we get

there and comply, is there going to be a market there for us. I think the whole thing is very onerous, is very time consuming and we will wait to see who is around. I think the big boys will, but they will all be creaking and groaning, and some will lose products. I think it will be the health care community that will suffer over the MDR, rather than anyone else

NMD: I totally agree, I imagine there will be acquisitions out of this where some of the smaller companies will be bought out by the bigger ones. Okay [redacted] I think I am going to wrap this up now [redacted], once again I would like to thank you for your time. You have given me great insights into your thoughts. I am going to be writing up this thesis during the summer, so I am happy to share with you the final results of that when I have it written up. Once again, thank you [redacted], I am just going to stop the recording now.

Appendix F Transcripts from Interview C4

Interview with Noeleen Mc Devitt (NMD) and C4.

NMD: Hello [redacted]

Thank you for taking time for doing this interview with me today. This interview is purely for the purposes of research purposes. This interview is confidential. You will not be identified by name or by organisation. The topic that I am doing my research on is the challenges for the regulatory affairs professionals in complying with the new MDR regulations.

I would love to hear your opinion on what you think are the main challenges as you see it for this regulation which we have been talking about for years and its now upon us and we are in the thick of it. I have certainly seen changes as someone who is working in industry as a regulatory professional. I would like to hear, what do you think are the challenges.

C4: I guess because the regulations are quite broad and have a lot of detail I think one of the key challenges if the resource requirements. It is difficult to get the right personnel that is required for the expertise under the various chapters. There is a person responsible for regulatory compliance that you need, the authorised rep will need that also, so manufacturers and authorised reps will need those personnel. I guess this can be compared to a QP on the pharma side. The qualifications for this will be set put. The qualifications will not be same as it is on the QP side but still need regulatory knowledge and experience in the field to be able to ensure the regulatory requirements are met. So that's one thing with resource needs. Also, Notified Bodies will be faced with the same thing. The Notified body chapter specifically calls out the need for competent people so it's important that notified bodies are sufficiently resourced and have people permanently at their disposal to be able to carry out the necessary reviews and to be able to make the decisions on devices.

For us as competent authorities, as well we have resource challenges as well. If everyone is competing for resources, how is that going to pan out. The commission also needs a lot of experts. You have the expert panels that needs to be resourced, the joint assessments teams needs to be set up to carry out the notified body audits, so the national expert will be required, and competent authorities will have to provide resources into that field as they have their own obligations at national level. There is a huge impact on resource for all the stakeholders. Authorised reps, manufacturers, distributors I guess also have requirements on meeting the requirements of the

legislation as well. Previously they were not covered or were in the scope of the previous directives. Now there is a whole raft of requirements that they (distributors) will need to familiar with and carry out verification checks and be able to work at that national level with their supply chain to ensure that there is a closed loop mechanism to ensure there is safe products on the market.

NMD: So just in relation to the resourcing which is huge, and I absolutely agree with you. How has your organisation dealt with resourcing so far?

C4: I guess in trying to understand the resource needs we have had to go through the regulation to see what is new, what has changed or what needs to be done differently. Are there gaps in terms of competency needs? Skillsets? And do we need to improve on those? I guess we will find that there is a significant need for resources in the clinical area, in the notified body area, to ensure we have the staff and resources to carry out all the admin. So, it did involve a line by line review of the legislation for organisation to learn what we need to do and to know to add numbers and upskill.

C4: It is important for us to retrain the existing staff we have. In terms of implementation of the regulation there is a whole implementation project in place. So, we are looking at classification, notified body, market surveillance, vigilance and Eudamed. All the elements are being looked at and being project managed to identify the training needs, the process engineering requirements, what does that mean resource wise and ensuring we have accounted for that as best we can be for 2020.

NMD: Ok so it sounds like you guys have a good handle on the training needs.

[redacted] Its really to identify all the training needs and now have to develop the material. And there will be guidance coming out. We certainly do not have answers to everything yet, so we need to keep best informed as to what is coming down the line and contribute where we can and ensure that that is captured in any future training plan and any training need development.

C4: I guess the way it is developed at a European level and it was split under the health function, so they still look after the inspections and audits, and the quality and regulatory aspects are under a different function.

NMD: Do you think the class IIb implantable being treated as class III's is going to have a lot of impact?

C4: Goes on to talk about the scrutiny process, This was one of the debated topics during the negotiations and it was in recognition of, we were very close to having pre -market approval in the new regulation so really it was to have another layer of approval to ensure those devices are as intended, The scrutiny process while it is a big change for the industry, it has merit for those high risk devices which may go to expert panels for review. We may end up having a lot of different types of expert panels to figure out how the devices are going to be filtered out and sent to the commission for the scrutiny process. Those expert panels can't decide we know about these medical devices, we know how long they have been on the market, they may decide they are ok and that they don't have to be sent to the commission and issue an opinion themselves. So, it's not a case that everything will go through the scrutiny process. There is a lot of discussion ongoing at the minute how these panels are going to be set up, how they are going to run, what is going to be going to them and what is going to be prioritised. There has been a lot of joint work coordination going on with the joint actions that are under way. Things like developing common specifications. so, if you have a common specification those devices may not necessarily go through the scrutiny. There are no common specifications at the moment, so they do need to be prioritised.

We have done some work to develop a process to prioritise the need for common specifications as well but there is a long way to go on it. Hopefully there will be a strategy around that expert panel shortly, we recognise that is a challenge.

NMD: And I guess updating the standards is so important since we use those to claim presumption of conformity with the essential requirements. What are your thoughts on that and getting those updated?

C4: I think standardisation in general is going to be a big challenge. There is a mandate. The way the standardisation process works is that the commission need to issue a mandate to CEN to develop a European standard or to adopt a standard to the European system, so it's like a process that has to go through. There has been a lot of issues in the past with Annex Z's, like while you have a presumption of conformity, if you demonstrate compliance with a harmonised standard, a lot of the standards won't be a requirement of the new regulations as they are a lot more robust now and a lot more detail of what is required, so those standards are going to have to be reviewed and amended. That process will take @ 3 years, so I guess it's a case of prioritising horizontal standards first and having those in place and then working out a priority for the technical standards underneath. It is a massive undertaking and while standards are not legally binding , if you are using a standard to demonstrate conformity you will also need to refer to the regulations

to see where are the gaps, where else do I need to demonstrate, or how do I demonstrate that I meet this higher requirement, so it's like a two stage process.

NMD: So, until such time that the standards are updated will it be acceptable for us to use the standards to support our GSPR's.

C4: you need to follow the regulation.

[redacted] - They have a lower level. They are at the level of the directive and there is a gap between that and the regulation.

NMD: But if there isn't anything else available? And I know they are not mandatory.

C4: A gap would need to need to be done between the standard and the regulation and show how you have addressed that gap and you meet that requirement. While they are not legally binding you still need to work around it. The standard will only take you so far and then you need to fill what will bring you in compliance with the regulation.

NMD: That is going to be a challenge.

C4: Yes, and I guess even looking what is available in other regulatory regions, you know if there are some of the harmonised standards are European standards, they might have been adopted from an ISO standard, there might be other regions who might have guidance's, that this might help somewhat if there is no other available guidance.

NMD: What are your thoughts on post market surveillance requirements?

C4: The timeframe has changed around these requirements, so I guess this is going to be a challenge as timewise there is so much more that needs to be recorded in much shorter timeframes. The timelines are a lot smaller.

C4: The timelines on the vigilance system that [redacted] refers to a form has been developed to be suitable to take on the changes under the new regs. It is very focussed on the information that is being portrayed through that form, so it is exactly the information that a competent authority would need.

There is more reporting required as part of the post market surveillance plan, but I guess it's all about us capturing post-market surveillance data and the lifecycle. The reporting should be used as a tool to demonstrate a lifecycle approach to compliance. There will be templates to facilitate this and we are certainly aware that there is a lot of burden coming on to the industry to report

back but I guess it is necessary as well and that the technical files are not just a static timepoint for checking.

The shorter timeframe is a challenge for the competent authorities as well as they are getting all that information from ALL manufacturers.

NMD: Absolutely, their workload will have gone up so much.

C4: To try to triage through the information you are getting in, it is important to separate out through risk to try to get a priority in place. This ties into the discussion on resourcing as well.

NMD: Is there any other challenges that stands out as a big one?

C4 I would see Eudamed database as a challenge which will be a phased approach. The obligations related to Eudamed do not go away, the use of Eudamed as a tool to transfer information. If for example it says through Eudamed it is looking for a specific point, and Eudamed is not available you would need to look at information be available and in a lot of cases you would fall back on emails. All players will need to use Eudamed from manufactures, notified bodies and competent authorities.

NMD: Eudamed is going to be huge alright but it is going to be a great tool when we get it populated.

C4: It is really fundamental to having the system working to increase transparency, having access to data for healthcare professionals, for patients, that they have access to that data. I guess traditionally medical devices has been quite closed in that data isn't available to the public and clinicians, so I think it is important that the device users do have access to that data to show how effective the device is, and that they have the data to show any issues with it, or limitations it might have. Having more publicly available data will help the system as well. It has gotten a few dents over the years and it is important to the first release of Eudamed that there is publicly facing piece, but there are challenges on this as well as for manufacturing industry we have heard of some arguments that they may be less inclined to report if this information is publicly available. There is a lot of clarification required as to what will be available publicly. You don't want to have any commercially sensitive data available but it's about getting that balance and at what levels the information is available.

NMD: Yes, that's a good point.

C4: Are you covering IVD'S

NMD: No, I am not.

C4 Ok

NMD: I think we can leave it at that. Thank you so much ladies for your time.

C4f you have any other questions at any time you can email us.

Appendix G Transcripts from Interview C5

Interview with Noeleen Mc Devitt (NMD) and C5.

NMD: Good morning [redacted]

C5: Good morning Noeleen.

NMD: My name is Noeleen McDevitt. I work in Regulatory Affairs in Boston Scientific. As you know, I am currently doing a master in Regulatory, at the minute and as part of that course I am writing a thesis. The topic that I chose to write my thesis on, funnily enough, is on the MDR. Its specifically focusing on the challenges for the regulatory affairs function in the medical device sector in bringing our files in compliance with the new regulations in Europe. As we well know, clinical is one of the huge challenges within our industry, so that's is a challenge for us, it's a challenge for the regulators reviewing our files and we could talk about this for a long time, and we could write many thesis' specifically on the challenges of clinical, but purely because of that, I am excluding it from the scope of what we are going to do talk about today. I am purely going to focus on the regulatory function. I would like to thank you for taking time out of your very busy schedule because I know how busy you are. I want to reassure you that everything will be in confidence, you will not be identified by name, or by organisation. This interview is going to be a semi- structured interview, where I am going to ask you a specific question at the beginning and we will let it be flexible and explore the issues that arise spontaneously

C5: Okay.

NMD: If I ask you a question that you are not comfortable with answering, just ask me to move on, it is no problem. I am recording it, and as I said, and I will be transcribing it. I expect us to record this for maybe twenty mins, half an hour, we will see how it goes. Do you have any questions for me before we start into it[redacted]?

C5: No nothing, thanks Noeleen.

NMD: Okay perfect. So, [redacted] can you tell me a little about yourself and your role and involvement into regulations to date?

C5: Okay, I am [redacted]. I'm director of Regulations Affairs [redacted]. I have been involved in the evolving medical device regulations for many years, because this is not been a new thing, this has been evolving for some time, and then was finally published in 2017. My role has been

to watch the MDR evolve, to help understand the content of the regulation, specifically for what is new compared to what is current, compared to the directives and then support the business in reaching compliance to the MDR and at the same time continuing to work with MedTech Europe on understanding any ongoing advocacy work. There is some work we are able to be involved in, specifically around interpretation into certain parts of the regulation, as well as supporting guidance. It is important for us to be very engaged in that throughout the whole three-year transition period.

NMD: Wow, so you have excellent experience in this area, very in-depth knowledge by your description of your involvement to date.

C5: Yes, and even though I am one of those people who have read the seventy odd pages, it is still very difficult to understand certain parts of the MDR. It is not just us, who find it difficult, industry as a whole have challenges around interpretation. None of the guidance that we need is really ready yet, so even though you can read it and have lived with it for many years, there are still elements of it that are unclear.

NMD: Okay, yea. I totally agree with you, absolutely. And so, as my leading question into this interview Karen, and it is a fairly leading question [redacted], and I am sure you can talk on it for more than twenty minutes on it, but what do you foresee are the challenges for the regulatory affairs function in our day to day roles for the foreseeable few years as we work through the MDR regulations.

C5 Well, I think one of the things is that the regulatory teams, they own the technical documentation and the process for CE marking. We know that the technical documentation format is going to change, so we are all going to have to adapt as to how we have previously written our technical documentation and we adjust ourselves to the extra requirements and the different format of the MDR. The MDR also requires a great deal more detail and they have also changed the essential requirements that we have all have known for decades into these GSPR's. There are some new ones in there as well, because they have obviously combined the directive and the active and plannable directive into one regulation. It is a big cultural shift, I think, for everyone to learn this all over again, something we have been so used to and one of the unknowns is no one has made a submission to MDR and it is unlikely that anyone will be able until later this year because there are no notified bodies ready to take MDR submissions just yet. It is a un known as to how that will go, so we will do our best to write it, in accordance with the regulation but this will be the first time the notified bodies will have seen technical documentation to the

MDR and we don't know the expectations will be yet because they haven't anything to judge it against.

There is a lot more information, also new requirements to include new additional post market information, as well as these post market update requirements which are new under MDR.

There are extra things we need to be collecting to put into the content of that technical documentation. The term itself is also changing to because we are used to design dossier's for class three products and technical files for lower class products. Under MDR everything is called technical documentation, so there are some new terminology issues that we need to learn and adapt to as well.

Of course, there is unknowns about class three implants and the extra clinical evaluation process that will happen for those projects. We don't know what that will really look like when we make a submission, so the clinical portion of the technical file will go to this expert panel, which is independent of the notified body and then they will bring an opinion. Although, it is meant to be done in parallel, we really don't know what that will look like in practice and neither do the Notified Bodies. Those expert panels aren't even built yet, so they are not even ready to take any work and unlikely to be ready until the end of this year. The timing of everything is tight, because we are moving towards that three-year transition period in just over one years' time. It is a combination of a number of factors.

NMD Right, yea I agree with everything you said there and no matter what we look at it, the review time for our files for the Notified Bodies will increase, I would imagine is going to extend through this process, through additional requirements to review, and through it being new for them as well.

C5: Yes, and we know there is going to be more fees. We have no visibility on those, and of course the timelines are unpredictable, and I think we will find it more unpredictable with our Notified Bodies then we do with some of our other Notified Bodies. They are more committed to giving you a timeline that they will respond to you, whereas we know Notified Body [redacted] in particular won't make those commitments to us and already taking longer to review even under the directives. So, under the MDR, it can't get any better, put it that way and it continues to be the single biggest risk to MDR implantation is Notified Bodies readiness but also Notified Bodies capacity. It is possible as we go into this unknown, that we will see it take longer to get the CE mark then we do now. I don't think it will be, say it's six to nine now, we could say it is nine to

twelve months. It is very hard for us to guess at what that might be, but I think everyone is comfortable adding a few months onto where we are now as a prediction of what that might be.

NMD: Yea, I totally agree. [redacted] do you see impact to our change management process as we work through the next year or so?

C5: I'm not that close to it to be honest. I think one of the things that has been a challenge is what we identify as a significant change or not. I don't know if that's what you are referring to Noeleen.

NMD: It is more the number of changes that a manufacturing operation wants to make and getting at the Notified Bodies capacity to take them in along with everything else that is happening at the minute.

