CHAPTER ONE : THESIS INTRODUCTION

This Doctor of Business Administration (DBA) thesis seeks to explore how experienced physicians make regulatory decisions for clinical trials to guide compliance with a new international standard. It is structured on Perry (2001)'s chapter approach to a doctoral thesis. The first chapter outlines the thesis overview, research study background, study aims and objectives, decision theory and research scope. Chapter two examines the literature to critique medical and naturalistic decision-making (DM) theories from organisational, psychological and sociological published works in order to identify and select themes to research empirically within the main study. Chapter three presents the research design from interpretive philosophical choice through the methodology, methods used, data gathering and analysis. Chapter four displays the findings gathered from physicians' assertions. Chapter five considers the findings in light of the DM themes identified from the literature review, and introduces two conceptual frameworks empirically constructed from this research. Chapter six draws together suggestions and recommendations from the findings, considers research implications and future options from this work.

1.0 RESEARCH OVERVIEW

The field of medical devices is expanding rapidly and there is increasing complexity of both devices and their clinical applications. Consequently, it is one of the most tightly regulated industries in the world today being constantly challenged to meet rising standards of quality, safety and product efficacy through meeting rigorous requirements (Food and Drug Administration, 2014; Medicines and Healthcare Products Regulatory Agency, 2014). Medical device legislation mandates regulatory compliance across many areas where impacted organisations must bear the economic, legal, professional and ethical obligations concerning the risks and benefits of their products, policies and services (Griffen, Posner and Barker, 2013). Although the regulations mandate compliance they are not prescriptive. However, ensuring regulatory compliance is maintained during continued business operations is a major challenge (Berkan-Sesen *et al.*, 2010). So, decision makers must interpret diverse device requirements against clinical applications and settings, coupled with effectively and efficiently managing business compliance, prior to any decision being made, which can be more onerous than pharmaceutical drugs (Raber, 2010).

Within the clinical research field, decision-making for regulatory compliance is increasingly falling to company physicians but environmental constraints often influence and impact on the behaviours individuals would normally display (Christ, 2014). Practice of medicine research highlights that physician's make patient-orientated decisions, from alternatives, over various stages of a clinical lifecycle (Groopman, 2007; McWhinney, 1997). However, in clinical research organisations patient needs dominate but patients are noticeably absent (Griffen, Shaw and Stacey, 2006). So, this study seeks to ascertain what influences affect and impact physician's making compliance decisions in this context.

1.1 BACKGROUND TO NEW INDUSTRY REQUIREMENT

A new industry requirement is the primary external factor acting as both driver and focus for this research. In 2011, the regulatory environment surrounding good clinical practice (GCP) for medical device clinical trials changed following publication of a new international standard, ISO14155:2011, Clinical investigation of medical devices for human subjects - Good Clinical Practice (International Organization for Standardization, 2011). This standard seeks to ensure good clinical practice in human clinical trials via assessing and checking medical device performance and safety for regulatory purposes (Smith, 2012). Although other industry legislation is in effect, the principles set forth in ISO14155:2011 should be pursued as far as possible now, contingent upon the clinical trial scope and additional ancillary national regulations (International Organization for Standardization, 2011). For example, ISO14155:2011 has tightened general requirements protecting the rights, well-being and safety of trial participants. However, the three current European medical device directives mandate scientific clinical investigation conduct, validity of results, defines the responsibilities of regulatory agencies and notified bodies, trial physicians, and assisting study sponsors and ethics committees, involved in audit and medical devices assessment (World Medical Association, 2014; International Organisation for Standardisation, 2011). So, is there any overlap? It appears that ISO14155:2011 trial requirements have evolved to cover enhanced safety monitoring, evaluation and inspection, such as gathering and assessing data from all adverse event cases (Smith, 2012) but how the new standard affects regulatory compliance DM of impacted organisations is unknown.

1.2 LOCUS AND CONTEXT FOR STUDY

The main internal factor to assess in this study is a real world organisation directly impacted by the new requirements. The locus and context for study is an American Clinical Research Organisation (CRO), Pharmaceutical Product Development (PPD). PPD is a global, full service CRO with offices, clinics and laboratories in 84 locations (46 countries) and has provided services for clinical trial studies in over 100 countries over the last quarter century. PPD maintains operations consistency via a hierarchical organisational structure, physicians appointed to critical departmental roles, supported by a global quality management system and standard operating procedures (Pharmaceutical Product Development, 2010; 2009). Since 1997, PPD has provided medical device services to the market, with over 300 experienced staff located in various geographical locations, including Bulgaria, China, United Kingdom and the United States of America, to assist clients with medical device services (Pharmaceutical Product Development, 2009). So, this new standard will impact.

Additionally, since 2000, the traditional medical product development model (figure 1.1) has undergone transformational change from the traditional, in-house, company-does-all, globalised approach to outsourced partnerships and collaborations with specialised pharmaceutical and biotechnological service providers, such as PPD, that focus on certain aspects of the medical products lifecycle value chain from discovery through commercialisation (Sabatier, Mangematin and Rouselle, 2010).

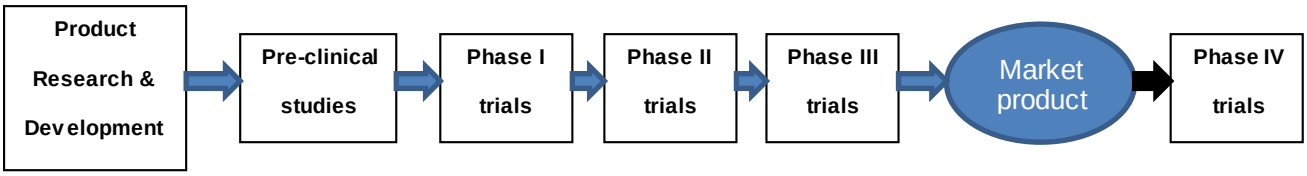

Figure 1.1: The traditional medical product development value chain. (Adapted from Ribeill, 2013:4; Sabatier, Mangematin and Rouselle, 2010:433).

This changing value chain has forced pharmaceutical manufacturers to reconfigure their strategic approach to discovery pipelines, reorganising their knowledge base and structures to better detect new opportunities, consider merger and acquisition approaches, optimize processes and improve the links and interdependencies between them to improve cost-efficiencies and speed development (Ribeill, 2013; Sabatier, Mangematin and Rouselle, 2010; Suresh and Basu, 2008). However, the

industry change has impacted regulatory compliance interpretation globally as it varies by market and product. Within each country national laws are in place that are directly binding on people, organisations and operations but, within the industry, key understandings are interpreting the requirements, ascertaining how compliance differs from market to market, how best to address country anomalies and whether any difference constitutes a non-compliant legislative breach in another country (Abdel-Aleem, 2009). American and European pharmaceutical regulation has been in existence since the 1960s and has been successfully extended from controlling the requirements for placing product onto the market, backed by all necessary data to satisfy safety and efficacy, allied to all aspects of dealing with a medicine from research and development, through manufacturing, clinical research, marketing and advertising. In contrast systemic medical device legislation is more recent dating back to late 1970s (US federal legislation) and early 1980s (European Directives) (Griffen, Posner and Barker, 2013; Zuckerman, 2011). Pharmaceutical drug regulation is based on two well-controlled phase III studies that demonstrate the safety and efficacy of the drug. However, the medical device regulatory pathway is based on one confirmatory, well-controlled multi-centre trial. Additionally, there are key differences associated with the plan and conduct of the pivotal study: with devices requiring a randomized sample size ranging from 500-1000 patients, whereas pharmaceuticals range from 1000-3000 double-blind subjects. However, the central difference is that many pharmaceutical trial activities require prior health authority clearance, which is not the same for devices, as an independent notified body has to assess and certify both organisation and product(s) against pre-market and/or post-approval legislative requirements (Griffen, Posner and Barker, 2013; Abdel-Aleem, 2009).

For pharmaceutical clinical trials involving human subjects many organisations attempt to follow the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines (International Conference on Harmonization, 2015). This is an international ethical and scientific quality standard for designing, conducting, recording data and reporting from clinical trials. ICH GCP was developed for the United States, European Union, Nordic countries, Australia, Japan, Canada, and the World Health Organisation (WHO) with the aims of providing a unified practice standard and to facilitate the mutual acceptance of clinical data by the regulatory authorities under these jurisdictions. Compliance with ICH GCP provides public assurances that the

rights, safety and well-being of trial subjects are protected, consistent with ethics principles originating in the Declaration of Helsinki, and that the clinical trial data are credible (International Conference on Harmonization, 2015). However, although ICH GCP can provide assistance to industry and healthcare professionals on how to comply with governing regulations, statutes and policies they are administrative instruments only, are not enforceable by law and, as such, allow for flexibility in approach. Furthermore, although ICH GCP serves to provide high level clinical trial compliance guidance to medical staff, it is not directly applicable to medical device trials.

The changing regulatory landscape has provided PPD with opportunities to grow the business organically via expansion of high value-added service provision to clients. For example, the company has developed outsourcing solutions involving strategic alliances, innovative collaborations and partnering opportunities to meet industry challenges by working with clients and sponsors on new approaches fuelled by organic growth and acquisition (Pharmaceutical Product Development, 2014). Furthermore, to meet growing demand for clinical development services, PPD have opened new offices in the Philippines, Malaysia, China, Bulgaria and Germany; partnered with US companies for medical imaging and early stage businesses (including translational research out-licensing); and strengthened the clinical research bench strength through acquisitions in eastern Europe and Japan as well as expanding vaccines and biologics laboratory infrastructure in recent years (Pharmaceutical Product Development, 2014; 2010). To stay ahead of the curve, PPD relies on effective monitoring of regulatory authority, ethics committee and other applicable official requirements for changes and trends. These trends may affect PPD deliverables, including clinical operations on a country-specific, regional or global scale. In addition to surveillance, there is a need to summarize and disseminate actionable regulatory intelligence not only to PPD staff but to clients and partners too.

However, PPD is a service provider, where people are seen as the greatest asset, and so to deliver enhanced offerings headcount has increased steadily, with experienced healthcare professionals recruited into roles with increasing responsibility, including the appointment of physicians into senior management positions (PPD, 2010, 2009). However, with mergers, acquisitions and changing regulatory positions, the constant

challenge is to keep skillsets current, stay ahead of the curve in terms of service provision but also enhance regulatory compliance that offers benefits to all parties.

Within PPD, the highest ranking physician is the Chief Medical Officer (CMO), who reports to the Chairman and Chief Executive Officer (CEO) (figure 1.2). Reporting to the CMO are physicians who lead specific compliance functions such as regulatory affairs, safety vigilance, phase I clinic, laboratory units with medical assessment of clinical data allied to ethical standards and good laboratory practices, phase II-IV clinical trial operations and therapeutic areas. An abridged PPD organisational chart is depicted in figure 1.2 illustrating where physician leadership appointments fit within the company hierarchical structure. This organisational structure is broadly consistent with other industry companies that employ physicians, albeit functions and job titles may differ (Aitken, Perahia and Wright, 2003).

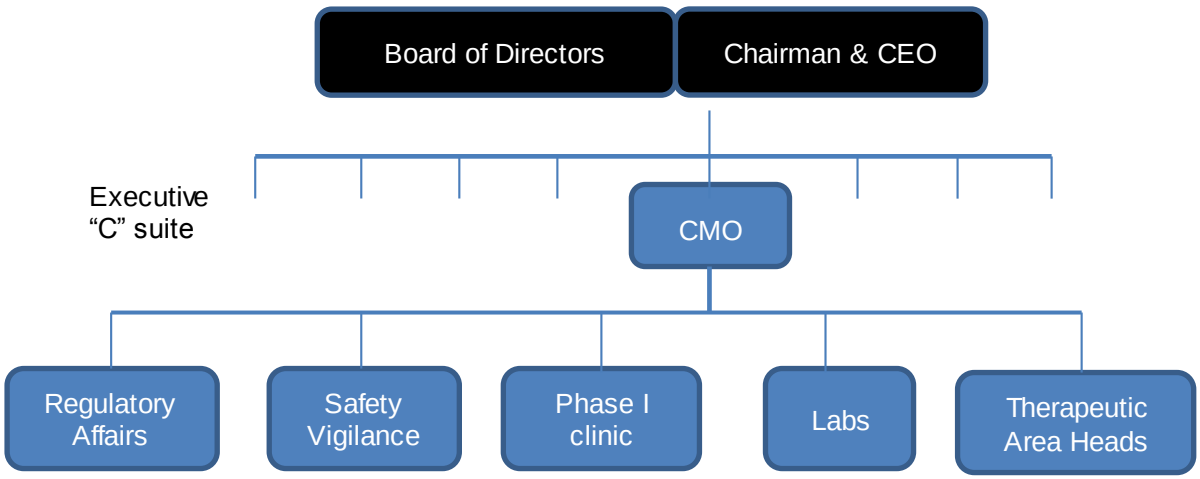

Figure 1.2 Abridged PPD organisational chart depicting physician roles

Through the 1990s only a small number of physicians were employed by PPD but they occupied strategic positions within the organisation such as Chief Medical Officer and Regulatory Compliance Lead. However, over the past decade the demand for medical services in clinical trials has increased resulting in an expansion of physicians being employed in strategic and tactical roles. Today physicians bring medical expertise to the heart of client clinical programs by shaping regulatory strategies from target compound decisions through regional and global pre-market and post-market approval activities (Pharmaceutical Product Development, 2014). PPD physicians also engage in variety of medical device regulatory compliance decision activities ranging from

reviewing health outcome and business intelligence information; assessing and analysing efficacy, technical and laboratory data on client projects; identifying, understanding and evaluating epidemiological risks and benefits related to device safety in both pre-clinical approval and post-marketing environments, as well as executing medical writing services (Pharmaceutical Product Development, 2010). The physician roles are to educate key stakeholders and internal groups about regulatory compliance requirements and therapeutic considerations, inform strategy and enable compliance decisions to be taken in the best interests of patients with implementation in a timely and informed manner. For example deciding how best to implement a client-centric commercial strategy to overcome medical device market access challenges such as how to navigate the FDA's Refusal to Accept Policy given that the US agency will no longer accept 510(k) regulatory submissions that are incomplete or inadequate. Some physicians are actively engaged in PPD's compound partnering program which features an accelerated "fast and furious" approach to product development, where PPD shares financial risks with partners by applying medical expertise in global development-to-discovery efforts of partners to shorten timelines. Essentially these activities seek to bridge compliance steps in the clinical research lifecycle (figure 1.1) by engaging physicians to make timely regulatory decisions that ensure the rights, safety and wellbeing of trial subjects are upheld; the scientific integrity of data is maintained, products are safe and effective. This effectively places PPD physicians across multiple trial phases, striving to expedite the compliance process, but also safeguarding future work. However, despite physician roles being outsourced, those employed by pharmaceutical organisations can be regarded with suspicion and curiosity by colleagues and peers who often possess misconceptions about their functions and responsibilities (Aitken, Perahia and Wright, 2003).

Additionally some of the PPD physicians lead therapeutic teams covering specific disease indications as shown in table 1.1. Infectious diseases, oncology, immunology/rheumatology, neuroscience and urology are the leading therapeutic areas in PPD as ranked by revenue, number of active phase II-IV studies and the clients' research and development priorities over the past five years (Pharmaceutical Product Development, 2014).

Therapeutic Area	Indications
Infectious diseases	Pneumonia & influenza; infections of skin and subcutaneous tissue; HIV, viral hepatitis, viral and chlamydial infection, staphylococcus, respiratory syncytial virus, progressive multifocal leukoencephalopathy, neonatal candida infection
Cardiovascular	Congenital heart anomalies, arterial embolism and thrombosis, atherosclerosis, primary pulmonary hypertension, ischemic heart disease, acute myocardial infarction, heart failure, cardiac dysrhythmias, varicose veins
Central Nervous System	Epilepsy, Alzheimer's disease, multiple sclerosis, intracranial injury, alcohol dependence syndrome, affective psychoses
Dermatology	Urticaria, psoriasis
Endocrine / Metabolic	Diabetes mellitis, cystic fibrosis
Gastroenterology	Ulcerative colitis, chronic liver disease, cirrhosis
Immunology	Osteoporosis, rheumatoid arthritis, gout, lupus, psoriasis, transplant
Neuroscience	Neurology, psychiatry, pain management, sleep research
Oncology	Virtually all major tumour types including breast, bone, colon, connective tissue, skin, prostate, ovary & uterus, bronchus & lung, liver, bladder, lymphoid tissue, multiple myeloma, myeloid & lymphoid leukemia, head, face and neck.
Pulmonary / Allergy	Asthma, idiopathic fibrosing alveolitis
Urology	Prostate hyperplasia, erectile dysfunction, overactive bladder, premature ejaculation, kidney/renal disease

Table 1.1 Breadth of PPD physician therapeutic experience covering phase II-IV trials (Pharmaceutical Product Development, 2014).

In order to meet client needs PPD actively recruit clinicians who possess core competencies heavily focussed on the therapeutic specialities highlighted in table 1.1. The key medical features being a comprehensive understanding of how the human body works at the molecular level, possessing an excellent grasp of disease pathophysiology, verifiable medical degree, 5+ years clinical based experience following full registration, with no prior, or pending, professional / legal issues or sanctions listed against the individual (Pharmaceutical Product Development, 2010). However, other essential skills include good spoken and written English and excellent presentation skills which are tested at interview. As a consequence the majority of PPD physicians are native English speakers and are recruited into European or North American office locations. Additional value add-ons include supplementary professional specialist qualifications (e.g. dermatology); geographical location; the ability to embrace and use new technologies to virtualise the clinical research process and thereby expedite clinical development; and proven collaboration and experience with industry, academia, governments, regulatory agencies and healthcare providers.

To maintain knowledge and skills PPD encourage and support leadership development and continued professional development (CPD) through attendance and/or presenting / networking at conferences, symposia, specialist external training courses as well as building in-house expertise through initiatives to improve processes, systems and operating efficiencies. Examples include finance training for all leaders; in-house programs to develop broader business or soft skills, or developing additional medical skills via clinical self-development in working hours reading professional journals (British Medical Journal) or using company supported subscriptions to online information (OvidSP). However, in some countries, such as the UK, physician CPD is now a mandatory requirement for maintaining professional registration, which is actively encouraged and supported by the company (General Medical Council, 2015; Pharmaceutical Product Development, 2014).

To meet client needs and compliance requirements more efficiently the phase II-IV therapeutic groups have been globalised to align with PPDs four operational regions: North America (NA); Latin America (LA); Europe, Middle East and Africa (EMEA); and Asia Pacific (APAC). This broad regional alignment serves as a matrix to ensure that therapeutically experienced physicians are positioned to train, monitor, manage and provide support for multi-national medical device trials within key markets.

From a strategic perspective meeting and maintaining regulatory compliance is a core business process within the industry and, within PPD, the way to achieve this is by meeting the main market (US and Europe) requirements, as described by the American Food and Drug Administration (FDA) Code of Federal Regulations and European Commission directives. Although other market requirements exist and are applicable nationally (such as Japan, Taiwan, Brazil and Australia) the FDA and European laws are the main ones applicable to PPD. In order to achieve compliance PPD references industry guidance such as international standards (ISO) and International Conference on Harmonization (ICH) allied to a comprehensive compliance culture, structured mechanism and coordinated effort across the entire organisation. As a global company PPD meets regulatory compliance across the world by following guidelines, implementing validated systems and processes, linked to harmonised procedures (global and local) allied to robust quality assurance applications. This is the quality management system which is regularly assessed by

governmental agencies and regulatory bodies such as the American Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for compliance against national and international legislative requirements (Food and Drug Administration, 2014; Pharmaceutical Product Development, 2014).

From a tactical perspective regulatory compliance can vary from simple submission filing tasks to complicated outsourced compliance services depending on client needs. However, they all involve dealing with applicable health authority regulations or regulatory agencies in specified markets. The challenge is to navigate the regional and local nuances compared to international requirements and the lack of consistency between the various agencies (e.g. EMA and FDA) such that all elements of the PPD quality management system are kept up-to-date. Within PPD the company physicians are at the forefront of the company efforts pertaining to gathering the necessary data for and taking and implementing informed compliance decisions. To help aid improvement in safety and efficiency assessment PPD has invested heavily in innovative technological solutions both bespoke and off-the-shelf. The latter includes functional test and validation packages for Oracle's datacentres and life sciences suite of applications. The former includes PPD ProjectView (an efficient and cost effective clinical project management tool with in-built quality deliverables) and PPD DirectConnect (web portal that allows clients secure and timely access to key study data and information). Use of these applications provides the PPD physicians with the means to perform an expedited data review and potentially enhance precision with their decision making capabilities. For example, China's Food and Drug Administration (CFDA) updated their existing provisional Good Manufacturing Practices for medical devices (New GMP), and issued the country's first Good Supply Practices for medical devices (GSP) in December 2014 (Wang, 2015). Within PPD the direct reports of the CMO (figure 1.2), led by the regulatory affairs lead, assessed these rules against the quality management system service provision in China, made compliance change determinations based on their analysis and updated the in-house Chinese regulatory flag pages accordingly.

Although PPD senior management have recognised the need to implement new ideas to support the industry model break-up (figure 1.1), the implementation of novel or innovative approaches has been slow and sporadic. Some elements of continuous

improvement have been deployed successfully, however, there have been drawbacks such as problems introduced by management decision only; focus on individual tasks causing sub-optimization to occur throughout the organisation; computerizing poor processes, creating departmental silos, fostering regional differences, making errors faster, fragmenting communication, which has introduced redundancy and re-work (PPD, 2010, 2009). A potential avenue for addressing these internal short-comings could come from social psychology literature which has identified that social, environmental and structural characteristics guide how group members interact, and influence decision-making. Examples include cohesiveness, communication networks, roles, socialisation, shared mental models, and team norms (Klein, 2008; Nutt, 2008, Paris, Salas and Cannon-Bowers, 2000; Endsley, 1997) and merits further exploration in the main study. Within PPD, although each department head is ultimately responsible for the decisions made, it is often a sub-group that guides the regulatory compliance decision-making process. Psychological literature indicates that where groups comprise two or more individuals with specialized roles and responsibilities, other factors can influence such as utilising multiple sources of information, bringing forth relevant task knowledge, using adaptive strategies to help respond to change, and forming expert groups to achieve specific tasks to achieve mutual common and valued goals should be explored (Salas, Muñiz, and Prince, 2001; Paris, Salas and Cannon-Bowers, 2000; Brannick, Salas and Prince, 1997).

However, as many PPD compliance leaders are physicians, the business problem being considered in this thesis is exploring how company physicians use prior experience, knowledge, skills and available information when making specific regulatory decisions for compliance with the ISO14155:2011 standard in medical device clinical trials.

1.3 RESEARCH AIM, OBJECTIVES AND RESEARCH QUESTION

The research aim is to identify how company physicians make regulatory compliance decisions in PPD, particularly those needed for medical device trials following the recent ISO14155:2011 update. Therefore, the research objectives of this study are:

- To ascertain, understand and critically reflect on the theory and literature regarding decision research in contextual settings,

- To explore ISO14155:2011 to identify key factors, parameters and relationships that could influence regulatory compliance decision-making in the vigilance department of PPD,
- To investigate and explore key decision-making themes with the company physicians' practicing in the vigilance department of PPD,
- To ascertain how PPD physicians would make regulatory decisions for facilitating ISO14155:2011 compliance.

Therefore, the research question posed by this study is "*how can decision-making principles facilitate and guide compliance with ISO14155:2011 for expert physicians undertaking medical device clinical trials?*"

1.4 INTRODUCTION TO DECISION RESEARCH

In order to position this research a brief introduction to decision research follows. Key theories are introduced and categorised using classical and descriptive decision-making models (Herfield, 2013; Baron, 2008; Bazerman and Moore, 2008). In this chapter, Yates (2001) DM definition will be used which describes DM as a

> "*process that leads to the commitment to an action, the aim of which is to produce satisfying outcomes.*" Yates (2001: 10)

<u>Decision research</u>

Making decisions is a fundamental human cognitive function that occurs many times daily and has been researched via human psychology over the past seven decades. (Edwards, 1954). Decision Theory, or rational choice theory, involves studying human cognition and rationality, particularly the uncertainties, preferences and influencing effects pertaining to the construction of optimal or rational choices (Herfield, 2013; Baron, 2008). Over the past seventy years it has been extensively researched in many fields such as philosophy, economics, statistics, mathematics, management science, medicine, sociology and computer science, contributing both theoretical perspectives and methodological rules (Mäki, 2009; Baron, 2008; Dickens, 2004; Edwards, 1954). According to some authors decision theory can be divided into three components. Firstly, normative decision theory which explores

what an ideal (perfectly rational) agent with infinite computing power would choose. Secondly, descriptive decision theory considers how non-ideal (human) agents actually choose, that is essentially real behaviour. Thirdly, prescriptive decision theory which explores how humans can improve DM (relative to normative model) despite known defects (Herfield, 2013; Grant and van Zandt, 2009; Baron, 2008; Bazerman and Moore, 2008). Prescriptive components are covered in chapter two but summaries of the former streams follow in the next section.

Classical Decision Theory

Classical decision-making models (CDM) typically revolve around what people should ideally do, but not necessarily describe how people actually perform a decision-making task (Fischhoff, 1988). The underlying assumption being that DM influences move around a central concept of utility which is either the overall value of a choice, or how much each outcome is worth to the decision maker. For example, researchers specify the costs and benefits associated with different choices so that mathematical models can apply values to those variables giving rise to an optimal choice.

In classical decision theory, also known as traditional or normative, two approaches dominate within a positivistic-systematic stand: information-processing theory (IPT) and analytical decision-making theory (ADMT) (Zsambok and Klein, 2014; Klein, 1998).

ADMT presumes that impartial cognition predates action whereupon analytical reasoning occurs via step-by-step, systematic process following logical rules until a decision is taken (Nutt, 2008; Hammond, 1996). Since publication of the Expected and Subjective Expected Utility theories in the 1950s, CDM research has concentrated on the study of rational, optimal (normative) decision-making of consequential choice. This is the traditional approach to decision-making that assumes that decision makers have the right information, the ability to make correct decisions and that the decision makers agree about goals.

Contrastingly, IPT is a psychological theory used in medical research, characterized by a scientific approach to DM where the central assumption is that the decision

process in humans is cognitive split into two elements: long- and short-term memory. The latter contains the stimuli information that acts as a catalyst to release experiential (episodic) and factual (semantic) knowledge saved in longer term memory (Hamers, Huijer Abu Saad and Halfens, 1994; Joseph and Patel, 1990; Carnevali *et al.*, 1984). For example, the hypothetico-deductive approach (H-DA) was the most common inductive method of scientific medical observation used extensively through the 1980s and 1990s based on a 4-step memory interface comprising: gathering preliminary patient clinical information; initiating speculative potential hypotheses about patient's presenting symptoms; interpreting cues in view of these hypotheses; then balancing decision options before choosing the best one that fits the evidence collected (Banning, 2008, Lauri and Salanterä, 2002, Thompson, 1999; Hamers, Huijer Abu Saad and Halfens,1994). However, H-DA is based on theory that confirms a hypothesis only where a prediction-observation (p-o) gap is narrow (Rakover, 2002). Although a null hypothesis can be confirmed when the gap is large, H-DA is not able to account for other demands when it does not hold. Furthermore, H-DA assumes linear sequences but they were not observed in practice and healthcare staff often overlapped process stages and changed their order (Thompson, 1999; Corcoran, 1986; Jenkins, 1985). Following this criticism alternative approaches, such as reconstruction from memory or adaptation of similar behavioural decisions, were suggested (Rakover, 2002; Yates, 2001).

When faced with many competing theories decision-makers have often questioned which approach to follow. However, there is no easy answer and this dilemma continues to present a challenge to practitioners and researchers alike (Virani *et al.*, 2009). Okasha (2011) argued that there is no rational way to choose between scientific theories thereby potentially undermining the view that science is a rational enterprise. Contrastingly, Bradley (2013) suggested that scientific rationality needs to be more content and context specific and suggested utilising a considered and measured approach, such as modification of Kuhn's (1992) choice rules algorithms. However, given these anomalies, observations and alleged inconsistencies research into other decision-making areas, such human behaviours, evolved.

Behavioural Decision Theory

Within decision theory behavioural research acknowledges how individuals make judgments and choose action courses. As a research field behavioural DM is interdisciplinary, acquiring ideas and accessories from business, management, economics, medicine, political science, psychology and statistics (Nutt, 2008). Since decision-making applies widely across many disciplines, behavioural decision theorists claim that their human behaviour models are more authentic than classical ones since they focus on trying to explain real world decision scenarios. So, to illustrate this, descriptive behavioural decision-making models were developed to depict how humans typically made decisions. One early example is Simon's *Satisficing* model where a decision maker generates and considers choices until one is found that is acceptable (Simon, 1957). However, the main issue with this model is that the decision maker considers only a few scenarios before choosing the first one that seems satisfactory.