C5: The significant change that guidance seems to be applied to every classification device which I think is different to what we are used to doing now, so I think it is possible that we will be submitting more changes. As a business, I think we need to look at how we are making those changes, so that we don't overwhelm ourselves with something that needs to go to a notified body because what we did in the past is going to change and I think that that if we do end up in the situation where we are submitting more of these changes to the Notified Bodies, it can only be added to the resource and capacity issue that they already have. I think a lot of that will be down to planning and giving visibility to the Notified Bodies as far in advance as possible, so that they can plan their resource.

NMD: Yea, I agree and they all seem to be struggling a bit with the resourcing piece of it.

C5: Yes.

NMD: From your organisational perspective[redacted] have they hired more people or how has your organisation dealt with resourcing for the MDR to date?

C5: Yea, so we have one new head count coming in 2019 to support additional work associated with the MDR, but the rest of the work will generally be absorbed by the teams that are already doing it. So, we are the authorised rep. for the business, so we act on behalf of the Brussels address for CRM, and the Galway address for legacy products, and the Dutch office for EMS currently. We are the authorised address, we are the contact point for the competent authorities within the EU member states and the wider economic area. We are thirty-two countries in that part of the region. The authorised rep. responsibilities are going to change. We will have to have a storyboard in place to show the authorised rep. connect into the person responsible for reg. compliance and

we also need a way of us verifying the DOC and technical documentation have been drawn up correctly and the business is doing what they are supposed to be doing in accordance with MDR.

We are also going to have more interaction with our distributors and our economic operators under MDR, where they will need to come to us for certain documentation so that they can do their verification processes as well. And then, of course, the Competent Authorities themselves are more active and will be even more active under EUMDR. We will also be responsible for registration for Eudamed for all economic operators. We will be doing that directly within Eudamed and how we do field actions is going to change. We will, instead of submitting field actions to every country, we will go through the Eudamed single application process and then we will also have an impact in terms of clinical studies, so my teams do clinical studies on all the SE reporting for studies. All that is going to change with the Eudamed is live for clinical studies application. Although there is a lot more work, our work will be a lot broader. There may be some VIP opportunities in there for us, because instead of sending thirty-two applications to every single agency, we will send one through a single portal within Eudamed, so it's not all bad. I would say, that even as Eudamed goes live as this single database we are still going to manage and maintain all of the in countries database for an unknown period of time. That's all the database we currently manage throughout the EU. We are still going to have to manage those.

NMD: So, I would imagine [redacted], you will probably end up hiring more people then, with all this additional work that you have just described?

C5: We have EOP planning coming up, and we will certainly be looking at headcount and resourcing, again for next year.

NMD: Okay perfect. Can I ask you about training within your organisation? Do you feel people have the right level of knowledge in the MDR, and what are the plans within your organisation for rolling out training to the various different functions, that need to be aware of it and to understand their role within the MDR compliance?

C5: Even before the MDR was published, there were opportunities to visit every division. And then after it published, to revisit all those divisions again and to present on EUMDR and ask questions. We had the chance to do this with every single division on two occasions. As the project kicked off, and we had a communications workstream established, we developed training tools so the regulatory workstream actually developed its own training materials specific to the reg. teams. I was responsible for creating something that was more generic, that anyone interested in MDR could follow and we have rolled all off that out and communicated that in our

newsletters. Every couple of months they go out to give everyone an update on where we are with MDR, and we post things on tv screens etc., and we had posters put up throughout the regions as well. We have communicated very well, we take the chance to keep people updated at functional review for example, at management review is another one. Within the QMP itself, there is now various communications going on at a functional level. The labelling teams now own everything to do with labelling. The materials work group, they have specific needs that are material related. We have a really good network of people who are building their own knowledge and experience, and now communicating that throughout the business. Within my own team, we have done the brain chart training and we do individual sessions as needed, for those who are interested into deep diving into some areas and my team who were responsible for clusters of countries take the opportunities to present at the CLT meetings that take place, to keep everyone up to date. Any questions that originate, they come to me and I can answer those as needed. It is an opportunity for me as well to keep the Vice president of the region up to date on MDR.

There is more we can do as we evolve, but I think we've done a lot at the moment and I am confident that the awareness within the organisation, right up to executive level is good.

NMD: It seems like excellent training. You sound like you have covered so many angles already with the training and I agree with you from being on the ground here in Galway, I think Boston Scientific have done a great job of rolling out training at the different levels it needed to be rolled out at and on a periodic basis. It is every couple of months you are hearing of something, so it is all good.

C5: It is interesting that there are still companies, mostly the smaller to medium sized companies, who still have not read the MDR and that is a fact we have heard through various sources. Some smaller companies in particular just don't know what to do. They generally don't know what to do. We can't do anything to help those companies. They may very well be acquired by companies, because we do see opportunities for companies of our size. It is a shame to hear there still are companies who are way behind where we are. We are as far ahead as anybody can be at this point.

NMD: Yea, and that leads me onto just overall within the regulatory framework, do you think there is a certain lack of clarity across the Commission, the Notified Bodies, the Competent Authorities, the manufacturers? What's your thoughts on that [redacted]

C5: Well we had done a lot of work with the government affairs group as well in terms of raising awareness of implementation readiness of the MDR and there was a lot of work been done, even

through to MedTech and vice versa. A lot of voices communicating that we need more time. Things aren't ready for us to be able to implement and smaller companies may be suffering from lack of skills, money and ability to transition and there could be potentially be a risk to supply at some point because products will be lost from the market and the last year was very, very strong. We felt that we were close to the Commission listening to industries voice. However, towards the end of last year, the consortium movement of investigating journalists began a campaign against industry, against the Notified Bodies, highlighting the very poor framework around CE marked products and risked patients and it was very damaging. Although, that has stopped, it's not as bad this year. It was very bad last year. We spent a lot of time mitigating the risks of that and MedTech did a very good job of giving our perspective to those journalists.

The problem is then, by doing that the Commission has is that they don't want to be looking as if they are supporting industry anymore, so the chances of an extension to the three years or any kind of modification to the regulation, those opportunities are gone. We all just have to get on with it. Even though, the Commission understands the risks, they are not prepared to put their head over the parapet and say we are going to help industry here because we have a risk to supply chain. They are just not prepared to do it, they are too scared.

In the background, we do want to still continue to message that, so we are working with the government affairs groups to look at a way to messaging this and supporting MedTech but at the moment I don't see us having any change to the timeline. The risks we have still exist, implementation, readiness, guidance missing, expert talent missing, Notified Bodies readiness and capacity still exist.

NMD: You know, you have summed up a lot there in the last sentence alone [redacted]. That was fantastic information that I got from you there. I've thoroughly enjoyed listening to you and hearing your perspective on it because I appreciate the amount of knowledge you have. It was just great to hear all that directly. I don't have any more questions for you at this point in time [redacted]. Do you have anything else you'd like to cover before I wrap this up?

C5: Maybe I am being a bit controversial.

NMD: No, it is reality.

C5: It is. If we were to go back to the directives we had and we had enforced those directives correctly, we wouldn't have had a need for regulation because the regulation was brought in because everyone was sacred and something that was going to happen and they were going to get blamed so the PIP implant scandal was a terrible thing that happened but it was a genuine case of

fraud. What they did was they used that to tarnish the whole of industry as people who CE marked products without any clinical data, who used Notified Bodies and payed them to get CE marks. This is how it was all portrayed, so the Commission was forced into having this big regulation that was supposed to revamp the whole framework. But actually, for what's in the box that goes to a customer it is going to be exactly the same. So, what we have got is fancy labelling, fancy DFUs that nobody will read, I guarantee it. We have a database that we could have had anyway under the directives that we could still have had transparency for patients. The single biggest thing that was missing was enforcement of the requirements and standardisation at the competent authority level and the notified body level. That is what was missing and if they got that right, they wouldn't have needed to have done what they needed to have done what they did now which is to cost companies like ours hundreds of millions of dollars, potentially at the end of all of this to transition products that will essentially be the sane in the box that they are now. I have a huge problem with that because what they are doing is a bureaucratic exercise and we could have given patients what they needed without all of this massive project around it, which many companies cannot manage. They don't have the skillset, they don't have the money and we will inevitably lose products to patients because of the political decision. I know that is controversial.

NMD: it is so true [redacted] you are so right in what you are saying there. I totally agree with what you said. Nothing has changed there in that product going out the door, only there will be more robust technical documentation within our companies but you are absolutely right. When you think about the amount of money that companies are spending to get us to this place is phenomenal.

C5: Yea, and the thing is that those other companies who were abusing the process, but it was perfectly legal, who were using Eastern European Notified Bodies, providing no clinical data, that was the problem. It wasn't BSI, it wasn't DEKRA, TUV SUD, it wasn't Boston Scientific or Medtronic. It was those companies and those Notified Bodies and those Competent Authorities who spoiled it for everybody else, and the control is ultimately with the Commission.

NMD: Yea, you are right. Well [redacted], thank you again. I appreciate you taking the time and I am going to be working with this thesis over the summer, I would be happy to share the final product with you when it's done in July frame time.

C5: That would be great.

NMD: Thanks again [redacted], I am going to switch off the recording now.

C5: Okay thank you Noeleen

Appendix H Transcripts from Interview C6

Interview with Noeleen Mc Devitt (NMD) and C6.

NMD Good morning C.6 thank you for taking time to meet with me this morning.

C.6: Your welcome Noeleen

NMD: As you know C.6 I am doing the MSc in reg affairs and for the research I am doing the thesis on the challenges for the regulatory professionals associated with the MDR.

As we all know clinical is a real hot topic as a challenge for the MDR, and we could talk about the clinical challenges all day, but for the purposes of this research I am going to exclude discussing clinical.

I would like to thank you for taking the time to talk to me and just before I start I want to outline a few things.

This will be a semi structured interview where I will ask one leading question and we will see where it flows from there. I may ask you some probing questions later on in the interview. As I said everything will be confidential and I will be recording the interview and we have signed up to that. I will be transcribing the interview for further review and analysis and possibly discussing the top few themes or challenges. I expect this this interview to take around 45 minutes. If I ask any questions that you are not comfortable with we can just move on.

Do you have any questions for me before we start the interview?

C.6: No

NMD: Would you be able tell me a little bit about yourself, your background and your involvement in the MDR to date.

C.6: My background is a science degree, working in BSC for 19 years, 18.5 of them in regulatory so I have a good understanding of the European system both the directives and now the regulation. I have been working on the regulations now on the MDR coming up to 2.5 years on the Corporate QMP team so I have a good understanding on the MDR and what lies ahead of us from an industry perspective.

NMD: Yes, that great experience.

C.6: I think the MDR is a good thing as a potential patient at some stage in the future of needing a medical device. I think of the changes that are coming and introduced are good. I think transparency etc, the regulation is only of benefit to us. But from a challenge perspective, overall, I'd say the system isn't ready. We don't have a system. The commission are building it as we are trying to move into it. So, we have to maintain the existing system and move products to a new system and the new system is not ready. I think the analogy is – that we are living in the house as it is being built around us.

NMD: Can you explain that to me in layman's terms?

C.6: I suppose we are working at the moment, the team I am working on is we are looking at our technical documentation and we are looking to see how we will structure it with respect to BUDDI numbers. This is the new basic UDI DI that we are trying to understand how we best set up for our technical documentation and our DOC's. But we can't because the commission has issued guidance that we need to make the number structure, or how we should do the groupings, we don't know the nomenclature that they are going to decide on , we don't know if we have to register existing devices, or just new ones, they were meant to make a decision at a meeting on February 14th , they decided no, they needed more time, and they changed the next date to April 2019. It is just over a year before we are due to go live with this and we will potentially be finding out some of the rules around how we are meant to structure our technical documentation, which again is just hard.

NMD: It's a challenge?

C.6: Yeah. It's beyond a challenge, a dangerous level is probably the wrong word, but a level where we are going to have to make decisions, and if we make the wrong ones it's going to cost us money to come back out of them again, because we are going to set up numbers (BUDDI) for the entire company and if we get that wrong it is going to take a lot to reverse out of it.

We are deciding on how we are going to structure files, how we are going to structure declarations of conformity, to align and basically utilise this BUDDI number. If we get it wrong we are just going to create work for ourselves, because we just didn't understand the rules, because they were not available to us. So that to me is one of the biggest challenges we are having right now, so we have our technical documentation all structured, we understand how we are going to write it, yet we don't know, well is it, from a family perspective, how will we know that we have the right number of families in a file, or will we have one file for every family, just it is not clear to us.

NMD: Ok, so at this point do you think you are going to have a timeline that they will come up with this guidance?

C.6: So, at one stage they said they would have it in February 14th, which was a closed meeting that nobody from industry could attend, so no, they decided they needed more time and more discussion. They then said we will not have an answer before April 10th, 2019, and who's to say when they come to April 10th that they won't do the same thing again. So, we are kicking the can down the road and the clock of 26th May 2020 is not that far away. That to me is the biggest challenge we are now facing at the moment. One of the biggest challenges for the regulatory function is how to structure our files from a grouping perspective.

Thereafter we go into all the areas of supporting information. In our technical documentation and again some of the rules are unclear. There is no guidance available to us, we are asking our Notified bodies to interpret the regulation. The response from our Notified bodies is that "we can't", we are not allowed interpret. The competent authorities and the commission say we can't do it, yet the competent authorities are not available to answer our questions.

The response we have got from the competent authority is, "send us an email, and we won't answer your question directly, we will consider it and it will appear in guidance's at some stage in the future. Which again is no good to us, we want an answer and we don't want the answer in 3 years' time, we want an answer now.

NMD: Yeah, you can't proceed without the guidance.

C.6: Yes, and examples of that are "change management". We don't know how to deal with change management. We have loads of questions on change management in the transition period and after it, and we do not know what to do with it. There are certain parts of the technical documentation requirements that are unclear, and again, we are going to make a best attempt at meeting the requirement, but we do not know for definite. We are going to start a submission process not knowing if we have interpreted the requirement correctly because there is no guidance available to us. They don't want to answer our questions.

NMD: Just touching back to the topic of change management, how will that impact you on a day to day, week to week, purely from a business perspective how will change management impact your organisation?

C.6: The way we are assessing it is, the ability to make changes is going to be reduced. Leading up to the MDR date of application, and then after it, we think the bar for change assessment is going to change. So, leading up to it, the Notified bodies have told us they have less resources available to us as they are maintaining two systems, so just the sheer volume of changes they can accept has decreased.

Then the regulation introduces a clause that says "you cannot make significant design changes or changes to the intended purpose if you are selling your device under a directive cert after May 2020.

So again, that limits our ability to make certain key changes that we as an industry like to make to improve and innovate our products, and then once the product is MDR compliant there is no guidance as to what exactly we are meant to report from a change perspective. So, the language is different to the directives with regards to "you should assess this in the directives" and it is different in the regulation, but when take that and try to break it down to see how it applies to our current decision models, we don't know. We have no guidance. So, we have been told, continue as is until told otherwise, which again, is back to the original problem, we are building a system and moving into it at the same time.

As an industry we like predictability and transparency. The leaders of the business are shouting asking if about making changes, and we can't answer them an honest answer. We can give them a best guess based on what we know today and what we don't know today.

NMD: And that guidance document that you refer to, what form will that come in, what sort of document will that be?

C.6: That's part of the problem, we don't know. Currently they exist as NBOG's or MEDDEV's, but we don't know for definite is those will continue to exist post MDR. We assume the NBOG's will as the NBOG organisation will continue under the MDR as that is a technical group within the MDECG group. We think they will exist, but MEDDEVs will go away because they are a tool for a directive as opposed to a regulation, but again we don't know.

We are all scrambling to find out what is the best guess at what may be available to us. Consultants are having a field day as they are available to provide an educated guess at a price, but it's no better than our guess at the minute.

NMD: How has your organisation dealt with resources for this project, have they added any headcount, have they created any specific roles for this project for people working solely on MDR?

C.6: So, I would say yes, there is a variety of things that has happened here. There is a corporate QMP team. There is a variety of people across functions that are dedicated to MDR and in each divisions have created a team within each division with the understanding and tactical execution of MDR. At a corporate level it's all about trying to provide strategic guidance and make sure we are coherent and consistent in our understanding and sharing information down, so there are functional representatives on that team, that team feeds into the divisions, where there is a dedicated leader whose sole job is the tactical execution of MDR and they are supported by a cross functional team. Again, we are there to provide that strategic guidance to the divisional teams as they execute. All in all, across all 6 divisions there is probably up to 200 people working on MDR in our organisation.

NMD: Would that be on a full-time capacity?

C.6, No not all full time, there are probably about 50 people fulltime on this project and for the rest it is taking up a portion of their time and it is growing. Every week there are more people getting involved as we are working on files. Rather than just changing the system we are changing the files, thus the questions we are receiving are changing from small set of questions to a larger set of questions which is great as they are posing more challenges to us as team to understand this fully. But it is further exposing that the system is not ready. People are asking about going "EOL – end of life with products" because people are wondering what they need to do with my "end of life products" before may, after May, in the middle of May, and again it is not clear what we need to be doing. So yes, from a company perspective we have resourced it appropriately with both dedicated resources and ad hoc roles.

NMD: Do you feel that there is an understanding of the requirements for the MDR across the organisation. I am getting at training there. Does your organisation provide internal training, or do they have people go to external venues for training? How do you feel you are dealing with training since there is a lot to learn for all of the functions and there is a lot of extra roles?

C.6: The training is a challenge for sure, as everybody has a different level of knowledge need for the want of a better description, yet they hear about this gigantic project called MDR and they think they need to know everything, when in fact they don't need to know the ins and outs of everything. They need to know what is relevant to their function and what they need to do for

that aspect. Because MDR is so topical everyone feels they need to know it all, so it's about getting that balance that people have the right level of training. I am responsible for the regulatory training so it's a little easier to manage as we get the kitchen sink approach. We in regulatory do need to know a lot. I think when you go beyond our function and you are into design assurance, and clinical for example, you are touching on certain aspects of the regulation so our approach has been a lot through general awareness training that is available to the entire organisation, and then dedicated work instructions and SOP training where they are reading their procedures as to how it is being brought into their particular function. I think the general awareness training is being underutilised at the moment. People have not engaged in it enough yet. It is really good, and it does answer most people's questions. But I think with training the challenge is making people aware of what they need and what exists to meet their need. With a company of 28,000 people we are finding it a challenge at times to meet that need. It has to consider all manufacturing sites and all divisions. As a team I believe we have the tools there, it's trying to get the awareness of the tools in now. We are getting it on TV screens around the buildings and getting it into newsletters. But have put a significant effort into creating the training.

NMD: Yes, it sounds like you have, it sounds like they are solid plans you have in place there.

NMD: This has been great chatting, it has been a very informative interview. Maybe to sum it all off, if you were to pick one challenge, as we know there are many of them. What would that be?

C.6: Em, I think from a reg specialist perspective, so it's not the clinical, not dealing with labelling etc, some of the new processes we are going to encounter, we do not know how they are going to work. Currently we submit a file today to our Notified body, we understand the sequence of steps it is going to go through, with the new system there are a few other new steps built into the process, the clinical consultation process being one of them. This is applicable to class III implantable products. We do not know anything about that process. So as industry we are preparing our files, some of them will be submitted by the end of this year. They will get to that gate in the process and if the committee is not established they may just sit there and wait. Again, it is going back to the commission have not built a system. So, we are going to have some of our highest risk, innovative products sit and wait until the commission have established expert panels to review this product.

To me, just that unknown to something I do every day, where I submit a file and what is the next step? I don't know where it goes next as they system is not there. To me it is just unacceptable that stage just over a year to go to implementation, we don't know how the actual process of submitting the file will actually work. We can deal with some of the lack of knowing what all the labelling requirements where we don't have all the symbols, they are things we can manage. But the actual process for getting approval, we still don't know how that is going to pan out. It's just not good enough and it causes us an amount of angst as business leaders want to know what is the process, how long is it going to take to get approval? Is it going to six months, nine months or twelve months and we cannot give them that answer. From a current perspective there are current European leaders looking for a Strat plan, are we able to launch products in 2 years' time, in 3 years' time? We can give them a best guess but there is always going to be a big red flag because there is part of the process we just don't know enough about. To me purely looking at regulatory that is the biggest challenge. The unknown.

NMD: I agree, but maybe when we get a year into this we will understand it all a bit better.

C.6: It should not have to take a year though? We should know now. We should know before we submit the first file. We know when will submit the file, it will go so far in the process and then it will stop.

The guidance from the commission, or the roadmap from the commission, it says for this particular process we will try to get an implementing act and try by the end of 2019 or it may be early Jan 2020. So that's an Act, does that mean then that the Act will need to be executed to create the panels, that will take another 6 months, we don't know. It's just a bad situation to be in.

NMD: It sure is C.6 and there are a lot of challenges ahead.

C.6: Did you get what you needed?

NMD: Yes, I think I did, I would like to thank you again. I have enjoyed hearing your perspective on what you perceive as the challenges because you obviously have a wealth of knowledge and you have been living this MDR for some time now.

I can make this thesis available to you C.6 if you are interested in seeing it towards the end of the summer.

Appendix I Transcripts from Interview C7

Interview with Noeleen Mc Devitt (NMD) and C7.

NMD: Good morning [redacted]. My name is Noeleen McDevitt. I work at Boston Scientific as a senior regulatory affairs manager. I am doing the masters in regulatory affairs and I am currently starting up writing my thesis. The thesis that I choosing to write about is, the challenges for the regulatory affairs function in the medical device sector in bringing our files in compliance with MDR. As we know, there is loads of changes happening with the MDR and clinical is one of the big challenges facing us. We could stay here and talk about clinical all day or for ten days and we recognise that is a huge challenge but purely for the purpose of this thesis and research, I am excluding the topic of clinical.

Just to set the scene. I would like to thank you for taking time to talk to me. This will be a semi- structured interview where I am going to ask you one leading question. We will be flexible and just explore it and see how it goes after that. I may probe some towards the end with some probing question's, but we will see how the flow goes. I am recording the interview as you know, and I am going to be transcribing it. I expect it to last maybe twenty minutes at this stage of recording. If I ask you a question that you are not comfortable with, please just say I don't want to answer that question and move on, but just to remind you that everything is confidential.

Do you have any questions for me, [redacted]before we start into it?

C7: I actually do have one question. When you say clinical that is a fairly broad terms as you have clinical trials and clinical evaluations. Are you speaking about both?

NMD: I am excluding all things clinical from this discussion. As we all know it is a huge challenge and I am going to leave it to the experts and there is a thesis in itself there on clinical, but I am not the person with the expertise in that area.

C7: So, if I do veer off into that, just pull me back.

NMD: Ok, I will.

So, [redacted] can you tell me a little bit about your role and your interaction with the MDR to date.

C7: I am the Director of Regulatory Affairs with Europe responsibility for two facilities, one is based in [redacted] and the other is based in [redacted]. There are various different types of products, specifically I am responsible for CE marking of products out of those facilities. The products come with all shapes and sizes. We have implants which are class III's and have material of animal origin combined with drugs, so that is on one end of the scale of complexity right down to class I devices that non-sterile non-measuring function which are reusable.

In relation to interaction with the MDR I led the efforts of the gap assessment for the company and co-ordination of that with various different chapter leaders.

We broke that assignment into project streams and we had various Corporate people leading those efforts and then that was mapped to the different sites and depending on the specific chapters and working with the different functions too.

So that's how we set ourselves up. I am also the chapter leader for Clinical evaluations as well as clinical investigations. We have interactions with the Notified Body and the various different authorities through industry association meetings.

NMD: Clearly you are very familiar with the regulation to date and are very knowledgeable in that area and you understand the impact it is going to have on industry.

Here is a leading question then [redacted], what do you foresee is the challenges for the regulatory affairs professional as we work our way through MDR.

C7: So, let's start. There is a huge amount of unpredictability within the system, there is a lot of unknowns, so the business needs to plan ahead. It needs to look in advance and plan ahead. Projects bringing them to commercial takes a number of years so need predictability with our products on the market but also what is in our pipeline. So that is an absolute huge thing.

What does that really mean? The frustrations are the challenges and I would use those words interchangeably at this point in time, would be that we have a very good intended regulation that came out somewhat coloured through political influences, somewhat coloured through different regional interests that evolved. Be that what it may, it is a good regulation, we think it makes sense, the intent behind it in terms of traceability and patient safety focused information is a really good thing. There is no doubting that the system behind it, the authority system behind it, has not evolved.

So, they have a proposal, and I say they, meaning the Commission and the intermediaries which are the Notified Bodies don't have the associated support structure. What I mean by support structure is that is the associated implementing Acts on the legal side of it and guidance's, best practices, the associated resources and the associated timelines. We seem to be caught in a roadmap of quarters, like tabs of years.

One thing that is unchanged is May 2020 and onwards. So that is a challenge from the industry side. Internally, I would say that regulatory is a technical function, it needs to be able to interact well with different departments and it provides consult at the round table where there is lots of other functions there. I think that will be a lot more of focus with this MDR and one of the challenges for us is communication.

Making sure people are aware of developments, leading, coming out from the backroom in front of the microphone leading this project which is MDR focussed.

NMD: Yes, you are right, that is good information. You make some very good points there.

Can I ask you [redacted], how is your organisation dealing with change management over the coming months coming up to May 2020 and beyond? Are you finding that a challenge?

C7: Do you mean systems or products?

NMD: I mean changes to products? Making substantial changes to products.

C7: We have a very good planning system for making changes. Many of our changes impact international so we have a very good robust system for that. There will be a lot of knock on effect from the labelling updates around the globe.

We have a lot of acquisitions also. We integrate their systems. So, change management is a big thing for us for legacy products.

We try not to do too many changes with our legacy devices. They are well monitored though our complaints system.

NMD: So just on another question on change management.

Are you restricted by the number changes that you can make to your products between now and May 2020? Are your Notified Bodies restricted you on changes there based on workload and their capacity etc.

C7: Yes, I would say absolutely off the bat without giving you any numbers.

Last we were given different signals that Notified Bodies would be ready. Shock, horror, that did not come to pass. We came to a decision to we should renew all our certificates under MDD. We made submissions for all our products by December 2018, so we were ahead of other companies there.

Our company has a project plan to deal with MDR. We are having test cases of products being put forward to get a flavour for the type of questions which will be asked though MDR. We do have approximately 200 products' so we do have a lot to get through. We will be working of a sampling process for the lower- class products. We also do work with three (3) different Notified Bodies and we are finding that some are readier than others. Brexit of course is having an impact too, so we will have to wait and see how that works out.

Our company goal is come May 2020, we want to be able to transition as much as possible over to MDR. There are devices in our portfolio that we need to reclassify and there are devices that we are not going to pursue in the future.

NMD: In relation to resources [redacted], how has your organisation dealt with that.

C7: Like any project it is built into objectives and resources would be part and parcel of that. Resources are tethered to budget but are also tethered to the MDR.

Yes, we have looked at resources and we are resourcing and are hiring. We are also looking at using outside consultants. We are also going to be adding medical writers as this will come in under the regulatory function. They will be involved in writing the clinical summaries and will be involved in the post market work also.

NMD: So, you sound like you are ramping up.

C7: Yes, we are indeed. The medical role is going to be a new type of position coming under the regulatory function.

NMD: You touched on something earlier which was in relation to lack of clarity. Would you agree that there is lack of clarity between the Commission, the Notified Bodies and the Competent Authorities and then back to the manufacturers. Do you feel a sense of that?

C7: Yes, is a simple answer. To expand on that there is a lack of clarity with the lack of resources and the timeline. The guidance's have not come through. They are on a timeframe that is not on the Gregorian calendar. Irish MedTech has done a really good

job of trying to pull information together for industry. They are pretty open, and we are sharing things within industry. That is a really positive thing.

We are still waiting on guidance documents. There is a lot going on with the Commission. Brexit is not helping. There is a lot of noise in the system. The people at the Commission and Competent Authorities. The system is just not in place. We have management asking us about timelines. We know how long it takes to get labelling updates completed for all products, especially on a global scale.

The Notified Bodies are caught in the middle. You could construe as the victims or not, you could put them on two different podiums but depending on which podium you put them on they say different things.

NMD: Yes, they do tend to change their minds.

C7: Based on that you don't get consistency, and so based on that you cannot predict.

We need to be able to make decisions, we need to be able to advise people. And we just don't have the support. Speaking for myself, I would say I am conservative, I like to know everything, I am cautious, that's me.

NMD: You want to be prepared for this and that is very hard when we have so many unanswered questions.

C7: Internally we have set up procedures and then we find out guidelines have changed so it is very frustrating.

We are still figuring out which, if any of our class III products needs to go through the consultation process for the scrutiny mechanism. Even as of last week the Competent Authority did not know.

The Commission is busy trying to figure this out.

NMD: And the time has crept up so quickly. May 2020 seems so far out but it is very soon approaching. It is right upon us.

C7: I do think it is interesting times. From a business perspective, we are thinking FDA are doing a much better job at giving guidance, giving predictability, and are very approachable, very straight.

NMD: One of the things that was interesting at the last MedTech conference was FDA came out in a shining light.

C7: Yes, well if you make the wrong call it could cost a lot of money. So, some of the comments made at the conference was valid.

NMD: Ok [redacted], I don't have any more questions for you.

C7: I would like to see when you get all these interviews back what message you would give out to the wider audience. I think it would be great for the wider audience.

C7: I think it is very relevant. It is an interesting time. Our goal is the patient should win out.

NMD: Thank you [redacted] for your time and I will share my thesis with you during mid-summer 2019.

Appendix J Transcripts from Interview C8

Interview with Noeleen Mc Devitt (NMD) and C8.

NMD: Good afternoon [redacted]. This is Noeleen McDevitt here from Boston Scientific. As you know [redacted] I am currently doing the master's degree in Regulatory and as part of that course I am writing a thesis. The topic that I've chose to write about is the challenges for the regulatory affairs function in dealing with the MDR and bringing our technical documentation and our files in compliance with the new regulation in Europe. As we both know, there's a lot of changes and there is one in particular that is a huge challenge and that is the whole topic of clinical evidence. I know we could do a lot of discussion over talking about that challenge but purely for the purposes of this thesis, I am going to exclude that topic. We will talk about everything else, but the clinical challenges. This interview is set up as a semi- structured interview. I am going to ask one leading question [redacted] and I would like you to be flexible from that one leading question and explore issues that arise spontaneously. I would like to assure you that this interview is confidential, you will not be named by name or organisation. I am recording it and I will be transcribing, and I will send you a consent form for you to be okay with that. We will record this for around twenty minutes or so. If I ask you, [redacted] any question that you are not comfortable with, that is no problem. Say "move on" and we will move onto the next question. So, do you have any questions for me [redacted] before we start into this?

C8: No, Noeleen that's fine.

NMD: Okay perfect. [redacted], can you tell me a little about your background and organisation. I believe your organisation would be classified as a small organisation and correct me if I'm wrong there but maybe if you could describe your role and your interaction with the dealings with the new regulation to date.

C8: Okay, so my organisation would be a small organisation. My role is head of quality and regulatory. Basically, that means I have responsibility for ultimately implementing the MDR and all the interactions with the notified bodies, the regulators would go with that and leading the project to get the company ready and relevant to the MDR and engaging with all the key stakeholders in the business to bring them up to speed on it and then to put the process around getting us compliant so that's where we are.

NMD: Excellent, so it sounds like you are in the thick and you are the main person who would be leading these efforts up.

C8: Pretty much Noeleen, there is a team that works under me in Regulatory and they will be doing a lot of the pushing and shoving but I suppose I am the key person to get it across the line.