From the 1980s onwards many DM researchers sought to ascertain and understand how behavioural themes influenced and impacted. Foremost amongst healthcare DM was the intuitive-humanist model which was utilised by professionals using expertise and intuition rooted in a person's ability to recognize patterns of cues developed from direct experience in the field (Benner, 1984). Essentially, the intuitive-humanist model can be summed up by referring to the Thompson (1999) definition which states

> "*intuitive judgment distinguishes the expert from the novice, with the expert no longer relying on analytical principles to connect their understanding of the situation to the appropriate action*." Thompson (1999: 1224)

The spread of research devoted to ascertaining and understanding how behavioural themes can impact decision-making within this field has expanded to include context, decision criteria, emotion, expertise, interpretation, motivation, risk, uncertainty, time, strategy and spending, but there appears to be gaps in the selection, interpretation, utilisation, interplay and execution of these themes by decision makers. For example, Duchon, Dunegan and Barton (1989) found that engineers and project managers made decisions based on previous team successes or failures, whereas

Lipshitz (1993) indicated that some people made decisions without explicitly evaluating any alternative outcomes at all. Furthermore the developing naturalistic decision-making (NDM) paradigm suggests that understanding the influences and perceptions on the decision-makers' cognition in real-world contexts is of paramount importance (Godin *et al*., 2008; Reyna, 2008a, 2008b; Klein, 2008; Elwyn *et al*., 2000; Elwyn, Edwards and Kinnesley,1999).

Within the clinical trials field, research has focussed on product discovery and development with most new strategies concentrating on improving the predictive value of pre-clinical and clinical evaluations (Nirmalanandhan and Sittampalan, 2009; Elgen, Gilchrist and Reisine, 2008). However, this has opened a knowing-doing gap between clinical and managerial research and actual healthcare practice, as reconciling and harmonising scientific guidance is time and labour intensive, extremely difficult, underfunded and comprises many regulatory interpretation pathways (Koliadis *et al*., 2010; Bansal, Arnold and Garofolo, 2010; Raber, 2010; Pfeffer and Sutton, 2000; Kitson, Harvey and McCormack, 1998). This implies that the classical and behavioural approaches do not fully explain, or account for, decision-making processing by experts in the apparently different realities of clinical environments and decision theory. Therefore clinical situational decision-making contexts will be explored in detail within chapter 2.

1.5 MOTIVATION & RELEVANCE OF UNDERTAKING THIS STUDY

The researcher is a PPD employee, has worked in the pharmaceutical industry since 1988, and will be directly affected by the implementation of this regulatory change.

From a personal perspective, the author is interested in expanding personal, business and practice knowledge by undertaking this research in combination with meeting organisational and industry compliance requirements for the new standard.

From an organisational perspective this research will potentially offer a new mechanism to help PPD meet organisational compliance goals and objectives separated from the company's continual improvement program. Additionally, from a business perspective, this research could contribute to both knowledge and practice at individual, group and departmental level by offering a compelling rationale and

alternative methodology for ascertaining how physicians make and take decisions in non-medical contexts impacted by regulatory change.

From an academic perspective this research contrasts with the traditional and positivistic DM perspective, which typically requires adherence to scientific method and uses experimental research designs and structured, standardized methods (Bowling, 2009). Although many decision-making models have appeared over the last two decades covering healthcare professionals, studies of safety vigilance physicians making decisions and judgments, under clinical research legislative and contextual conditions, appear to be missing from the literature. Additionally, some authors have argued that there is no convincing basis for explaining clinical DM but there is a place for a framework that possesses characteristics of the main DM approaches (Thompson, 1999: White *et al*., 1992). This thesis attempts to explore DM literature to ascertain, and potentially bring together, the supposedly different worlds of physician reality and decision theory.

1.6 RESEARCH RELEVANCE

This research is important on several levels. Firstly, from the perspective of organisation stakeholders which include PPDs executive management, vigilance department leaders and PPD physicians; secondly, from the researcher's own personal perspective, and thirdly, from an academic viewpoint, when considering how physicians make regulatory compliance decisions in non-medical roles and contexts. This thesis argues that this research provides evidence to support all these perspectives.

It is hoped that the study design, using interpretive methodology and qualitative methods will allow the research question and aims to be addressed in a clinical research social situation in which there is little pre-existing knowledge. This will maximize the opportunity for exploration and, coupled with individual curiosity, study the relationships between a new industry requirement and physician DM in context. It will enable the researcher to satisfactorily fulfil the requirements of the Edinburgh Napier University Doctor of Business Administration degree program but also provide PPD safety vigilance physicians with a potential discretionary mechanism to

aid regulatory decision-making in the department whilst helping shape compliance with the new standard for medical device trials.

1.7 SCOPE AND BOUNDARY OF THESIS

The scope of this thesis is to explore and examine decision-making themes considered relevant by the author to achieve the thesis aims as outlined in section 1.3. In contrast to industry and company approaches this is not positivistic research but an interpretative study designed to bring forth experiences, ideas, thoughts and perceptions of physician decision-makers to aid compliance with a new industry standard within the vigilance department of a global clinical research company. The following chapters describe the research journey by detailing the literature review, philosophical positioning, research design, methodology and methods used. The penultimate chapters present the research findings and emergent themes from the large amount of rich data collected via semi-structured interviews and mini focus groups. The thesis finishes by reflecting on contribution to practice and academia with a consideration of potential implications, applications and future work allied to further research suggestions.

CHAPTER TWO : LITERATURE REVIEW

2.0 CHAPTER INTRODUCTION

This literature review critiques themes relevant to this thesis, namely how physicians make decisions and the factors influencing regulatory compliance decision-making in a clinical research environment. The literature review commences with a synopsis of medical devices regulatory compliance. It then leads into medical decision research, where theory is introduced then categorised using classical and descriptive decision-making models, highlighting important and relevant themes pertaining to the influences and mechanisms behind medical DM. The literature review then explores contextual cognitive and behavioural aspects of decision-making to identify themes relevant for research in the main study. The chapter ends with an illustration of how academic literature has informed the study area and provides a guide to the empirical research of physician regulatory compliance DM in a non-clinical context.

2.1 MEDICAL DEVICES REGULATORY COMPLIANCE

The biggest issue facing companies operating in the medical device industry is how to meet all regulatory compliance requirements prescribed by applicable legislation in their markets of choice. Globally countries have implemented similar regulatory requirements which are broadly based on manufacturing, packaging, clinical trial, and cleanliness requirements with an additional contemporary focus on mobile medical applications (Yetisen *et al.*, 2014; Dacy, 2010). However, national legislation differs from country to country based on medical device definitions, classifications, local controls and specific requirements. For the purposes of this thesis a short synopsis of the main medical devices regulatory compliance legislature follows.

Medical devices manufacturers are subject to various quality system regulations intended to ensure the overall quality and safety of products. For example, in order to ensure that medical devices entering the US market are safe and effective, the FDA requires that manufacturers follow Good Manufacturing Practices (GMPs) as part of its Quality System Regulation (QSR: 21 CFR 820) such that manufacturing processes are controlled and validated to ensure consistent performance (Fotis and Bix, 2006). This means that domestic and foreign manufacturers of medical devices

must put in place a quality system that addresses the design, manufacture, packaging, labeling, storage, installation, and servicing of finished medical devices for use in the United States (Zuckerman, 2011). In Europe the essence is similar but a more complicated core legal framework exists consisting of three directives issued by the European Commission to harmonize the technical requirements across the region. These aim to remove trade barriers and dispel uncertainty for economic operators and facilitate free movement of goods inside Europe. These consist of:

- Directive 90/385/EEC for active implantable medical devices
- Directive 93/42/EEC for medical devices generally
- Directive 98/79/EC for in vitro diagnostic medical devices

Together these European directives constitute a medical device legal system that aims at ensuring a high level of protection of human health and safety and the good functioning of the single market (Griffen, Posner and Barker, 2013). These directives have been supplemented over time by several modifying and implementing directives, with the ultimate authority for interpretation resting with the courts. However, each member state must designate a government authority for implementing the directives in their member state. In the UK it is the Medicines and Healthcare Products Regulatory Agency (MHRA) and the legislation is the Medical Devices Regulation 2001/618 (as amended) (Griffen, Posner and Barker, 2013).

Many medical devices are sterilized in their packages, so another regulatory compliance focus area is packaging, as sterility must be maintained from manufacture through the supply chain to final use by patients and /or physicians. To ensure that packaging meets regulations and end-user requirements several specific standards have been introduced to test the packaging ability to retain sterility (American Society for Testing and Materials, 2014). Examples include:

- ISO 11607 Packaging for terminally sterilized medical devices
- EN 868 Packaging materials and systems for medical devices to be sterilized, General requirements and test methods
- ASTM F2097 – Standard Guide for Design and Evaluation of Primary Flexible Packaging for Medical Products
- ASTM D1585 – Guide for Integrity Testing of Porous Medical Packages

Since 2000 medical device cleanliness has come under greater scrutiny following high profile patient complaints of manufacturing residues appearing in metal hip implants and concerns with cleanliness of re-usable devices (Spiegelberg, Deluzio and Muratoglu, 2003). This has led to the American Society for Testing and Materials (ASTM) introducing new medical device technical standards (American Society for Testing and Materials, 2014).

Contemporary regulatory oversight has focused on electronic medical devices, particularly the software development process and system-level testing, given some devices can be remotely controlled. This has raised concerns about privacy and security issues around human error and technology glitches but only a few studies have looked at the susceptibility of medical devices to hacking (Fu and Blum, 2013). Although there have been no known incidents of a hacked medical device injuring or killing a person, cyber-threats and risks remain (Burleson *et al.*, 2012; Maisel, and Kohno, 2010).

In short, medical device manufacturing, packaging, cleanliness and software standards are important but are not in scope of this regulatory compliance investigation. On the other hand Good Clinical Practice is in scope given it is an international quality standard provided by ICH that defines standards on the conduct of clinical trials, as well as the roles and responsibilities of research sponsors, investigators and monitors (Dixon, 1999). By following GCP, physicians and clinical study teams can work to gather quality data and uphold patient safety standards. However, those running clinical studies must focus on the right safety parameters, product efficacy and what is needed from a regulatory standpoint. There is some room for interpretation of GCP regulatory review but covering certain essential elements is mandatory such as:

- Informed consent
- Safety management
- Quality source documentation generated and available
- Administration and control of the investigational product to confirm efficacy and safety to support study claims
- Protocol compliance given its focus for regulatory agencies

Although ICH GCP compliance with legislation is mandatory for pharmaceutical trials, ISO14155:2011 is the new GCP standard applicable to medical devices studies. However, a consistent industry principle is that each company must decide how to interpret applicable laws then work out how best to respond to changing market demands. This can typically involve adhering to industry compliance standards such as ISO13485 (Medical devices - Quality Management Systems - Requirements for Regulatory Purposes) and ISO14971 (Medical Devices - Application of Risk Management to medical devices) (Smith, 2012; Abdel-Aleem, 2009). A further complication is that suppliers to the medical device industry, such as design firms, contract manufacturers and CROs, must also establish and maintain compliant quality systems in order to ensure that the services they provide meet these same quality requirements. Therefore, as PPD physicians are seen as the key compliance decision makers within the organisation, this research seeks to explore regulatory compliance decision making from their perspective in light of the new ISO14155:2011 standard for medical device trials.

2.2 MEDICAL DECISION - MAKING

The practice of medicine involves physician's making decisions at various stages of the clinical lifecycle but it is complicated given the need to integrate ill-structured, uncertain, and potentially conflicting data, then assess options from various sources in the time available (Groopman, 2007; Kushniruk, 2001; McWhinney, 1997). In an attempt to find an optimal approach to medical decision-making, various theories and models have been put forward over the decades with concepts and ideas borrowed widely from other disciplines, such as economics, mathematics, statistics, psychology, and business contexts (Reyna, 2008a; Allen, 2006. Patel, Kaufman and Arocha, 2002). In medical and healthcare literature the terminology used to describe physicians' thinking includes clinical decision-making and medical decision-making (Groopman, 2007; Gale and Marsden, 1985). However, for the remainder of this thesis, the term decision-making will now be re-defined as how a

"*physician judges an appropriate course of action, via an unspecified process, comprising steps needed to produce a decision.*"

(adapted from Chapman and Sonnenberg, 2000)

The clinical environment is primarily functional in nature and, in this environment, classical DM recommends that treatment should conform to guidelines (Eddy, 2005), where DM is presented in view of traditional, positivistic-systematic approaches, such as analytical decision-making (Hammond, 1996) or information processing theory (Joseph and Patel, 1990). These classical research theories focus on reason, backed up by research methods, such as the randomised controlled trial, adaptive design and evidence based medicine, which have been used to aid physicians acquire and appraise clinical results (Christ, 2014; Tonelli, 2011). However, although classical DM provides powerful mechanisms to collect and analyse data, they do not fully account for variances in cognition and behaviour (Reyna, 2008).

Contrastingly, behavioural approaches emphasise clinical expertise and intuition in reaching case-specific judgments (Falzar and Garman, 2012, 2010, 2009) which can be traced back to the Intuitive-Humanist Model (Benner, 1984) and the original Satisfying model (Simon, 1957). However medical DM requires physician's to consider various factors comprising their clinical knowledge and expertise, personal and professional ethics, training, practical and theoretical reasoning, whilst assessing the presenting situation against paradigm cases from literature and experience (Tonelli, 2011).

However, over the past three decades DM research has attempted to arrive at an optimal DM approach centred around a pair of interdependent aims: firstly descriptive, to ascertain how physicians take decisions in real world contextual situations and, secondly prescriptive, to identify and construct ways to aid the decision operation involving people, process, procedure, technology and/or training in isolation or in combination (Lee *et al*., 2010; Reyna, 2008a; Spring, 2008; Patel, Kaufman and Arocha, 2002). In this field the descriptive models represent relationships but without any course of action, whereas the classical approaches require formal action to attain some defined objective (Griffen, Shaw and Stacey, 2006; Allen, 2006).

However, how physicians determine which approach to follow is uncertain. Some studies have explored physician's experiences of, and preferences for, types of decision-making in healthcare settings. Murray *et al*. (2007) indicated that physician's DM styles can fall into 3 broad categories. Firstly, paternalism where a

physician makes a healthcare decision and informs the others; secondly, shared decision-making, where options are discussed and the group makes the decision and, thirdly, consumerism, where for and against options are discussed and others then decide what to do (Murray *et al*., 2007; Murray, Charles and Gafni, 2006). However, although physicians' consider themselves as practicing their preferred clinical DM role much more is needed when targeting physician DM in alternative clinical-based scenarios (Murray *et al*., 2007; Tonelli, 2006). For example, some qualitative studies have investigated whether third parties play a greater role in DM than physicians (McKeown *et al*., 2002); the extent and comfort level of physician's with shared DM (Charles *et al*., 2004); and the perceived barriers to shared DM amongst participants (Charles, Gaffney and Whelan, 2004; Stevenson, 2003; Elwyn *et al*., 1999). Furthermore cognitive DM theories indicate that physicians rely on heuristics to overcome rationality limitations and help them make decisions but can lead to cognitive bias (Gorini and Pravettoni, 2011). It appears that contextual decision-making of this type is some form of risk-benefit calculation that weighs up potentially conflicting topics such as experiential knowledge, evidence from empirical research, pathophysiological understanding, organisational goals, personal values, healthcare costs and patient safety data (Tonelli, 2011).

The most prominent peer-reviewed, empirically-based, examples of medical DM theories and models over the past 30 years are listed in table 2.1 with key facets summarised. However, despite years of field research and physicians appearing to have the capacity and ability to execute such tasks well, there is no single DM theory, format, or approach, for use as a generic prescriptive framework to a presenting clinical situation (Tonelli, 2011, Mäki, 2009; Baron, 2008). Some argue that this is due to the complexities of medical decision-making, characterised, in broad terms, as juggling multiple inputs comprising science and art, gut instinct and intuition, evidence and analysis with knowledge and experience (Woolever, 2008). Others, in contrast, contend that medical DM research is not driven by theory explicitly, and could be at odds with it, because it addresses practical problems in time sensitive conditions but, the tools, techniques, themes and tasks are not adequately versed in evidence-based explanatory description regarding the fundamental structures of real human understanding, reasoning and DM (Reyna, 2008 a,b). Alternative viewpoints suggest that the conceptual framework of science

is not appropriate for human systems because cultural and artistic matters are separate from scientific matters; experience and intuition influence DM implicitly, or that assumptions made via modelling reduce the description of reality (Allen, 2006; Altmann and Koch, 1998).

Theory / Model	Author / Year	Summary
Prospect Theory	Tversky and Kahneman (1981)	Most popular. Researched extensively. Explains irrational human DM where people choose between loss/gain risk probabilities evaluated by heuristics.
Expected Utility Theory	Edwards (1992)	Individual statistical preference regarding popular choices that have uncertain outcome(s) (gambles) vs expected.
Cognitive-Experiential Self-Test (CEST)	Epstein (1994)	DM occurs via 2 separate systems for information processing: analytical-rational (deliberate, logical, slow) and intuitive-experiential (fast, automatic, emotion-driven). Parallel operations.
Support Theory	Tversky and Koehler (1994)	Subjective probability statistical model to evaluate an individual's beliefs.
MINERVA-DM	Dougherty, Gettys and Ogden (1999)	Memory-based model of choice, probability judgment, and frequency judgment to account for common heuristics and biases.
Appraisal Tendency Theory	Lerner and Keltner (2001, 2000)	Situation appraisal causes an emotional (affective) response. Describes why people react to things differently.
Illness Script Theory	van Schaik *et al*. (2005)	Expert clinicians reason by recognising, weighing up & prioritizing symptoms by comparing contrasting clinical influences then making a diagnosis.
Behavioral DM Framework	Fischhoff (2008)	Assessment of DM competence via consideration of multiple social and affective factors that influence behaviour.
Reasoned Action Approach	Fishbein (2008)	Framework of behavioural intention where behavioural approaches, perceived patterns, and control determine people's intentions, whilst people's intentions predict their behaviours.
Fuzzy Trace Theory (FTT)	Reyna (2008b)	Utilises gist based memory information (advanced intuition) integrated with verbatim info (analysis). Based on dual-trace impressions to forecast and describe mental phenomena, particularly in memory & cognitive analysis domains.
Trans-theoretical Model (TTM)	Prochaska (2008)	Assesses people's ability to act on healthier behavioural data, then implement change strategy / process to guide patients through all change steps and stages to action and maintenance.

Table 2.1: Medical decision-making theories (Adapted from Reyna, 2008a).

Given the fragmented position of clinical DM, questions have been raised on how physicians actually think, including integrating their knowledge into practice, with suggestion of a knowledge hole between that gathered from medical research studies and the kind of information required by a physician to make an optimum decision (Tonelli, 2011; 2006). This has led to suggestions that physicians use various DM approaches and decision tools including speculation, analytic thinking,

affect, sharing assumptions of human judgment (Epstein, 2013; Reyna, 2008a). However, others have suggested that personality, intuition or cognitive style (attitude and habitual strategy) may determine a physician's decision-making preference, or style, such as spontaneity or decision-avoidance (Dewberry, Juanchich and Narendran, 2013; Bruin, Parker and Fischhoff , 2007). Some of these DM approaches are illustrated in table 2.2. The DM dilemma faced by a physician is whether to fall back on what is known already or use a novel empirically supported tool, but where the mechanisms behind the results are poorly understood, validity is questionable and not easily generalizable to DM for disease, patient or setting (Lee *et al*., 2010; Reyna, 2008a, 2008b; Woolever, 2008; Groopman, 2007).

DM method / tool	Influencing factors	DM approach
Scientific method	Compile problem statement, generate hypothesis, collect and analyse data, accept or reject hypothesis	Normative
Probabilities	Observe patient, gather symptoms data, establish an early opinion on likelihood of given outcome. Can focus too soon.	Normative
Tests	Time consuming. Expensive. Subject to limitations. Results questionable. Repeat tests or alternative approach required.	Normative
Heuristics	Informal problem solving methods	Descriptive
Pattern recognition	Process interpreting indicators	Descriptive
Differential diagnoses	Generate options list. Many take probabilistic approach. Focus too soon?	Descriptive
Treatment thresholds	Choice of options. Once diagnosis made new decision on treatment needed.	Descriptive

Table 2.2: Physician decision-making approaches. (Adapted Woolever, 2008)

The effect of all of this is that some authors have called for DM to move beyond the traditional and behavioural formats, as they do not adequately characterise the medical DM process, and seek alternative improvement strategies (Milkman, Chugh and Bazerman, 2009; Milkman, Rogers and Bazerman, 2008). Some authors have suggested exploring themes that better represent DM within specific clinical encounters utilising contemporary methodology such as shared decision-making, evidence-based medicine, medical ethics and proactive considerations of non-clinical influences on physician decision-making (Guerrier *et al*., 2013; Lipworth, Strong and Kerridge, 2012; Hajjaj *et al*., 2010; Woolever, 2008; Groopman, 2007; O'Connor, Llewellyn-Thomas and Flood, 2004). Within each theme, a variety of considerations have been put forward, and the following sub-section attempts to present a brief consideration of the research in these areas.

Departures from traditional medical decision-making

The first departure from traditional medical DM is demonstrated by **shared decision-making (SDM),** also known as patient-centered care and informed decision-making (Woolever, 2008). Essentially, it is a humanistic, bio-psychosocial and dynamic perspective that combines a physician's ethical values with psycho-therapeutic theories of medical DM taking a patient's view into account (Elwyn et al., 2000; Bensing 2000; Charles, Gafni and Whelan, 1997). SDM is a process where physician and patient interact at the expert level to arrive at a value added, informed choice amongst clinically acceptable options, so tuning medical care to patient needs and preferences (O'Connor, Llewellyn-Thomas and Flood, 2004; Towle and Godolphin, 1999). However, although SDM does not exclude considering physician's preferences, values and experiences, there appears to be scant organised assessment of their assertions in this contextual setting (Guerrier *et al*., 2013; Briss *et al*., 2004; Elwyn *et al*., 2000; Makoul, Arntson and Schofield, 1995).

The second departure from traditional medical DM is demonstrated by an active **consideration of medical ethics in biomedical research**. Human medical research considers two forms of ethics: individual and collective ethics (Lipworth, Strong and Kerridge, 2012; Palmer, 2002). Individual recognises the right of the patient and targets what is best for the subject in the current trial (Lipworth, Strong and Kerridge, 2012). However, collective ethics aim to determine optimal options for future patients based on the results from a current trial (Griffin, Posner, and Barker, 2013; Lipworth, Strong and Kerridge, 2012). Although strain can occur between these two fundamentals, the Declaration of Helsinki (World Medical Association, 2013) clearly protects individual patients when it states that

> *"concern for the interests of the subject must always prevail over the interest of science and society"* (World Medical Association, 2013).

To help aid physicians reconcile the ethical component of their decision-making it appears that university medical ethics training covers two moral, but impartial, traditional theories of philosophy: consequentialism and deontology (Jackson, 2013; Lipworth, Strong and Kerridge, 2012). Consequentialism requires results based on forward-looking decision-making action guided by actions linked with the best

consequence for an individual or group (Kelly, Magill and ten Have, 2013; Scheffler, 1988). Deontology only has concern for duty, where looking to the past for precedents and rules shape professional ethical duty on four principles - autonomy, beneficence, justice and non-maleficence (not doing harm) and is the foundation of bio-ethics (Kelly, Magill and ten Have, 2013; Pojman and Fieser, 2009). Both approaches are based on Kant's guidance principles that perception, reason and understanding were the sources of morality (Jackson, 2013). However, other authors have added many minor ethics elements over the years so that prior understanding has changed, blurring meaning and making the concepts difficult to clearly define (Kelly, Magill and ten Have, 2013; Pojman and Fieser, 2009; Clewis, 2009). This has led to suggestions that teaching medical ethics is, at best, trivial and unnecessary or, at worst, futile as the subject needs to be taken seriously by developing appropriate assessment methods (Hope, Savulescu and Hendrick, 2003; Hope, 1998).

In contrast, alternative ethical theories have been put forward for consideration, as they are more people and situation-centric, covering topics such as virtue or communitarian ethics (Jackson, 2013; Faunce and Jefferys, 2007; Nussbaum, 1999). Virtue ethics focus on the character of the individual rather than on the nature or consequences of the act, or its omission (Jackson, 2013). For example, where a physician makes a decision based on conscious knowledge, integrity or virtue rather than theory (Faunce and Jefferys, 2007). Communitarian ethics occur where the clinician acts in a way that favours specific particulars of a distinct part of the community (Faunce and Jefferys, 2007). However, critics of these approaches argue that there are few points of agreement between these positions, none are fundamentally distinct from each other, nor qualify as rival approaches to deontology (Nussbaum, 1999). The main healthcare criticism of these approaches concerns the lack of academic foundation and, to address these concerns, some researchers have requested that philosophy and sociology training be included in medical schools' curriculae (Lipworth *et al*., 2012). Contrastingly, others have deployed mechanisms such as clinical governance pathways in context (Faunce and Nasu, 2009) or via the Training and Resources in Research Ethics Evaluation (TRREE) program, albeit the latter is mainly aimed at African countries (World Medical Association, 2014).

Given the potential influence of medical ethics on a physician's DM process, which could be a factor of age, exposure to the subject, medical school attended, teaching methods and individual preference, it appears that further exploration is needed. The interesting component for this research is not what ethical approach is in use but rather the physician's cognitive and moral reasoning concerning how that individual thinks and balances the ethical dilemma. In some respects this follows sociology, in particular Trevino's (1986) interactionist model, which suggests relationships between individual, situational variables and cognition, such that determining the interplay between the components determines how an individual is likely to behave in response to the ethical dilemma decision. McNaughton and Rawling (2007) have expanded this suggestion by indicating that there is no definitive correct answer to medical DM, as ethics options often clash, but the important point is to justify ethical reasoning, then document the approach for the record.

The third departure from traditional medical DM is demonstrated by the emergence of **evidence-based medicine** (EBM) (Hajjaj *et al.,* 2010; Bensing, 2000). In the 1990s EBM appeared in scientific literature adopting a biomedical and positivistic viewpoint focused on physician's interpretation of available objective evidence to guide the most appropriate patient treatment (Bensing, 2000). Medical DM has been revolutionised by technology, multimedia and the internet which can facilitate the provision of synthesized clinical evidence at the point of care, via electronic diagnostic tools such as DynaMed, ePocrates and UpTo-Date; access to medical databases such as CIHNAL, Embase, and Medline; the availability of academic theses and dissertations via Proquest; and internet search engines such as Google (Webb *et al*., 2010; Godin *et al.,* 2008; Woolever, 2008).

However, despite an increased EBM focus since the millennium, with an expanded choice and availability to these resources, a breadth of criticism exists. Uptake by practising physicians has been limited. Time, cost, prejudice, variable technological strategy and adoption, organisational resilience, adherence to clinical practice guidelines, unfamiliarity with contemporary research and SDM incompatibilities being cited as reasons for low acceptance and utilisation (Guerrier *et al*., 2013; Hung, Ku and Chien, 2012; Spring, 2008; Wainwright and Waring, 2006). Additionally, the accuracy, generalizability and applicability of available evidence is still questionable

(Hung, Ku and Chien, 2012; Woolever, 2008; Alper, White and Ge, 2005). In this setting, randomized controlled trials are still viewed as the pre-eminent standard on which to base medical decisions, but some study constraints, such as patient generalizability with co-morbid conditions, multiple and complicated problems, poor prognoses and poly-pharmacy treatments have been increasingly recognised (Christ, 2014; Starfield, 2006; Rothwell, 2005; Kravitz, Duan and Braslow, 2004). Furthermore, EBM is seen as a cognitive and rational operation that diminishes the importance of human relationships, such as patients' uniqueness, consideration of individual needs, preferences, and emotional status, all of which still appear to be discounted as relevant contextual DM factors (Kelson *et al*., 2012; Bensing, 2000).

Although this refreshed activity in pursuing the physician DM process point of view within individual medical scenarios is encouraging, it has not produced a gold standard for medical decision-making, resulting in renewed calls for challenging current research practices when evaluating physician DM interventions and active consideration of alternative approaches (Christ, 2014).However, the challenge for researchers is how to bring these separate worlds together. Some author's urge caution, others consider particular models, theories or themes and yet more advocate further research using other philosophies (Lipworth *et al*., 2012; Légaré *et al*., 2007). Some suggestions include highlighting tendencies that physicians' should avoid in their medical DM. These include search satisfaction – returning to lower level DM rules when eliminating alternatives; diagnosis momentum - ignoring findings that could lead to an alternative direction; commission bias - doing something rather than wait and watch and intuitive leaps - jumping to diagnosis without support of evidence or logic (Groopman, 2007).

Contrastingly, Woolever (2008) suggested that the best physician DM resources were not academic papers, scientific books or electronic applications but rather

"*the physicians you practice with*" (Woolever, 2008: 32)

This builds on the works of Norman (2006) and Bowen (2006) who postulated that physicians should utilise their colleagues and peers' wealth of experience and knowledge of working with the same patient population to promote informed clinical decision-making. In this study the researcher believes that this idea can be further

expanded by exploring how company physician's knowledge, skills and experiences can influence decision-making in non-medical contexts. This leads to the fourth departure from traditional medical DM. That is the emergence of **non-clinical influences on physician's decision-making**, which has also been seen as an important test of evidence-based practice (Burkle *et al*., 2012; Hajjaj *et al*., 2010). Around the turn of the last century the medicine focus grew beyond the doctor-patient interface as clinicians assumed a more central role in society (Porter, 1997). Due to the complexities of contemporary health care systems physicians now serve in a variety of non-clinical roles such as health authority executives, hospital administrators, insurance company representatives, business consultants and clinical research monitors (Uchitelle, 2006). So, for the purposes of this research non-clinical roles are defined as

"*roles filled by physicians that are outside of direct patient service but where patient needs still require active consideration.*" (adapted from Sade, 2007;11)

However, the challenges facing physicians working in these contextual roles has prompted repeated calls for guidance (Guerrier *et al*., 2013; Hajjaj *et al*., 2010; Hafferty, 2006; McKinlay, Potter and Feldman, 1996). Although not universally binding, and perhaps driven by fears of loss of professional status and respect, the American Medical Association published ethical obligations to maintain the integrity of the medical profession, the public trust in medicine, and guide clinicians in non-clinical roles, to the extent that those in such situations should primarily rely on their medical training, professional experience and own counsel to protect the health of individuals and communities they serve (Lipworth *et al*. 2013; Sade, 2007). However, identification and consideration of other non-clinical influences on physician DM are not so clear cut or prescriptive but merit further exploration (Guerrier *et al*., 2013; Hajjaj *et al*., 2010).

It appears that the biggest challenge to physician decision-making in a non-clinical environment is to understand the influences and perceptions on physician's cognition in context (Godin *et al*., 2008; Elwyn *et al*., 2000; Elwyn *et al*., 1999). Patel, Kaufman and Arocha (2002) called for development of a new framework to provide a greater suitable illuminative explanation of the DM process highlighting both adaptive and

sub-optimal characteristics of decision makers. This call appears to reference Fischhoff's (1982) work on reducing bias and heuristics which indicated understanding an individual's cognitive processing was a potential fruitful DM research area. This point suggests that physicians operate in social worlds, populated by other players, constraints and artefacts which could potentially influence their decision process and so should be explored.

Non-clinical influences on clinical practice fall into three main categories: firstly, direct patient-related influences including quality of life, socio-economic status and patient expectations; secondly, physician-related influences such as individual characteristics and peer engagement; thirdly medical practice policy and/or health authority / industry guidance (Hajjaj *et al*., 2010; Gill and Lambert, 2004).

In seeking a way forward for the clinical DM process and constructing a means to improve, the greatest amount of research over the past fifteen years has focussed on how patients' wishes and preferences can influence management decisions, such as in SDV (Guerrier *et al*., 2013; Hajjaj *et al*., 2010; Elwyn *et al*., 2000; Elwyn *et al*., 1999). However, physician non-clinical roles vary in the degree to which patient interfacing exists. Some suggest that reliance on medical expertise, knowledge and training in this environment is diminished, but their decision-making can still indirectly impact on the health and well-being of patients (Hafferty, 2006). Other authors have suggested re-evaluating physicians' DM perspectives in context, as the industry has neglected these aspects to the detriment of stakeholders (Lipworth, Kerridge and Day, 2013; Guerrier *et al*., 2013).

Alternative lines of enquiry suggest exploring overlapping influences from medical DM themes in detail. For example, probing physician's individual traits such as ethnicity, gender, age and personality; professional interaction with peers, their community and the pharmaceutical industry and physician-related influences such as capability, specialism and tendency to intervene (Bernheim *et al*., 2008; Hardy and Smith, 2008; Whitney, Holmes-Rovner and Brody, 2008). Furthermore, other exploratory avenues could be consideration of how business policies, managerial techniques, company procedures, environment and organisational constraints could introduce additional levels of complexity and influence physician's DM (Gill and Lambert, 2004; Herbert-Croteau, Brisson and Pineault, 2000). However, it does

appear that exploring the changing nature of the physician-patient DM relationship will form part of the main study exploration.

However, over the past decade, **dual-processing strategies** have attempted to improve medical DM by amalgamating intuitive and analytical models combining reasoning with interpretation. Although uptake of this call, in terms of emerging medical DM models, has been limited, some progress has been seen. The theories of reasoned action and fuzzy-trace, Illness scripts and the trans-theoretical model being the most notable examples of published works in this field (Lee *et al*., 2010; Milkman, Chugh and Bazerman, 2009; Reyna, 2008a; Allen, 2006). A brief outline of each approach follows.

The theory of reasoned action (TRA), and the updated version, theory of planned behaviour (TPB), describe how an individual's intention to execute a behaviour is a good indication of their inclination and motivation to make decisions (McEachan *et al*., 2011; Fishbein and Ajzen, 2010; Fishbein, 2008; Spring, 2008). This can be determined via researching an individual's thoughts (cognitions) which are seen as processes amidst noticeable stimuli and reactions in real world situations (Fishbein and Ajzen, 2010; Montaño and Kasprzyk, 2008; Fishbein, 2008). The study of social cognitive theories influencing clinical-related behaviours of health professionals was covered in depth by Godin *et al.* (2008) and their systematic review of scientific literature identified 78 papers discussing intention and behaviour factors that could influence healthcare professionals' behaviours built on social theories of cognition. The majority of perspectives were descriptive and behavioural, linked to either TRA or TPB, but although Godin *et al* (2008) concluded that TRA and TPB could be utilised to investigate sources of health professional's behaviour via the study of intuition and pattern recognition, the majority of papers were theoretical, few empirically-based and fewer still physician DM specific.

Fuzzy trace theory (FTT) suggests that individuals rely on subject gist instead of the verbatim detail for decision-making and judgment (Reyna, 2008b). This idea appears to explain why specific facts, such as risk profiling or statistical data, are not automatically used to support medical DM, despite the individuals receiving the information but then fail to use it or derive the correct meaning (Reyna, 2008a,b).

Essentially FTT assumes that that contextual DM processing using intuition is more capable and sophisticated than evidence-based medicine.

Illness scripts is a medical reasoning concept that provides a theoretical framework for physicians to illustrate how clinical diagnostic knowledge can be depicted for diagnostic problem solving. It involves using a knowledge-driven model of pattern recognition superimposed on a formal 5 step philosophical structure where physicians use mental shortcuts to make diagnoses (Lee *et al*., 2010; Bowen, 2006). However, inadequate data collection can lead to poor problem representation, inadequate hypothesis generation and low diagnostic accuracy (Bowen, 2006).

The trans-theoretical model (TTM) offers a means to conceptualise patient's decision-making about behaviour change and comprises four key pillars: change stage, change process, balancing decisions, and self-effectiveness (Prochaska, 2008; Prochaska and Velicer, 1997). Over the past dozen years TTM has been researched empirically within many therapeutic areas, such as diabetes, smoking cessation, obesity, pregnancy and sexually-transmitted disease (Tuah *et al*., 2010; Salmela *et al*., 2009; Aveyard *et al*., 2009; Aveyard *et al*., 2006; Bridle *et al*., 2005). However, although stage of change thinking has established itself within medical practice, there is scant supporting evidence to confirm that TTM may really be associated with health-related behavioural changes (Spring, 2008). Furthermore one critical point of view suggested that the model makes incorrect assumptions and predictions that are worse than rival theories (West, 2005).

Overall the theories of reasoned action and fuzzy-trace, Illness scripts and the trans-theoretical model have broad similarities but several significant differences. The similarities include all being supported by empirical evidence with each one declaring a contrasting view on behavioural change and medical decision-making risks (Reyna, 2008a). All have a fairly clear stand on what is prescriptively possible through researching subjective perceptions of reality to shape decision-making, for example via perceived gist, risk pros and cons, mental representation and values retrieval, intuition and conscious awareness (Spring, 2008; Reyna, 2008a). However, the differences manifest themselves in terms of DM approach with TRA and TTM approaches accentuating reason, Illness scripts needing patients and FTTs focusing on intuition of the decision-maker (Reyna, 2008a).

In this study the researcher is interested primarily on the physician perspective so has chosen to discount TRA and TTM, given their focus on reason over behavioural variance, and Illness scripts given their patient-centric core. However, although FTT appears to be a dual-process theory that could be used to account for behavioural phenomena, via researching effects such intuitive reasoning, it appears to have been vilified as clinical opinion (Spring, 2008).

Despite criticism of these models and the apparent literature gap in terms of empirical evidence of DM dual processing gathered from physician experience in non-medical contexts, the concept itself appears to have merit. However, to actually ascertain which dual processing influences are relevant, and identify the best means to incorporate within this research, further exploration was needed.

The concept began with the Cognitive-Experiential Self-Theory (CEST) model of individual perception, which suggested that people actively use two distinct but interactive systems for processing information: intuitive-experiential and analytical-rational (Epstein, 1994). Although, useful in understanding various social behavioural influences, this model failed to describe how decisions were made. Criticisms of CEST included incomplete modeling of conflict between intuitive and rational processing, and a ratio-bias limitation of the experiential system in ambiguous situations where individuals choose a higher absolute number rather than ratios (Lieverman *et al*., 2007). However, some authors extended this framework to other fields with a prominent example being the Stanovich and West (2000) linear framework, that distinguished between cognitive System 1 (automatic, fast, implicit, intuitive, emotional but effortless) and System 2 (explicit, conscious, slower reasoning, logical but requires effort) processing. Additional opinion suggested that dual processing application could reduce system 1 errors via bounding awareness; system 2 thinking had potential to reduce bias; but system 1 thinking needed to be understood in context (Milkman, Chugh and Bazerman, 2009; Bazerman and Moore, 2008; Bazerman and Chugh, 2005; Moore and Lowenstein, 2004, Epstein, 1994).

Contrastingly, two theoretical frameworks incorporated various non-medical have contextual factors on physician's DM processing. Firstly, the **Rapid Clinical Decision in Context (RCDC) model** suggests that experienced clinicians use a naturalistic decision-making (NDM) process via a cognitive framework to illustrate

how recognition-primed contextual factors enter into physician's mental processing (Tamayo-Server *et al*., 2005). Although the RCDC model specifies pattern-matching, mechanisms and flows, potentially amenable to DM, criticisms include it being theoretical, race / ethnic biased, based on a physician-patient interaction, and specific to clinical treatment (Tamayo-Server *et al*., 2005).

Secondly, the theoretical concept of **emotion-primed NDM**, is a constructive and destructive emotion-based modulation framework for use under life threatening conditions which produces either a satisfying outcome, or vice-versa (Rahman, 2009). Although, this model attempts to explain how altering the probability of taking a clinical decision could lead to a satisfactory outcome, the key element for the researcher is not the emotional probability perspective but rather that Rahman demonstrated construction of a NDM-based framework for use in a clinical-based contextual setting.

However, other authors have indicated that clinical practice decisions are individual professional decisions, and so a better understanding of physician decision-making mechanisms could be explored by focussing on social psychology theories (Mohan *et al*., 2012; Grol *et al*., 2007; Eccles *et al*., 2006; Michie *et al*., 2005; Connor and Sparks, 2005). In order to account for social phenomena on medical DM, effects such as exploring practitioner DM experiential perspectives (Kordeš, 2009), researcher's having access to, and pre-understanding of, the social environment and institutional conditions (Gummesson, 2000), and constructing new decision support tools (Guerrier *et al*., 2013; Reyna, 2008a) have been requested.

To sum up, this subsection has focussed on medical decision-making processing and highlighted some physician DM influences within clinical encounters that could be explored in non-clinical settings. This includes physician experiences, ethics and engaging other clinicians. However, this medical DM review suggests that further study of social cognitive and subjective influences on physician DM in context could offer a means to address decision challenges faced by physicians working outside of direct medical practice, in roles that do not directly involve patient care, such as in vigilance processing roles within a clinical research organisation. Of particular interest to this researcher is exploring the dual-processing approach which suggests that combining intuitive and analytic reasoning appears to be better than either

alone. The RCDC and emotion-primed NDM approaches illustrate that the NDM cross-disciplinary research paradigm has begun to be applied to medical DM. It is this author's suggestion that investigating a dual process approach, utilising a NDM lens, could bring a new and distinct perspective to understanding physician DM as it occurs in non-clinical settings, particularly if key influencing factors were clearly identified. For example, via identification of literature-derived, evidence-based, cognitive and behavioural DM influences for exploration in a non-clinical context. Consequently, naturalistic decision-making will be considered within the next sub-section of this literature review.

2.2 NATURALISTIC DECISION - MAKING

Over the past two decades behavioural decision-making research has moved towards researching cognitive DM as it exists in real-world, dynamic, but complex, environments, which has seen the emergence of a new field termed naturalistic decision-making (Klein, 2008; Nutt, 2008; Salas and Klein, 2001; Zsambok, 1997; Orasanu and Connolly, 1993). NDM has been described as both a communicative theory and DM approach which is rooted in sociological analysis, focused on contextual description, categorisation and its impact, emerging from empirical study of how individuals take decisions within real world settings which are recognizable and meaningful (Klein, 2008, 1998, 1993; Lipshitz *et al*., 2001; Yates, 2001; Zsambok, 1997). Although it inductively evolved out of a descriptive inquiry (using cognitive task analysis) into how fire fighters handled time pressure and uncertainty, NDM research can be characterised by five components; namely, experienced decision-makers, pairing situation-action decision rules, contextual-bound framing, shaping processes, and prescription from empirical study (Klein, 2008, 1998; Lipshitz *et al*., 2001; Rasmussen, 1997; Endsley, 1997).

In the 1990s the earliest definitions of NDM were spent clarifying the paradigm against traditional research (Orasanu and Connolly, 1993), and the evolution of NDM was described by Cohen (1993) as a consequence of NDM researchers taking issue with comparing the quality of decisions against traditional, rational standards. This approach viewed classical DM as appropriate for laboratory settings but failing to take account of contextual influences that accompany DM in real world settings (Klein, 2008). Formal models were seen as not adequately portraying the adaptive

characteristics of real behaviours and so a clearer understanding of what defined NDM in positive terms was needed. However, in the intervening period, the NDM approach has attempted to study human cognitive performance by researching how experts typically take decisions in real-world, natural contextual situations (Nemeth and Klein, 2011). Latterly NDM explores approaches individuals deploy when making difficult decisions in variable conditions comprising instability, risk, time pressure, high stakes, multiple decision makers, uncertain conditions and vague goals (Schraagen, Militello, Ormerod and Lipshitz, 2008). Individuals in these situations are not generating and comparing different courses of action, as believed by traditional decision-making research, but rather, referencing past experience to categorise situations and make judgements (Klein, 2008). So, for the purposes of this research, the NDM definition used is that of a study which

> "*asks how experienced people, working as individuals or groups in dynamic, uncertain, and often fast-paced environments, identify and assess their situation, make decisions and take actions whose consequences are meaningful to them and to the larger organisation in which they operate*."
>
> (Zsambok, 1997: 5)

2.2.1 Naturalistic Decision-Making models

NDM models and theories have been utilised to aid researchers observe links and form proposals as, minus them, many interconnections will typically be unseen. The main NDM models and key themes within this paradigm are depicted in table 2.3. Three key examples: Image Theory (Beach, 1993), Cognitive Continuum Theory (Hammond, 1993) and Recognition Primed Decision-Making (Klein, 2008, 1993, 1989) have been selected for consideration within this section. The main elements from each theory will be presented in turn with key components pertinent to this research identified and discussed. In addition, three sub-level NDM models will be contrasted - SRK Decision ladder (Rasmussen (1983, 1993a), amended by Lintern (2010); Situation Awareness (Endsley, 1997) and Recognition-Metacognition (Cohen, Freeman and Thompson, 1997) as they extend specific NDM themes into behavioural and cognitive areas that could potentially impact physician decision-making in a non-medical setting. Each model will be critiqued for consideration and potential exploration in the main study. At the end of the chapter the identified NDM

elements will then be presented in a NDM schematic for guiding the empirical research.

NDM theory / model	Key Features	References
Image Theory	Decision-making occurs in two phases where alternative options screened versus overarching goals, values, beliefs and ethical standards with links to the application of a compatability test.	Beach (1993)
Cognitive Continuum Theory (CCT)	Decision maker's judgment oscillates between intuition and analysis depending on cues presented. Linear process.	Hammond, (1993); Hamm (1988a;b)
Recognition Primed Decision (RPD) Making Model	Decisions flow from recognition of familiar situations by experienced individuals or groups, working on realistic organisational tasks, in typical contextual conditions, constrained by executive level operational objectives. Linear process.	Klein (1998; 1993)
Skills-based, Rules-based, Knowledge-based (SRK) model of task performance	8 stages of decision making in decision ladder with focus on situation analysis, value judgment, planning and execution. Accommodates both rational and heuristic decision processes. Allows for associative leaps (shortcuts) between any of the decision stages, particularly in unfamiliar situations.	Rasmussen (1983)
3 step model of Situation Awareness	Internal conceptualisation of situation comprising perception and understanding of current position then anticipation of how the situation will evolve.	Endsley (1997)
Recognition – Metacognition (R-M)	Extends recognition situation awareness into object and meta-level cognitive activities where information flow and control characterise the decision-making relationship.	Cohen, Freeman and Thompson (1997)
Updated decision ladder	Template used to depict all possible cognitive stages and processes, including non-active ones.	Lintern (2010)

Table 2.3: Naturalistic decision-making theories, models and key features.

Image Theory

Image Theory (IT) is a descriptive DM theory where individual experts simulate and envisage data as a series of informative images (Beach, 1990). The first image consists of a quest to reach specific objectives. The second image shows an illustration of some future state resulting from achieving those goals. The third image depicts the plans and actions implemented in the endeavour to attain these goals. The fourth image illustrates the forecasted results of these arrangements. The value of IT occurs when a possible decision route is incompatible with at least one of a person's images, such that that route is filtered out via a pre-choice screening of options. So, a compatibility decision is made to either adopt, or reject, existing goals, plans, or principles versus a potential candidate's images of the desired state, or the potential loss/gain offered by the goal or plan (Beach, 1993). Although IT appears to

offer an alternative to normative decision theory by describing how people use their overarching goals to guide DM, its focus is consumer research with most IT studies involving simulations (Galotti, 2002; Beach 1993). One author claimed that it is unclear whether IT is a normative or a descriptive model given its use of equations (Galotti, 2002). However, the researcher is interested in this model as it introduces the idea of conceptualizing schematic knowledge structures and cognitive elements of DM, separates screening from choice, and implies that other factors, such as organizational goals, objectives and tasks are involved in the decision-making event.

Cognitive Continuum Theory

Other researchers, however, have suggested that DM processing occurs somewhere along a cognitive spectrum commencing with intuition and finishing with analysis (Hammond 1996, 1993; Hamm, 1988a, 1988b). This is Cognitive Continuum Theory (CCT) where analysis and intuition are viewed, not as separate systems, but merely as end-points between which cognition is located. This has been introduced as quasi-rational cognition where many decision events need cues that lead to mental fluctuation between intuition and analytical cognition (Hammond, 1996). Determining whether a decision maker utilises an intuitive or traditional DM approach occurs by the task location on the spectrum which comprises three dimensions; complexity, ambiguity, and nature of the presentation of the task (Thompson, 1999). However, influences, such as a person's organisational position, can exert influence on the mental doctrine available to them for deployment (Thompson, 1999).

According to Hammond (1996), the key principle infers that

> "*judgment is a joint function of task properties and cognitive properties.*"
>
> Hammond (1996: 83)

The key feature of CCT is that processing intuitively is characterised via little governance or slight consciousness, expertise, fast processing and great assurance with any result (Hammond, 1993; Hamm, 1988a). This appears similar to clinical DM approaches that emphasise clinical expertise and intuition in reaching case-specific judgments (Falzar and Garman, 2012; 2010; 2009). However, this is in contrast to analytical processing, which could be considered similar to Rasmussen's (1983)

knowledge-based processing within the SRK model (section 2.2, page 48). It appears that Hammond (1993) is suggesting that processing analytically or intuitively is established via two critical features. Firstly, specific judgments generate either analytical or intuitive processing, and secondly, that breakdowns when using one format results in flipping over to the other.

This model is of interest as it appears that DM tasks can induce processing in various ways – intuitively where a relatively large number of cues are simultaneously and briefly displayed but DM relationships amongst the cues are processed in a relatively short time period. Contrastingly analytical processing occurs with lesser clues, strong belief in the task, or processing lengthy sequences of available cues over time (Hammond, 1993). This model appears to echo comparisons with physician's clinical DM approaches in industry. For example, physicians making decisions emphasizing clinical expertise and intuition, or recommending that clinical treatment should conform to guidelines (Falzar and Garman, 2012; 2010; 2009; Eddy, 2005).

The CCT model is important to consider as it suggests that DM fluctuates rapidly between intuition and analysis depending on current circumstances and experts' analytic and intuitive cognitive activity (Hamm, 1988b). However, to understand how mental processing, or conceptual representations, influence problem solving relationships, Klein (1993) described an alternative model of decision-making describing how individuals use their experiences to take decisions in naturalistic contexts (eg: comprising changing conditions, diminished data, group engagement and time constraints). This was the Recognition Primed Decision-Making (RPD) model which incorporated two cognitive processes: situation assessment and mental simulation (Klein, 2008; 1993; 1989; Klein and Klinger, 1991).

Recognition-Primed-Decision Making Model

The RPD model is the most empirically researched NDM approach describing what decision makers actually do under changing conditions with ambiguous information, time constraints, ill-defined goals and objectives (Klein, 1998). RPD focuses on several NDM factors particularly staff experiences, working in complex, uncertain conditions, facing personal consequences for their actions. The model is descriptive,

addressing how individuals make decisions, without comparing outcomes, using situation awareness and problem solving as part of the DM process (Klein, 2008; 1993; Klein, Orasanu, Calderwood and Zsambok, 1993) and is depicted in figure 2.1.

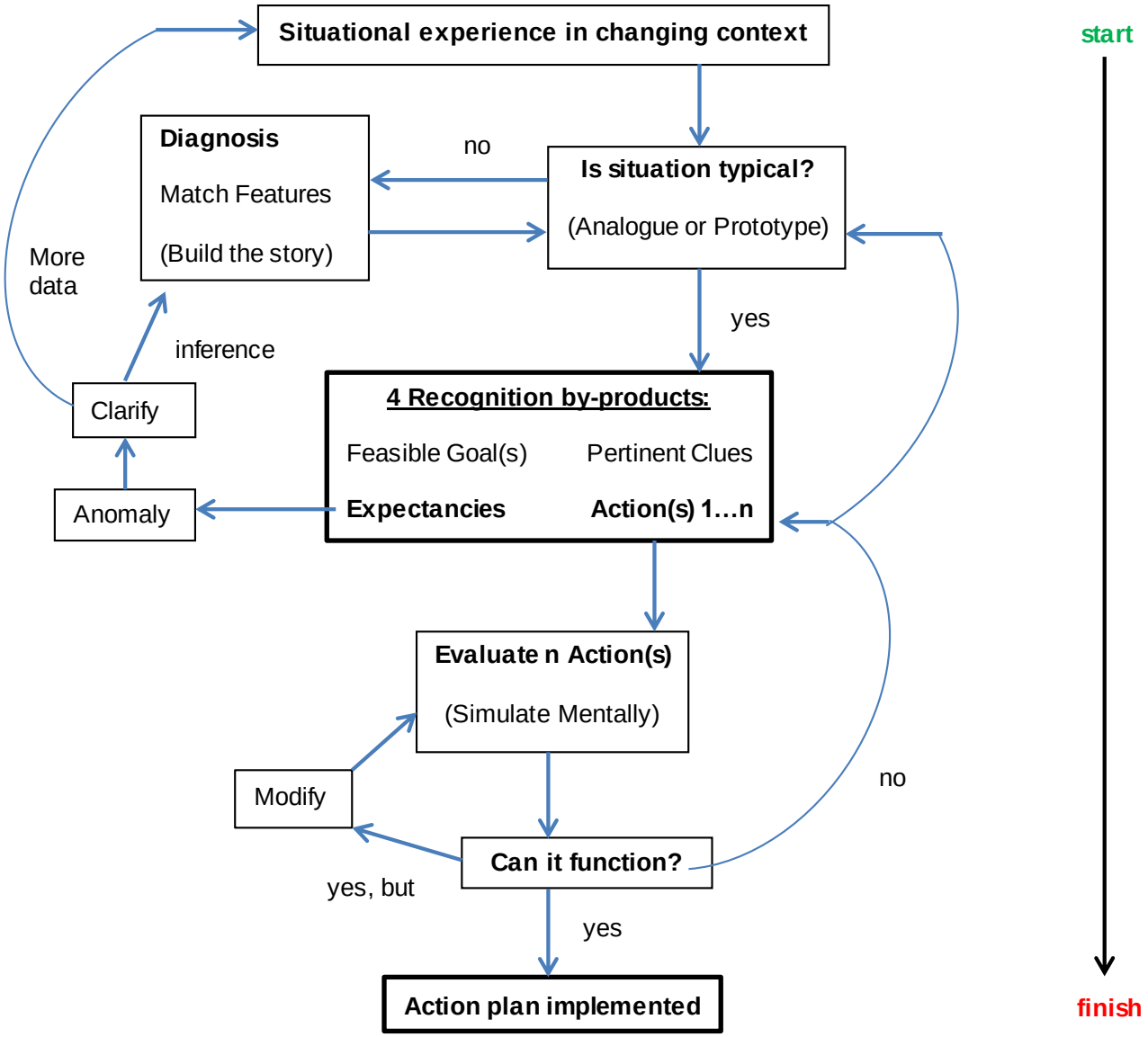

Figure 2.1: Unified Recognition-Primed Decision Model (Klein, 2008)

Within RPD a decision maker picks up certain cues which cause mental patterns to form for any given situation. The decision maker chooses one action course (action script) that they consider will achieve the outcome based on these conceptual patterns and any judgment that requires to be taken (Klein, 1993). Essentially, the decision-maker runs this action script through a form of mental simulation based on some internal cognitive process developed from their existing and prior experiences

(Klein, Orasanu, Calderwood and Zsambok, 1993). The RPD model's objective is the means by which individuals utilise prior experience to recognise situations and take effective decisions save having to compare alleged pros and cons of different courses of action. It suggests that people use experience and intuition to size up a situation, providing them with a sense of typicality, as shown in figure 2.1, via recognition of goals, cues, expectancies, and courses of action. Analysis can then be utilised to corroborate that intuition is relevant to the situation (Klein, 2008). Although RPD appears to give decision makers more options to choose from, it has been shown that the first option chosen was actively constructed via rapid and effective movement through the model and that functioning is what makes them experts (Klein, 1997a; 1993).

RPD has been considered relevant to this study because it has been used successfully to model how experts in their chosen field make decisions via an intuitive ability to recognise and categorise patterns accumulated from experience. This would appear to be useful in a clinical research situation, such as physician DM, where monitoring environmental actions and their consequences is required prior to implementing an action (Klein, 1998; Roth, 1997). Additionally, the validity of the RPD model has been tested and evaluated in various environments providing empirical evidence for the success of the model but also demonstrating the typicality of recognition-based decision making (Klein, 1997). This diversity is crucial as it shows that the DM is a universal human process rather than a domain-specific one.

Despite the RPD model's dominance in NDM research, it can be a barrier to looking anew at a phenomenon, if followed too closely. It does not address all the concerns of NDM given influences such as group effects, organisational constraints, memory, attentional or metacognitive processes are missing (Klein, 2008). As a result some researchers have deliberatively chosen to avoid RPD because it can get in the way of observing phenomena (Klein, Phillips, Rall *et al*., 2007). Instead, alternative approaches and frameworks, such as the data frame model (Klein, Phillips, Rall *et al*., 2007) or naturalistic exploration (Fadde and Klein, 2010) have been put forward. However, although the data-frame model is empirically grounded and consistent with RPD, it emphasises alternative processing and interdependencies to RPD, namely: causal reasoning; commitment to hypotheses; feedback and learning; sense-making

as a skill; and confirmation bias. Although initially seen as a RPD enhancement, it was shown to be flawed because in each data-frame area, the model and the research it was based on, did not align with common beliefs (Klein, Phillips, Rall *et al*., 2007).

Contrastingly, other investigators have used naturalistic exploration of deliberate practice to accelerate performance and enhance expertise in natural settings rather than amend the data-frame sense-making model flaws (Fadde and Klein, 2010). However, although four deliberate performance exercises were described: estimation, experimentation, extrapolation, and explanation, business people did not have time for practice, indicating that these updated models cannot be considered a depiction of common-sense views (Fadde and Klein, 2010).

In this study the key consideration is whether elements of CCT, IT and RPD could form the foundation of a NDM investigation within the main research. For example, RPD indicates that an intuitive pattern-matching process lies at the core of DM where context and situation awareness are key contextual components of problem solving, whereas IT and CCT show that other influencing factors such as mental modelling, experience and addressing errors within a changing landscape would require to be explored in decision-making. In order to potentially help address these gaps the next sub-section highlights and critiques four NDM themes (context, situational awareness, experience, and errors) and discusses each one in turn linked to additional NDM models.