NMD: Okay, so I'm going to ask you one leading question here, [redacted] and we will see where it takes us and that is what do you what do foresee as the challenges for the regulatory affairs function in bringing our existing medical devices in line and compliance with the new regulation?

C8: For me and for organisation, as a small organisation it's still a lot about the unknowns and where exactly things are going to go and I suppose, the key challenges for us as I seem them is, first of all we have a strategy in place to continue with our MDD cert and role that out so that we are not having to be immediately MDR compliant. That is an initial challenge in itself and the fact that the notified bodies are not particularly snowed under and they are given timelines now that you must have three-year research, or your recertification process done. The other challenge that us straight on top, that is front and centre at the moment is that is around significant changes and that you can't make significant changes after a certain time, and obviously that's May 2020 but it's actually earlier then that again now with the notified bodies wanting stuff in. That is an immediate challenge to us, just how we continue to supply the market with our current project under the MDD and that's until we are ready to go and become MDR compliant. Subsequent to then to that, I look at the MDR, the next challenge for us and I will only talk about us as opposed to the general challenges, the next challenge for us is the quality system element and what kicks in in May 2020. One of the key ones for us certainly as a small business that relies heavily on distributors in Europe to put our products out there is going to be the whole stuff around economic operators and all that is going to entail and the additional burden of documentation and stuff that comes with that, along with the PMS and all that other stuff. We are lucky in the classification in so far as where our structure is from a post market surveillance perspective, although we will have to do further and additional stuff, so probably okay there and we are in a reasonable peace and obviously risk management and other bits and pieces like that. That is the next step for us and then the other challenge for us is looking at the gap assessment and trying to put a gap assessment around the product itself and when we think we will be ready to go in under the MDR, what do we think we need to do. Obviously because it is a completely new submission and that has some advantages as so far as we may be going in under different products as we have done under the MDD as long as we line up all the testing. But then, as well as that because you can't leverage off of certain stuff and because we have the benefit of being in the market for a certain

length of time and being able to feed of it, that's all now gone where there is certain standard and certain things will have to raise the bar on our products. We will have to go back and do testing, we will have to change some of the things we have set up to this point around maybe cleanliness or aspects of that in order to get it MDR compliant so there is a whole body of work there that needs to happen because obviously come the Technical file and all the other documentation that comes with around making sure that we meet all the standards. Making sure we are MDR compliant and just raising the bar around that documentation and our essential requirements and all that. I suppose they are the key things at the top off my head. I would context that Noeleen by saying that, we probably still in a very much wait and see aspects to some of that and that is a challenge in its own right because there isn't really enough visibility out there to some of the aspects of what's going to happen. As a small company, we have made the position to stand back until we see more direction and that might not be the same as large companies have done or things like that. That in its own right is a challenge because we may find ourselves that may have been the wrong strategy and we might get caught and it may take us longer to get MDR compliant then maybe we have anticipated. They are the real challenges for us.

NMD: Yea, I agree with everything you said but just to touch on your strategy from a small companies' perspective with a lack of clarity. We feel as a larger organisation the same thing. There is lack of clarity across the key players in the regulatory framework from the commission to the competent authority through to the notified body. We ask our notified body questions and they can't answer us either. It is a lot of unknown is how I would see it at the minute and you are obviously feeling the same.

C8: Yes, we do, and we might feel because we are a small organisation that the larger organisations with more resources are in a better position than us, that may be a misconception to be honest with you. Talking only from inside our own four walls, I've a board of directors that I need to present updates on. The updates have been pretty much the same in the last three, four meetings where I have been saying we are in a holding case at the moment, there is a little more information I can share with you but there isn't a lot. It is all going to either come in flooding at the one time or that alone is difficult to manage.

NMD: it is, yea. You talked about change management there, do you think it will prevent you making changes in operations, do you think the operations side of the business will struggle with the restrictions we have with change management?

C8: Yea, I think they could do. Certainly, at the moment, I am having the conversation with our R&D and our Operations group to say we have dates now, but we know come November, December we won't be able make any more changes rt our MDD product. We are trying to line up what does that mean, what changes would we like to have in as soon as possible, what changes can we wait for the MDR and then people need to become aware. Is that going to cause drift in our product offering in Europe versus our product offering in The States. If we are ready to go in the states, will we submit in The States? In other markets as well like Japan and china, will we update the product in there. That causes its only differentiation from a labelling and a DFU perspective. Some of them are different anyway, but it is further differentiation and it's further widening of those, until a months' time where you'll catch up with the MDR products hopefully. There is definitely that and from an operations perspective just even in the system, again it's just bringing people to the fact they are either going to be differences that are coming in even trying to communicate to the business that they're going to be business the MDR is arriving in different ways and that there's ways coming first that are quality systems related and they will make changes to the business that we will have to be very clear on and then there is ways that are coming that are more product orientated and that is more the licence to sell or the certification to sell, even communicating that a bit and making sure people are tuned in to that can be difficult enough.

NMD: I agree, the whole May 2020 thing but then we have until May 2024, and the whole recertification of files that you talked about. I think as a regulatory function, we get all of that, but it is hard enough for the other functions to grasp the whole certification thing and what you can and can't do within those timeframes.

C8: Yea I would say, here now in my company, they have struggled understand what you do mean they can't make changes? A key question which I've brought to them is if you have a safety issue in that timeframe, will you be forced to make a change there, and if you are asked to make a change there because it's seen as a safety thing can you put other changes in on the back of that? That's the questions that I am getting. For instance, if our complaints were pushing us in a particular way and we felt we are not ready to go MDR, but we definitely think we should make this change for the good of this patient and then we went to the notified bodies and said I think we need to make this change. If we were given the go ahead to do that, could you then load other questions in on the back of it is the type of questions I'm getting.

NMD: Yea, and they are all valid questions as well from a business perspective.

C8: Oh yea, absolutely.

NMD: [redacted] has your notified body given you a cut off time when to stop sending in changes under the MDD?

C8: Yea they have given us a general one and I have a meeting with them next week them to just discuss it but I have heard even though they have given a general timeframe , a general cut off timeframe, they are now struggling even to that because a load of people have come in to say okay I want to book a slot and I want to. I'm having a meeting with them next week and at this stage, Noeleen, it looks like we'd be just booking a slot for the sake of having a slot and if we use it, we use it and if we don't, we will just let it go. I don't know are other companies doing that as well.

NMD: Which month do they mention?

C8: They're saying November.

NMD: It's funny you say November for your notified body and we're dealing with two large notified bodies and one is saying March, end of March

C8 2020?

NMD: Yea. No. no, March 2019.

C8: Oh okay.

NMD: This month. The end of March is with one of our notified bodies, is the cut off period for sending in changes and with the other notified body it's August. Your notified body is saying November, so they are all a bit different in how they are managing this.

C8: What has been communicated to us Noeleen is with any recertification, they have to be in by May and then they have to be by the end of May for with any recertification with MDD and then they won't be looked at until during the summer. We have a date for ours to be in May, but it won't actually be reviewed until July. What we have been told for significant changes, and this was an informal communication now at this point, was that November was our timeframe. Now when I meet with them next week, they may tell me that has changed but even as I say I have spoken to one of the people in the notified bodies just in the last week and he had told me that that date of November is actively getting filled up and they are not even sure if they can meet that now at this stage. They might even come out and say "look no more significant changes. We can't deal with them all, there is so many". That is what I have to meet with them next week and understand.

NMD: That is a challenge. When do your notified bodies expect to get designated [redacted]

C8: From memory, I think it is the last quarter of this term.

NMD: Like that, one is saying Q2 and another is saying Q3 in our case

C8: I think it is between Q3 and Q4 was what they were saying.

NMD; Can I ask you on resources [redacted], has your organisation hired any additional headcount on top of the extra workload that is going to be coming down the line or have you absorbed that into existing headcount at the minute?

C8: I suppose, we are lucky a small bit Noeleen, in so far as that we are growing. We are a small company, but we are growing eight years, so we have done as we budgeted each year, we've added in what is coming down the track. I have budgeted for the fact that MDR is coming and we've added headcount that will be involved in that MDR. In the R&D organisation, we have done something similar. Now, would I say specifically we have hired specifically for MDR, probably not but we have blended as part of our growth and said right if we are going to be, there are a couple of new projects we need to think about and there is a new hire for those projects and MDR is included in that hire if you know what I mean, and similarly across the organisation. It is probably a bit of half and half, we probably haven't scoped it to the level where we have said we are going to need X amount of FTDs to do MDR and is to do with some of the unknowns. We have done it more on the basis, we know MDR is coming, we know this other project is coming, we know this other thing is coming, that means we'll need some extra resources in those areas and we are going after those. Do you know what I mean?

NMD: Okay, yea. That all make sense. Excellent. Can I ask you about training in your organisation in relation to the MDR? Is this something you are doing internally or are you going to external programmes? How would you say you and your staff are getting up to speed with learning and all the training on this new topic? How are your organisation dealing with that?

C8: Both a mix really, Noeleen. We are probably utilising IMDA, regulatory forms and we are going to those and we are looking at other things externally. There is an extended notified body that run a few things and we have gone to those. It's probably very much just at the moment, the reg. group, my own group that are getting the training related to it. We are in early days in terms of training the rest of the organisation and that is purely just down to my previous comments about the unknowns and we need to actually actively bring the organisation up to speed on but is probably a mix and what I would say, what we will end up doing is, it will continue to be a mix. We will probably end up getting to a stage where as we complete out our gap assessment and

understand the area that we are weakest in, and that we need the most knowledge and we end up external and finding out, how did we get that. That might be through going out to training courses, it might also be to go out and get a consultant whose knowledgeable in the area and get them in here to both help us with the project and also train people so there might be an element of that in it.

NMD: Okay, okay. Do you envisage [redacted] that the MDR will, I think we know the answer to this, but I would like you to talk about it a little bit, that it will cost your company money?

C8: I think like you said, you know the answer to this. There is no doubt, it is going to cost us money. Certainly, in the short term and medium term because obviously it's a more whole burden of everything. In reality the true cost of that won't be seen until we get into the actual testing and filing from a MDR perspective because you know what I will say is this and I don't know have you seen this with your notified bodies but the last significant changes we've done, they have cost us a lot more money and unseen that they were going to cost us more money and a lot of the reason that we have been given back is that everything is going up and we need to get ready for MDR, even though, my feedback on that is that we are still in MDR here. Everything is getting scrutinised, so if that continues into the MDR, my expectation is that it will cost an awful lot. We can expect that the notified body will send an awful lot of time reviewing every-time we make a change, spend an awful lot of time reviewing even the application. That is only that part of it. I think the economic operator's stuff could cost us more because we may have to fundamentally make some changes there because I envisage that there may be economic operators that just won't want to come to the party. Some of the guys who just won't want to do what jobs they are being asked to do and we may have to make a change. That may be more costly because you could have to go to someone who is a bigger player in the market in a particular country who we may have avoided in the past just for commercial reasons, on the basis that they are too big for us or their portfolio is too big. We may have to go to them now though, but that will come at higher costs as well.

NMD: Even all the labelling and DFU updates, so it's inevitable there is going to be huge tasks associated with this. That has been really good to hear your perspective. I have enjoyed listening to you [redacted] and hearing the challenges you have as well. They are similar to mine, and they are similar to a lot of other people I have talked. I actually don't have any other questions for you. Do you have anything you'd like to bring up before we wrap up the interview?

C8: No, that's fine Noeleen.

NMD: Okay, well thank you again for your time and I am going to be writing up this thesis during the summer and you are welcome to have a look at it when it's all finished.

C8: No problem Noeleen, best of luck with it.

Appendix K Transcripts from Interview C9

Interview with Noeleen Mc Devitt (NMD) and C9.

NMD: Good evening [redacted] this is Noeleen McDevitt from Boston Scientific. Thank you for taking time to talk to me this evening [redacted] As you know, through our mutual friend [redacted] am doing the master's degree in Regulatory Affairs. As part of that course, I am doing a thesis and for my thesis, the topic that I'm choosing to write about is on the challenges for the regulatory affairs function in the medical device sector in dealing with the new medical device regulations in Europe and bringing our technical documentation and files in line with those new regulations. As we both know as well, clinical is a huge topic as we talk about the MDR and purely for the purpose of this thesis and me wanting to narrow my scope, I am going to exclude clinical from our discussion because we could get wrapped up and talk about clinical the whole time and I don't intend writing about the clinical challenges, so just to set the see on that from the outset. It will be a semi-structured interview here Martha where I am going to ask you one leading question and we will see where it goes. We will be flexible and just explore challenges as they come up. I am recording this interview for transcription, so I will get you to sign the consent form on that. I will record now you for fifteen or twenty minutes and we will see how it goes. If I ask you any questions, [redacted] that you are not comfortable with or you don't want to answer just ask me to move on, that is no problem. Do you have any questions for me [redacted] before we start into the interview?

C9: No, not at all Noeleen at all, but I would love to get a copy of your thesis when you are complete. That would be great actually, if you don't mind?

NMD: Absolutely, absolutely. I'd love to share it. I don't know how good it will be.

C9: That topic seems so on point, it's not funny.

NMD: I know, I know. The way I'm doing my research is by interview first of all, so I have twelve interviewees from a mix of small and large companies. I got an interview with competent authority, across three different notified bodies, so I have a good mix of people. I would assume your company would be considered a small company, would that be correct?

C9 I suppose it would, Noeleen. I think we would kind of be in the mid region. I do know that there is between 1,000 and 2,000 employees worldwide, so I suppose we are midsized.

NMD Okay, so you are certainly not the big, multinational. You are on the smaller side.

C9: In [redacted] we are 130 strong, 130 head count. We are responsible for a lot of the neurological devices but there are multiple different manufacturing sites around the world.

NMD: Okay, excellent. I must do a bit of digging around on your company because I don't know a lot about them, so I must take a bit of time to understand a bit more about what they do. Just before we start then, can you just tell me [redacted] a little bit about your role and how you are involved in the Regulations at this point in time.

C9: No problem at all. I suppose I am working for [redacted] now for almost 18 months, Noeleen. I was hired as Senior Regulatory Affairs Specialist and I was promoted last May to Regulatory Affairs manager.

NMD: Congratulations

C9: Oh, thank you very much. One of the responsibilities I have within the group is that we are responsible for the Global Registration of all the neurological devices that we make. Some of those are manufactured in The States, some of those are manufactured in Canada and then some are manufactured in [redacted] and basically it is the Global Registration for each of those devices. China is our primary market, I suppose like everybody else. The registration's there are priority and always will be. As well as that, and in my current role, I am responsible for the technical file that [redacted] currently hold.

They are for our Class IIa devices. For our needles, our invasive needles, they are used to administer medicine. That would be where we have active medical devices which are connected to those needles and we administer a little shock basically. We monitor how the muscle would be impacted and the muscle responds to that simulation and that simulation is then recorded. They are used for diseases and illnesses on a lower scale all the way up to severe cases of epilepsy.

We also manufacture the ESD devices so if you enter into a hospital, the R room or A&E, you will see our devices mostly on trollies. Our active devices are class IIa as well, but we also manufacture Class IIb's. They have operable functions when they are in a higher classification. We also manufacture, not in [redacted] but In [redacted] the Class III catheters. There are ICT catheters and we also have the monitors which are sold with those, so we are responsible for the technical files in relation that range of products.

NMD Right.

C9: There is a little bit of a shake up going on at the moment with regulatory and we do think in the coming months that [redacted] will be responsible for all technical files of all products that are manufactured by [redacted] That brings on the audiology business, which is manufactured in

[redacted] and it also brings in our new born share product range which are manufactured in [redacted] but at the moment I don't know a huge amount about those products. It's going to be a learning curve.