2.2.2 NDM theme one : Context

All naturalistic decision making theories and models attempt to explore and ascertain how individuals take calls within real contextual world settings which are familiar and meaningful (Lipshitz *et al*., 2001). In workplaces NDM research usually focusses on the connection between cognitive resources and contextual constraints without relying on normative models of choice as the starting point (Klein, 2008; Elliot, 2005; Endsley, 1997). Furthermore, NDM research from other fields show that experienced decision makers know just what to do without deliberation, often relying on contextual expertise, where exploration and analysis of real world environments often results in the construction of a descriptive DM framework to illustrate the

natural setting effect (Klein, 2008, 1998, 1993; Elliot, 2005; Endsley, 1997; Cohen, Freeman and Thompson, 1997; Rasmussen, 1988). Additionally, other features such as their innate ability to reason, think, and judge; amount and type of knowledge and experience, or DM activities, not clearly identifiable, but embedded in complex workplace practices, appear to be important too (Benner, Hughes and Sutphen, 2008; Klein, 2008; Nutt, 2008; Alby and Zucchermaglio, 2006; Elliot, 2005; Endsley, 1997).

Throughout this research two large contextual influences appear to run in parallel. Firstly, the new industry requirement, ISO14155:2011, (chapter one, section 1.1), and secondly, the clinical research organisation and physicians impacted (chapter one, section 1.2) (International Organisation for Standardisation, 2011; PPD, 2009). However, there does not appear to be any literature on the effect of these contextual influences on physician DM either individually or collectively.

In this research the author suggests that a clinician's ability to execute decision-making processing could be influenced by contextual factors and naturalistic features and so, researching the interplay of physicians' non-medical DM practice with regulatory requirements within the contextual constraints of a clinical research organisation is needed.

2.2.3 NDM theme two : Situation Awareness

Naturalistic decision-making processing commences with a situation assessment (SA) where people gather environmental information, which is then used to construct a mental illustration of the decision problem at hand (Elliot, 2005; Endsley, 1997). NDM research indicates that experts make decisions in field settings using intuitive and holistic processing that involve situation recognition, current information, prior knowledge and experience linking pattern matching to memory structures (Klein, 1998, 1993, 1989; Klein, Calderwood and Clinton-Cirocco, 1986; Dreyfus, 1981). However, decisions are rarely made in a stationary environment, which contrasts with the singular choice points highlighted in traditional normative DM models (Klein, 1998). So, rather than reliance on fixed information sources, a decision maker needs to assess the changing environment frequently to update and constantly advise their DM. As DM influences change automatically and with each decision formed, NDM

depends upon continuous situation assessment of the influencing factors such that continual assessment produces situation awareness (Elliot, 2005). This has similarities to the CCT model (chapter 2, section 2.2).

Although recognition forms the core of proficient decision-making, it is deficient when no recognizable form fits the presenting situation (Cohen, Freeman and Thompson, 1997). So, from the literature, two supplementary naturalistic situation-assessment-based models (Endsley, 1997, 1995) and Recognition/Metacognition (R/M) (Cohen, 1993) have been identified by the researcher as offering potential decision-making aids to help understand novel situations. For example, the role of mental models (specific situation representations) and schemata (abstract cognitive structures that guide the construction of mental models), appear to be crucial themes to augment the information from recognition. Each is outlined in the next section to potentially highlight how they can help clarify the physicians' decision-making processing.

Endsley NDM model

According to Endsley (1997, 1995) an individual's situation awareness (SA), or internal conceptualisation of the presenting scenario, is the key task that drives an effective DM process. In this context SA considers

"*perception of the elements in the environment within a volume of time and space, the comprehension of their meaning and the projection of their status in the near future".* (Endsley, 1988:97)

However, SA concerns more than simply observing and distinguishing data from the environment. It includes understanding information meaning in an integrated format versus all their objectives, and providing forecasts of the environmental future state (Artman, 1998; Endsley, 1995, Brehmer, 1990). In this way the cognitive image forms a lens via which a decision maker illustrates the situation and aids formation of goal construction and determination of expectations (Elliot, 2005). This is mental simulation and depicts the mental models role in processing current situational information where higher SA layers can subsequently enable decision-makers to operate in an effective and timely manner (Elliot, 2005; Endsley 1995). Endsley's (1995) model, as illustrated in figure 2.2, provides a general cognitive framework for conceptualizing the factors, mechanism and processes that impact SA across three

layers: perception, comprehension and prediction. First layer SA comprises a perception of the environmental critical factors. Second layer SA involves comprehending what those influences mean, especially when integrating altogether with respect of the decision-maker's objectives. Third layer SA (highest) consists of comprehending what will occur within the system in the near term.

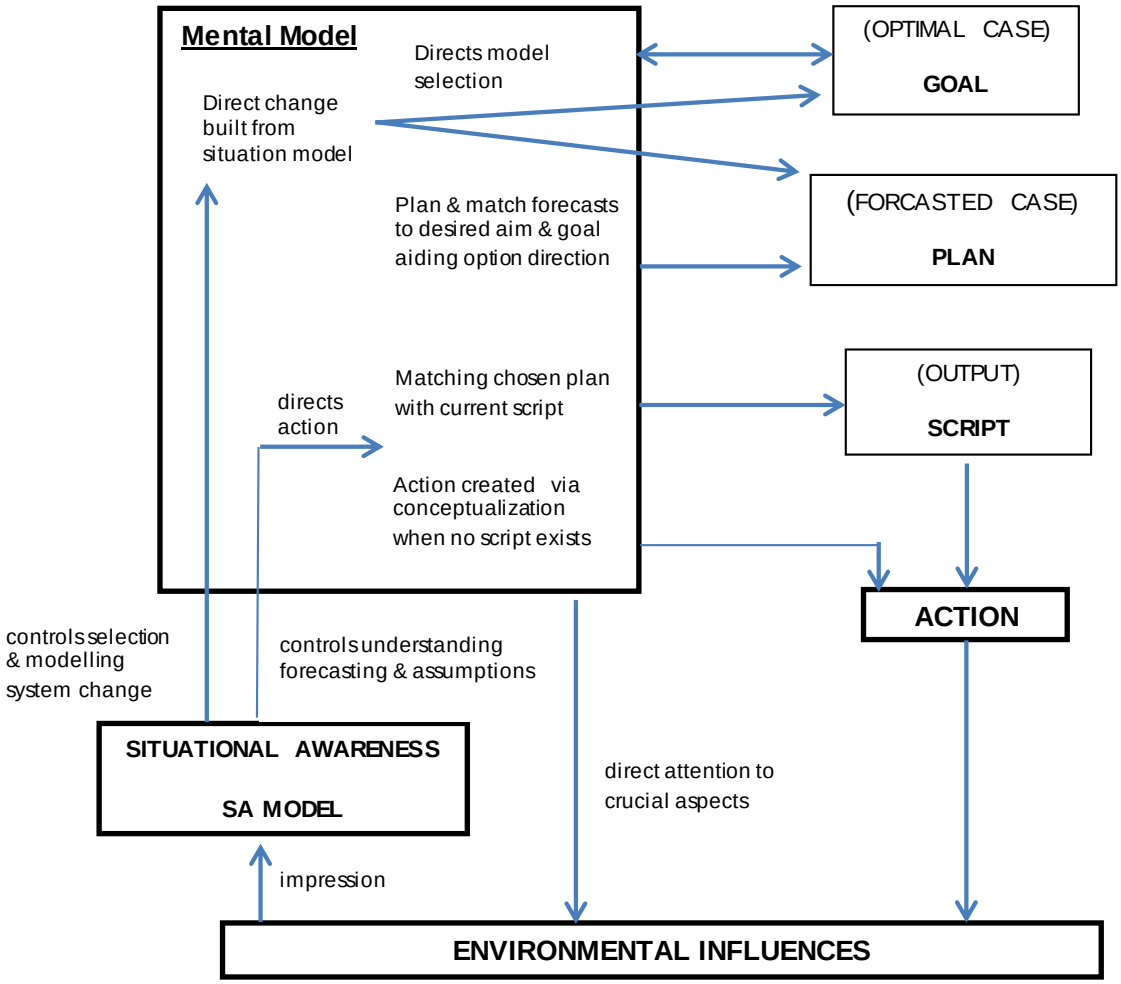

Figure 2.2: Mental model roles when dealing with presenting influencing situation data (adapted from Endsley, 1995).

This model is particularly useful within this study as it suggests mechanisms for goal selection, categorization of information, considering crucial clues, pattern matching, expectancies concerning future state and ties, SA linkages and DM action. In this regard Endsley's (1995) model is similar to other models of human performance and naturalistic decision making, such as the RPD model and Image Theory, (chapter 2,

section 2.2.1). However, Endsley's (1995) model emphasizes the role of SA within the decision event.

In this research it appears that SA could be a key influence in how a physician characterises the ISO14155:2011 situation, which can then influence the decision process used to solve the compliance problem. For example, some authors have indicated that different problem framings can induce contrasting situational comprehension and information integration, given that a person's situational comprehension determines mental model and strategy selection for use in solving the problem (Manktelow and Jones, 1987; Tversky and Kahneman, 1981). So, it would appear that in Endsley's (1995) model (figure 2.2) detailed situational data is provided that directs selection of decision strategy but also the way the pieces are compiled and constructed, constrained by organisational goals and plans.

Although the Endsley and RPD models appear to offer a means to explore key situational specifics that could influence the mental model adoption by physicians, neither, however, supports unfamiliar situations (Klein, 2008, Endsley, 1995). However, the Recognition-Metacognition (RM) Model (Cohen, Freeman and Thompson, 1997) explains how metacognitive reasoning supplements recognition processes within decision events involving novel scenarios and will be covered next.

Recognition / Metacognition Model

The Recognition-Metacognition model depicts how to integrate situational schemas (organised thought, or behaviour, patterns that classify information and the relationships between them) under the influence of meta-level control (Cohen, Freeman and Thompson, 1997; DiMaggio, 1997). This includes processes to critique (problem identification via recognition schemas and developing situation model); correction (instigate observation, retrieval, reinterpretation or mixture to produce better situation model) and; quick test (to consider error costs, degree of novelty or uncertainty; and identify time available) (Cohen, Freeman and Thompson 1997).

The key component of the RM model is the appreciation of metacognition which is a mixture of skills supporting and extending SA process recognition. This involves splitting cognitive processing into two levels (object- and meta-level) where an information flow-and-control mechanism characterises the relationship. Firstly, the

object level consists of processes recognition which activates schemas in response to external and internal clues. Then the meta-level controls the process. This process is comparable to meta-perception competencies that proficient readers utilise to construct mental models based on printed text information (Cohen, Freeman and Thompson 1997).

In this research, there are several elements worthy of consideration from this model, namely; identification of key situational assessments; checking the constructed stories of physicians for completeness and consistency relative to decision-making assessments, and then generating alternative descriptions, if and when, too much conflicting information is encountered, unreliability is exposed or DM is too general or has gaps (Cohen, Freeman and Thompson, 1997). So, in this research, it appears that to fully explore the construct of SA, and to develop an understanding of its role in physician DM processing, this study needs to be fed by understanding how expert physicians make use of their cognition, past experience, environment, organisational goals and resources to make decisions relating to ISO14155:2011 compliance within their complex and dynamic environment. To supplement DM situation awareness the next section will delve into two additional NDM themes: expertise and cognition.

2.2.4 NDM theme three : Expertise

NDM researchers broadly consider that real-world DM is heavily schema-driven, grounded in the present, but strongly influenced by the past experiences and expertise of practitioners (Lipshitz and Ben Shaul, 1997; Zsambok, 1997; Klein, 1993). However, although decision-makers can all assert to possess experience and knowledge of their environment, definition of contextual expertise is difficult and not adequately defined in literature, because phrases such as *previous experience* and *specialised domain knowledge* have still to be defined clearly (Elliot, 2005). Thompson and Dowding (2002) argued that when making decisions, decision-makers draw on a variety of information sources: experience; a combination of theoretical, tacit, and experiential stored knowledge or facts; the expertise of other practitioners; expert groups and occasionally the experiences of many others in the form of research evidence. However, these latter points appear to be overlooked areas in this field, but important ones, that provide a focus area for this research.

Some authors have suggested that the focus of medical decision-making be on physicians alone given their technical expertise, the ability to think critically, experience, and clinical judgment which informs independent and interdependent decision-making (Benner, Hughes and Sutphen, 2008; Bogner, 1997). However, in nursing contexts, physicians are employed in expert roles, and act as decision-makers either individually or collectively, but conflict can occasionally occur depending on how DM event is viewed (McConnell, 2011). For example, in some healthcare environments a practitioner professional often has a managerial role and faces a dilemma of respecting professional practice versus the managerial tasks of addressing broader issues and functions (McConnell, 2011). The same dilemma occurs within clinical research, as the physician decision-maker is often the same professional expert, who has to manage and balance industry requirements versus client and organisational expectations as well as patients' needs.

Although individual experts make and take decisions in NDM situations, some scenarios require other groups of people to assist with decision-making (Klein, 2008; Orasanu, Martin and Davidson, 2001). In such scenarios the decision-making focus expands from the individual to requiring comprehension of the DM situation in the context of a specialist group (Stout *et al*., 1999). For example, understanding process and performance factors, incorporating shared and distributed team DM and collecting the views of key influencers (Légaré *et al*., 2011; Stacey *et al*., 2010; Makoul and Clayman, 2006; Salas and Fiore, 2004; Fan *et al*., 2005).

In these situations, the distributed nature of organisational group decision-making is complex and has been presented in various ways, such as using situational diagnosis which can be shaped by flexible roles, distributed responsibilities, absent participants, and narratives as specialised discourses (Alby and Zucchermaglio, 2006; DiMaggio, 1999). To address making decisions of this type other researchers have pointed to identifying key features of decision-making processing that are very successful, or, strongly ineffective, which may involve the nature, tenure and extent of prior expertise; the need for cognition; team mental models; reflective-impulsive styles, or the way expertise is used when making difficult judgments and decisions (Nutt, 2008; Lim and Klein, 2006; Elliot, 2005). Furthermore, Cannon-Bowers and Salas (2001) identified three internal and five external factors that could affect

shared group decision-making. The internal factors were identified as cognition, skills and attitudes whereas the external factors were context, group structure, group design factors, process factors, and contingency factors. However, Hu and Liden, (2011) suggest improving DM via exploring organisational goals and process-clarity. Contrastingly, Brown (1998) claimed that group DM was usually subsidiary to individualistic DM. Some authors suggesting the contrast could be due to social or process malfunctions (Postmes and Lea, 2000). The latter arising from group setting or structural characteristics that offer disproportionate chances to communicate, or participate, thereby impacting DM (Postmes and Lea, 2000). Social malfunctions arise from limitations in the form and structure of meetings leading to conformity strains, evaluation apprehension, socialising stress, or domination due to status imbalance (Postmes and Lea, 2000; Strobe and Diehl, 1994).

Although NDM research studies depict how decision-making works in complex, uncertain, dynamic situations, such as anaesthesia in emergency rooms, there are some situations where an expert's experience may not have an immediate and intuitive response (Klein, 2008). Consequently NDM research has gravitated to comparison studies of novices versus experts in decision-making or expert group differences in clinical settings (Elliot, 2005; Zsambok, 1997). Similarly, in transparent intuitive coping, a decision-maker must assess a situation and generate action plans, drawing on their expert understanding, rather than falling back on normative models, which can cause the decision-maker to lose touch with their expert intuition completely (Dreyfus, 1997). However, Ollis, Button and Fairweather (2005) argued that there was little conclusive evidence for optimal practice structure but situation complexity and professional experience were mediating factors that influenced the potency of contextual interference in real-world settings.

Therefore, in seeking to ascertain how, and what factors, can affect and influence physician decision strategies for compliance with ISO14155:2011, a key component appears to be understanding how professional physician expertise, gained from prior clinical situations, is brought forth, considered and balanced with current role, legislative requirements, social and organisational decision-making strategies and other influences within PPD. This is a theme that will be explored in the main study.

However, another presenting theme that overlaps throughout DM literature is the influence of cognition on the decision-maker. Although prior NDM theories have touched on this topic to some extent, two specific NDM cognitive models, Noble (1993) and Rasmussen (1983) appear to offer a means to potentially explore the cognitive DM role in some detail. Each will be considered in the next sub-section.

2.2.4 NDM theme four: Cognition

A recurring NDM theme is the importance of cognition and behaviour, such as shared mental models (SMM), which are knowledge frameworks, or mental representations, common to group members, utilised for organising information, enabling similar understanding of events, guide group interaction, make predictions, and enable decision-making (Cooke *et al*., 2003; Kushniruk, 2001; Stout *et al*., 1999). Additionally, others have indicated that specific characteristics such as planning before a task; proactive communication; providing information in advance, can contribute to the development of effective SMM (Stout *et al*., 1999). To illustrate how previously solved problems and DM experiences were stored in memory Noble (1993) proposed a cognitive model.

Noble's Cognitive Model

During SA, a decision-maker constructs a solution to the issue that is considered reasonable from cognitive comparisons (Noble, 1993). This depicts NDM as being proceduralized; indicating that DM's unequivocally related to action and its circumstantial application (Means *et al*., 1993; Rasmussen, 1983). In clinical settings this is akin to rule-based DM which is used by novices who study and learn from procedures for frequent or risky conditions (Flin, Youngson and Yule, 2007). With time and practice, a shift occurs, with rule(s) being retrieved from memory automatically with little conscious deliberation. At this point DM becomes intuitive, as outlined by the RPD model (Klein, 2008; 1998, 1997), which was covered in section 2.2.1 from page 41.

This shift suggests that expertise consists of decision-makers recognising familiar stimulus cues and learning what influences to attend to, and which data to screen out, via cognition and direct experience (George *et al*.,1996). The implication being those with wider range of skills and experience would have more recognition cues to

fall back on when making workplace decisions. Furthermore, other NDM research indicates that an expert decision maker could deliberately explore problematic cues or situations using Rasmussen's Skill, Rule, Knowledge model, which explains three differing layer of cognitive control that occur during decision-making (Rasmussen, 1993a; 1993b; 1983). This model is presented in the next section.

Skill-Based, Rule-Based, and Knowledge-Based (SRK) Model of Task Performance

The SRK (or decision-ladder) model of task performance is represented by three performance layers (skill-base, rule-base and knowledge-base), that correlate to diminishing acquaintance of task or environment (Rasmussen, 1983). The SRK model is illustrated in figure 2.3 and shows how and where individuals engage with one of the layers, conditional on the decision at hand and their degree of experience with the particular scenario.

At the skill-based layer, stored mental impressions representing pre-programmed instructions located in a space-time domain directs performance. The rule-based layer applies when dealing with familiar scenarios where the DM solution and action is controlled by retained rules (productions) of the variety, if (state), then (diagnosis), or if (state) then (remedial action). The knowledge-based layer comes into play in atypical scenarios where execution needs to be planned utilising conscious stored knowledge and analytical processing. However, as expertise increases, the main control focus shifts from knowledge-based to the skill-based levels; however all three layers may co-exist simultaneously (Rasmussen, 1993a; 1993b; 1983).

Rasmussen's contribution to DM has been to chart the shortcuts that human decision makers take in real-life situations (Reason, 1990). Essentially, instead of straight-line sequencing, the SRK model is comparable with a ladder, where the skill-base (activate and execute stages), allied to the knowledge-base (interpret and evaluate stages), forms the frame. The rule-base stages (observation, identification, goal selection and procedure selection) act as steps in the middle. In SRK cognitive flexibility is crucial, with shortcuts taken between the various standings, typically comprising some type of situational reaction, where observation of system state leads to natural selection of fixing procedures without slow and arduous intervention of knowledge-base processing (Rasmussen, 1993a; 1983; Reason, 1990).

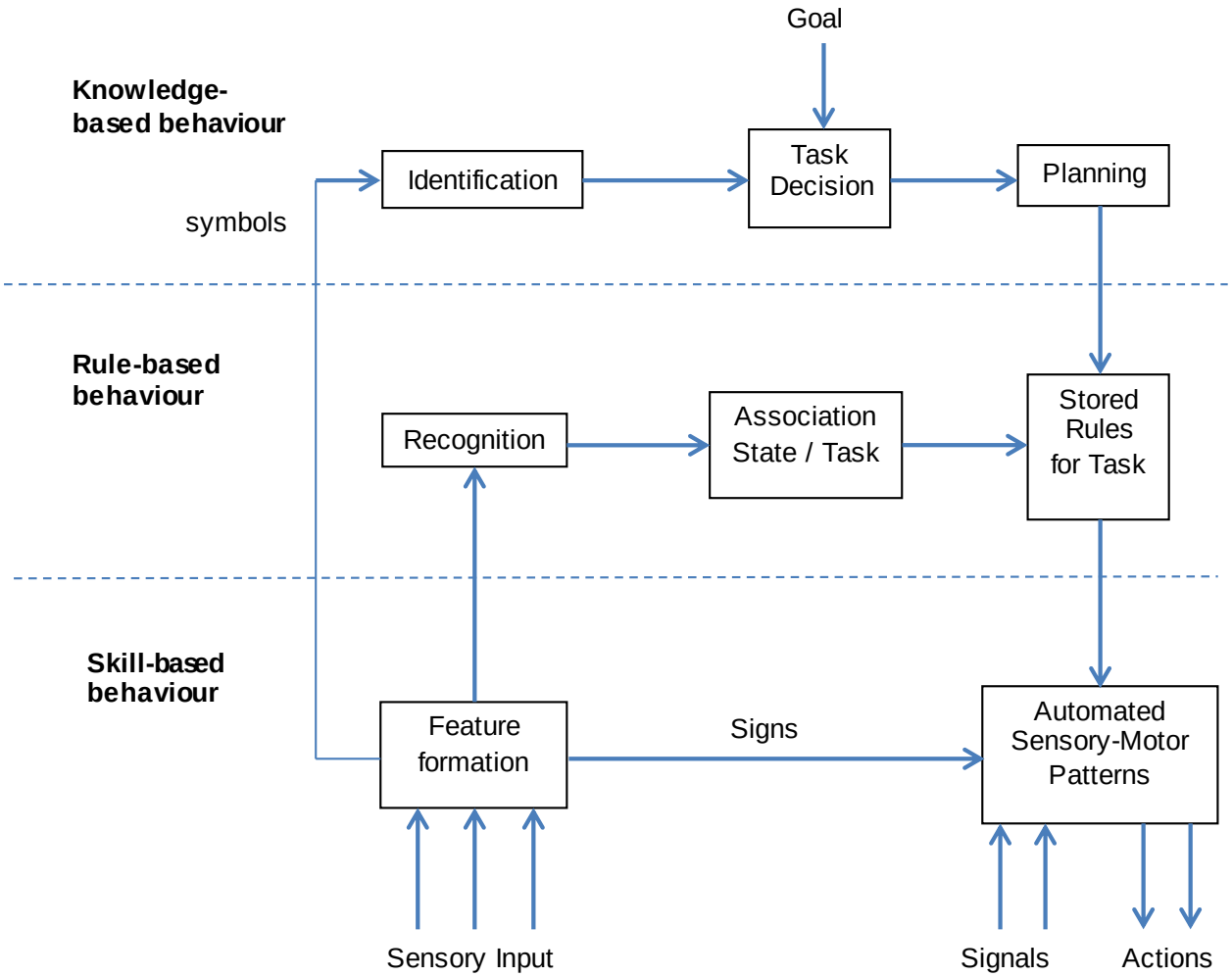

Figure 2.3: Rasmussen's Skill-base, Rule-base, and Knowledge-base (SRK) model of cognitive control (Adapted Goodstein, Anderson and Olsen, 1988).

However, although the standard SRK decision ladder is the benchmark for work or task analysis, it has remained unaltered for many decades, prompting one author to postulate that some NDM aspects are missing, such as not taking full account of the situation awareness models, distinguishing betwixt explicit and implicit mental processing, or the tenets of NDM (Lintern, 2010). However, other researchers have suggested that underestimated task performance factors require consideration, such as the nature of subjectivity or objectivity, uncertainty within DM events in context, or questions on whether a relationship existed between context, organisational factors and cognition, as they can contribute to NDM error (Shaban, 2005; Hammond; 1996, 1993; Hutchins, 1996). These points echo Hammond (1998) who suggested that a level of uncertainty exists in all NDM, arguing that all decisions and judgments are imperfect and erroneous at some level. Others have claimed that decision makers'

experiences are generally contorted by hindsight, and individuals are judicious when bringing forth data and assertions they think is needed, requiring modification of first principles as new intelligence ousts old knowledge (Thompson and Dowding, 2002).

Despite these latter points, the SRK model is of interest for exploration in this study because this model of cognitive control is error-orientated, originating from study of staff engaged in organisational trouble shooting, and so it is primarily aimed at identification and reduction of serious errors made by those in responsible roles (Rasmussen, 1993a). Additionally, the symmetry and completeness of the decision-ladder appears to be a convenient guiding mechanism to potential cognitive states and DM processing; allowing for associative leaps between decision stages; and could be open to upgrade by potentially mapping NDM concepts onto the decision ladder (Lintern, 2010). The idea being that an alternative DM path (actual and/or feasible) could be explored in the main study, where NDM themes guide consideration of a new potential conceptual DM approach.

Although ascertaining whether this SRK approach to decision-making can be applied to physician DM in context will be investigated in the main study, a key feature of the decision-ladder is consideration of decision-error factors (Rasmussen, 1993b). This is the final NDM theme and will be discussed in the next sub-section.

2.2.6 NDM theme five : Decision Error

According to Klein (1998) there are two main categories of decision-error within the naturalistic paradigm. The first one locates error causality as external to the decision-maker by looking at the decision's contextual surroundings. The other positions the error as internal to the decision-maker indicating taking place via cognitive processing. This sub-section explores situational context and the cognitive schools of decision error and highlights NDM features that could help address how decision-error factors can be identified and potentially reduced in the workplace.

Context

Klein (1998) maintained that lack of contextual information has the ability to significantly impact on the decision-maker developing good situation awareness and thereby potentially leading to decision error. However, Woods *et al*. (1994)

suggested that attention is paid to all accessible situational information, company goals, and decision-makers' experiential levels to reduce the prevalence of errors. The work of Orasanu, Martin and Davidson (2001) indicated that four contextual factors (ambiguity; dynamic risk; stress; organisational and social pressure) influenced expert error and they are depicted in table 2.4 together with associated contextual frames and subcomponents. However, there does not appear to be any objective rules or guidance for determining which contextual error factors are applicable in specific environments, nor whether an appropriate screening frame is needed for interpreting a particular chain of events or decision process.

Contextual Error Factors	Contextual Frame	Context subcomponents
Ambiguity	Physical	Stable environment vs Dynamic environment – Specific cues (triggers for expert schema?)
Dynamic risk	Temporal	Time of day Length of day
Organisational & Social pressures	Relational	Relational networks Communication (implicit vs explicit) Morale/Mood
Stress	Emotional	Working memory capacity Stress and anxiety levels Individual personality Emotional trigger

Table 2.4: Areas of contextual expert error, contextual frames and subcomponents for predictive categories for error (adapted from Orasanu, Martin and Davidson, 2001).

Although Orasanu, Martin and Davidson (2001) indicated that the context surrounding NDM is important they also recognised that individual experts could make errors in developing situation awareness or in their selection of an appropriate action. However, what may seem to be an error using one conceptual framework may actually make sense using another frame (Lipshitz, 1997). So, in this research the areas and applicability of contextual error in DM required exploration.

Despite ambiguity, dynamic risk and stress being listed as potential contextual error factors, the researcher is interested primarily in ascertaining and exploring the organisational and social factors that could potentially introduce error into the physician DM process. This is because compliance with ISO14155:2011 is a

mandatory industry requirement, requirements are clear and the industry has a grace period in which to plan compliance activities and execute. However, the organisational and social triggers for decision-error are considered in the next sub-section.

Organisation and social triggers for decision-error

Organisation psychology literature has identified certain organisational factors that potentially adversely affect performance outcomes. Bruggink (1985) found that errors were influenced by policy factors. Others identified triggers for decision errors could be attributable to high level management decisions; communication breakdowns; organisational culture; power or role structures (Buchanan and Huczynski, 1997). Contrastingly, social psychology suggests that social group biases are important considerations in decision-making with Jones and Roelofsma (2000) indicating that group decision errors can be introduced via one of four mechanisms: false consensus, group polarisation, groupthink and commitment escalation in a group.

False consensus is an effect where individuals overemphasize the degree upon which their personal choice and judgment is comparable to others (Ross, Green and House, 1977). This bias affects groups with respect to presumptions made when incomplete data is acquired then used to make decisions. Presumptions can be made regarding group membership; the decision-maker; the situational context; other individuals, departments or groups in the company. However, Fischhoff and Johnson (1997) indicated that false consensus can develop from imprecise or faulty group conceptual modelling of the constructed assumption. Therefore, this bias requires further research within the clinical research environment to ascertain its effect on decision error and whether present or absent.

Groupthink occurs when the group's appetite for consensus overrides the need for identifying the best decision consideration (Janis, 1972).This mode of thinking may lead to inadequate consideration of alternatives, examination of too little goals, or erroneous data searching (Janis and Mann, 1977). Although Groupthink has been criticized as a theory it appears to have been widely accepted and used (McCauley, 1989; Leana, 1985). So, it could be an important factor for potential consideration as an influencing bias within this research.

Polarisation infers a propensity for group decision making that is risky and extremely higher than the average leaning, albeit heading in a similar way (Lamm, 1988). Two forms exist: risky-shift (tendency to choose more risky action course than group norm); and cautious-shift (more cautious action course than group norm). Polarisation takes into account group norms where severe decisions are taken to corroborate the group barometer (Lamm, 1988). However, there appears to be precious few studies carried out within clinical research settings.

Group escalation is a tendency for groups to commit and seek a particular path of action despite objective evidence suggesting it is declining or inadequate (Staw, 1976). Within this bias, issues of poor and/or irrational management, and leadership, are brought into question and indicate a potential valid research area for this study.

Overall, it appears that numerous conditions for decision error exist at a social and organisational level. However, the researcher needs to accurately explore the prevailing attitudes, norms and values within PPDs decision-making culture, and expert group sub-cultures, so that the background, impact and consequences of regulatory DM by physicians is understood within the CRO context. However, Jones and Roelofsma (2000) indicated that mental conceptual triggers, as well as social and organisational influences, could impact decision-making error in groups. Therefore, the next section explores how cognitive decision errors can occur in individual experts and potentially influence the NDM approach.

Cognitive decision errors

Most of the research on human errors in the NDM paradigm was a by-product of root cause analysis of disaster situations from real life environments such as emergency operating rooms, military conflict and nuclear power plants (Lipshitz, 1997). Although this work has attributed expert errors to poor decision-making in three areas: problems with cognitive, interpretative, and/or adaptive/systematic perspectives (Lipshitz, 1993a, 1993b) its applicability in clinical context has still to be researched.

The cognitive perspective

Human experts make many decisions non-analytically, often intuitively (Dreyfus and Dreyfus, 1986; Simon, 1983), and focus on situation assessment as the most critical aspect of decision-making (Klein, 2008; Endsley, 1997; Kampf and Klein, 1994).

However, Endsley's (1997) model (chapter 2, section 2.2) indicates that errors can involve problems with situation awareness rather than the action phase of DM processing. Essentially perception is erroneous but a correct decision was taken based on the decision-maker's situational perception. However, this is a completely different decision error categorisation from where the precise scenario was accurately diagnosed but a poor decision taken regarding optimal execution, requiring different types of remediation strategies.

On the other hand, Klein's (1998) RPD model (chapter 2, section 2.2) indicated that cognitive decision errors could be due to lack of decision-maker experience or poor cognitivel simulation, where decision makers observe problem signals but explain them away. Although Lipshitz, (1997) suggested a probabilistic relationship between decision errors and bad outcomes, other research suggests bad outcomes could be traced to faulty cognitive processes in complex causal chains consisting of i) a bad outcome; ii) an inappropriate action, or substandard performance of an appropriate action; iii) a fault in a single step of the decision-making process (situation awareness, action selection, action planning and/or implementation); iv) breakdown of the cognitive mechanisms that control action; and v) situational factors such as time stress, or a task structure that overloads or misleads the cognitive system (Lipshitz, 1997; Rasmussen, 1993a).

All of this implies that decision errors have different causes and that they can potentially occur at different levels of cognition action control. This would appear to link with Rasmussen's (1983) SRK model (chapter 2, section 2.3). For example, at the rule-based classification level, errors are associated with misclassification such as application of the wrong rule, incorrect activation of action owing to underspecified rules, inaccurate recall of rules and omission of acts that are isolated from well-rehearsed action sequences. At the knowledge-base layer, execution is explicitly controlled via formulated goals and situation analysis, whereas at the skill-based layer, errors are linked to underlying variables of force, time or space distribution (Rasmussen, 1993a; 1993b; 1983). This indicates that error mechanisms are not as well specified as in the two lower action control layers (Lipshitz, 1997; Dorner, 1987). Reason (1990) elaborated on this cognitive perspective by adding situational error classifications to Rasmussen's (1983) SRK model. This included classifying

mistakes as errors in planning; *slips* as errors in execution; and *lapses* as errors in storage. Furthermore, skill-based lapses and slips, plus rule- and knowledge-based blunders were seen as opposites of the *attentional* and *schematic* modes of the cognitive control of effective action (Reason, 1990). This implies that rule-based action is controlled mostly by the schematic mode where mistakes are activated by a readily available, but irrelevant, or inefficient, action (s*trong-but-wrong)* routine. These mistakes are by-products of two heuristics; *similarity matching and frequency gambling,* from vague situations. Although these heuristics appear to be generally effective, they tend to rely on familiar cues and well-tried solutions in situations when risk taking is needed (Reason, 1990).

Knowledge-based mistakes appear to have two explanations: bordered rationality and incomplete information (Reason, 1990). Some authors have indicated a mistake of this type does not have a typical form but is, ad hoc and arbitrary, based on bias and fallacy within expert's deductive and inductive reasoning (Rasmussen, 1993a; 1993b; Reason, 1990). However, others have suggested that deficiencies in the construction and use of mental models that drive decision-making (*buggy knowledge*) could be alternative mechanisms responsible for knowledge-based mistakes (Lipshitz and Ben Shaul, 1997; Cook and Woods, 1994).

To minimise these DM errors Lipshitz, (1997) advocated training on the attentional mode to consciously set goals and to design, implement, monitor and modify action, if required. Additionally, the schematic mode should be used for out-of-attention cases and reference the expert decision-maker's highly specialised knowledge packages or information processing (schemata) (Lipshitz, 1997).

The interpretive perspective

The interpretive perspective suggests that decision errors are introduced via the final analysis, by analysts and researchers. This is conceptual thinking involving tracing effects to causes independently of the measuring method where *what* is observed is inseparable from *how* it is observed (Lipshitz, 1997).

The adaptive/systemic perspective

The adaptive/systemic perspective suggests that tracing back bad outcomes to decision errors of individual decision-makers produces erroneous conclusions (Lipshitz, 1997). For example, where outcomes linked to individually innocuous tendencies (latent error) occur, then bad decisions can lead to lethal outcomes (Lipshitz, 1997) or inappropriate action occurs via suggestions from situational cues (Cook and Woods, 1994). Alternatively, when a change of standards is needed, decision errors can be adaptive and should be made rather than avoided (Lipshitz, 1997). The impact of adaptive/systemic perspective on this study is that improving an individual decision-maker's ability to detect errors should be considered as a design counter-measure, following the work of Cook and Woods (1994) and Rasmussen (1993a; 1993b).

In summing up decision error, it appears that context, organisational factors and cognitive standards appear to be the three main categories for consideration within the naturalistic paradigm. Additionally, it appears that the NDM cognitive standards for identifying decision-errors pertain to situation assessment, mental modeling, sequential option generation and evaluation rather than concurrent choice. However, to fully understand the possibility of DM errors in the clinical research environment, this study requires exploration of the cognitive, organisational and social perspectives to understand how, where and when physicians' decision errors can occur and the influencing contextual factors that could possibly derail a NDM decision-making process for compliance with ISO14155:2011. However, careful construction will be needed, as the use of poor, or inadequate, mental models has led to significant drops in performance and introduced decision errors with fatal outcomes (Rettinger and Hastie, 2001; Lipshitz *et al*., 2001; Passaro, Cole and Wala, 1994).

2.3 CONTEXTUAL DECISION - MAKING OVERVIEW

Medical decision-making in clinical settings involves many different branches of decision theory which has seen researchers explore either classical or behavioural approaches in an attempt to construct a gold standard for the field (Falzar and Garman, 2012; Tonelli, 2011; Reyna, 2008; Patel, Kaufman and Arocha, 2002; Klein,

1997). However, despite much research, no single DM approach has found universal acceptance. This is also true of medical DM in the CRO environment. However, where complex and dynamic systems are involved, such as those within the clinical research environment, establishing an on-going awareness and understanding of the important situational components poses a major task for the decision-maker (Zsambok and Klein, 2014).

This literature review has identified that NDM offers models and potential elements with which to explore the research question within the main study. Although single NDM models have been tested in medical and healthcare activities, ranging from anesthesiology to tobacco control, they are too narrow to address the research question in this thesis (Zsambok and Klein, 2014; Liu *et al*., 2012; Schraagen *et al*., 2008; Gore *et al*., 2006; Bogner, 1997). Individually, NDM models appear to signpost some influences affecting physicians making decisions in non-clinical settings. For example, concepts such as expert group influence, metacognitive processing, organisational and contextual constraints, and proactive error consideration appear in single models but are missing from a collective NDM approach. However, Lintern (2010) suggested a potential way forward via mapping NDM concepts, then framing for context, to provide an alternative insight from a situational awareness perspective linked to a consideration of cognitive processing. This is akin to medical DM dual-processing which attempts to blend evidence-based, cognitive, social and behavioural influences to medical DM. However, key differentiators within this study are physician DM in a non-clinical context, consideration of patient needs but they are absent from decision event, and a new industry compliance requirement.

2.4 CONCEPTUAL RESEARCH FRAMEWORK

In this research a conceptual framework (figure 2.4) is proposed to illustrates how the key NDM themes identified from this literature review (situation awareness, context, decision approach and decision error) flow from the highlighted DM theory and models and potentially intertwine into factors for consideration within the main study. It appears that situational awareness is a naturalistic linchpin for the decision process and can be instrumental in informing DM and is depicted in figure 2.4.

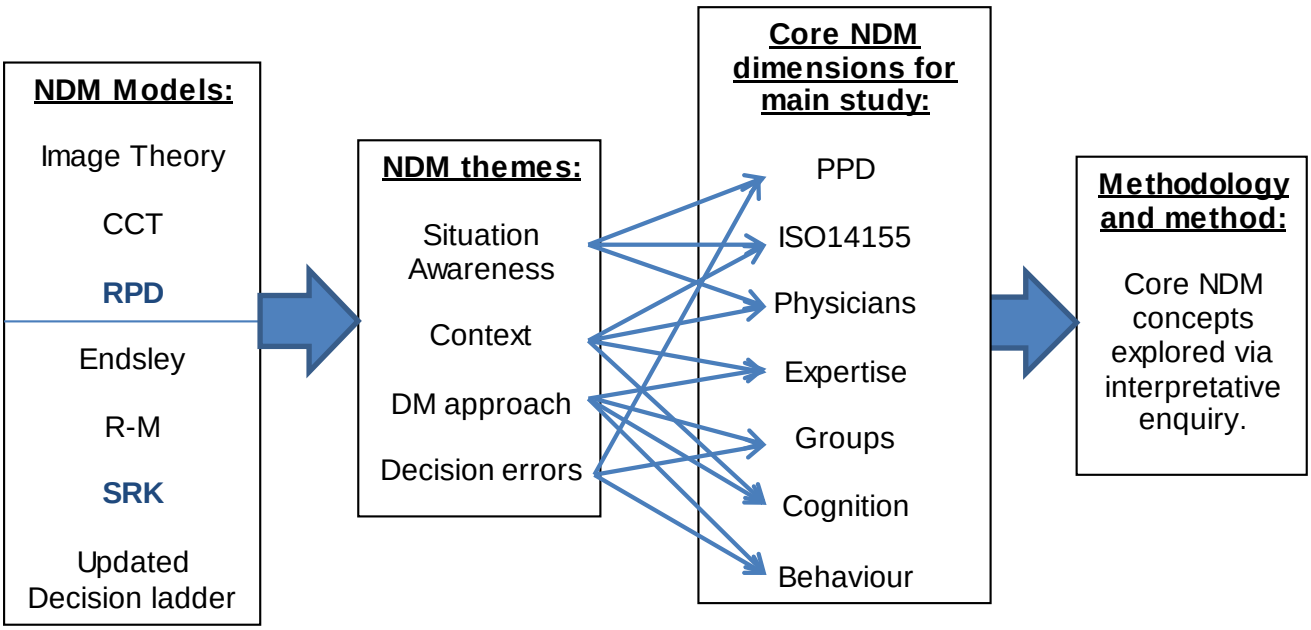

Figure 2.4: Research framework of important NDM themes (developed from this literature review).

However, Klein's (1993) RPD model describes only simple, or routine, activities where actions follow patterns and observations agree with expectations. Other authors have argued that RPD oversimplified the NDM process and required modification to include other influences such as cognitive representations, context, expertise and errors (Lintern, 2010; Klein, 2008, Nutt, 2008; Endsley, 1997; Lipshitz and Ben Shaul, 1997; Beach, 1993; Rasmussen, 1983). Although the integrated RPD model (Klein, 1998) addresses some of these concerns, it does not cover all. For example elements such as team influence, organisational constraints, memory, attentional or metacognitive processes are still missing (Klein, 2008).

Therefore, in this research, the author suggests that Image theory and CCT could link dual-processing and iterative DM fluctuations between intuition and analysis; where elements from the R/M and Endsley models could cover novel situations and more complex cognitive decision-making environments; with the SRK decision ladder potentially providing a baseline for work tasks in the organisational environment. So, this literature review suggests exploring the NDM themes identified from literature review via the research frame depicted in figure 2.4.

2.5 CHAPTER SUMMARY

This chapter introduces, defines and discusses relevant and important DM themes and shows that research into physician DM within clinical encounters have been studied in-depth using various means. However, despite many years of research into this field, there is no single DM theory or approach for use as a generic DM framework to a presenting clinical situation. Following this exploratory review the researcher believes that there is a literature gap, as consideration of expert physician DM in non-clinical regulatory compliance settings is missing. This literature review illustrates how indirectly related DM positions could potentially inform the main study via combining dual processing from Medical DM with specific NDM themes gleaned from academic theory and models. Although integration of ideas from different theories appears to be a relatively new approach within this DM context, it is not academically unique (Adams, Khan and Raeside, 2014:40).

To help answer the research question (chapter 1, section 1.3) four NDM themes appear to offer avenues for consideration in this research. They are decision-making approach, context, situation awareness and decision error. In this research a focus on developing an understanding of these concepts, and the interrelations between the dimensions, will be important considerations when exploring PPD physicians' compliance DM. However, in order to depict how these themes could apply in this environment, a conceptual research frame (figure 2.4) was constructed to guide the main study (Adams, Khan and Raeside, 2014). This frame helps to guide exploration of cognitive, organisational and social perspectives in the main study by highlighting how, where and what factors could potentially influence physician DM processing for ISO14155:2011 compliance.

This literature review has demonstrated that first research goal, exploring DM theory, (chapter 1, section 1.3) was accomplished but the remainder are unfulfilled. The next chapter discusses philosophy, methodology and methods considered for close examination of physician's experience, perceptions and thinking in a non-medical, clinically-orientated setting to ascertain more about DM within this specific domain to aid in answering the research question as well as addressing the remaining research goals.

CHAPTER THREE : RESEARCH PHILOSOPHY & STUDY DESIGN

3.0 INTRODUCTION

This chapter charts how the research aim (chapter 1, section 1.3) was realised using strategy and design. This chapter is organised into sections commencing with explaining the options associated with resolving the research philosophy and design components for this study. It covers ontological, epistemological and axiological positions, explores the choice and use of an interpretive phenomenological approach, qualitative data collection and analysis methods, plus addresses ethics and reflexivity elements. The chapter ends with a consideration of study feasibility with the key study design decisions tabulated and summarised.

3.1 PHILOSOPHICAL OVERVIEW

In academic research, philosophical positioning can relate to the researcher's understanding of the nature of knowledge (epistemology), of reality (ontology), researcher's view of the role of values (axiology), but it can also be the lens viewing the development and nature of knowledge in a particular field, commencing with research background, but also questioning the assumptions influencing research strategy, design and, approach (Saunders, Lewis and Thornhill, 2009). However, although study design is an essential component of academic research, presenting philosophical strategy may take several differing forms depending on the research purpose, its subject matter, allied to the positions and assumptions underpinning the research strategy (Cresswell, 2009; Saunders, Lewis and Thornhill, 2009; Eakin and Mykhalovskiy, 2003).

In this study the initial key elements were to understand the nature of reality given the assumptions, perceptions and beliefs of those involved could influence the research (Moule and Goodwin, 2009). Secondly, it was important that the research approach reflected the nature and aims of the study by connecting back to the research problem, such that research biases were identified, considered and minimised (Holloway and Wheeler, 2010; James and Vinnicombe, 2002). So, design transparency was built into this thesis, by describing the research philosophy using key terms such as ontology, epistemology, axiology and research paradigm,

highlighting methodology and methods chosen, thereby demonstrating the research approach and upholding research integrity (Topping, 2010; Cresswell, 2009; Saunders, Lewis and Thornhill, 2009; Easterby-Smith, Thorpe and Jackson, 2008; Blaikie, 2000). These topics will be discussed in the next section.

3.2 PHILOSOPHICAL CONSIDERATIONS

Although many research philosophies exist, and various mechanisms can be used to refine exploration, management research typically falls to one of four key research philosophies: positivism, interpretivism, realism and pragmatism, which have been developed in both contemporary and classical forms, each one being constructed from a basic ontological position coupled with an associated epistemology to classify different research approaches (Saunders, Lewis and Thornhill, 2009; Denzin and Lincoln, 2003).

Literature examination shows that research can be roughly classified into three groups: (i) quantitatively-orientated researchers working within the post-positivist tradition, where a positivist paradigm supports a fixed reality and that impartial knowledge can only be created via rigorous methodologies, emphasizing experience in general, observation and testing in particular, and primarily interested in numerical analysis; (ii) qualitatively-orientated researchers working within the interpretivist (constructivist) tradition, where knowledge is socially constructed, reality is ultimately subjective and primarily interested in analysis of narrative data with interpretation, based on a skeptical or anthropological relativism, and (iii) mixed methodologists working within other paradigms (for example, the transformative-emancipatory paradigm or pragmatism) and interested in both types of data (Tashakkori and Teddlie, 2010; Saunders, Lewis and Thornhill, 2009; Holloway and Freshwater, 2009; 2007; Barry and Hansen, 2008; Easterby-Smith, Thorpe and Jackson, 2008).

Within the medical field, academic literature is dominated by positivist studies, emphasizing the importance of research theory-building, providing a framework for analysis, facilitating efficient development of the field, which is used and applied to practical, real-world problems (Christ, 2014; Polit and Beck, 2008). However, although this industry is predominantly scientifically based and procedure-driven, where quality equates with proper execution of research methods and techniques, critics continue to

question clinical decision-making and research findings from these studies given the prevalence of patient adverse events (Wacker *et al*., 2013).

Similarly, within the clinical trial arena, study designs require rigour with many sharing similar epistemological and methodological orientations, where the methodologies used are mainly analytical-conceptual, empirical-statistical and case study in nature, paradigms deployed are skewed towards positivism, and simple, single variable statistical analysis methods dominate (Creswell and Plano Clark, 2011; Cresswell, 2009). Although healthcare organisations regularly utilise positivistic methodology and methods, this approach has been questioned in terms of its suitability for contemporary organisations on the grounds that social factors, involving choice, values and preferences, influence the research process to such an extent that it is difficult to achieve objectivity (Bryant and Cox, 2013; Hansen, 2009).

Although the researcher is a positivist by education and professional practice, and despite the clinical research organisation being a suitable environment in which to observe, capture and analyse quantitative, numeric data, positivism was deliberately rejected for this research in order to pursue an alternative, meaning-based philosophical approach centred on the social actors to answer the research question (chapter 1, section 1.3)**.** This follows authors who have argued that paradigmatic stances should not be focused on positivism alone, but be expanded to include approaches such as critical management research, post-modernism, pragmatism and other methodologies (Creswell and Plano Clark, 2011; Plano Clark, 2010; Cresswell, 2009). However, approaches such as critical management theory, post-modernism, anti-positivism and pragmatist approaches have had little impact in this field as questions have been raised as to whether they can reliably inform decision-making (Alvesson and Deetz, 2006; Freeman, Wicks and Parmar, 2004; Milner, Bailey and Deans, 2003; Alvesson and Deetz, 2000; Linstead, 1993).

3.3 RESEARCH PHILOSOPHY CHOSEN

The choice of paradigm used is congruent on the research question posed (Holloway and Wheeler, 2010; Moule and Goodwin, 2009). An interpretive philosophy was deemed the most appropriate for use in helping to answer the research question (chapter 1, section 1.3) for several reasons. Firstly, it enabled the researcher to

explore context and behaviour within the environment in which the social actors were situated, and secondly, understand the nature of language itself given DM is comprehending how words are used and how social actors recognize their use and meaning (Wittgenstein, 2010; Pope and Mays, 2006). Thirdly, in this research the intention and focus was to gain insight into the decision-making perceptions, thoughts and experiences of qualified physicians in a non-medical contextual environment. Joseph *et al*. (2009) suggested a means to do this within medical DM research using qualitative methods such as phenomenology and hermeneutics. Fourthly, the approach chosen allowed investigation of the organisational DM phenomena by utilising description, not by gleaning new information, but by interpreting and arranging what was already known (Shotter, 1990). The rationale for using an interpretive approach, and the impact on the main study design, are described in the next section, utilising the funnelling approach, illustrated in figure 3.1 as the guiding principle (Carter and Little, 2007).

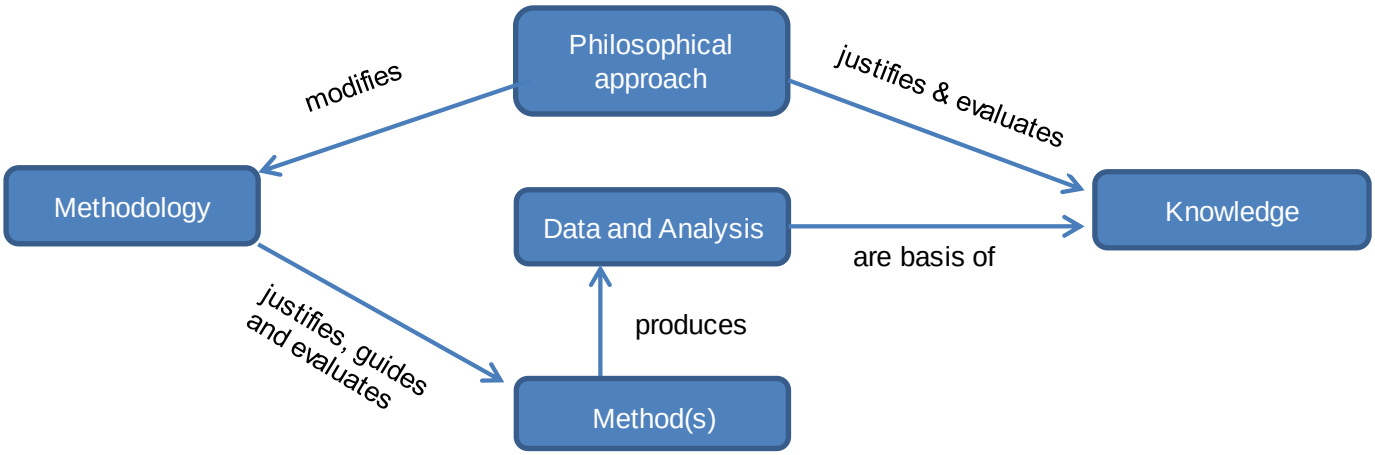

Figure 3.1: The relationship between philosophical approach, methodology, method and knowledge (adapted from Carter and Little, 2007).

This funnelling approach depicts how the key components of interpretive philosophy, methodology and qualitative methods for data gathering and analysis, helping to highlight relationships between them and aiding DM knowledge generation that flows through this thesis. The funnelling approach guides the next section which covers the research philosophy, paradigm and methods deemed most appropriate for this study and justifies those selected.

3.1 Interpretivism

The academic pedigree of interpretivism grew from classical organisational theory and covers notions such as Weber's (1947) *versehen* (to know); the hermeneutic-phenomenological tradition, where human action oscillates constantly between the whole, its constituent parts and back again (Schutz, 1962; Hughes, 1990); and symbolic interactionism, where people develop and rely upon symbolic meaning from social environmental interaction (Blumer, 1962; Hammersley, 1989; Collins, 1994). In this study interpretivism was selected as the research philosophy given its focus on making sense of social situations based on people's beliefs, memories, expectations and values as adequate justification to answer the research question (Easterby-Smith, Thorpe and Jackson, 2008). It has been described as post-positivist (Blaikie, 1993) or anti-positivist (Hatch and Cunliffe, 2006) given the fundamental differences between subject matter in the social and natural sciences. Essentially the interpretivist ontology is subjective and socially constructed, with the epistemology focusing on understanding meaning and the interpretation of the social actor's world from their perspective (Saunders, Lewis and Thornhill, 2009; Easterby-Smith, Thorpe and Jackson, 2008; Eriksson and Kovalainen, 2008). So, as the researcher was seeking to ascertain how physician's think, feel, and use language to communicate their experiences in context, actively choosing subjective research and value-bound axiology enabled the researcher to be internal to the study, not separated from it (Saunders, Lewis and Thornhill, 2009; Easterby-Smith, Thorpe and Jackson, 2008; Eriksson and Kovalainen, 2008).

As interpretivism is highly contextual, but rarely generalizable, it can be used to understand a specific business situation where research uses a small sample then undertakes a detailed evaluation to comprehend the issue affecting the population at large (Kasi, 2009; Saunders, Lewis and Thornhill, 2009). In this social world meaning is constructed, and re-constructed constantly over time, using experience to describe many differing interpretations of social reality where people interact (Saunders, Lewis and Thornhill, 2009). Within this approach the key feature is exploration of the contextual factors and meanings that influence and affect the individual's interpretations (Hatch and Cunliffe, 2006; Denzin and Lincoln, 2003). From an epistemological perspective, interpretivist research proposes that researchers

navigate a social realm of the study subjects by comprehending the world from their perspective including viewing the distinctness of humans within the social actor roles (Saunders, Lewis and Thornhill, 2009).

However, various interpretive approaches exist. Although it is associated with qualitative methods and data approaches, identification of a suitable interpretive paradigm, based on how folks questioned and made sense of the environment about them, was needed for the main study (Eriksson and Kovalainen, 2008).

3.2 Phenomenology

All social science qualitative research paradigms possess shared apprehensions focussed on the compilation and interpretation of meaning, as well as the texture and quality of experience (Willig, 2008). Some authors have described the key branches of qualitative research as phenomenology, discourse analysis, grounded theory and narrative analysis (Smith, Flowers and Larkin, 2009). These concepts appreciate investigation of thought, emotion, meaning and sense-making; respect clarity of epistemology, and look to understand aspects of life perspectives. For example, grounded theory uses structured and specific procedures for analysis such as open coding (Strauss and Corbin, 2008); Discourse analysis is focused on how language can be constructed and alter facets of the world but requires considerable time and experience (Dick, 2004; Phillips and Hardy, 2002); Narrative analysis focuses on stories, provides meaning to facts but does not have sufficiently rigorous means to substantiate the findings (Saunders, Lewis and Thornhill, 2009).

Phenomenology is a philosophical paradigm concerned with how people question, evaluate and interpret the world about them allied to methods by which research sets down pre-conceptions of their comprehension of the explored world (Bryman and Bell, 2007). To this end phenomenology has been described as

> *"a body of knowledge that relates empirical observations of phenomena of each other in a way that is consistent with fundamental theory but is not directly derived from theory"* (Thewlis, 1973: 248)

In this way the investigator concentrates on the actual occurrence alone (intentional analysis) then expresses how the specific experience was compiled (Dowling, 2007; Polkinghorne, 1983).

Contrastingly, phenomenology has also developed as a research method built around nursing and clinical experience, since nurses were not pursuing the standard phenomenological aims given reflexivity was missing (Crotty, 1996). Known as American, or new, phenomenology this method uses a phenomenological reduction process, vital for illustrating the essences of the phenomenon under investigation, but brackets concepts together, rather than the philosophical phenomenological foundation, as a focus for the proposition (Crotty, 1996).

In this research several factors suggest the use of phenomenology in the main study; namely, bringing forth assertions and perceptions of individuals from their own experiences, surfacing deep issues from contextual situations, making voices heard and challenging complacency, structural and normative assumptions (Lester, 1999). Essentially this is the interpretive phenomenology approach that does not try and distinguish betwixt interpretive and descriptive phenomenology, but remains oriented to asking research questions about the nature of the phenomena as a typically human experience (Dowling, 2007; Donalek, 2004; van Manen, 1990). This is based on personal knowledge, industry experience and an organisational subjectivity paradigm, with an emphasis on understanding and exploring the personal perspective and interpretation, to gain insight into decision-maker's motivations, tasks and actions via study of organisational assumptions, experience and conventional wisdom (Lester, 1999). Thus phenomenology is the epistemological approach selected for use in this study.

This approach is being taken for several reasons: firstly, because the researcher wants to utilise a social science paradigm within a domain of the natural sciences (i.e. humans in their workplaces). However, this reasoning is not accepted by positivism's supporters and users (Bryman and Bell, 2007). Secondly, although comprehending an alternative viewpoint is limited, interpretative phenomenology proposes the means to augment naturalistic comprehensions of health, expertise and reality, by bringing forth individuals' assertions of the researched phenomenon (Langridge, 2007). In essence this approach enables experiences to be expressed

and enables a more rounded view of the individual's relationship with their world, thereby resulting in better experiential understanding (Carel, 2008; Brajtman, 2005). Thirdly, the researcher's interest is in individually socially constructed knowledge from professional practice where understanding the phenomenological experiences of individuals connects the physicians to the practitioner research and frames the subject (Fox, Martin and Green, 2007). So, in this study the interpretive phenomenological approach attempts to explore in detail the specific DM phenomena identified from the literature review ascertaining the actors lived experience perspectives within the clinical research legislative context.