NMD: Wow if you inherit all that, that will be a huge extension to your portfolio, won't it?
C9: Oh definitely. It would be massive. Now as I say, we would be responsible for the technical file, we wouldn't necessarily be responsible for the quality of the manufacturer or anything like that. That would still happen at the [redacted] but we would be the point of contact for the technical file.

NMD: Okay, so that's definitely going to increase your work burden for sure.

C9: It is definitely and, on my team, as well, an increase on headcount definitely.

NMD: So where do you see, [redacted] the main challenges that you and your team will have as you work through trying to comply to the new regulations?
C9: We are discovering more and more, that in particular for our older products which would have been on the market for years, there have been an awful lot of grandfathering in relation to some of the testing, in relation to the technical file information that has been put together. That is our biggest issue. We have the milestone to bring our files in compliance with the standards. This will be where our products that are manufactured in [redacted] where they are sold as part of a system, that our system verification has been carried out. This seems to be where we will see an awful lot of our issues, but I suppose, the biggest one will be the material composition for us.
NMD: Yes.

C9: That is all around being the first part of the project where we have to have the material composition, so we really wouldn't have any of that information on file and that is where our biggest issue is going to be, is finding out did the components that we put into our system to see if the part. numbers, to see if the manufacturers of those components and the composition of those components. I think we can. I think that is going to be our new biggest milestone and then basically the lifting off that product where there is content of greater than 0.1 percent week by week. I think that is going to be our biggest issue.
NMD: Okay, yea. You are right. I agree with what you are saying for sure. When you say system verification being a challenge [redacted] what exactly do you mean by that?
C9: I suppose, with [redacted] and the way [redacted] grew its business, it grew by acquisition. We tended to buy out a lot of our competitors or I suppose those companies that used our products in combination with theirs. Let's say our systems, our [redacted] which is one of our big sellers

across Europe, they were manufactured in [redacted] and they were manufactured by a company called [redacted] who subcontracted the business out to another business. [redacted] would have bought a lot of the supplies that made it, our needles, our electrons, our cables, a lot of that and then they would have matched those with the systems they sold but [redacted] are responsible for the supply and they accept in relation to the needles and the [redacted] were responsible for the system. When they bought [redacted], the technical files were indeed merged to change to [redacted] However, system verification had been carried out so in a lot of [redacted], a lot of our electrical safety, our safety and ESD report, we haven't referenced all of the individual components which were used with our devices. That requires a significant amount of testing.

NMD: Okay, I understand it better now. I am with you now.
C9: Because now they are all manufactured by [redacted] It is now all of our responsibility.

NMD: Absolutely. Tell me which notified body are you with[redacted]

C9: We are kind of with [redacted] and we have recently changed to their [redacted] due to Brexit obviously as well.

NMD: We are doing the same thing ourselves. Are you finding any challenges associated with change management within your organisation, and if so can you maybe talk a little bit about that?

C9: Do you mean change management in relation to the change we would carry out ourselves, Noeleen or those ones that we would have to report to [redacted]

NMD: The ones that you would have to report, so say product changes, technical changes, significant changes basically where you would require to be submitted and approved by notified body. Are you having challenges with that, with respect to resourcing or time to get those done by May 2020?

C9: At the moment Noeleen, we've come to the stage where we won't be making any significant changes to our product until after we have been certified to the new MDR. That was a company decision that was made because we just feel, we need to take it bit by bit, and we need to slow down in relation to our changes and to incorporate MDR first off and then start with our changes. The last significant change that we would have to submit to [redacted] which where we [redacted] one of our needles. Now silicone would be added to one of our other needles and it is one of those products that's added because it will go through the stages easier once it has silicone on it. Now while it was a significant change that needed typing itself and it was a significant change. [redacted] renewed that, turned that around in a matter of three weeks. It was significant in the case that we

finished looking at that needle, but I suppose it wasn't significant because we had already been carrying out the process of adding stuff going to the needle. We haven't had any issues with our notified body in relation to the turnaround of any changes.

NMD: So, you don't have any class III products? Is that what you said at the beginning, [redacted]

C9: Yes, not in [redacted]

NMD: Okay, that explains why you're not coming up too much again with that challenge.

C9: Where we are finding challenges with the notified body and while [redacted]s a small one at the moment, we still haven't received our MDSAP certification certificate. We had our audit and a successful audit last September, but we still haven't received our ISO updated certificate, so that is where we are finding issues. A number of our major sites are having the same issues with [redacted] where we are finding it increasingly difficult to get our cert handed over and sometimes they won't be handed over until the eleventh hour, which holds up a lot of our registrations then.

NMD So how are you managing with Canada then, if you don't have MDSAP cert?

C9: What we did was we literally informed Canada that we had a successful audit through our edit 202 form. We showed them our Z1 form which from the successful audit, and they will allow us to continue based on that.

C9: Okay, that is interesting. I thought it was a no go after the 1st of January 2019 if you didn't have a MDSAP cert.

C9: No, Canada issued guidance, on how you could continue to supply into Canada after the 1st of January. This is one way that would allow you to do it.

NMD: Okay excellent that sounds good. From a resourcing perspective [redacted] has your organisation added any headcount to deal with the resources or has that piece of the puzzle hit you yet in terms of having to hire? How have you handled that one?

C9 Thank god it has, Noeleen. We have three open requisitions at the moment. We have four additional head count in [redacted] in order to help with the MDR. One of those has been killed and we currently have three openings in the division, so if you know anybody who wants a job, send them my way.

NMD: Oh really? So, you have three reg. positions open at the minute.

C9: Yes. Three open at the minute.

NMD: Wow. Is it hard to find people?

C9: Yes. I think we are like gold dust Noeleen. We are valuable in the knowledge we have. It is difficult to find good people with well-rounded experience.

NMD: Okay thanks for that. Will your organisation be able to convert by May 2020? Do you feel that you have enough time on your side or how are you going to deal with that?

C9: I think it's going to be tight, Noeleen. We're concentrating on our Class 1 at the moment. They are mostly our complies and our cables. We are concentrating on the Class 1 first because by May 2020 and because of the declarations we self-certified our Class1 and we really don't have as such notified body oversite of our Class 1. We have no regulation as of May 2020 for our Class 1, so we have to convert all of our Class 1 to MDR by May 2020. That's going to be difficult.

NMD: Is that a big percentage of your business?

C9: Our class 1, yes. Our supplies and accessories, that would probably be 50% of the business, I would say.

NMD: 50% is that what you said?

C9: 50% it would indeed.

NMD: Oh right.

C9: The remaining 50% is probably 40%, 10% split between Class IIa's and IIb's and then the class III's would be the remaining 10.

NMD: And even the class IIb's, do you think you'll have those? Are they implantable?

C9 No, the class IIb's are not implantable. Its only our Class III's are. What we have decided to do and what we have agreed with our notified body is that a lot of our certificates are coming up for renewal this year, and what we will do is they will be issued in a new, which means we have in some cases up to 2022 and 2023 in order to stay compliant but as I said to you previously Noeleen, we will not be making any significant changes to our product for that time and the sooner we get them in the better. We probably have a timeline in place between 2022 and 2023 in order to have all technical files transferred.

NMD: Obviously ye won't be submitting all of your technical files until they've been done on a sampling basis, will you have many to submit to get to actually submit to get reviewed by the notified body?

C9: I think if we can reach May 2020 for our Class1, the notified bodies won't want to see our Class1's. They don't, they are not part of our certificate and the certificate is not required for our Class 1's. I do think though after May 2020, we will put a plan in place in order to submit the Class IIa's and IIb's then eventually the class III's. I think that will be on a rolling basis. We probably as of May 2020, maybe June, July 2020, I feel we will have some of our Class IIa ready to submit and that would be ahead of schedule.

NMD: In relation to knowledge within the regulatory framework, do you feel there is a lack of clarity within the Regulatory framework, right from the commission to the competent authorities, to the notified bodies to the manufacturer? Do you feel there is a lack of clarity there in relation to the MDR?

C9 Yea I do think the MDR reads better certainly then the MDD. Now there are a lot of similarities between the two and some of the requirements haven't changed at all. I think the article at the start are very beneficial and I do think they read well, in comparison to anything similar in the MDD. What were the essential requirements have now been clarified, I think the language is difficult to interpret and I do think there is a more clarity in relation to that. However, interpretation is still there, and interpretation between peers, interpretation between Industry and the notified body and I think the industry and the competent authority that still remain. I was of the opinion that MDR will clear a lot of that up.

NMD: Okay, okay great. One last question then [redacted] in relation to training, how is your organisation, how are they dealing with training for the new regulations?

C9: At the moment, Noeleen where we are with SDR is basically our corporate organisation, corporate have rolled out to SDR. What they have done then is they have rolled out to the directors and managers and procedures. Corporate procedures have been found out and they updated to include the requirements of SDR. In some cases, we have to significantly rewrite the procedures, and, in some cases, we have to generate new procedures. As a training perspective corporate director and then managers have been involved for planning the implantation as training has been implemented that way. For the seniors, the associates and the specialists, really that hasn't been addressed properly through the company I feel. They have been given a very high-level PowerPoint presentation on the requirements but no real detail as to how it will be done. There certainly hasn't been any training provided to our engineering team who will be the ones who will have to satisfy a lot of the requirements in relation to texting and reports that have to be provided. You will probably know yourself at the moment there is so many standards currently recommended in the official journal, but they are currently going through updates at the moment.

[redacted] certainly aren't too quick with the amount of changes that are going through on those at the moment. We do have a regular monthly meeting and how we discuss these changes. We have gap analysis process set up at the moment. We found that out in engineering and we get an official communication or documentation back from them on the changes that need to be made through their own devices and **into** our technical file, but certainly that weak at the moment in relation to our organisation. The process is there but we need to move with it now. I feel in relation to the harmonised standards, its weak and I feel in relation to the requirements of the SDR, it's particularly weak, particularly at our seniors, our specialists, and our associates' level.

NMD: Yea, and I think you are not alone there. I think a lot of us companies are in the same boat, small or large. Even if the notified bodies were designated in the morning, I don't think any of us are in a position to be able to convert our files at this point in time.

C9: No, I don't think so and I think that's the feeling in general I am getting too. We are certainly really only updating our quality manual at the moment to deal with the MDR. We do have a template around new technical files and how that's going to look but we have certainly not started to populate any of that. I think our next step is teaming up with engineering and R&D on how the report will be written in order to classify the technical file. I think that will be an area where we can roll out to our specialists and our associates.

NMD: Yea, I agree. I think we will all be doing something similar and that's going to take a good bit of time as well. That training across all the functions is going to absorb a lot of time and resources as well. [redacted] I don't actually have any other questions for you at this point. Do you have anything else you would like to say before I wrap it up?

C9 In relation to the major milestone that companies are going to face Noeleen, in particular, and I know you mentioned it at the start CER's are massive and that you had asked me that question before saying that. That's an area that we are going to be hugely wide open and vulnerable on. The rest of it then is going to be in relation to our design history file and how that's going to happen and also our material composition is going to be the next area. With any other company Noeleen, was there anything that was a little off the wall when you were interviewing other people? Were there any other areas of concern that other people and other companies had?

NMD: The biggest thing I think that is coming through is, because I am nearly at the end of the interviewing cycle is resources. I think resourcing, time and lack of clarity are the three main things that are the frustrations within Industry and the notified bodies. I mean the notified bodies themselves are struggling. I actually managed to get a few interviews with the notified bodies, so they are the main things that are coming up. Some companies are struggling with change

management including ourselves, and particularly in working with [redacted] so we are really struggling with that particular topic and that is a huge challenge for us. Some of the people, I have talked to, it is a huge challenge, but again it is more in relation to the Class 3 where there are more significant changes and there are more prior approvals being needed.

C9: You probably need to sign off on.

NMD: Exactly, so that is one of the biggest challenges for us here as a large multinational. I'm started doing these interviews with a leading question. I haven't done the analysis yet but definitely there are trends coming across all the interviews, a top three or four that's hitting everyone. You also hit upon those things as you just talked naturally and as the flow went you also hit upon many of the same issues. I think regardless of if you are a small or a large organisation, we all have the same issues and I think we all have job security, that's for sure.

C9 I know. That is one thing for sure, anyways. We all have job security.

NMD: Well listen [redacted] thank you so much. I am going to stop the recording now. As I said, I'm going to be writing the thesis over the Summer and I am quite happy to share the final research with you when it's complete.

Appendix L Transcripts from Interview C10

Interview with Noeleen Mc Devitt (NMD) and C10.

NMD Good afternoon [redacted]. My name is Noeleen McDevitt. I work at Boston Scientific as a regulatory affairs manager. I am doing the masters in regulatory affairs and I am currently starting up writing my thesis. The thesis that I choosing to write about is, the challenges for the regulatory affairs function in the medical device sector in bringing our files in compliance with MDR. As we know, there is loads of changes happening with the MDR and clinical is one of the big challenges facing us. We could stay here and talk about clinical all day or for ten days and we recognise that is a huge challenge but purely for the purpose of this thesis and research, I am excluding the topic of clinical.

Just to set the scene. I would like to thank you for taking time to talk to me. This will be a semi-structured interview where I am going to ask you one leading question. We will be flexible and just explore it and see how it goes after that. I may probe some towards the end with some probing questions, but we will see how the flow goes. I am recording the interview as you know, and I am going to be transcribing it. I expect it to last maybe twenty minutes at this stage of recording. If I ask you a question that you are not comfortable with, please just say I don't want to answer that question and move on, but just to remind you that everything is confidential. Do you have any questions for me[redacted] before we start into it?

C10: No nothing, that's perfect.

NMD: Okay great. [redacted] could you tell me a little about your background and your association or interaction with the MDR to date?

C10: I am a senior regulatory specialist, so I have been in regulatory for coming up to five years. With regards to MDR, I have been peripherally involved with it for the past probably year and a half but within the last six months, I am now fulltime working on MDR.

NMD: Okay great, so have great experience and you're in the thick of it, as we say at the minute.

C10 Absolutely

NMD: [redacted] what do you foresee are the challenges for the regulatory affairs function as we work through, the mammal task that's ahead of us, the MDR?

C10: For me, I would say the big thing would be the transition, the actual transition of product from MDD to MDR. One thing is meeting requirement but then another thing from an operations perspective and keeping products, being able to make changes and keeping up products that are in the market and working on implementation,, I think that implementation of the change over from MDD to MDR and management of that is the biggest challenge for a regulatory professional, and just linking with your operations and R&D, that all your stakeholders there to manage that and insure that they can keep making the changes that they want to make and we also move over in a timely manner and we never end up off the market

NMD: And just on that, I totally emphasise with you [redacted] because we are going through the same thing here. Do you foresee any changes where you won't be able make them, purely because of resourcing or timing etc.?

C10: Absolutely, I suppose even in the essence of the whole MDR project has been that resources haven't been allocated to new project development, so by default, has the money been allocated to MDR and this actual transition, which doesn't actually bring in any new projects into the market is something, is actual growth in other areas or actual operation fixes. MDR resources have been allocated as much as we can for now.

Going forward it is going to affect us how we make changes as we transition to MDR.

NMD: Yes, it is going to be a juggle to manage all that. Obviously regulatory are very familiar with what is going on with the restrictions with MDR, do you feel that your operations folks are in tune with this MDR and the implications of same with respect to restrictions around making changes for this and how it is going to impact them.

C10 Yes, to be hones the focus for the past few months has been working on getting that message across to operations as to what they should be expecting with the whole restrictions of changes on MDD products post May 2020. We have made a big effort in getting that message across to operations over the past few months. We probably won't see how this is going to impact anyone until we see how MDR will stop something happening. Then it will be a big realisation when that happens. We are aware that operations are one of our big stakeholders, so we have put a big effort in there and we have worked with operations to help us get that message across.

NMD: Right, ok that sounds good and really important.

How have your organisation dealt with resources to date?