3.4 RESEARCH DESIGN

3.4.1 Methodology

Methodology is the design process for carrying out research and in this thesis it is specifically defined as

> *"how research should be undertaken, including the theoretical and philosophical assumptions upon which research is based and the implications of these for the method or methods adopted"*
>
> (Saunders, Lewis and Thornhill, 2009: 595)

In this study the ontological approach is subjectivism meaning that social entities are thought to be social compilations constructed from perceptions, assertions and descriptions of the social actors allied to their subsequent actions (Saunders, Lewis and Thornhill, 2009). This approach is part of the constructionist, or constructivist, paradigm, which views social phenomena as social actors' creations (Bryman and Bell, 2007). As constructionism contends that a social phenomenon and its meaning is continuously achieved from contextual experience as it is lived, felt and undergone by the physicians, Remenyi et al. (1998) stressed a need to investigate

> "*the details of the situation to understand the reality or perhaps a reality working behind them*". (Remenyi *et al*., 1998)

This position follows Schwandt (1994:125) who argued that a constructivist view of the world is formed by users and using the word, but that there is no generically

accepted perspective on this paradigm. However, certain characteristics appear fundamental (Guba and Lincoln, 1994; Schwandt, 1994; Weick, 1995).

In the first instance, realities are *specific* and *local* from the perspective that they may alter betwixt individuals and groups in the same environment (Guba and Lincoln, 1994:110). Secondly, *constructions,* are ontological reality elements, not exactly correct or true, only less or more sophisticated and informed (Schwandt, 1994:129). Assuming constructions are valid some will be poor however, given inconsistently or simplistically constructed. So, construction deformity depends on which social paradigm the constructivist operates in. Thirdly, the facts of existence are firmly built, not simply exposed. Therefore, epistemological and ontological division is obscured given all that establishes the real world relies on the individual and their beliefs and feelings (Guba and Lincoln, 1994). Within this scenario an unbiased, valueless individual fails to live. Fourthly, although reality is built *socially* the conceptions are not technical or personal (Dahlbom, 1992:101). However, thinking and perceiving is individualistic, and so conceptualising incorporates additional behavioural, cultural and societal influences thereby becoming social.

These points illustrate that constructivism is aligned with interpretivism epistemologically with exploration of subjective meaning being necessary and desirable but motivational to social actors' activities but also enabling the researcher to comprehend the individual deeds (Saunders, Lewis and Thornhill, 2009). However, in order to reflect the distinctiveness of physicians in the PPD social world a methodology was needed that could connect descriptive and interpretive approaches but make visible the meaning structures joining paths to knowledge with practical approaches (Dowling, 2007). One such mechanism that accounts for an individual's personal experience, pre-understanding and assumptions, while recognising that it is all inherently tangled in their interpretation of the phenomenon, is van Manen's methodology (van Manen, 1997; 1990). This methodology is located in the Dutch school combining interpretive with descriptive phenomenology, via acknowledgement of the phenomena in its entirety and including the investigator's role within the research process too. It achieves this by combining Husserl's descriptive phenomenology and emphasizing researching the real-world prior to any reflection (Dowling, 2007; Cohen and Omery, 1994). Additionally a scientific

argument has been proposed via asserting that phenomena and experience are one-and-the-same thing but involves interpretation (van Manen, 1997, 1990). Van Manen's methodology has been used in medical practitioner studies as it provides a framework for conducting investigation and analysing the data built on four existential procedural activities (Mak and Elwyn, 2003). They are:

- Exploring seriously interesting phenomenon that commits to the social world
- Investigating lived experience, not just conceptualised
- Reflecting on essential themes characterising the phenomenon
- Description of phenomenon via writing and revision (van Manen, 1997)

However, in order to execute van Manen's (1997) methodology within PPD a means to explore the physician's DM phenomenon in a systematic manner was needed (Dadds, 2006). The means covers study design, sampling, methods and ethics and each will be covered in the next section.

3.4.2 Study design

In this study the empirical research involves a single case study within PPD's vigilance department exploring how DM concepts can influence regulatory compliance using an interpretative paradigm with qualitative methods that rely on face-to-face interaction with several key departmental contacts (Yin, 2009). The justification for this approach comes from Lewis, Glenton and Oxman (2009) and Thomas *et al*. (2004) who reported that qualitative research in healthcare is becoming increasingly advocated, respected and used. Lawton *et al.* (2012) and Cheung and Hocking (2004) indicated that qualitative studies allow researchers to explore specific issues from the perspectives of the individuals directly involved. Lawton *et al.* (2012; 2011) and Sayre (2000) suggested that qualitative research methods are suitable for investigation of meanings, perceptions, interpretations, social and cultural norms that impact health-related behaviour, medical practice and health outcomes because of their potential to inform by drawing on health professionals experiences, understandings and viewpoints. Additionally, phenomenology methods are a satisfactory means for investigating lived-in experiences to enable comprehension of individual's perceptions of living and working real-world environments allied to ascertaining the essence and implications for them (Langridge, 2007). However, despite these justifications, Lewis, Glenton

and Oxman (2009) have indicated that qualitative studies focusing on the dynamics of clinical trial delivery are limited. Therefore, to execute the phenomenological paradigm suitable sampling, ethics, and methods for gathering and analyzing data were needed linked to the research question in chapter 1, section 1.3. These elements are discussed in the following pages.

3.4.3 Sampling

Two major sampling approaches have been linked to qualitative research: purposive and theoretical. Theoretical sampling relates to the selection of individuals to a sample based on the contribution they can make to a developing theory. This has strong associations with grounded theory and involves an iterative approach between data collection, sample selection and analysis. Contrastingly, other researchers use a purposive sample deliberately choosing informants to be involved in studies that expose salient features or categories pertinent to their research question because of the key qualities possessed by the individual (Lewis and Sheppard, 2006; Ritchie and Lewis, 2003; Bernard, 2002). In this research study purposive (non-probability) sampling was selected and used, not to create a randomly selected group, but to identify

> "*people who either possess characteristics or live in circumstances relevant to the social phenomenon being studied.*" (Pope and Mays, 2006:12)

This decision was strategic and unavoidable because the researcher was seeking to develop a socially constructed insight into the topic but constrained by subject specificity, time, small number of key physician informants and the expert nature of this qualitative research (Adams, Khan and Raeside, 2014; Lewis and Sheppard, 2006; Bernard, 2002). For this study sample size was determined by three constraints; time, relevance and feasibility (Adams, Khan and Raeside, 2014). Inclusion criteria were that the physicians selected were full time members of PPD staff, medical degree qualified, possessing a minimum of 5 years clinical practice and 3 years direct experience of successfully conducting medical device clinical trials from study start-up through to closure. Other recommendations adopted included that the data be gathered from native English-language speaking respondents, who were accessible, could be easily persuaded to participate, were available and who

appeared to be pleasant, normal, subject matter experts (Davies, 2007). In this thesis the researcher used prior knowledge to explicitly select and approach eighteen physicians within the organisation based on an expectation that their knowledge, experiences, geographical location, situation and position would help in the exploration of the research question (Davies, 2007). The demographics of the purposeful sample are illustrated in Appendix A. All other PPD staff were excluded.

The study participants appeared to share some purposive characteristics described by Ritchie and Lewis (2003) namely *homogenous samples* - company physicians working in the same field; *heterogeneous samples* - various physician roles working in the environment; *typical case samples* - experienced staff working in the same field and *critical case samples* – experienced practitioners and conveniently available to the researcher. However, although the researcher identified and targeted individuals to participate in the research, who were believed to be 'typical' of the expert population being studied, there was, however, no way of knowing to what extent the sample chosen is indeed representative of the whole, or what the so-called 'typical' qualities actually are (Ritchie and Lewis, 2003).

Nevertheless, Aveyard (2007) suggested that a small number of subject matter expert participants can provide information-rich data that is more important than a larger sample from which the data would not be so enlightening. As all 18 PPD physicians approached accepted their invitation to be a research participant and, given the wealth, breadth and depth of data gathered (chapter 4), no extra interviewees were deemed necessary. Additionally some authors indicated that qualitative research sampling could be linked with specific methods such as interviews and focus groups (Ritchie and Lewis, 2003) which are discussed in the section 3.4.4.

3.4.4 Methods

Methods are the techniques, instruments and procedures utilized for obtaining and analysing data (Franklin, 2012; Saunders, Lewis and Thornhill, 2009). According to Langridge (2007) phenomenological methods are suitable for exploration of lived-in experience and providing comprehension of individual's world perceptions by bringing forth the value and what that means to them. In this study, as the research

question (chapter 1, section 1.3) attempts to ascertain how physicians make regulatory compliance decisions in a clinical research context, execution of the research framework (chapter 2, figure 2.4) was by selection of mini focus groups (MFG) and semi-structured interviews (SSI) to gather the data. The justification for choosing these methods follows Brajtman (2005), who referenced van Manen's (1990) qualitative research, which used a phenomenological approach involving focus group and individual interviews in the main study.

Mini Focus groups

The initial empirical data collection was by mini focus group. MFG is a form of group interview where dialogue occurs between less than four invited research participants with common experience (Davies, 2007). The value of MFG is the interactive element of the approach to explore and map reasons for attitudes and behaviour, understanding how the target audience approaches the issue by enabling participants to bounce ideas off one another. It is also useful as a data collection method since the ideas expressed by one participant may trigger a response in another informant (Krueger and Casey, 2000). Additionally, these sessions can also enable participant's reactions to be monitored, and so lead the researcher to probe interesting issues when necessary (Bryman and Bell, 2007). Contrastingly, the use of MFGs initially did not appear to belong with phenomenological research principles that explore an individualistic experience (Webb and Kevern, 2000). However, Spiegelberg (1982) outlined a procedure for cooperative, or group, phenomenology and some authors have used group interviews in their phenomenological studies such as Brajtman (2005), Hassouneh-Phillips (2003) and Benner (1985). This indicated that group interviewing can be utilised in phenomenological research if considered to be suitable (Racher, 2003).

So, for this study, two MFGs were formed, each comprising three subject matter physician experts per group, who are responsible for PPD vigilance decision-making. All group participants were invited to participate in a one hour scheduled session in a neutral and local PPD office for the extraction of their views and perspectives. Advance notice period varied from two weeks to one month. All invited physicians accepted their invitations. The researcher facilitated all interview sessions.

The primary purpose of the MFG was to gather a breadth of opinion on PPD regulatory compliance DM by eliciting a wide variety of views and stimulate debate. This approach follows Davies (2007) who advised care when executing MFG to ensure all shades of opinion get aired with the venue being comfortable and convenient.

In order to help answer the research question (chapter 1, section 1.3) a list of study questions (Appendix E) was compiled by expanding the four decision-making concepts identified from literature review (chapter 2) and using how, where and when type questions (Kvale, 1996). The constructed questionnaire (Appendix F) shaped each session, but not too intrusively, given the accent was on interaction within the group, joint construction of meaning where the individuals debated and challenged each other in relation to what they deem to be important and significant (Bryman and Bell, 2007, Kvale, 1996). The questionnaire acted as both prompt sheet and probing technique for the invited physicians facing regulatory change in their practice (Gummesson, 2000; Krueger and Casey, 2000; Kvale, 1996). The questions were open-ended, scripted to stimulate exploration, assertions and descriptive perceptions from the physicians (Merriam, 2009; Kvale, 1996). Each interview session discussed how the participants viewed and perceived PPD DM issues and to ascertain their thoughts and assertions around what influences and constitutes regulatory compliance. However, being semi-structured the researcher had flexibility to explore areas of interest brought up by the participant, whilst having at the back of their mind the overall research purpose and topics from the schedule, and the need to guide the conversation to relate to them. At best this method could lead to advancement of theoretical understanding of the social reality but more routinely it allows first person perspectives of the staff on the focus of the research subject (Gummesson, 2000).

The first MFG (Raleigh, June 2013) comprising US-based physicians, formed the initial exploratory phase and acted as a MFG pilot study to test the selected DM approach and demonstrate competent research due diligence. The session produced a wealth of relevant data and indicated that the group responded well to the questions posed and that the format and structure of the MFG was sound. However, after this MFG session the questionnaire (Appendix F) was updated with

supplementary questions on decision error given the in-depth focus on this topic. The second MFG took place in Cambridge, July 2013, with UK-based physicians. Although each MFG comprised a differing set of PPD physician staff, each selected informant performed similar organisational roles, with comparable ranges of industry experience and company tenure. Each group session was conducted prior to the semi-structured interviews.

Semi-structured interviews

The other form of empirical data collection was by semi-structured interview with individual PPD physicians. Semi-structured interviews were directed towards twelve individual PPD physicians strategically selected for their beliefs, opinions, attitudes, social position in the company, time in post and industry knowledge and experiences Merriam (2009). Each one hour interview was scheduled within the interviewees' office. The aim was to elicit specific discussion on the informant's insight and experience of regulatory decision making within safety vigilance and generate rich data through one-to-one dialogue (Kim, 2011). Two SSI sessions took place in July 2013 – one in Cambridge, UK and the other in Raleigh, US and essentially acted as a pilot for this method. The semi-formal questionnaire (Appendix F) again acted as the interview schedule. The outcome was such a breadth and depth of physician response on DM and regulatory compliance influences that, like the MFG findings, all material was retained for inclusion in the main study. The remaining ten other SSI sessions were scheduled and executed through the rest of the year. The physicians interviewed via SSI did not participate in the MFG sessions.

3.4.5 Ethics

Clinical research physicians work under a plethora of compliance legislation, regulation and professional practice codes such as the European Clinical Trials Directive 2001/20/EC, Declaration of Helsinki, Council for International Organizations of Medical Sciences (CIOMS) guidance, European Data Protection Directive 95/46/EC, TRREE program, and World Health Organization (WHO) guidelines for human subjects' research (World Medical Association, 2014; ACRO, 2012; Smith, 2012; Bowling and Ebrahim, 2005; de Roy, 2004). So, given the CRO industry setting, the company and academic governance requirements, research ethics

conditions were incorporated into the study design. Therefore, this research study is bound by the Edinburgh Napier University code of practice on research ethics and governance and PPD's corporate compliance program. This study design was reviewed, and approved, by the Edinburgh Napier University Business School Research Ethics and Governance Committee on the 10th January 2012 and assigned the internal reference number ENBS/2011-12/002.

By anticipating and considering potential ethical problems during the specific stages of the research design, factors were identified, addressed via research design and conduct of the research process, thereby building integrity within this study (Saunders, Lewis and Thornhill, 2009). Table 3.1 illustrates the main study design stages and depicts where ethical issues were present (topic identification, research design, data collection, data analysis and reporting) and the means used to protect both participants and the researcher. For example, a participant information sheet and informed consent form was provided to each participant in advance of data collection to digest and reduce potential coercion. All potential interviewees were asked if they wished to be research study participants. Those who wished to participate completed and signed an individual copy of the informed consent form prior to start of MFG or SSI. Data was only collected from participants who followed this process (Adams, Khan and Raeside, 2014; Saunders, Lewis and Thornhill, 2009).

As this decision-making research involved serving company physicians, it was necessary to consider the ethical implications of protecting the anonymity of the participant interviewees, so that enough relevant background information could be gleaned whilst protecting staff identities (Yin, 2009; Carroll and Johnson, 1992). Additionally, by guaranteeing anonymity, a deeper relationship could be cultivated with all participants thereby uncovering potentially more valuable and sensitive data than if the subjects were readily identifiable (Carroll and Johnson, 1992). Therefore in order to address general ethics issues such as the voluntary aspect of study involvement, informed consent, confidentiality of data provided, privacy, avoidance of harm and identification of potential risks, the potential for ethical problems arising in this research was identified early the study and built into the design from the outset (Saunders, Lewis and Thornhill, 2009; Yin, 2009). These are shown in table 3.1.

Research Stage / Ethical issues	Researcher	Sponsor	Participant	How addressed?
Topic identification	Absence of Coersion	Useful research Quality research	Subject matter expert	Independent Case study PPD approval
Design	Coersion absence Right to safety	Quality research	Fully informed Privacy	ENU ethics approval PPD staff access Create study info sheet Create IC form
Data Collection	Coersion absence	Quality research	Informed consent Right to withdraw Deception Confidentiality	PPD staff access Study info sheet IC form Qualitative methods
Data Analysis & Reporting	Coersion absence Non-disclosure	Confidentiality Quality research Non-disclosure	Individual rights Personal data Confidentiality Anonymity	Contextual data Purposive sampling Code respondents Embargo DBA thesis

Table 3.1: identification of stage specific ethical issues and means to address (adapted from Saunders, Lewis and Thornhill, 2009).

Furthermore, given the research locus is a biopharmaceutical research organisation where physician's personal information, clinically sensitive data and valuable organisational knowledge will be studied, it potentially could throw up issues that the company would rather be kept out of the public domain (Bryman and Bell, 2007). So, to safeguard all parties this DBA thesis will be subject to a one year embargo.

3.4.6 Data collection procedure

There are many ways in which the collected qualitative data can be collected such as observation, descriptive written field notes and use of technology such as laptop computers, audio recorders and digital cameras (Merriam, 2009). However, in this

study primary data was audio-recorded by the researcher using a portable Olympus hand held, battery operated digital recorder, from each interviewee session. The use of this device was noted in both the participant information sheet and the informed consent form. The main study research took place between June & December 2013 in four PPD locations (Bellshill & Cambridge, UK; Morrisville & Wilmington, US).

All recorded sessions were transferred onto a laptop computer, given a unique name and number for identification purposes, then stored electronically on the researcher's computer and backed-up regularly. Each recorded session was subsequently transcribed verbatim by the researcher for accuracy and consistency of approach (Merriam, 2009). An example of one physician's (Cairngorm) interview transcript has been included in Appendix B. A back up copy of each electronic file and transcript was stored on the PPD company network.

To protect subject identities, ensure confidentiality and anonymity, each transcript was assigned a pseudonym drawn from the names of Scottish mountain ranges comprising Cairngorm, Campsie, Cuillin, Galloway, Grampian, Lammermuir, Lowther, Moffat, Moorfoot, Munro, Ochil, Pentland, Sidlaw and Torridon. The Sidlaw and Torridon pseudonyms were applied to the MFG sessions. The pseudonyms and demographic profile of each physician interviewed as part of the purposive sample are illustrated in Appendix A.

Some researchers advocate that interview transcripts are returned and reviewed by interviewees in order to check for errors, inconsistencies and validate the participants' transcript's content for accuracy (Hagens, Dobrow and Chafe, 2009). However, Barbour (2001) argued that this was time consuming and an unnecessary burden on the informants, who may not remember the interview or may not wish to revisit the content of the interview. Therefore, in this study, no transcripts were returned to the informants as the researcher did not want to alter the content of the interview data and thereby affect its validity (Aveyard, 2007).

3.4.7 Data analysis

In this study all material gathered during small sample interviewing was used in analysis and write-up, as suggested by Davies (2001:155), who indicated that there

are no strict data collection boundaries in this context. Additionally, data analysis followed Merriam (2009) who advocated a preliminary review of data during the collection process rather than commencing the activity once all data had been gathered. At the initial stage, the researcher began an in-depth data analysis via identifying segments of the data that could help answer the research question. This involved identifying text portions, ranging from a few words to several informants' sentences but, irrespective of portion size selected, the individual portions had to stand alone with only supporting context supplied as well as being relevant for the research. These portions were referenced as categories (Lincoln and Guba, 2000).

When determining which conceptual categories were present in the interview documents the researcher read all transcripts and wrote down questions, comments and notes pertaining to data gathered during the study. This data analysis processing stage was assigned the phrase '*open coding'* since the interviewer was amenable to all potential positions worth exploring (Strauss and Corbin, 2008). Detailed data analysis occurred via Thematic Analysis of the transcripts which attempted to make sense of the codes, categories and themes to find and describe patterns across the collected qualitative data (Braun, 2006).

According to Ritchie, Spencer and O'Connor (2003), Framework Analysis (FA) is an extremely useful and pragmatic approach for considering practice related questions and providing an intuitive, but structured, means of organizing qualitative data. It has been utilised within healthcare settings covering nursing (Swallow *et al*., 2011), psychology of health (Tierney *et al*., 2011), and midwifery (Furber, 2010), providing clear results and suggestions which may be traced backwards to source data (Johnson et al., 2011).

In this study FA was divided into five stages: familiarization with data (via thorough immersion in collected material and reading each transcript three times); identifying thematic segments (via key issue identification by open coding) from each physician transcript (see Appendix B); transposing the physician data (via key issue labelling emerging over data set - see Appendix C) ; constructing sets of themed charts (by exploring and reviewing full pattern across the full physicians data set) (see Appendix D); then attempting to map and interpret data (by seeking links, conceptualizing and forming explanations, spotlighting key ideas and characteristics)

(see Chapters 4 and 5). This follows the guidance provided by Ward *et al*., 2013; Smith and Firth, 2011; Ritchie, Spencer and O'Connor, 2003.

The results were preliminary analysed using open coding of themes and presented as narrative categories (chapter 4). Detailed framework analysis and subsequent interpretation of the data gathered from each physician transcript (see Appendices B, C & D) generated an understanding and insight into physician perspectives of organisational and regulatory compliance context and enabled the researcher to ponder links to/from the DM themes (chapter 5) identified from the deductive literature review (chapter 2). For example, following three reads of the physician transcript (Appendix B), key segments were identified and highlighted in yellow. Appendix C illustrates the Cairngorm coding framework where each in-vivo physician segment is given a key issue description, transcript code and thesis reference. In this data eight key issues were identified within the decision making core concept (highlighted within red lines). They comprised both intuition and a reasoned approach to DM allied to process and procedure. Seeking a second opinion and use of reflection occurred occasionally but decision tools were not used and emotion rarely affected decision making in this context. Furthermore the key issue information (highlighted in green text) from this informant was subsequently transposed into the big picture coding frame summary (Appendix D).

Chapter 4 presents a breakdown of the framework analysis core concept results and overall findings via narrative discussion and tabulated presentations (Chapter 4; tables 4.1, 4.2, 4.3, 4.4 and 4.5). Each of the four core concepts is presented in turn using narrative text as a guide and verbatim quotes to demonstrate and reinforce the most representative categories of physician perspective (Lincoln and Guba, 2000). Each quotation is highlighted in italic text with inverted commas, together with pseudonym and numerical postscript referring to the original page from the respondent's transcript from where the quotation was recorded (see Appendices B and C). Each core concept is sub-divided into dimensions and key issues. A tabulated summary concludes each chapter sub-section highlighting links between dimensions and key issues presented (Chapter 4, tables 4.2, 4.3, 4.4 and 4.5).

This approach follows inductive reasoning principles, advocated for healthcare studies, given data analysis purpose is to assure data gathering is focused, not

repetitive, with investigators feeling confident that sufficient data has been collected to solve the research question (Bradley, Curry, and Devers, 2007; Lincoln and Guba, 2000). Use of FA enabled the researcher to undertake an inductive process of themes arising in the data, based on anticipated and unexpected categorisation, as well as separating physician perspectives into similarities and differences between sources. In addition, it enabled the researcher to write-up the findings in stages, using categories and themes to describe results, focus areas, as well as the broader body of analysis (Saunders, Lewis and Thornhill, 2009; Strauss and Corbin, 2008).

3.5 STUDY FEASIBILITY

Qualitative research design has been criticized on several levels and as such this study has the same potential limitations. Namely investigator's personal values and attitudes could influence the findings (Polit and Hungler, 1999); qualitative research is not academically rigorous (Horsburgh, 2003) and that the diverse character of qualitative studies marks the approach as challenging to appraise (Aveyard, 2007). To counteract these points, and address the limitations, a hybrid design was developed comprising elements drawn from different disciplines (Kvale, 1996). This incorporated a robust philosophical and ethical approach and addressing researcher bias through reflexivity (Cohen and Crabtree, 2008; Nutt, 2002); solid study design focused on investigation, checking, questioning (Kvale, 1996); re-evaluating the quality of the research process iteratively (Morse *et al.,* 2002); immersing the researcher in the empirical research (Lincoln and Guba, 1985); constructing specific contextual frameworks (Horsburgh, 2003) and keeping an accurate quality record of the research study process to build in credibility (Aveyard, 2007).

Methodological and ethics concerns were specifically addressed earlier in this chapter. Although a purposive sampling process was followed, giving a detailed understanding of the DM subject, enabling conceptual ideas to be empirically investigated, to develop explanations and generate ideas, it was still accidental as it offered no improvement on convenience sampling and did not estimate the prevalence of the phenomenon (Davies, 2007). The qualitative research methods (SSI and MFG) selected provide great flexibility and a repeatable means to seek out views of the research participants, but limitations can include variability in terms of

output, types of questions posed, interviewer technique and experience, balance and bias, ethical sensitivity, sampling, quality of data recording and transcription (Bryman and Bell, 2007). However, use of these methods enabled the researcher to use purposive sampling to identify and interview physicians known to hold different views from their own and gather a breadth and depth of data unprecedented in this subject.

A further limitation is that the researcher is involved in, and indeed shapes, both the data collection and analysis process, and so it will not be possible for the researcher to remain detached from the collected data. However, Aveyard (2007) indicated that it was not necessary, or desirable, for detachment as the richness of qualitative enquiry arises from researcher and researched dialogue, and the insights obtained are only possible because of the interaction between the two.

3.6 CHAPTER SUMMARY

In this study an interpretative phenomenological paradigm was deployed to ascertain and understand how PPD safety physicians make sense of the regulatory changes being applied to their industry and make organisational compliance decisions based on their roles, experience, cues and sources of information available. The research strategy was designed to enable an inductive approach to be taken where the principal orientation was to iteratively gather data empirically from the social actors.

Element	**Comment**
Research Philosophy • Ontology • Epistemology • Axiology	Interpretivism • Subjective. Socially constructed. • Phenomenology. Focus on social actor's view. • Value bound. Researcher internal to study.
Research Paradigm	Interpretive phenomenological approach where individual makes sense of, and constructs, own world reality.
Methodology	Van Manen methodology. Practitioner research.
Methods	Qualitative methods. Ethics approved. Informed consent. Purposive sample. Pilot study. Main study. MFG. SSI.
Data Collection	PPD locations. Data are words. Digital recording. Researcher transcription
Data Analysis	Preliminary read through. Open coding. Thematic framework analysis.

Table 3.2: Table highlighting the key elements of philosophy and research design within this study

Literature review provided the vehicle to explore the context by drawing on decision theory focused on CDM and NDM. The key elements of philosophy, methodology and method applicable within this research study are illustrated in table 3.2.

Empirical research occurred via a descriptive, interpretive study involving a single, participative, case study of regulatory compliance decision-making within PPD where a purposive sample of physicians acted as the unit of analysis. The research vehicle used a phenomenological approach using van Manen's methodology to explore and describe how and what influences regulatory decision-making within PPD's vigilance department especially for compliance with ISO14155:2011.

Qualitative methods were used in an ethically designed case study to collect data. This involved obtaining informed consent from all participants prior to mini-focus group sessions and semi-structured interviews. A semi-formal questionnaire was constructed from the DM literature themes identified, and was used by the researcher as a probing technique for the selected PPD physicians facing regulatory change in their practice. Each physician was invited to answer the same set of interview questions (Appendix F) with supplementary questions being asked in order to clarify meaning and expand on points discussed. Although time consuming, all data was digitally recorded and transcribed verbatim by the interviewer for accuracy and consistency. Analysis of the gathered data was conducted via preliminary reading of the transcripts, open coding of data categories, followed by detailed thematic analysis using framework analysis. This approach enabled structuring of the data and iterative refinement of the key verbatim categories by condensing meaning within tables.

The use of these methods produced a wealth of regulatory compliance and decision-making related data from the physician's assertions (chapter 4). Although not unexpected, this was a surprising outcome indicating a high correlation between the research design and contextual questions asked and themes under investigation. It also indicated that two underlying features were present in this study, namely physician DM in context and ISO14155:2011 compliance decision-making requirements. A review of the empirical findings follows in the next chapter.

CHAPTER FOUR : RESEARCH FINDINGS

4.0 INTRODUCTION

This chapter demonstrates the execution phase of the research framework (chapter 2, figure 2.4) by presenting the physicians' responses, stratified by open coding and framework analysis of the four core concepts (decision-making approach, error, ISO14155:2011 compliance and situation awareness) identified via literature review (chapter 2, sections 2.4 and 2.5). The chapter commences with a tabulated overview of findings (table 4.1). Each core concept is presented in turn using narrative text as a guide and verbatim quotes to demonstrate and reinforce the most representative categories of physician perspective (Lincoln and Guba, 2000). Each quotation is highlighted in italic text plus pseudonym and numerical postscript referring to the original transcript page from where the quotation was recorded. Each core concept is sub-divided into dimensions and key issues. A tabulated summary concludes each chapter sub-section highlighting links between dimensions and key issues presented. A summary of the preliminary findings concludes this chapter with detailed analysis and interpretation of the research findings presented in chapter 5.

Core concept	Dimension	Key issues
Decision-making	At PPD Physician approaches Physician influences Types and tools	No formal model; C-suite versus department; Physician involvement. Instinct; intuition; reasoned thought; hybrid method(s) & skillset(s). Individual versus Group DM; Emotion; Reflection. Criticism. Strategic, tactical, transactional Some versus none.
Decision error	Correction Effectiveness Improvement measure(s) Error prevention	Identify, confirm, react and fix. Check that fix works. Lessons learned so get better. How to stop errors occurring?
ISO14155:2011 compliance	Awareness Understanding Planning Study execution Analysis & reporting	Info source: internal vs. external. Clarity, interpretation & impact. What is needed? Who to engage? How & who to do it? Check, act & execute.
Situational awareness	ISO14155:2011 impact PPD implications Environmental influences	Compliant decision-making factors. Company vs. vigilance department; People; Process; Procedure. Client; Patient; Clinical site; Regulatory Authority.

Table 4.1: Summary of regulatory compliance decision-making core concepts, dimensions and key issues as discoursed by PPD physicians

4.1 DECISION - MAKING

Each physician discourse commenced with an exploration of the interviewee's approach to regulatory compliance decision-making to ascertain what factors influenced it in their contextual setting and role. Initial analysis categorised their responses into four dimensions which are listed below:

- **Decision-making at PPD**
- **Physician's approach to decision-making**
- **Decision-making influences**
- **Decision-making types and tools**

4.1.1 Decision-making at PPD

There was consensus that no single model for making decisions exists in PPD. However, many compliance decisions are made daily within the company with DM authority firmly in the hands of company physicians. This concept is important as it guides all regulatory compliance DM affecting many areas across the business as the following quotation illustrates:

"…. regulatory compliance is only one of the key tasks of a physician, takes a fraction of our time, but one that has a significant impact on the entire department, if not the whole business, as it defines not only the individual, but can impact company performance and results." Moorfoot,5

However, the physicians indicated that various approaches are utilised depending on *"…. problem complexity, level of expertise, and impact any change will have*."

Sidlaw,2

Regarding **problem complexity**, the majority of physicians commented on the mandatory nature of industry regulation and how compliance with GxP was at the heart of all decisions made within the company.

"…. regulatory compliance decision-making is an absolute." Torridon,2

"…. everything is in context of the regulatory requirements because we're dealing with drugs and devices in patients." Grampian,3

However, many indicated that the nature and scope of these decisions were complex and challenging requiring input from senior leaders, various functional areas and staffing levels comprising

"…. regulatory intel, therapeutic and business experiences, silo specific experience in both pre- and post-approval, then involving others as needed." Torridon,9

Contrastingly, some physicians inferred that, when it came to decision-making, commercial and client influences influenced heavily and perhaps took precedence, by stating that

"…. serendipity and ad hoc is the PPD model." Torridon,9

"…. PPD trades on the quality and speed of its service provision." Sidlaw,1

"…. for strategic clients PPD favours a three-tiered governance process for decision-making to guide the work of study teams focused on delivering the overall strategic imperatives and initiative goals." Moorfoot,6

Other physicians suggested that compliance DM was challenging in this environment because everything is project based, involving multiple time-zones and geographies, different personnel, resulting in many conflicting variables to deal with.

"…. it can be difficult to make a call which applies across all projects. We certainly try where we can and where we have influence over the processes." Galloway,3

However, the over-riding caveat was that when any regulatory compliance decision occurs the expectation is that it is

"…. ratified against us as a company and the position of our clients." Sidlaw,2

Regarding the **level of expertise** needed for regulatory compliance DM, there was consensus that the senior decision areas of the company were well covered by scientifically minded people, each of whom have been in the industry for more than two decades. However, DM distinctions were expressed, ranging from senior individuals making them at departmental level through to physicians participating in

executive level debate on regulatory decisions that affected the whole company. All physicians interviewed were involved in the former but only some, based on their organisational role, were invited to participate in the latter. Furthermore, it appears that compliance DM can be individualistic or operate via group consensus in strategic and tactical DM areas using resources as required. For example Lowther and Sidlaw talk of collaboration versus Torridon and Cuillin who say that the leader makes the decision.

"…. C-suite decision-making is collaborative but data driven also." Lowther,9

"…. engage legal counsel, as well as internal regulatory, clinical and operational specialists, before any decision can be contemplated." Sidlaw,2

"…. At times it's all about balancing the conflict between people who think differently so that we tease out alternatives positions and points of view." Lowther,9

"…. PPD is very good at delegating upward and so everyone looks to the captain of the ship to take the ultimate decision and we all sheepishly follow." Cuillin,5

"…. In the end the final decision always resides with the leader who can make a balanced decision." Torridon,9

In assessing the **level of impact a change will require** it appears that common factors were evident, including inputs and the cyclical nature of DM, comprising

"…. information you have at that moment in time, the knowledge you have and past experience. You decide but have to measure the decision outcome." Campsie,4

"…. decision-making is cyclical but open for amendment. If it is not the outcome expected, you just go through the cycle again." Torridon,4

However, despite best intentions, some physicians indicated that failing to adequately consider the breadth and/or depth of opinion or impact could result in inconsistencies, problems, sub-optimal decisions and re-work. For example

"….. we'll question a decision among ourselves. If we don't go into it then fine. Otherwise we do a review, some action is taken, then shared with a few people, but it doesn't get generalised across the business as a whole." Ochil,6

"…. the decision there (executive management) *is not the right decision here* (vigilance department)." Cuillin,5

In order to combat these perceived gaps some physicians suggested balancing decision-making by actively taking specific factors into consideration, such as:

"…. a bigger picture view is needed." Galloway,3

"…. don't consider impact on one but make decisions based on the many." Cuillin,7

4.1.2 Physician's approach to decision-making

When discussing their compliance decision-making most physicians were ambivalent; rarely from an indecisiveness perspective, more in the psychological sense given various contrasting decision-making styles, approaches and perspectives were utilised. In determining which approach to follow, when a compliance situation presented itself and required a decision to be made, there was general consensus that it was inconsistent, personal, ad hoc and discretionary.

"…. people are put in place based on their skills and knowledge but I haven't seen any structured, engineered model to make those kinds of decisions. I think they are embodied in the directors and those tasked with leadership and in their individual experiences." Lammermuir,5

Although the gap is known and acknowledged, the DM situation persists because no specific guidance exists.

"…. I don't believe that I've received, or been given any specific training or guidance, that there's a specific process that PPD follows." Galloway,1

Additionally, most physicians indicated that they were unaware of how they actually determined how to move forward. This can be summed up in the following quotation:

"…. I don't think I have a recipe." Campsie,4

Further questioning of the physicians determined that their decision-making approach could involve some, or all, of the following elements: instinct, intuition, prior experience, formal procedures, applying reasoned thinking, either individually and/or collectively, running sequentially or in parallel.

Instinct, intuition and experience

Many physicians described how gut instinct, intuition and industry experience influenced their PPD compliance decision-making as the following quotations show:

"…. 99% of the time regulatory decisions are instinctual." Sidlaw,5

"…. more based on a hunch than on any decision-making process." Cairngorm,5

"…. I draw on intuition and prior experience before coming to PPD, or experience of things that have happened within the organisation." Grampian,1

The consensus appears that instinct, intuition and experience act as drivers for compliance decision-making but utilisation, in this context, is inconsistent. This appears partly because physicians fear replicating previous mistakes or breaching regulations. Similarly, if an approach is associated with prior success the perception is that it can be emulated and repeated. In short, these influences were important because

"…. experiences shape your subconscious decision-making overall." Moorfoot,4

Process and procedure

PPD is a highly proceduralised company but determining how to make regulatory compliance decisions is not covered by any process or procedure. Although options exist the actual decision-making approach chosen lies with the decision-maker. When faced with regulatory compliance DM some physicians make decisions in a

"…. systematic process with clearly defined elements and in a distinct sequence of steps where the key is to make effective decisions by not making too many but concentrating on the important ones." Moffat,2

Physicians that engage and interact with the executive realm appear more likely to incorporate methodical DM approaches given the presence of

"…. analytical and statistical people with varying scientific backgrounds …. with decisions linked to detailed rules and smart incentives." Grampian,2

"…. policies and procedures determine if they meet the requirements, yes or no." Pentland,2

However, physicians at the department level seem to be more flexible in their use of process and procedure when it comes to DM. One approach involves

"… trying to understand who and what the recipient of that information needs and how to justify that." Galloway,1

However, this approach introduces speculation, opinion, interpretation and subjectivity into play leading to various viewpoints and variability within the DM processing area, so some control mechanism is needed. For example,

"…. if you ask 3 physicians, you get 4 opinions at the best of times." Cairngorm,4

In such cases an informal DM check process gets implemented where a senior physician oversees the medical monitors for consistency on studies since

"…. some things are open to interpretation. When subjective it's difficult to ensure everyone doing the same thing, unless very clear directives on a task-by-task, or study-by-study, basis are given." Cairngorm,4

Contrastingly, other physicians are more strategic, focused on solving compliance problems and achieving some defined end-point. They acknowledge that tactical knowledge can be weak and so some surround themselves with PPD process or procedure orientated staff to help plug the gaps and guide their regulatory DM.

"…. I step outside the box, look at it from an alternative perspective, but surround myself with process orientated people to balance the argument." Lowther,3

Reasoned approach

Other physicians described their DM approach as measured which involved thinking and mentally focusing on the gathered data, considering and interpreting the influencing factors, then taking a decision. One physician's description used diagnostic terms but all responses implied that time available influenced DM greatly.

"…. When it comes to regulatory decisions you're obliged to approach matters in a cold, calculated manner with patience." Lammermuir,4

" ….. I take the history first. So that gives you the story. Then do some investigations to get more information from different sources that are more detailed. I try and make a mental list of options and form hypotheses. Then you have chunks of information that would support or refute those hypotheses." Cairngorm,6

"…. one draws on education to bring some analytical foresight and ask what is it that you're trying to achieve and what are the motivations for making the decision? Part of it is a factor of time but often decisions are made under duress." Sidlaw,5

"…. I weigh evidence in my mind and apply common sense. Does it follow logic and did we consider all of the potential consequences of this decision? I try to make an informed choice but not to get into a quandary of indecision either." Lowther,3

"…. my decision-making is based on interpreting data in a time crunch." Grampian,1

Hybrid consideration

Other physicians expressed that they were comfortable making decisions under ambiguous conditions because the mind-body interaction was not a predictable model of how the human body reacts to stress and illness. So they learned to adapt. When assessing these contextual cases, some physicians articulated their preference for an informal hybrid DM approach considering multiple potentially conflicting factors such intuition, reasoned thinking, available time, problem complexity, amount and type of data, and seeking input from others. Typically,

physicians accepted or rejected data or proposals based on some internal, but unknown, benchmarking mechanism.

"…. It's looking at the whole issue. Gestalt." Lowther,3

"…. Medicine is a mix of science, experience, intuition, guesswork, and luck. I use the strongest hard evidence, such as from a randomized placebo-controlled trial, where I try make sense of available data given what is known about the condition or others like it. When data is absent I seek out the opinions of my peers." Moffat,4

"…. I use a blended decision technique asking questions when considering the need for a decision. What is the objective of the decision? How does the information support the objective? Is it complete / incomplete? Do we know if there is more or there are gaps that no one can fill? What options are there and have all been considered, including vetting their impact positively and negatively?" Torridon,3

"…. For bigger things I assign a team to study it first who then come back to me with recommendations." Munro,2

"…. I don't have it formalised but when something doesn't make sense I tend to discard it as internal intuition just overrides it." Lowther,8

4.1.3 Decision-making influences

Skillsets

The physicians offered some insight into applicable competencies and skills needed to make compliance decisions in PPD. From a high level clinical research context, it appears that physicians' perceive regulatory compliance decision-makers to be both scientists and physicians requiring

"…. mastery of two skillsets: business and medicine." Galloway,8

At a lower level physician skills ranged from interpreting the context in which decision-making flows, gathering data on each case, fluctuating use of medical knowledge from none to specific based on the presenting scenario, then having the practical wisdom and the moral skill to figure out what to do. Examples include using their scientific medical background in interpreting

"…. regulation changes, potential grey areas, things not covered or inadequately addressed." Galloway,1

"….protocol development and clinical study execution but in day-to-day business I don't necessarily pull on the academic side of my education at all." Grampian,5

For some physicians, proactivity and subject curiosity drives an initial individual data screen to raise awareness and build momentum for the compliance DM event.

".... I'll work on something to start with then bring in others to modify it." Galloway,4

"…. but in the majority of instances you have to get additional information and engage with others." Sidlaw,4

However, not all compliance decisions have positive outcomes as patient safety concerns can result in significant ramifications for affected parties, such as a

"…. signal indicating that trial product is potentially carcinogenic, demonstrates life threatening problems, QT intervals, or whatever, where we say halt this program, inform the agency, and do it in real time." Torridon,4

Therefore, most physicians indicated that they needed to be strong willed, focused, resolute and capable of defending their decisions.

Second opinion

Consistent amongst all physician responses was a desire to consult and/or solicit alternative opinion across regulatory DM levels as, and when, needed. This was especially prevalent when considering compliance decisions that affected others such as the primary study endpoint for the medical device in question, either in isolation, or in combination with other therapies, drugs, or determining the health or survival rate of patients. This was characterised by asking for a lot of data in a short time period. The implication appeared to be that the physicians needed to weigh up the data and determine if the trial continued, required modification to address new mid-study information, or had to stop early because of a lack of clinically meaningful efficacy.

"…. I can't know the detail of absolutely everything so I do take advice and delegate, but not the accountability or absolute responsibility." Torridon,2

"…. many times I get a perspective that I never had by actively listening to them and getting their input on a topic." Lammermuir,4

"…. this is where broad experience across therapeutic areas counts." Torridon,2

"…. if we are in consensus then typically we'll move forward." Sidlaw,2

"…. rare that there's no consensus, or absolute dichotomy, Someone will speak out, voice an opinion, we consider it and come to a consensus somehow." Cairngorm,4

Contrastingly, although all respected peer opinion, others urged caution, when accepting advice given there are so many parts to safety vigilance such as triage, case processing, medical, risk management, reporting and the affiliate pieces. The implication was that advice could be contradictory, outdated, poor or wrong depending on level of peer involvement, making the decision path still unclear.

"…. it works well when everyone has an equal say within a particular discussion. I am not convinced that it's always the case, even in the C-suite." Campsie,5

"…. just because you do a job for years doesn't mean you have a lot of exposure or are necessarily any good." Cuillin,4

"…. from a purely epidemiological perspective the PPD medical opinion may not necessarily be representative of that decision-making body of people, either through a lack of medical speciality or because those who have chosen to leave that environment might have chosen to leave for a reason." Galloway,7

"…. most have only studied a tiny fraction of all medical conditions, usually those which affect many people, which appear financially promising to drug/device companies, or are controversial for one reason or another. Also, experts can be wrong. Then I have no idea what to do, in which case I do nothing at all. I park the issue, then revisit it later." Moffat,4

Emotion

A couple of respondents commented on the effect of emotion on physician decision-making. However, although it can apply in clinical settings, when facing a casualty or trauma, it does not appear to be a significant influence in PPD.

"…. in a medical emergency emotion can affect but I found that it doesn't really take hold. Your training kicks in regardless of what you are confronted by. However, in PPD it's a non-event really as those clinical scenarios never occur." Cuillin,5

"…. emotion can influence decision-making but I've no experience of that here. PPD don't tend to discriminate or act on it to guide thinking or action. If anyone did then you'd revisit the decision when feeling less emotional." Cairngorm,5

Reflection

For some PPD physicians reflection can influence DM comprising considering past scenarios, retrospectively identifying alternative options or learning from experience to improve performance. However, it's a personal influencing factor, timing based and inconsistently applied.

"…. it's not always clear what's being asked. Sometimes it takes a little time to do that. So, I look at it, then I'll go do something else for a bit. Coming back to it helps me to really try to think about the subject and think of alternatives." Cairngorm,1

"…. I do look back and say to myself what would have happened if I take this scenario and try and put it back there. I think it's a human ability to step away from ourselves and view from someone else's point of view." Campsie,4

"…. being a sort of reflexive person, I ruminate and draw on past experiences all the time. It's always about improvement in the sense of my performance." Torridon,5

"…. I sit at home some nights thinking have I answered that e-mail, did I do that correctly, was my response appropriate? I'm quite critical of myself. We all make mistakes in our careers but, for me, it's very important to understand what I did and how I can do it better in the future to allow me to move on." Cuillin,6

4.1.4 Decision-making types and tools

Decision types

The contrasting approaches to PPD compliance decision-making can impact organisational function and staff engagement via the decision types which are categorized as strategic, operational and transactional.

"…. In our company many decisions are made every day. Most involve a degree of compliance consideration but there are various levels and types of decisions that have to be met ranging from strategic to the tactical." Moffat,4

"…. decisions about how we are conducting a study, about how a study is to be executed, is on a strategic level before it gets down to the operational staff because a lot of the operations staff at PPD are young, new to the industry and are in need of some guidance." Ochil,4

"…. the operational side is very tactical and transactional." Grampian,1

"…. some are snap decisions because the scenario is familiar and the choice among decisions is narrow and there is only a clear path to the right decision. So there is no ambiguity. However, some decisions, based on the nature of what is going on, require pause because there could be multiple paths to the correct answer but the path to get there may not be obvious." Lammermuir,5

Decision-making tools

Literature review indicated that tools exist to aid decision-making. However, the general consensus from physicians was that DM aids were rarely, if at all, utilised.

" ….. in a past life I've used decision trees." Grampian,2

" ….. I might use S.W.O.T. analysis but I don't consistently do that." Lowther,2

" ….. we certainly map out various process flows for some things we do routinely where we try to diagnose and seek additional, or new, evidence but not really for making decisions." Galloway,5

" ….. I don't believe so. I think people make decisions based on their previous experiences, knowledge and the nature of the work that we do." Cuillin,3

" ….. never had to follow any decision-making tool other than logic, if you consider logic to be a tool." Campsie,3

" ….. I suppose my mind might be organised that way, but it's subconscious rather than conscious." Torridon,3

" ….. do not really use them in PPD" Cairngorm,1

4.1.5 Summary of decision-making within PPD

In summary, it appears that PPD regulatory compliance decision making occurs daily via the company physicians but a variety DM approaches exist based on problem complexity, level of expertise and impact of change. Some decisions require juggling diversity of opinion, balancing disagreement and vigorous debate, where physician executives appear to engage in a form of discourse that can be explained in a logical and systematic way showing that they have weighed up different arguments and perspectives. Contrastingly, for others, it appears that their intuition, knowledge, skills, experience, reflection, as well as following due process and procedure, all impact and shape the decision-making capabilities to a varying degree. Many physicians seek out peer advice and second opinion to aid with their DM process but this can introduce some contradictory, and potentially negative, positions too. This inconsistency with compliance DM can lead to organisational confusion and staff frustration. Some suggest that problems with the current DM approaches are because of physician variability, contextual complexity, differing experiences, skillsets and lack of consistency. A few physicians engage in self-reflection but the practice is not widespread and there is little to suggest process improvement result as a consequence. The following quotations summarise the dilemma:

".... decision-making is so complex. Although it is supposed to meet patient and client needs, it is frequently opaque. We need to make it simpler." Munro,5

".... each individual at executive management level has differing requirements depending on what they know about the situation, client or study, department, the function at hand, finances, etc … but whoever it is wants to have some baseline knowledge of the issue, a minimum rate of information exchange, and be able to make an effective decision. But that varies by individual" Grampian,3

So, in developing the core concept, labelled compliance decision-making, the physician in-vivo responses were refined by the researcher into four dimensions using open coding and preliminary framework analysis as shown in table 4.2.

Initial categories (In-Vivo codes)	**Key Issues**	**Dimensions**
No formal model or process *Tiered approach* *Make decisions … go with them* *Collaborative … data driven* *Serendipity and ad-hoc* *Balance conflict* *Cycle*	No set model. Convoluted, fragmented decision-making approach	**Decision-making at PPD**
Don't have recipe *All about people* *Medicine is mix of science* *Gut instinct. Gestalt.* *Internal frame of reference* *Methodical approach* *Take history … mental list of options* *Blended technique* *Context*	Contrasting physician decision-making styles & perspectives: Instinct, intuition, experience Process & procedure Reasoned approach Hybrid consideration	**Physician Decision-making approaches**
Skillsets mastered : business & medicine *Interpret regulatory change* *Work alone* *Not make decisions in isolation* *Engage others* *Emotion not take hold* *Reflexive person*	Skillsets Second opinion Emotion Reflection	**Physician Decision-making influences**
Many decisions made every day *Compliance consideration* *Fraction of time* *Significant impact* *Decision making complex*	Strategic Tactical Transactional	**Decision Types**
Don't use them *Decision trees* *S.W.O.T* *Previous experience & knowledge* *Logic*	Decision-making aids	**Decision Tools**

Table 4.2: PPD physicians' perspective of compliance DM. (constructed by refining in-vivo categories into key themes and dimensions to develop the core concept).

The four dimensions were decision-making at PPD, physician decision approaches, physician decision influences, decision types and tools. The refinement of the raw collected data into their respective dimensions is illustrated in table 4.2 moving from left to right. The left hand column depicts the physician responses (in-vivo codes) combined together as initial categories. Refinement of these codes occurs in the middle column entitled key issues. Finally the dimensions are constructed by condensing the key issues into succinct labels, which are highlighted in bold text on the right hand column of table 4.2.

4.2 DECISION ERROR

In response to the physician answers provided on the subject of decision errors, four dimensions were identified and are listed below:

- **Reactive correction**
- **Effectivity checking**
- **Improvement measures**
- **Error prevention**

4.2.1 Reactive correction

PPD is a global company with many people working on multiple clinical trial projects simultaneously. Occasionally decisions are taken and actions occur that potentially result in adverse organisational outcomes. So, all physicians were asked how decision errors were identified and addressed within PPD when things go wrong. Although these events were rare, it appears that investigation commences quickly via a series of reactionary steps commencing with error confirmation.

"…. identifying that we have a problem." Grampian,5

"…. when an error is confirmed a whole host of meetings occur, with appropriate level staff identified. Then the problem resolution kicks in immediately." Lowther,7

"…. the error severity is classified as critical or non-critical. That typically determines our approach which is a factor of the given circumstances, the client interactions, the overall expectations and nature of problem or issue that has arisen." Moorfoot,5

When critical errors strike, PPD has several formal internal processes and departmental procedures that are utilised to help guide and coordinate the flow of information, thereby helping with decision-making. These include:

"…. CAPA (Corrective and Preventative Action*) *process, CRRM* (Clinical Rapid Response Mechanism*)*, or escalation to the CCC* (Corporate Compliance Committee*) *for serious breaches."* Sidlaw,4

Contrastingly, non-critical error handling within PPD's vigilance department is ad-hoc and non-proceduralised but also very reactionary. Once details of a situation emerge, an informal process begins comprising a review of the anecdotal evidence, understanding what is the issue and impact to PPD, then confirming the details, discussing with others, prioritising tasks and fixing as a group. It appears that the communication channels both upstream and downstream in the organisation are vital in making decisions and correcting the problem as quickly as possible. This has been described as

"…. communicating to top management so that they are aware, can set strategy and act as an escalation point." Grampian,5

"…. investigate quickly what has gone wrong, then sort it. Essentially it's reactive trouble-shooting." Campsie,4

"…. This is one of the things that PPD does very well." Lowther,7

4.2.2 Effectivity checking

Following error corrections, checking how effective the change has been seems to be the second error-related sub-theme. This appears to involve retrospective track and trace analysis of the error incident by reviewing the investigation process via

"…. revisiting and assessing the correction measure implemented after a fixed time period to check that there have been no repeat incidents". Lammermuir,6

"…. questioning the original decision-making strategy and approach." Munro,6

Footnote * acronyms expanded by researcher for reader clarity. See List of Abbreviations on page xii

Additionally, others felt extending the effectiveness check to cover the client's perspective was needed because assessing commercial due diligence was of paramount importance

"…. as a service provider the impact of our remedial action can affect the nature of our business relationship with our clients. So, we need to establish whether the consequences of our corrections could adversely affect trial outcome, time to market, potential revenue implications or future potential commercial opportunities." Ochil,5

4.2.3 Improvement measures

Once an error has been corrected, and the effectiveness check made, the third error-related sub-division appears to be an improvement discussion with department leaders. Although an infrequent exercise, it appears to be a quality review of gathered data where analysis indicates problems coming from

"…. CAPA or complaints" Pentland,2

"…. critical audit report findings." Ochil,3

"…. rate queries, such as number of CRFs, data queries generated per subject or number of protocol deviations per patient" Moffat,3

"…. monitor visit reports and observations" Munro,4

Other physicians indicated that correcting errors could occur following management review when things were failing but there did not appear to be any set way to fix these errors. It seems to be

"…. arbitrary, on a case by case basis, or at the discretion of the head of department who, if interested, will ask impact type questions." Sidlaw,5

Examples of questions asked during the impact analysis stage include

" ….. how did we identify the error? How did we classify the error? What escalation steps were needed? How did we track the error? How did we reduce the impact and risk of the error to the client, the sites and our business?" Lammermuir,5

4.2.4 Error prevention

The fourth error-related sub-division appears to be consideration of errors for lessons learned debriefs and input into improvement conversations to potentially help get things right in future clinical trials. However, this point was not actively considered by many of the physicians questioned. Those who did comment indicated that errors occurred because

"…. people were rushed and pressurized, by senior management, clients or both, into making quick decisions with incomplete data, usually because of a time crunch"
Grampian,6

"…. the wrong decision was made in the first place. Not from lack of awareness, integrity or training. Just that things can, and do, go wrong sometimes." Cuillin,6

Both scenarios were seen as uncommon, with pro-active error discussion being extremely rare, viewed as
"…. patchy. It is not institutionalised." Pentland,8

However, anecdotal comments suggested that decision errors could be used as catalysts for future state process improvement initiatives such as introducing

"…. a new way to work linked to a set standards for errors." Lowther,6

or as a

"…. formal error correction mechanism linked to personal accountability and departmental responsibility." Pentland,8

4.2.5 Summary of decision error

In developing the core concept, labelled error, the physicians' in-vivo responses were refined by the researcher into four dimensions. These were reactive correction, effectivity checking, proactive improvement and preventative measures. The refinement of the raw collected data into their respective key issues and dimensions, ranging from current to future state, is illustrated in table 4.3.

Initial categories (In-Vivo codes)	Key Issues	Dimensions
Notification. *Immediate investigation response.* *Determine how & why errors occur.* *Reactive trouble-shooting.* *Anecdotal evidence.* *Failure determination.* *Identify error type: human, process, system, procedure.* *Correct the error.* *Communicate fix.*	**Current state** Error Identification Reaction Confirmation Categorisation Remedial Action	**Reactive correction**
Consequence? *Client effect (external)?* *Company effect (internal)?* *Question DM strategy & approach.* *Effectiveness of correction?*	Perceptions of current service provision. Confirm fix working	**Effectiveness check**
Lessons learned. *Determine need for change.* *Impact assessment.* *Determine best way to fix?* *How identify error?* *How classify?* *Escalation steps?* *How track?* *How reduce impact and risk?*	Lessons learned Support needs How to get better?	**Improvement measures**
Need new way of working? *Set standard(s) for errors.* *Correction mechanism.* *Accountability.* *Responsibility.*	How to stop errors occurring? Pro-active **Future state**	**Error prevention**

Table 4.3: Physicians' conceptual understanding of how errors influence ISO14155:2011 compliance, and refining dimensions within the core theme.