C10: I suppose like any project it has been set up something similar. Resources have been assigned, budgets have been set up, tasks have been assigned. So yes, similar to other big projects so it has all been accounted for. Obviously, [redacted] is a very large organisation like yourselves. It has been broken down per business unit and has its supporting teams.

It is not being run out of regulatory, it is seen as a stand-alone project on its own.

NMD: OK, so have you hired extra headcount at this point or is more using the resources that you have and juggling around with those resources?

C10: It is a bit of both. It depends on the function. Some functions have hired additional resources such as clinical at this point whereas other functions are using existing resources for a certain length of time and may end up hiring at a later stage. It just depends on the function and how they decide to manage it.

NMD: What is your opinion on clarity, do you think there is enough clarity for the manufacturers and the Notified bodies on how we move forward on MDR. What are your thoughts on that?

E: laughs…. If I were to go with a straight answer I would say no.

NMD: yes, and I agree

C10: Even between different Notified Bodies we see a difference in the message and I think that is going to be the state of affairs over the next year or so. We have had to make assumptions in order to move forward, otherwise we know we are not going to be given the answers by our Notified Bodies. So, we have taken some risks and have moved on.

NMD: What would be an example of that [redacted]e where you would have taken your own initiative to move forward.

C10 Well I suppose the basic UDI, and clinical would be two areas where we are making our own decisions. What is sufficient clinical evidence. There are still no expert panels in place. There are lots of bits and pieces in the MDR where there is still lacking clarifications on what is sufficient. evidence. We are still not clear what the timelines regarding designation, so yes there are lots of bit and pieces where we are not sure.

We will work closely with our Notified Bodies to work with them ahead of time and stay closely aligned with expectations on technical documentation.

NMD: How is your organisation dealing with training. Is this something you are dealing with internally, or are you hiring outside expert people to provide this?

C10: It depends on what function you are talking about. For regulatory we hired in an outside consultant to give training to regulatory. This is something we just did not have the bandwidth to do ourselves, however I would envisage that as I get more involved that I will be rolling out more training. Corporate also plan to roll out training at a later time.

NMD: What are your thoughts on the additional reviews such as the scrutiny process. Have you any thoughts on how they will pan out.

C10: In reality we are not going to find out till we put our first files through it. What is important is that people understand that this additional review may lengthen the review time of their file. This is another example of where there is lack of clarity and with the expert panels not existing, yet it is hard to know at this point. It is hard to know how comprehensive it will be.

NMD: Is there any other challenges you think is going to impact regulatory you would like to share with me before we wrap up this interview?

C10 I just think there is going to be a lot of disruption over the next year or two. Once we get into it we are going to be ok. I think for regulatory we are going to have to deal with a lot of other functions expectations. We are always going to be the "go to" person once it comes to MDR. At the moment we are working of assumptions, even with the whole Brexit thing which also threw another complication into the mix. We are going back to the drawing board and trying to map out what the scenarios could be Brexit occurs and one of our main Notified Bodies are based in the UK. We are trying to be as flexible as possible, we are trying to do as much as we can with MDR filing. We want to make sure we can keep our products on the market and with restrictions on changes we are trying to juggle all of that and keep everyone happy, recognising that are a lot of "if's" and "but's "in there at the time.

It is a really difficult thing to communicate, especially when you are managing multiple products. My strategy is to keep a list of questions where I don't know the answer to follow up on same and revert back to whomever was asking the question in the first place, because I for sure do not know all the answers at this point in time.

There will be a bit of trial and error where we will send in files to the Notified Body for review and wait and see. In saying that, the business does not like that. The business always like to know what is going to happen, and to have precise answers, but that is not possible in working through MDR.

The business wants answers, they want to have timelines, they want to be able to plan, but we are not there yet with MDR.

NMD: Yes, I totally agree with you. It is so hard to plan

I would like to thank you [redacted] for talking to me today. I have enjoyed listening to you on what you perceive to be the challenges. I appreciate your honest opinions and feedback. It is always good to talk to someone in industry who is going through the same thing as we are ourselves.

I am going to wrap up the interview now. I will be working on this thesis over the summer and would be happy to share it with you if you wish.

Thanks again.

Appendix M Transcripts from Interview C11

Interview with Noeleen Mc Devitt (NMD) and C11.

NMD:

Good afternoon [redacted] my name is Noeleen McDevitt. I work in Boston scientific as a senior Reg Affairs manager. As you know I'm currently doing my master's in medical technology and reg Affairs. As part of that course I'm writing a thesis. The particular topic I'm choosing to write the thesis on is the MDR - specifically in relation to the challenges for the regulatory affairs function in the medical devices sector in developing their technical documentation to bring it in line with these new regulations. As we know clinical is going to be a huge issue for industry and surrounding clinical evidence and so I'm actually going to exclude the discussion of clinical in this thesis -because I think it is a full topic in its own right it's right and it's one of the big challenges but purely for the purpose of this thesis I'm going to go to exclude the clinical aspects. Thank you for taking your time out of your busy schedule. There're no right or wrong answers here. It's just set it up as a semi structured interview. I'm going to ask you one leading question and we'll see where that takes us. I am recording this interviewer, and I will send it to consent form to you for sign off. I'll be transcribing the interview. I expect to last about 20 minutes or so. If I ask you any questions [redacted] that you're not comfortable with you can just asked me to move on and we'll just go from the next question. So, do you have any questions for me before we start.

C11: No, I think everything is clear.

NMD [redacted], could you tell me a little bit about your background and how you have been involved in the regulations to date.

C11: OK the MDR regulations. I am a Notified Body Project Manager. being an auditor in [redacted] Review Application Manager. In terms of MDR, the level of involvement I have to date is within the notified body to try and implement the regulation within our own Quality Management System. Also, with general discussions with clients for to try and understand what their challenges are and to try and get some clarity in conjunction with clients on general MDR level topics. I am also involved in developing within our business – the transition phase from MDD to MDR, specifically in trying to deal with the timelines. From a high level, I have been involved in giving input to common specifications that are currently being drafted. The notified bodies have been requested to give an input. Some general level things.

NMD: From what you have described you are very much involved in the MDR regulation and would be very knowledgeable on them. I was wondering what you think are the challenges for the Regulatory Affairs professionals as we work through this project and try to bring our files in line with the MDR regulations. Specifically, for Regulatory and I would consider Regulatory be it industry, Yourselves as Regulatory professionals. What do you see as the challenges for this function over the next couple of years.

C11: Obviously the MDR regulation has provided us with much more clearer expectations with some topics. I think the main challenge is with lack of clarity for many other elements, as to how it is expected to be implemented. You did mention as to clinical being a challenge while excluded from this discussion but that is obviously a key example of what level of clinical evidence.

Some other topics regulatory professionals are having trouble grappling with

In the documentation section of MDR, it is extremely detailed as what is to be put into, but there are some intangible things, such as …All process validation data must be included. It is not always clear what is the industry standard. Do they really want all process validation data down to very detailed instructions?

Or as the person has written the MDR is just high-level report. I think the first issue is the lack of clarity on certain topics. Certainly, as for things like drug device combination there is a huge lack of clarity. It is not understood weather we are going to need to do full consultation with these products again. Or whether a gap analysis consultation can be done. It is very much coming from the commission for this kind of thing that full review must be done. And in a broader sense of technical documentation as well, it is a big challenge for the regulatory affairs function within notified bodies and within manufacturing sites. There is an expectation from the European commission that full Technical File Reviews will all be done.

Even for products reviewed and approved under MDD within the last year or two, you may not leverage any information from previous review and that has been very strictly told to us by the Commission. I think that is an extremely challenging aspect because???

in term of the amount of time to get all these things done. In terms of all the extra work that is to be done, managing the expectations for Regulatory affairs people within industry I imagine managing expectation of own Management is going to be extremely challenging.

How do you explain to a commercial manager, as to how that a product that is just approved two years ago, has to now go through another full File review? You need to put in lot of extra work into updating documentation, with information such as process validation data and much more detail like the . for material. Yes, I think managing expectations. Then, from other practical things, with materials as to all the new requirements regarding substances. That is quite a challenge for regulatory affairs people to get all that information together. To try and get from supplier of polymers, exactly down to the very smallest component to get what is exactly in their polymers, which previously information had not been asked to share, hadn't been asked to give. Challenging how much information you know along the supply chain and getting that information up - It is going to be difficult. I imagine for some products, it is going to cause an enormous amount of problems, as some of this information may not even be obtainable. Thus, people may have to make product changes because of this kind of thing. At the top of my head that is a very rambling things that jumps to me about problems.

NMD: You have described so many extra steps that are built into the various processes, extra documentation, which leads to resourcing. Obviously, your workload as a notified body is going to cripple with all this additional documentation to review. What are your thoughts on resourcing and workload with respect to that?

C11: I think I mentioned about you having to manage all expectations of your own management, and I think where the challenge is going to come is where companies are going to expect to get products reviewed in a prudent amount of time and are going to come up against this massive resourcing issue with certified body. We are estimating approximately taking a Class III device

With a typical previous review time of about 40hrs. We are anticipating the average review time will go up to 60hrs for an average Class III device without any drug device combination. Just the actual review time per product will increase and now obviously the fact you are going to have to review product that notified body has certified over the last approx. twenty years within the space of five years. All files must be submitted within the space of approx. four years. This feels like virtually an impossible task. The companies are going to get a big fright when they find out that products coming out of the Transition period in 2024, which just simply have not had the capacity from the notified bodies to review the appropriate documentation. There simply hasn't been capacity in notified bodies to review the documentation in order to approve a product.

If we take the current notified body workload, the average project manager within our business working with a 40hr week contract – people are working between 50 to 80 hrs / week on average.

That is just with maintaining the existing workload. Adding additional new file reviews on top of that, and additional audit plans. Audit times are going to be increasing with initial audits and with MDR requirements will increase. Audit times will be increasing. Effectively it is capacity we don't currently have to take up the MDR reviews.

NMD: That is not sustainable. Those hours you talk of are not sustainable for anyone. You can do that for so long, but you can't do that on a long-term basis.

Has your organisation hired many people as a result of the MDR project?

C11: We did a Technical file training in January and we had 17 new starts globally attend that training. We have all been recruiting, but that is an indication of how much globally we are recruiting. We have a new person starting approximately once a month. We just have a permanently open position rather than stating we have a specified number of positions open. If a person applies to us who is perfect for the job, we will just hire them. It's an area of constant expansion and we have ongoing recruitment agencies looking for people. The requirements for Notified Body Staff under the MDR has obviously increased. Previously people with good experience could be accepted or people with a strong academic background. But now you need to have academic background and experience to be clearly evident to go with all the qualifications.

NMD: Training seems to be a big emphasis for notified body staff. So that is obviously taking up a lot of your time training people

C11: Typically, it takes us 6 months to a year to train somebody up. For audits and specialised work it could take anything up to 18 months. Some people with appropriate background can be trained up in 4 months. Other people can take 18 months to get their qualification. We have introduced a new training program which is 4 or 5 weeks 80hrs of training. We expect people to have 160hrs of audit training… hands on audit training. The 80 hrs are just the initial training. It is not actual practice of carrying out audit review. You need to have x hrs of product review in order to be qualified. Auditing is 160hrs in addition to some auditing courses. An enormous amount of self-reading. Reading Standards, reading regulations, guidance and stuff like that.

NMD: That brings me on to my next question. Do you feel there is a lack of clarity presently within the Regulatory framework? There are certainly frustrations on our end, where there isn't answers from the competent authorities or the commission, and then the Notified Bodies are depending on advice or guidance from the commission. What are your thoughts on that, from a transparency as to how this system is supposed to work.

C11: I think for us, it doesn't feel very transparent at the moment, because as the way we get information is kind of through rumours generally and that's not great.

We have somebody who goes to Brussels regularly. Literally we get information that she has picked up from talking to commissioner lawyers. We sometimes get information from the competent authority. We do have a regular communication channel, but it is not like we are getting a weekly bulletin from anybody saying this is what is going on, this is what is at stake. There does seem to be lots of different things going on. Suddenly out of the blue we receive some common specification to provide input on. It seems to be the same steering group functioning, but we are not really sure. Sometime things come out of the NGPD. There is not one clear line of communication where we can get information on guidance as to when we can expect what. It is often a hard line we get back from the authorities saying that we must take the instruction without interpretation. We are told we can't interpret. In the end you have to implement the hardest version of what the regulation is going to say and that is very difficult to tell some manufacturers. It definitely feels like there is a lack of clarity in communication.

We have realised in our own government that those sources closest to Europe get more information as to those that stay in offices.?? We are trying to improve that and have more regular communication just to update people to be able to give progress update as to what we are hearing.

NMD: The next question I was going to ask you was in relation to change management. From an industry perspective and this is from dealing with a few notified bodies, we are starting to feel the restrictions of change management and leading up to May 2020. We are limited to the number of submissions that a given notified body will take into review and again this goes down to resources etc. What is your position on this?

C11: We haven't limited the number of changes we are going to accept but we have put restrictions on the bands as to when we will accept changes to ensure we have sufficient time to complete the review prior to the end of the MDD in May 2020. I think the main challenge about the changes is re this discussion on MDR no changes. No significant changes of intended design intent to be introduced are allowed after May 2020, but the question is coming what significant

changes entails.? Is this in line with what was documented in the NB MED document. Are there different interpretations of what is a significant change relating to MDR? As we don't have clarity on that so for changes all notified bodies are heading in the same direction to take that quite literally. We are talking of products qualified under the MDD. If that's the only guidance that is available for products, then that is the guidance we continue to apply until we receive clarifying information from the consular authority. In terms of changes we are just limiting the time period because we have processes that take time and hopefully we don't have to look at the actual number, but we haven't got to that point yet.

NMD: We have with one of our other notified bodies, that we are very much restricted with the number of changes that we can send in. That obviously has huge impact for Operations and functions outside of Regulatory that are not as close to MDR and the whole Certificate structure that we live with and understand. It is very hard to get that message across to other functions that they can't do certain changes- when that is all they want to do is to keep making changes.

C11: Again, that is managing expectations within your own organisation. It is such a big challenge for you then when they don't understand the impact of restrictions

NMD: I think like the MDR seemed like so far away. May 2020 seemed so far away but it is coming very close isn't it? In relation to that then and in relation to the amount of time we have left do you think there is any chance of that date being shifted out - May 2020?

C11: We have not heard that it will be. There are some people who hope, what they hear coming back from Brussels is that it is a very hard timeline to meet with all the stuff to the end of MDD and the start of MDR. It is not going to change. They are extremely determined to push this through.

NMD: We are recertifying everything under MDD to buy ourselves time. It's a pity that companies have to do that. As obviously we are doubling up on costs.

C11: A lot of this stuff is a tick box exercise to cover these aspects, but it could be a costly exercise.

NMD: A costly tick box exercise, exactly.

Is there anything else before I wrap up this interview? Thank you. You have covered a lot of ground there and you have covered a lot of challenges that other organisations are coming up with. So, it is great for me to see a trend coming up for the various different organisations, so that is good.

I'm actually planning to do a survey after when I analyse the interviews and come up with themes from the challenges. I'm going to do a quick survey which I might get you to participate in. It might be like a 5min survey. Is there anything else [redacted], you would like to call out as a challenge? There's lots of them I know.

C11: No. I think we have covered the main things. I'd be very interested to read your thesis when you are done.

NMD: Absolutely, and I will send you the consent form. I would love to share it with you. I have actually really enjoyed having the chats and interviews with all the people because it is not just us that is going through the pain. Everyone else is going through the same thing. It's kind of comforting and reassuring to hear the same thing from everyone. I think at the end of the day, we'll get there. It's just, it will be a windy road for a year or two.

C11: It will happen. It's one of those things that has to happen. At least we know that. We just push forward and get it done.

NMD: Great. Thank you.

Appendix N Transcripts from Interview C12

Interview with Noeleen Mc Devitt and C12

NMD: Good afternoon C12. My name is Noeleen Mc Devitt and I work in Boston Scientific as a Senior Regulatory affairs manager. I am currently studying a MSc in medical technology in regulatory affairs and as part of that course I am writing a thesis. The subject that I have chosen to research is "The challenges of the regulatory affairs professionals in bringing our technical documentation in line with the new regulations, the MDR.

As we know clinical is a huge challenge and a huge portion of the MDR, so what I am choosing to do is to purposely exclude that topic from the scope of our discussion. We sit here and talk about the challenges of clinical so for that reason I want to exclude it. The clinical function will be responsible for filling this gap and obviously regulatory will work with them on that, but it will primarily be clinical.

I would like to thank you for taking time out of your busy schedule. Everything you say will be confidential. You will not be identified by name or by organisation. I am setting this up as a semi structured interview where I am going to ask you one open leading question and we will see where that takes us. We will be flexible, we will explore what comes out spontaneously. I may probe you with some questions, or I may not have to. We will see how the free flow goes. I am recording it as I said to transcribe, and we have signed off to say that is ok. I would say it will take @20 mins, half hour maximum. If I ask you anything that you are not comfortable with you can just ask me to move on. Is that ok.

Do you any questions for me before we start?

C12: No

NMD: Can you tell me a little bit about your background and our involvement with MDR to date.

C12: My background involves having a degree in bio medical science. With that degree I started out working in a clinical laboratory setting testing blood, micro etc. I spent some time in the lab. I was not a fan of the lab environment, so I moved into industry. I moved to Australia and worked in the invitro industry where I was training people to use point of care analysers. So, I as training people to use that in emergency departments, operating theatres etc. I did a few years of that in Australia, then moved home and got a job with NSAI. It was a business development role.

Initially it was a standard role to increase client base and a very traditional business development role. That was September 2016. We knew the first draft of the MDR was out at that point. In April 2017 it was published. The focus with ourselves and anecdotally from other Notified bodies, the focus shifted from growing the business to working internally to preparing for the MDR transition and ensuring that our own client base is supported for their transition. I guess my job spec has become very fluid in a sense then. Very few Notified bodies have development teams out there trying to grow the business, purely because we don't have the capacity to grow anymore.

We are a little unique in NSAI in that we are a semi state entity. We report to the department of business enterprise. That is the same as enterprise Ireland. Part of our brief is to support the MedTech community in Ireland, regardless if they are our clients or not. That sort of keeps a slightly different focus for us and for me particularly in relation to information sharing. Just because of our day job as Notified body we get to learn a lot about the regulation and it is our responsibility to be responding back to the industry at large. As best we can do that with information sessions. We have an open-door policy in this office. We often would have companies, especially new start-up companies come in for a no strings attached chat about what it means to go through the regulation.

NMD: That's a great service, I did not know that this exists.

C12: Yeah, we are connected in with Bio innovate and Bio excels and various programs with NUIG. We give talks there and any company can talk to us in full confidence. It's not consulting, because we can't, as a Notified Body, but what we can simply do is tell them and explain to them what the requirements and these are the things we see companies doing. It is a useful service for companies to avail of.

NMD: Yes, this sounds like a fantastic service.

C12: So then, we have an internal MDR transition team within NSAI. Annex XII of the MDR outlines the requirements of the Notified body and basically that is an entire rewrite of our Quality system. It encompasses the requirements. That as you can imagine is an enormous body of work so there is a big team of us internally working on that. That would be replicated within other Notified bodies and that leads to capacity challenges also. At one point we probably had 30% of our review team off reviews and working on the MDR transition for on the audit and things like that. I have been involved in that, the Quality system transition so I got quite a bit of exposure to what was going on with the MDR as well as the public facing role also. I don't do technical file

reviews; my role is more on communicating on the process with clients and potential clients. I do have a technical background and I do get involved sometimes in some of the technical aspects. I am not a site auditor or a technical file reviewer.

NMD: Ok, good to know your involvement in it. With that said then, what do you see as the challenges for the regulatory affairs personnel in compliance with the MDR.

C12: Do you want to focus on the challenges for the team, like you said we could discuss Clinical for days.

NMD: Yes, how will it impact your regulatory folks.

C12: I think the impact of the MDR is far more widely impacting than just regulatory.

NMD: It is indeed.

C12: We know that because we work in regulatory, I am not sure how well it is known in the other functions across Operations, purchasing to Senior management. Companies are getting a lot better, there is no hard evidence for that, it's all anecdotal. People higher up in the organisation are becoming much more aware of the effects of the MDR, and I think that is a huge challenge for the regulatory affairs professionals because they know exactly what is required, and they need so much resources and buy in from the different functions.

If you look at, you are transitioning your essential requirements to GSPR's, general safety performance requirements. A big part of that is going back on the design history, going back to the R&D department, and bringing them up to speed on MDR. If their management team is supporting them on this. It is important for the regulatory professionals to have that support.

I know we are not talking about clinical but that is going to be a huge aspect. Does the organisation know that at the highest level that there is a chance that the company will have to do a clinical trial., which is a serious investment for a company? Infact that decision may be the balance on whether that product stays on the market or not. Obviously, that is a decision that is made at a very high level in the company. It is driven by information coming from the regulatory affairs department. It is the buy in and the visibility and the impact of the MDR is the challenge for the regulatory affairs professional.

The workload we know is a huge challenge and it comes back to resourcing. If there is not visibility all the way up the management structure that additional bodies are needed. It is the sheer volume of work in terms of, I spoke of us needing to overhaul our Quality system to be compliant with the MDR. There are very few supporting technical documents for products that

are going to remain untouched by the MDR. What is very important to understand when we look at a file for MDR, and it's not just we, its every notified body, we are reviewing the file as a brand-new product as if it has never been on the market, even though it may have been for 15 / 20 years. That changes the mindset of how a product is reviewed because if your product is on the market for quite a while and you go through these recertification cycles, some Notified bodies differ from what they look for in a recertification cycle. We know because we take transfers from other Notified Bodies, and likewise others take transfers from us, so we do get to see the level of detail that has gone into a review. Sometimes, I don't know if it is complacency or I don't know what it might be, but the standards that are being adhered to are not the most recent harmonised versions because the product has been on the market for 15 years.

Now there's no excuse because it is being recertified every 3 or 5 years. Apart from recertification the Notified body should be establishing that the product should be adhering to the most recent version of the standard. That is not happening all the time. BUT when MDR comes into the picture, the Notified Body has no option but to ensure it complies to the recent version of the standard.

There may be additional work that needs to be done here such as biocompatibility testing, there is software validation testing, human factors engineering testing, those are potentially new tests that will have to be done. Those tests are not done by the regulatory affairs department, but they need to highlight that they need to be done and make it happen. So, they are going to be reaching out to the other departments. You will have financial elements. I just think every aspect of a technical file's documentation will be impacted.

NMD: Yes, there will be a lot of interaction dealing with functions.

C12: The challenge is, do all of those other functions really understand the impact of MDR and who's responsibility is that. Is it the responsibility of the regulatory affairs function to sit down with these functions and let them know what's happening? Does this need to happen at a higher level? Do organisations need to invest in sending non-regulatory personnel along to information evenings and conferences and things like that? I don't know if that is happening in industry, but I do think that the more people know that this is happening and are aware, it is going to make it easier for everyone.

We have engineers in house here who are reviewing reports which comes from industry and sometimes they don't fully understand what is happening with the test method. They will contact regulatory affairs person in the company. The regulatory affairs person doesn't always

understand the test method either so they in turn rely on the engineer to explain it. So, you have scenarios of an engineer in a Notified Body that does not understand the testing technical aspect and then you have an engineer in industry that does not understand the regulations, the regulatory affairs person is the person in between communicating between the two of them and that is a really difficult position to be in. We have combated that in upskilling of other functions with regard to the regulations.

NMD: I think the people that I talk to in different companies have different approaches to training. Some are hiring specifically for MDR and then in other companies they are being absorbed into their current role. A % of their time dedicated to MDR.

I think it is interesting that we have been talking about MDR for so long and its really only now in the last 6 months that they are listening to us because it is upon us.

C12: Do you think they are listening?

NMD: Yes, I do think they are now.

C12: When you mention two words," label change" their ears prick up.

NMD: That brings us on nicely to another question I wanted to ask you. So, one of the things we are seeing in industry is how change management is impacting us. How would you say your Notified Body is dealing with change management? Can you talk to me a little bit about that to understand your perspective on change management and how you are dealing with it?

C12: It is a challenge. So, the directive is in place since 1993. Standards are continuously updated and we as a Notified body and we are a standards organisation as well. Our staff would be used to every now and then, there is a revision to the standard. Take for example 13485 2016. Our auditors have been auditing to the 2003 version and I know there was a 2012 version as well, some of them have been auditing that for years and years and years. So, change management is something that is inherent to life working in a Notified body. Things are constantly being revised. And our staff are constantly working on such a variety of things that change is always happening.

At an organisational level individual is used to companies presenting their documents in different ways, depending on their system. At an individual level, it would be something that our staff would be familiar with. At an organisational level it is certainly more challenging because the way we review files. We have a very disciplinary approach to reviewing files. We are lucky to have that because there is no way couldn't have that with the MDR.

We have someone who looks after sterilisation, possibly that person can look at biocompatibility if they are training in that area as well. If we have software to be reviewed we have a specific software engineer, we have a medical person who covers the clinical aspects, so you could have 4 or 5 different people reviewing a given file and that being co-ordinated by a file manager. Some Notified bodies would have had 1 or 2 people reviewing a file but that is going to change with the MDR as it goes back to the competency required of reviewers. The level of detail that each individual needs to have. So, we are lucky that there is not going to be an enormous change for how we review our files since we have several experts review the one file.

That may be a change for other Notified bodies. Change management is a challenge at an organisational level for us., how we are dealing with it is very much as a team.

We are one department within NSAI, we have other departments as well.

NMD: Can I ask about change management from a different angle? So, from the sheer volume of work that would be coming from your customers, do you have a cut off period of where you are going to say to your customers that they cannot submit after a certain timepoint. Can you bring me through your plans there, and when do you folks expect to get designated?

C12: We put out a communication in October of 2018 of our transition plan to the MDR. So, the last date of when we are accepting new products under the MDD is 27th May 2019.

The reason we picked that date is that it buys us 12 months from when MDR kicks in. If we begin reviewing a file under the MDD and we don't have it reviewed by May 2020 we can't review it because in effect the MDD has died at that stage. Now it does not normally take 12 months to review a file, but it is good to buffer in time.

We are allowing substantial changes to be submitted up to MID November 2019. I think it is 27th Nov. That is giving us 6 months to review a substantial change before the MDR kicks in.

Different Notified Bodies have different dates.

NMD: They do yeah.

C12: I think BSI is March 2019.

NMD: Yes, and DEKRA is October 2019. We have heard August 2019 and we have heard October 2019.

C12: Our Notified body is full in terms of new products under the MDD. We cannot take anymore. We have a certain number of slots available. I mentioned earlier that our position is a

little unique in that we are a semi state agency and we have a responsibility to the MedTech industry. The deadline of 27th May is a self-imposed deadline so there is a certain amount of flexibility there. It would be nice to get through a chat without mentioning the B word with Brexit, but it is very relevant because there are some Irish companies that are challenged as they use UK based Notified bodies, so we have allowed for certain flexibility internally should they try to approach us. Those deadlines are difficult as some of those companies will not be able to get the product in front of us for the 27th May date which pushes us to MDR and that's hard, as all along they have planned for it to be born under MDD, and then all of a sudden, they have run out of time and it will have to be submitted under MDR.

For our own change management, we had to put timelines in place. We can't have files coming in under the MDD continuously throughout the year. It's just too dangerous and it wouldn't work. We figure we are being upfront now by telling a company we cannot take any additional new products on. That is a whole lot better that getting 6 months through a review and all of a sudden having to change tack.

NMD: So just in relation to substantial change then for your current customers? Are you able to accommodate all of the substantial changes that your current customers want to make? Or do you have to put restrictions in place.

C12: We have not had to do that yet. We have a lot of substantial changes booked in all the way out to November, as obviously companies are looking ahead. Perhaps we will have an issue closer to the time, I can't say that for right now we have had to put restrictions on anything. I guess what we are seeing an awful lot of work now are companies recertifying their products under the MDD. Obviously, that will allow companies to get certs right out to 2024. Some of these might have certs currently out to 2021 or 2022 but they want to be able to have the opportunity to sell that product under an MDD certificate out to 2024. That's fine, I understand why they want to do that.

NMD: But it's like doubling up on the work.

C12: Yeah, we know when we issue cert now with 5 years when it is going to come back in. It is very cyclical for us. But now all of a sudden it is not as everyone wants their certs renewed now even though they are not due for another 18 months.

NMD: And then they will be coming in again for MDR.

C12: Well hopefully these companies will be pushing off on submitting out to 2023 timeframe.

You asked about our designation. We applied in November 29th 2017 and we had our designation audit in June 2018. It was an incredibly tough audit as we expected it to be. We had our competent authority plus two other competent authorities, plus the commission. We had 7 auditors for 3 days so again it was a hefty man day audit. It is what we expected. If you speak to any Notified body competency is a big focus. How are we qualifying our auditors, what are the criteria because obviously the criteria are been raised and how do we as a Notified body interpret that criteria.

Where we are then, there was non-conformities raised, and we are back and forth on that, and thankfully we are quite a way down that path. Now we are hoping for designation for end of Q2 this year. We are saying that, but it has to follow the caveat of a lot of moving parts. The final responses that we give have to be approved by the joint assessment team that actually carried out the audit.

You can imagine when you are co-ordinating between multiple people and then the HPRA need to come back in and close out the audit. It's going to be a really long road, we are out the right side of it now, but its availability of competent authorities as well, no more than ours from getting the responses done.

NMD: Its complex

C12: Yeah it is, it probably doesn't have to be as complicated as it is but to be fair we have put industry through this. Industry only knows that we are competent to do this when we go through such a rigorous designation process and that's only fair.

NMD: So, it is the right thing to do

C12: Absolutely.

NMD: Can I ask you a question on clarity. Do you feel that the Notified bodies are clear on how they are meant to be interpreting the regulations? I guess from an industry perspective there seems to be lack of clarity. Somebody described it to me as "you have moved into the house and you are building it around you" which I thought was a great analogy of how we are working through this MDR. What's your thoughts on that?

C12: I completely agree there is a total lack of clarity, and that goes right the way up. To be honest I know from speaking to so many different clients about the MDR, we encourage our clients to call us just to chat about it. Just run it by us as part of early stage planning. We want to know what companies are at, its ok if there are changes and we get a lot of questions and we

do not know what the answers are. That must be very frustrating for industry if the notified body does not know the answers then it's a big problem.

We have such a tiered system in Europe, if you compare it to the FDA. So, manufacturers speak to us, we speak to our competent authority, the competent authority speaks to the commission and it can get lost in translation.

NMD: Yes, its very political isn't it the whole circle.

C12: Yes, I suppose it's something that we get asked by an awful lot of our clients, if you look at article 120 transition provisions, that a medical device can remain on the market till 2024. That's fine, but after May 2020 you cannot make a significant change to the design or the intended use of the device. What if you change critical supplier? How do we handle those changes? We don't know yet how to do that. We are part of team NB as well, so we know a lot with what is going on with other Notified bodies. Everyone is flagging that with their competent authority, how do we asses something that is a significant change, but it is not a change to the design or the intended use? Do we assess that change against the MDD in 2021 OR 2022? The MDD will have no basis at that time, so that is something we have asked for clarity on and we have not gotten an answer, I assume because it's not there. I am sure that question has gone all the way up to the commission and I don't know will there be a guidance document or a common specification or we don't know what mechanism we will use to create a common understanding. But that's just one example of "what's the definition of sufficient clinical data? Who knows?

NMD: Yeah it's an open question.

C12: There is a guy from TUVSUD Notified body and he is like the rock start in MDR. He has stated that they are going to create their own version of what they deem to be sufficient clinical data. They can't wait for the guidance to come out anymore.

NMD: That goes against transparency then.

C12: I think it's more than transparency, I think it is the level playing field.

Notified bodies don't want manufacturers for example when they move from one Notified Body to another to get asked a completely different set of questions. There is always going to be some differences because it is going to be down to the reviewer but the actual basis of it should not change.

NMD: The nuts and bolts of complying to the MDR should be the same for all companies.

C12: Right now, it can be black and white, and night and day from one Notified body to another, but exactly that lack of transparency from a higher level is forcing Notified bodies. Right now, what we are doing on the clinical side of things that in the absence of a guidance document we are following the MEDDEV Rev 4, I know that is massively explicit, but we have nothing else to follow, and Notified bodies cannot come up with their own definition of what sufficient clinical data would look like.

I 100% agree with the lack of clarity. I don't think Notified bodies should come out with their own viewpoints of what every aspect is, then it's not that common understanding. I feel like I am passing the book when I say but it needs to be coming from higher, from the MDCG, - the commission, to get a shared understanding across the community. That I can only assume, an optimist, that it will come in time.

NMD. Yeah but we are just running out of time.

C12: Yeah, we are absolutely.

NMD: That has been great [redacted] You have covered a lot of the challenges that I was thinking of myself. I would like to thank you for taking time out of your busy schedule to accommodate this. I have enjoyed listening to you, I have enjoyed hearing your perspective on it all.

C12: Good

NMD: Do you have any questions for me before we wrap up the interview?

C12: no not really.

NMD: thanks again.

Appendix O Raw Data from the Interviews

Summary of the Interviews

Interviewee	Challenges identified
C.1	• Understanding all the changes that must happen • Lack of clarity, lack of guidance documents • Lack of standards being updated and harmonised against the new regulation, won't be done till 2024 • Post market surveillance requirements • Cannot grandfather in products, all old products treated as new product reviews again – huge burden • Material assessments • Enormous workload for industry • Enormous workload and capacity issues for Notified Bodies • Change management/ Prioritising changes • Additional reviews for products with drug/ animal tissue • CECP – Clinical evaluation consultancy process. • Keeping other functions and Operations informed on the impact/ restrictions • Up classification of product • Class IIb implantable will be treated the same as Class III • Running out of time
C.2	• Getting a handle on the whole document, sheer volume of additional information. • Interpretation of the regs- NB not allowed interpret • Commission needs to guidance on interpretation • Time is an issue • DEKRA - getting together in April as cannot wait any longer. • Change management – restrictions of timepoints of when can submit • Annex II capability- new regulations does not distinguish between classes- that is unclear • More changes submitted will take more time to review which will lead to cost. • No grandfathering – files treated as new products again, files will take longer • Resources / qualification criteria very strict – takes over a year to train someone, competency in codes etc. • Training – big challenge. Developing tools to help them internally. • Take more time to review files. Probably will be more questions. • Going to be a learning curve.

C.3	• More difficult for smaller companies • Don't have the budgets • Lack of time, most companies using the recertification of products under the MDD to buy time. • Some Notified Bodies may not be around, Brexit? • Post market surveillance – what is that supposed to look like? • Lack of guidance • Change Management • Training • Cost
C.4	• Resource requirements for Competent Authorities, Notified Bodies, Industry, Commission, expert panels, joint assessment teams • Specific expertise requirements under the various chapters, Authorised rep, distributers, supply chain. • Understanding what is new in the regulation and assessing what the competency gap is then with the current staff. • Training, upskilling, • The scrutiny Process • The standards not being updated in line with the regulation – creating a gap analysis • Post market surveillance and reporting • Eudamed database
C.5	• Understanding the MDR – Interpretation • Converting the technical documentation – format • ERC's to GSPR's • The unknown- nobody has made a submission, or a NB has not reviewed one yet • Clinical reviews • Timelines are unpredictable • NB readiness and capacity • Change management – the regulation does not distinguish between classification for significant changes – hence more workload • Resourcing – more responsibility on the authorised rep and they deal with the distributors etc • Will be adding resources • Eudamed – will have to manage in-country individual databases too with BSC. • Training – developing training – lots of training developed within BSC. • It is a challenge for small companies. • Lack of clarity – • Post market requirements

	• This interviewee gave a great summary in that if companies and regulators had worked properly to the MDD then there may not have been a need for the MDR.
C.6	• The system is not ready- great analogy, we are living in a house and building it around you. • Structuring technical documentation • BUDDI numbers, how they are set up. • Lack of clarity and guidance from the notified bodies and competent authorities • Lack of guidance documents • Change Management • Workload • Resourcing issues • Training – different levels of knowledge required for different functions • We do not know how file reviews are going to go with Notified Bodies • The unknown. How long will it take to get approval etc.
C.7	• Lack of clarity • No guidance's • Unpredictability • There is no system behind the regulation • Communication – Keeping other functions informed on the impact of the MDR. Trying to give timelines and that is difficult when guessing. • Post market surveillance • Change Management. • Timelines • Resources • The review process and # of steps for the Class IIb, Class III is unclear.
C.8	• The unknowns • Notified Body resourcing • Change management • Changes needed to the Quality system • Understanding the role of distributors and economic operators • Doing a gap assessment as to what needs to change I reality • No grandfathering allowed, products treated a new product again, may be gaps in testing. • What the technical documentation will look like • Lack of clarity from players in regulatory framework, Notified bodies, Competent Authority, Commission. • Resources • Training

	• Cost
C.9	• Writing technical files, knowing how to structure the files • Labelling, lots of systems and kits, we use distributors, so its complex, • Resourcing – small company and hiring 3 or 3 people • Lack of clarity • Training • Compliance to standards, many of these are old products so proving compliance may identify gaps.
C.10	• Transition of the files from MDD to MDR • Managing ongoing day to day changes • Making other functions in the business aware and up to speed on MDR • Resources • Lack of clarity • Clinical reviews • Getting things done in a timely manner.
• C.11	• Audit burden • Communication to other functions on MDR • Drug device combination – additional reviews by drug agency • Unable to leverage reviews previously conducted. Files have to reviewed in its entirety again despite nothing changing • Getting detail on materials information may be a struggle • Managing expectations to management • Extra steps in the review process • Increased workload- typically a regular class III device would take 40 hours, now they anticipate it will increase to 60 hours, and that is just the first round. • Resources- added 17 new people started in January. There are permanent open posts. • Recertifying a lot of products to MDD • Training – takes between 6 and 18 months to train people. Need to have 80 hours of technical file review training 7 need to have 160 hours of audit training at minimum. • Lack of transparency • Change management – what is a substantial change when the regulation becomes effective? • Limited time – Won't be designated till Q3
• C.12	• Converting their Quality system to comply with MDR. • Capacity / resource challenges • Making other functions outside of reg aware of the MDR • Resources required from functions going from ERC to GSPR. • Treated like new files new products again • Serious investment if a company has to do a clinical trial

	• Reg are the messengers from – getting buy in from the functional areas is a challenge • All way up through management must understand it • very few supporting technical documents for products that are going to remain untouched by the MDR • products transferring from other NB have different levels of documentation • workload of recertifying all files to MDD. • May be additional testing, bio, software etc to be redone. • Companies not always referencing the newest version of standard • Training – gave examples of engineers in NB does not understand the test method and vice versa the engineer in industry may not understand the regulations. • Change management – he answered it differently to how I anticipated. Re asked the question and he got into the cut off dates etc. Last date of products under MDD May 27th • Lack of clarity and guidance from the commission – he gave the example of changing critical supplier.

Appendix P Email to Survey Participants

Dear Participant

I am conducting research on **"The Challenges for the Regulatory Affairs Function in demonstrating compliance for existing CE marked devices to the new EU Medical Devices Regulation 2017/745"** (otherwise known as the MDR and referred to hereafter as same).

I would appreciate your support in completing a quick survey (<5 mins) to understand your challenges as we work our way towards the MDR. Your participation in the survey is completely voluntary and all your responses will be kept confidential. If you have any colleagues who also work in regulatory affairs, please feel free to forward to them also.

One of the widely recognised challenges with the MDR is the new requirements surrounding clinical evidence. For the purposes of this research I am choosing to exclude this topic to focus on additional challenges for Regulatory Affairs.

I appreciate you taking time to complete the survey. Please do not hesitate to contact me if you have any questions.

Please use the following link. https://www.surveymonkey.co.uk/r/HTRDJT5

Kind Regards

Noeleen Mc Devitt

Appendix Q Raw Data from Question 8 of the Survey

The following comments were made in addition to respondents answering the question

Do you think the MDR will have an impact on patient safety? Yes or No, please leave a comment to this.

1. It will create greater transparency within the regulatory framework.
2. Ensure producing safe products which are monitored throughout the product life cycle.
3. There will be more transparency and ownership of responsibilities.
4. Patients will have more access to device and manufacturers information.
5. MDR has the potential of minimizing risks posed to patient by medical devices, however, the more rigorous requirements may have the adverse effect of limiting availability of products needed by patients and stifling innovation and new technology introduction.
6. The more stringent requirements on clinical data rather than claiming equivalence should result in increased patient safety.
7. Increased awareness.
8. Increasing safety on patients due to increased frequency and volume of PMS.
9. it will improve patient safety.
10. Improved product information.
11. No, overall it will reduce innovation in EU and force manufacturers to develop device for other markets before EU which the pathway to market is predictable and have appropriate levels of guidance available to help novel/new device come to market in a predictable time-frame.
12. There will be greater scrutiny and continued vigilance of the product. Greater numbers of products to be covered by the MDR. The Eudamed database will allow patients to investigate, assess and make informed decisions about a device prior to use and after use to keep abreast of issues with their device.
13. One of the main drivers behind the MDR revision was public health and safety as a result of the PIP and hip implant scandals in Europe. From what I have read the PIP scandal was as a result of the actions of a fraudulent individual and there is no amount of legislation that account for this behaviour. We are not making changes to the devices we manufacture as a result of the MDR requirements, the devices are safely on the market today and will

continue to be on the market post MDR review. It was refreshing to read the article by the Irish journalist who was involved in the ICIJ ‘Implant Files’, a few months after writing the articles he was suffering from chest pain, he got it checked out and had to have coronary stent implanted. He recognised there is a need for safe medical devices and those safe medical devices are available today approved under the MDD.

14. Increased scrutiny and more oversight of Notified Bodies.
15. It will have a good impact on patient safety.
16. It will have a positive impact on patient safety in that it will enforce 'best practices'.
17. There were issues with diverging interpretation of the existing Directives and the MDR should help to level the playing field. However, concerns around capacity at a notified body level and the ability of small and medium sized companies to be in compliance by 2020 is concerning and may affect patient access to therapies.
18. We already have most requirements, it is just better or more documentation.
19. More clinical evidence.
20. Increased transparency.
21. An increased emphasis on post-market surveillance of medical devices will have a positive effect on patient safety.
22. More stringent clinical requirements will ensure a greater emphasis on patient safety.
23. Devices with current insufficient positive clinical risk/benefit will be cancelled.
24. I feel there will be a shortage or at the least a reduced selection of certain devices. However; it also feels like the MDR will positively impact patient care by improving the level of transparency in the EU system.
25. With all the new requirements there shouldn't be an impact to patient safety.
26. For devices such as reusables the more stringent requirements should improve patient safety. For high risk devices already strictly regulated it is debatable.
27. MDR provision intend to remediate all gaps that have been revealed through functioning of the MDD.
28. Yes, it will have an impact on patient safety, but a positive one. This is because there will be a higher degree of scrutiny on the safety of devices being placed on the market.
29. Unsure, the aim was to enhance patient safety (as a result of scandals) but will have to see how implementation proceeds before commenting.
30. It will not address the root cause of the issues associated with PIP etc.
31. focus on product related clinical safety and performance documentation.
32. It will enable greater transparency within the regulatory framework

33. The increased documentation, cost, and support burden is going to take current products off the market and limit the number of products companies will want to put into the EU market. In the end, patients will have less variety and may not be able to get access to devices required for their needs.
34. Reinforce and introduce more stringent requirements for high risk and implantable devices.
35. I think it will improve safety and there will be much more scrutiny on both legacy & novel devices.
36. Products may not be available after 2020.
37. I think in the medium term it will ultimately depend transition management for device critical to patient health and how their transition is managed to ensure continued supply instead of being dropped from the market.
38. Some products/companies will be off the EU market
39. Yes, it can only improve patient safety. However, if this is to be the case than we need clarity and guidance in relation to the Common Specifications and the use of Eudamed.
40. MDR will not generally improve device safety but will cause many safe devices to be pulled from the market and patients and MDs will have fewer options.
41. While there may be some products that will benefit increased clinical data, overall products that have been on the market and safe for years will not see a benefit. In fact, the cost of devices will go up in EU and technologies will be launched in other regions outside EU where regulatory requirements are better defined (this is already happening today).
42. Post-market surveillance will be enhanced.
43. It will enable greater transparency within the regulatory framework

Appendix R Acronyms

AIMD	Active Implantable Medical Devices
BSI	British Standards Organisation
CMR	Carcinogenic Mutagenic Toxic
CE	Conformité Européenne
COCIR	European Coordination Committee of the Radiological, Electromedical and Healthcare IT Industry
CECP	Clinical Evaluation Consultation Procedure
CER	Clinical Evaluation Report
DG GROW	Is the European Union's Directorate-General for Internal Market, Industry, Entrepreneurship and SMEs.
EU-	European Union
EC	European Commission
EEC	European Economic Community
EEA	European Economic Area
EFTA	European Free Trade Association
EUDAMED	European Database on Medical Devices
ERC	Essential Requirements Checklist
EN ISO	European Normative International Standards Organisation
EDC	Endocrine Disrupting Chemicals
EO	Ethylene Oxide
FDA	Food and Drug Administration
GSPRs	General Safety and Performance Requirements
HPRA	Health Products Regulatory Agency
IVD	Invitro Diagnostic Devices
IVDR	In-Vitro Diagnostic Regulation
IT	Information Technology

IFU	Information for Use
ISO	International Standards Organisation
MDSAP	Medical Device Single Audit Program
MDR -	Medical Device Regulation
MDD	Medical Device Directive
EEC -	European Economic Community
MHRA –	Medicines Healthcare Regulatory Agency
MD	Medical Device
MEDDEV	Medical Device Guidance Documents
MD	Medical Devices
MEP	Member European Parliament
MDCG	Medical Devices Coordination Group
MoM –	Metal on Metal
NB	Notified Body
NB-MED	Notified Body Medical Devices
NBOG	Notified Body Organisation Group
NB	Notified Body
NANDO	New Approach Notified and Designated Organisations
PIP	Poly Implant Prothèse
PSUR	Periodic Safety Update Reports
PMSR	Post Market Surveillance Report
PMCF	Post Market Clinical Follow Up.
PV	Process Validation
PMA	Post Market Approval
PMS	Post Market Surveillance
RSI	Reference Safety Information

R&D	Research and Development
RAPS	Regulatory Affairs Professional Society
STED	Summary of Technical Documentation
SSCP	Summary Safety Clinical Performance
Team NB	The European Association for Medical Devices of Notified Bodies
TD	Technical Documentation
TOPRA	The Organisation for Professionals in Regulatory Affairs
TUV SUD	Name of a Notified Body
UK	United Kingdom
UDI	Unique Device Identifier
US	United States
ZLG –	Name of the Competent Authority in Germany
QMS	Quality Management System
VIP	Value Improvement Projects
ROI	Return on Investment
WTO	World Trade Organisation