4.3 COMPLIANCE WITH THE ISO14155:2011 STANDARD

In response to the questions posed on the core concept of ISO14155:2011 compliance, five dimensions were identified (see table 4.1) and are listed below:

- **Awareness**
- **Understanding**
- **Planning**
- **Study Execution**
- **Analysis and Reporting**

4.3.1 Awareness

Each physician was asked if they were aware of the pending compliance change and what they knew about the ISO14155:2011 standard. All were aware of it and provided useful data. In a few cases, some physicians produced a plethora of

detailed opinion and commentary on the subject. For example, the physicians' answers indicated that they initially became aware of ISO14155:2011 via advice and commentary from industry providers such as the

"…. agency publishing the standard is the initial, and primary, source of the information but typically that is provided at a cost." Lammermuir,1

"…. competent authorities, such as FDA, EMA and MHRA." Campsie,1

"…. webpages of DIA, ASQ, RQA, and ACRO." Galloway,1

"…. updates by PPD internal mechanism run by global regulatory affairs called the Regulatory Intelligence Steering Committee. The purpose of the RISC committee is to keep on top of any emerging areas in clinical development." Sidlaw,1

"…. an-ex FDA inspector's blog called GxP perspectives. It's very easy to read and topics are very poignant as they really serve the industry." Moffat,1

All physicians indicated that it was important for them to find out about the pending ISO14155:2011 changes individually, as well as professionally, because
"…. as a decision-maker I need to understand what's it all about." Ochil,1

"…. keeping your finger on the pulse in terms of precedent matters is important in our business. They are the key drivers of what happens globally." Torridon,2
Contrastingly, one physician conceded that it was

"…. very difficult professionally to stay ahead of the implementation of regulations. But in most cases one has a grace period to become familiar and adapt." Sidlaw,1

4.3.2 Understanding

Once general awareness of the regulatory change occurs, it appears that a deeper understanding of the requirements, and its associated impact, is often required. This step is role dependent and seems to be the second compliance-related division. So, when confronted with a compliance subject that requires a decision some physicians refer to

".... the legislation, any guidance and any Q&As that come from the guidance in reaching a final decision." Torridon,4

"…. establish what is clear and what is not because that quite often gets lost in subsequent communication. If something isn't clear I like to get that out in the open first so that people I'm working with are on the same playing field, in the sense of, we established that there is no guidance on this topic." Galloway,1

From that position some physicians then move onto drilling into the requirements

"…. ISO14155 is a harmonized standard that defines the execution, management and performance of medical device clinical trial investigations." Munro,1

"….it carries several mandatory compliance elements and they are checked by the notified bodies such as BSI." Cairngorm,1

These comments indicate that the physicians start to comprehend the compliance requirements based on ascertaining key features from the standard. However,

"…. in order to fully understand what's actually involved you really need to go back to regulation and read the literal requirements, including any guides or documents published by the regulator." Galloway,1

because

"…. ISO14155 specifies conditions intended to protect patients by ensuring the scientific conduct of a clinical trial. It also supports clients, sponsors, medical monitors, investigators, ethics committees, regulatory authorities and notified bodies involved in the scrutiny and assessment of medical devices." Ochil,1

4.3.3 Planning

Many physicians indicated that after their preliminary legislative review, planning for change swiftly follows; initially at a fairly high level, before quickly delving into the detail. So, it appears that planning for change is the third compliance-related division. The following quotations illustrate this point:

"…. we need to start planning and communicating with the business to increase awareness and prepare for action." Grampian,2

"…. conducting a business impact assessment and determining the risks involved. Decide what that means and how that's going to be operationalised, set expectations and communicate, so shared understanding. Then interpret ISO14155 to determine its applicability, scope and impact on our business." Cairngorm,8

"…. if the standard is applicable then a comprehensive and robust plan is put in place that will cover all client and business study needs. This includes research and development activities of the medical device, its subsequent classification, interaction with the regulatory authorities and notified body, business planning, pre-study assessments, planning and scheduling the investigation activities and ensuring appropriate selection of the principal study investigators." Cairngorm,2

4.3.4 Study Execution

Study execution was deemed to be the fourth compliance-related division with some physicians suggesting implementing specific compliance requirements immediately given it was the cost of doing business in this environment. Execution involves

"….any on-going study or country affected by it. If necessary, we'll put a team together to start working with the client and doctors in that country," Sidlaw,1

"*….to ensure that the processes are in place for all stages and phases of a clinical study."* Lammermuir,3

"….from initiation and patient recruitment, through clinical monitoring, data management, vigilance reporting and study closure." Sidlaw,3

"…. and reviewing PPD's business rules and approved documentation in our quality management system for suitability with ISO14155 compliance." Moorfoot,1

"… then it's really about the resource and the tools to be able to do that, and the communication piece as well. It's all about making sure the relevant people know about the change, are aware what's happening and what's in place, then ready to go in time for that regulation change." Cuillin,1

However, other physicians took a wider study lifecycle execution view, by suggesting various external and internal compliance factors were required covering

"…. the business landscape and other departments." Galloway,2

".... the dynamic between culture and behaviour." Lowther,3

Contrastingly, a minority of physicians wanted to do more than just meet standard requirements at each study stage or product phase because there is pressure to do

"….everything to meet the minimum requirements rather than to meet a standard above that. Decisions are made too often using guidelines that are inherently loose and that's what causes us lots of problems. So, research deeply then make a call based on experience and the precedents set with other products." Campsie,1

However, one dissenting voice regarding implementing ISO14155:2011 as

"…. bureaucratic lunacy and just another obstacle to innovation." Munro,5

4.3.5 Analysis and Reporting

The fifth compliance-related sub-theme is the impact of ISO14155:2011 compliance on the analysis and reporting functions of a clinical trial. In this area the physicians' comments indicated that PPD was essentially acting for the sponsor on trials and so the data, analysis and specific reports generated needed to be complete, accurate, and timely as legislation mandates. Some physicians commented that this was a

"…. cradle-to-grave commitment from bidding on the original client request through to the final trial publication." Moorfoot,2

Additionally the physicians' consensus was that by using PPD analysis applications and reporting functions, the company was to continually deliver high quality outputs and speed processes to database lock without comprising quality or patient safety.

4.3.6 Summary of ISO14155:2011 requirements

In developing the core concept, labelled ISO14155:2011 compliance, the PPD physicians' perceptions described it as a series of overlapping dimensions covering

awareness, understanding, planning, study execution, analysis and reporting. This core concept is illustrated in table 4.4.

Initial categories (In-Vivo codes)	Key Issues	Dimensions
Information source *Internal mechanism at PPD* *Industry websites, blog* *Grace period*	Overview Information gathering Subject familiarity Timeframe	**Awareness**
What's it all about? *What is clear and what is not* *Read literal requirements* *Clinical trial of medical devices* *Pre-understanding.* *Shared understanding* *Cradle-to-grave commitment*	Comprehending scope of requirements	**Understanding**
Interpreting *Impact assessment* *Risk determination* *Business rules* *Fit with quality management system?* *How operationalized?*	Proposals for organisational applicability & impact	**Planning**
Cost of doing business *Rules of the game* *Study phases* *Other departments* *Systems and processes* *Approved documentation* *Necessary overhead*	Implementation and effect on other steps in trial process	**Study execution**
Study close down *Final reports* *Study publication*	Requirements at end of study	**Analysis and Reporting**

Table 4.4: Physicians conceptual understanding of how to achieve compliance with ISO14155:2011 & refining key issues and dimensions in the core concept.

4.4 SITUATION AWARENESS

In response to the answers provided on the subject of situation awareness, three dimensions were identified and are listed below:

- **ISO14155:2011 requirements**
- **PPD implications**
- **Other environmental influences**

4.4.1 ISO14155:2011 requirements

The majority of physicians indicated that situational awareness covered the ISO14155:2011 standard and its requirements, error considerations and all decision influences that preceded action, as described in sections 4.1, 4.2 and 4.3 of this

chapter. Contrastingly a few physicians cautioned that the new requirements could be onerous, adding layers of complexity with no real added value, with few experts to reference given it's so new.

"…. one of the challenges we have with this new stuff that has come out is that no-one is a SME. That applies to the industry as well as to us internally." Galloway,4

"…. it's been put together by people who don't really understand existing regulations." Campsie,5

Although these quotations illustrate that a spectrum of contrasting physician opinion exists in PPD, leading to inconsistencies and differences with regulatory compliance interpretation, it appears that many concerns could be addressed with supplemental DM information from elsewhere.

4.4.2 PPD implication

In response to the questions pertaining to the impact of ISO14155:2011 on PPD and its departments, four sub-divisions were identified and are listed below:

- **Company considerations**
- **People**
- **Process**
- **Procedure**

Company / department considerations

When considering the impact of ISO14155:2011 on the PPD business many of the physicians indicated that having full situational awareness was important because

"…. background and context can very rapidly change the decision." Campsie,3

However, within this organisational sub-division several contrasting points of view were put forward. The first considered the compliance impact on the PPD business and, although unknown presently, contrastingly different opinions were put forward; some positive and others negative.

"…. The absolute goal of compliance with ISO14155 will be to provide PPD with an assurance against the standard's essential requirements and, at the same time, deliver objective evidence of compliance to the regulators." Torridon,2

"….. just part of doing the job ….. standards are expected to change over time. It's a pendulum that swings back and forth between too onerous or too vague/simple. It's it's a struggle to find the sweet spot between what is overly prescribed and what is under-documented to what the expectations are." Lammermuir,3

However there was a general feeling that regulatory compliance can be restrictive in that once legislation is passed then you're stuck with it.

"…. There's very little in terms of reform. So, a lot of time and money is wasted and, will continue to be wasted, by mandating regulation that's completely and utterly falsely applied to clinical research." Sidlaw,4

However, overall compliance with ISO14155:2011 was essentially seen as a *"…. necessary overhead, but rules of the game, for without it we would have a free for all and patients would be put at risk."* Cuillin,2

The next consideration was looking at the bigger picture covering the business situation and working out how best to comply with the requirements.

"…. I try to keep a principle. The business mission is paramount." Lammermuir,2

"…. it's got to go across the whole organisation. Once the regulation's here you must comply. But it's the manner of how you comply where it comes together. I feel that it is mandatory to have voices from our safety physicians but also Quality Assurance, Regulatory Affairs, Legal and Operations. You could also argue that Finance is involved as well, depending on the nature of the wholesale change and where you are within the Corporation." Sidlaw,3

" ….. All safety vigilance professionals are driven by 3 main drivers: safety, quality and efficacy, covering the full spectrum of a product's life from initiation on-the-bench to final death on-the-market. This includes its licensing and post-licensing commitments. Post-licensing can make up 90% of product so, if the compliance approach is not right in the first place, you'll spend a considerable amount of time with the friction burns afterwards." Campsie,2

A further perspective was to consider balancing the risks associated with making the regulatory decision with the various impacting factors. Some risks were internal to PPD but others are external, including overlapping pieces of industry legislation and guidance, with some not applicable.

"…. Risk, experience, cost and the bigger impact are the things I think about. Risk to the company, to myself, and on the staff making that decision; the impact on other functions and departments because we are a cross-functional organisation" Cuillin,2

"…. with ISO14155 it is important to consider how risk management and risk-based decision-making processes impact but also how other ISO guidance such as ISO14971and its application to ISO13485 crisscross." Moorfoot,4

"…. there's a potential conflict in interpretation between the statutory instruments for GCP in humans, the European Clinical Trial Directive 2001/20/EC for pharmaceutical trials, versus the medical device directives and now ISO14155." Campsie,2

".... we look at the solutions, pros and cons for every decision we make then balance the pros and cons for each one. For most of the tasks we do it's about the speed of execution rather than the risk of it not getting there. Campsie,3

"…. however if a regulation doesn't impact day-to-day operations then I'll just ignore it." Lammermuir,1

People

In considering the impact of ISO14155:2011 on the company many physicians remarked that people factors were most important and heavily influenced their decision-making approach. Although the physicians' perspective was covered in chapter 4.3 additional comments indicate that

"…. PPD is all about people. We don't have, make or use products as in a regular business. Our product is service, made up of experience predominantly, as well as the education of the people who work here." Sidlaw,2

Therefore, in order to help make the best compliance decisions and interpret ISO14155:2011 the physicians indicated that it was essential to know where

"…. my skillsets are and who can interpret things." Munro,1

"…. skillset, capacity, availability, knowledge and experience are key. So, if you do not have those skills in the department then you have to reach out externally to get them." Cuillin,4

"…. stakeholders and practicalities of what to achieve go into the mix." Moffat,4

However, despite considering other people and their input, regulatory compliance DM conflict can still arise between physicians and their staff and vice-versa.

"…. I try to juxtaposition the needs of the company with the needs of the staff. However, the needs of the company are always more important than the needs of the individual." Lammermuir,2

Contrastingly, when receiving DM or compliance enquiries from other departments some physicians were very critical citing lack of context, hidden agendas or seeking out their opinion but not necessarily taking it on board when other factors conflicted.

"…. PPD is particularly bad at not having context around whatever people want you to do. People have their own agendas. So, they simply ask away but see no need to provide any background or justification for it." Cairngorm,3

"…. Too often doctors are seen as obstacles to getting something done rather necessarily as a solution to get you from A to B. Partially it's because of poor education within the Pharma industry but, especially within CRO departments. But in this environment some doctor's opinion gets pushed out as it is seen as being negative, rather than its true purpose, which is to help deliver safe, quality and efficacious medicines to the public." Campsie,5

Process

When considering the impact of ISO14155:2011 on PPD process the physicians remarked that alignment and communication are key particularly when assessing and determining impact on compliance functions. The following quotations illustrate this point:

"…. we've got global processes so we need to align those by engaging with global stakeholders. Having a consistent approach, with clear communication channels, when regulation changes are coming though for review, is critical." Cuillin,4

"…. when we have to change processes and procedures, the most important thing for me is that we update our processes first so that they are compliant. Even if the procedures lag behind slightly. If you only have the resource to do one or the other, the most important part is the compliance." Galloway,3

Procedure

All of the physicians questioned stated that a most essential component of compliance with ISO14155:2011 was the need to use an approved set of specific documents and procedures for conducting the medical device clinical trial. This was seen as a crucial element of compliance with the standard and can be summed up by the following quotations:

"…. *procedures are very important, and required as part of the legislation."* Ochil,3

"…. *identify new documents to be written, approved and used in situ."* Cuillin,2

"…. *focus prioritisation on getting highest risk procedures up-to-date."* Galloway,3

"…. *failure to comply with documentation requirements would be seen as a breach of regulations which can lead to sanctions on the company."* Moffat,3

From their experiences, the physicians relayed many examples of key critical clinical investigation documents required during a medical device trial and these are illustrated in appendix K. They include examples such as the Investigator's Brochure, Clinical Investigation Plan, Case Report Form, Ethics Committee approval and Informed consent forms. Additionally, other operational procedures were also put forward as essential documents and are also listed in appendix G.

4.4.3 Other environmental considerations

In response to the questions posed on the subject of other considerations that could potentially influence ISO14155:2011 compliance, four environmental sub-divisions were identified from analysis of the answers provided. They are listed below:

- **Client**
- **Patient**
- **Clinical Site(s)**
- **Regulatory Authorities**

Client

The first environmental sub-division was to actively consider the client's opinion regarding expectations and level of knowledge associated the regulatory compliance changes and decisions. So sharing information and engaging in discussions was seen as definite need given the client carries the liability for the final study decision.

"…. some clients know the requirements. Others look to us for expertise and knowing exactly what to do." Cuillin,3

"…. it's providing a spectrum of recommendations for the client to consider in terms of decision-making." Torridon,1

"…. interpreting the standard requirements enables much easier conversation with the client." Torridon,2

However, PPD has many clients and regulations to comply with globally and needs to be as flexible and adaptable as possible to service many differing perspectives and assumptions.

"…. we do things differently from big pharma. We need to understand the pharma perspective but modify and balance it within the CRO world." Pentland,7

"…. there's a modicum of vision and strategy needed to be able to look at current state information and juxtaposition that against potential growth, process improvement, new business opportunities." Lammermuir,1

"…. to help a client with regulatory decisions we look at any precedent, guidance and data with new molecule target profile the client maybe working to, and formulate plans around that. Of course those are open to discussion and review with the regulators on both sides of the Atlantic." Torridon,1

Contrastingly some physicians urged caution in that

" ….. it doesn't seem to matter that what we say is speculative." Cairngorm,3

" ….. one has to be considerate that our clients may have a different interpretation. It's very rare but has to be considered." Sidlaw,1

Patient

The second environmental sub-theme was to actively consider the patient perspective with any planned compliance changes.

"….. in this industry decision-making comes down in the end to be quite simple. It's about the safety of people and the ethical treatment of people." Sidlaw,8

"…. everything is in context of the regulatory requirements because we're dealing with drugs and devices in patients specifically." Grampian,2

"…. as a trained medic I'm always looking to see what are the risks to patient. In medicine, everything you do is based on the patient's history and examination of findings. I try to do this in PPD to a certain extent by seeking out what pieces of data are needed for completeness through the overall patient context." Cairngorm,3

However, the dilemma facing physicians' decision-making in this context surfaced in some commentaries where some physicians indicated that they operated in a

" ….. hybrid role. You have the right to make clear decision recommendations in terms of the actual words, but the actual meaning could be subject to amendment because my obligation is to protect the patient as well as to protect the status of the licence for that particular sponsor." Torridon,1

When considering patient perspectives some indicated that for clear cut issues study protocol was followed. However, occasionally help was needed as physicians are not experts in everything and pondered on whether

"….. have I got the right skills to meet patient needs?" Cuillin,6

"…. you just kind of figure out that things will be alright in the end. Which generally is the same in medicine, pretty much, as people get better despite what you do, not because of it often." Cairngorm,3

Clinical Site(s)

The third environmental sub-theme was to consider the clinical site's perspective with any planned compliance DM changes. Opinions ranged from no involvement, through delegation to proactive opinion generation.

"…. *Absolutely no involvement with the clinical sites."* Cairngorm,2

"…. just inform clinical operations of the regulatory change and get them to take all necessary action. They manage the sites so it's their responsibility." Moorfoot,2

"…. go back to the investigators to alert, query and deliberate on what's going on …. particularly with key opinion leaders or strategic alliance accounts." Munro,2

"…. Things on site I know need to be addressed and improved upon. For me it's a question of prioritisation; which ones are important and I can influence." Cuillin,6

"…. depends on what the decision is and what it is about." Ochil,2

Regulatory Authorities

The last environmental sub-theme involves some physicians interfacing with the regulatory authorities depending on their assigned role within PPD. The main comments indicate that the regulatory authorities are interested in being

"…. engaged with a strategic individual." Campsie,6

Where involved, PPD physicians spend the majority of their time reviewing and responding to queries and documentation from regulatory colleagues and agencies

"…. working with global regulatory affairs for consistency of safety messaging to the health authorities. If a compliance related decision impacts cross-functionally, then it's getting the right stakeholders on-board, prioritising highest risk and then ensuring that study is conducted efficiently and successfully." Cuillin,2

Occasionally additional regulatory nuances, or geographical commitments, go beyond standard requirements, but still need to be considered and addressed. So, where these cases exist, considering specific situational factors then taking decisive action was deemed to be necessary. For example, in some countries there are

"…. regulatory requirements which we must do by law but choose to stagger because of practical implications of delivering other documents in parallel. For example, delaying Spanish submissions by 3 weeks because we had to get ethics approval and ethics can only be submitted once." Campsie,3

"…. I'm not an expert in any one of them but I ascertain what the regulator wants, then make sure that our team delivers, balancing decisions based on what the authorities expect and judge us on, then share those experiences." Campsie,7

4.4.4 Summary of situation awareness

In short, developing the core concept labelled situational awareness, involved refining the responses into three sub-themes using framework analysis. These were the ISO14155:2011 requirements, PPD implications and environmental influences. The ISO requirements were described in sections 4.1, 4.2 and 4.3 of this chapter but the latter dimensions are tabulated and depicted in table 4.5.

Initial categories (In-Vivo codes)	Key issues	Dimensions
Knowing the full background, information and context. *Business mission is paramount.* *Engage global stakeholders* *How you comply. Back to basics.* *Balancing risk* *Safety, quality and efficacy* *Risk, experience, cost* *Bigger impact* *Communication is key.* *Specified documents* *Conflict with other legislation*	Company versus department People Process Procedure	**PPD implications**
Help client understand *Context around what want to do* *No one is a SME* *Risk to patient* *Safety of people* *Ethical treatment of people* *Go back to investigators* *Inform clinical operations* *Know what the authorities expect* *Engage with a strategic individual*	Client Patient Clinical Site(s) Regulatory authorities	**Environmental influences**

Table 4.5: Physicians' conceptual understanding of how situational awareness influences ISO14155:2011 compliance by refining dimensions and key issues within the core theme.

4.5 CHAPTER SUMMARY

This chapter expresses the wealth of rich data gathered from PPD physicians' perceptions of regulatory compliance DM reality stratified using the four core themes (decision theory, errors, ISO14155:2011 compliance and situation awareness) identified from the literature review (chapter 2). The findings depict a breadth and depth of knowledge covering decision theories and ways to meet regulatory compliance requirements. The diversity of physicians' perspectives and contrasting points of view acutely illustrates that no single model of regulatory compliance DM exists within PPD. However compliance decisions are not made in an irresponsible manner.

The findings illustrate that DM depends on problem complexity, available expertise and level of impact but the approach taken can vary each time as it is not formalised or proceduralised. Some physicians go alone, others engage peers or delegate but all retain autonomy and accountability. This has led some to describe their DM approach in this context as ad hoc, personal, confusing and inconsistent. Although PPD physicians do view regulatory compliance DM from different standpoints there appear to be similarities and overlaps with classical and behavourial DM approaches. Foremost amongst them is the way each physician blends DM themes and categories individually into some mental construct of the presenting compliance case using an unknown mix of instinct, intuition, experience, analysis and conceptual thinking. DM in this context appears complex, situated and appears to involve a reasoned approach, influenced by various factors such as business rules, contractual requirements, client needs, personal perspectives, engaging second opinion and patient considerations using available data in a set timeframe. Decisions made in this way can introduce occasional error but PPD internal mechanisms exist to correct and iteratively refine any pressing situation. However, the majority of physicians do not appear to be overly concerned with their individual DM style or approach, nor actively considered ways to change or potentially improve.

There is a good physician awareness and understanding of what is needed to comply with regulatory requirements, particularly the new ones applicable to medical device trials for ISO14155:2011. The findings show that compliance with the new

standard needs not only awareness and understanding but planning and preparation allied to robust study execution with good analysis and reporting activities from the trial data. The general consensus being that the regulatory compliance decision-making environment in PPD is constantly challenging, complex and always

"…. a learning platform." Cuillin,6

However, PPD is not perceived to be a learning organisation as compliance decision-making is viewed as situated, reactive, inconsistent, implemented whatever the consequences, error investigation can dominate, but limited improvement suggestions are carried forward. Consequently, DM criticism in this context ranges from irritation to annoyance as seen in the following irksome assertions:

"…. I get frustrated with dogmatic approaches to decisions when sometimes pragmatism is required. This applies to PPD as a whole, not just the department. That's easier said than done sometimes when you are faced with legislation which is very clear. Dogmatism works well when things go well. But when out of compliance, or suddenly facing an impossible task, you have to be pragmatic." Galloway,7

"…. you've got to decide more quickly and without much context than any other place I've worked. Quality is less important as long as you give an answer received according to people's timeframes but there's not much critique of whatever the deliverable is." Cairngorm,3

"…. there could be multiple paths to the correct answer, many destinations could be ok, but the path to get to the best may not be obvious." Lammermuir,4

"…. there isn't a set process within PPD whereby we examine all our successes and failures." Torridon,10

In essence, this chapter highlights that regulatory compliance decision-making by physicians is well established in PPD but, as a consequence of ambivalence and variety of approaches utilised, it may not be as effective as it could be. The next chapter attempts to analyse and interpret the physicians' situational responses and attempts to make sense of their perceptions in light of the literature.

CHAPTER FIVE : DISCUSSION OF RESEARCH FINDINGS

5.0 CHAPTER INTRODUCTION

This chapter builds on the research framework (chapter 2, figure 2.4) by developing the research findings (chapter 4) using the four core DM concepts (decision approaches, errors, situation awareness and ISO 14155:2011 compliance), identified from literature review (chapter 2), as a template for discussion. Some themes are discussed separately and others combined for synthesis where appropriate. The research output comprises two conceptual frameworks, which are constructed from the physicians' empirical assertions, guided by the four core DM concepts. Firstly, physician regulatory compliance decision-making in context and, secondly, covering regulatory compliance requirements for ISO14155:2011. The process behind this approach is illustrated in figure 5.1.

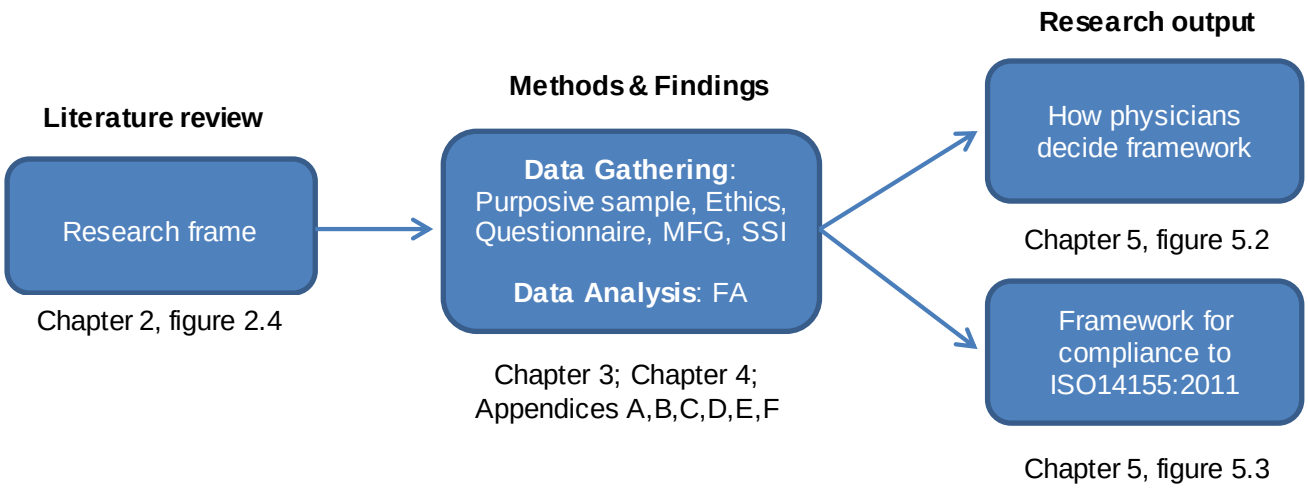

Figure 5.1: Linking the research frame to methods used, empirical findings and research output (compilation by author).

5.1 DECISION - MAKING IN PPD

The research findings presented in chapter 4 show that PPD is a highly structured clinical research company, where a traditional top-down DM hierarchy prevails comprising executive leaders, specific departmental areas with organisational charts, functional roles linked to job descriptions and documented procedures for running clinical trials. In this context regulatory compliance decision-making is complex and convoluted, led by company physicians using various DM approaches, a wide

knowledge base, various sources of information, in a broadly supportive environment. However, despite PPD having both a QMS and systematic approach to most things, physicians' DM is ambivalent given they ratify trial device and treatment, patient's preferences are absent and there is no formal decision-making process or procedure in the company. This appears consistent with DM messaging of authors working in other healthcare fields (Elwyn *et al*., 2014; Bjørk and Hamilton, 2011; Banning, 2008; Lauri and Salanterä, 2002).

When it comes to making specific compliance-based decisions the responses indicate that PPD decision-makers utilise a variety of styles comprising a blend of traditional, behavioural and hybrid approaches, which can be summed up as follows:

"…. within PPD making decisions is not necessarily formalised. I think the decision point of that is following an analysis whereby you have to assess whether that is really pertinent or not." Moffat,1

"…. I think there are various shades of that." Lammermuir,5

It appears that compliance decision-making appears to be loosely based on a mix of strategic intent, company goals and objectives, and granting decision-making rights to those who can gather and assess the best information in/from the functional departments relevant to the decision (chapter 4). The key to this approach being

"…. control over what is important to us as opposed to what is interesting or fascinating and how it aligns against the business strategy." Munro,3

The findings illustrate that in PPD decision-making rights fall primarily to physicians who occupy senior departmental posts and functions. In this environment regulatory compliance DM is a matrix covering strategic to tactical and from collaborative to individualistic. Although regulatory compliance situations differ across layers there are DM commonalities. Strategic compliance issues are escalated to executive management, with context and data presented infrequently, high level or generic implications determined, potential approaches identified, options and results of those actions assessed, with levels, impact and extent of service provision discussed. Following the presentation a decision occurs and actions implemented. Tactical vigilance decisions are more systematic and specific with various client, study and company risks identified with decisions made by physicians, or physician-led teams,

guided by procedures and formal agreements. Here, safety information is subject to regular review using standard operating procedures and product-specific work instructions that clearly define roles, responsibilities and tasks. Decision-making is deemed effective by minimizing risks to the intended study subjects via documented guidance and formal practice (chapter 4, sections 4.2, 4.3, 4.4).

Many strategic and tactical decisions occur daily frequently via group collaboration with multiple physician input. Contrastingly a small number of physicians avoid group input and make individual functional decisions in isolation. However, both approaches present problems. Firstly, company size, differing time-zones and geographies, linked to varying personnel availability results in alternative opinions and professional guidance being sought which can introduce inconsistencies

"…. the great benefit of PPD is that we make decisions and we go with them. The terrible thing is that we make decisions and go with them. I much prefer the former even if you are not guaranteed to make the right decision every time". Sidlaw,5

"…. it just depends on who's around on the day." Torridon,9

Secondly, it presumes that the decision-makers have all the commercial, scientific, regulatory and people skills to make an informed decision.

" ….. I think our people are put in place based on their skills and knowledge but I haven't seen, at my level, any structured, engineered model to make those kinds of decisions. I think they are embodied in the directors and those tasked with leadership and in their individual experiences." Lammermuir,5

Contrastingly, some respondents indicated that these DM approaches provide PPD with some flexibility when responding to client needs. However, others stated that it introduces risk, variability and error which can lead to frustration and confusion (chapter 4). So, currently PPD DM practice provides mixed messages.

5.2 PHYSICIAN DECISION-MAKING IN PPD

The lack of a formal DM process means that the physicians often seek second opinion, alternative counsel and/or are left to their own devices when it comes to

making regulatory compliance decisions. Although advances in DM theory have postulated ways forward to improve medical decision-making via classical extensions, such as evidence-based practice and shared decision-making (Reyna and Brainerd, 2011, Spring, 2008; O'Connor, Llewellyn-Thomas and Flood, 2004), PPD physicians' don't utilise them. The respondents tell how instinct, intuition and industry experience have shaped their ability to notice cues, assess situations using mental patterns, proactively address errors, whilst balancing other influencing DM factors such as regulatory requirements, peer opinion and organisational goals and rules (chapter 4.2.2). Although this suggests both analytical and behavioural elements, physician DM fluctuates frequently depending on the compliance situation and presenting contextual variables and influences.

Other comments appear to illustrate that selective NDM factors highly influence the decision process too. These include familiarity with the current situation, the values and perceptions of decision makers; the importance of cognitive interpretation; the organisation's construction of social reality; mentally labelling and categorizing events or experience into the organisation's decision types; the dominance of routines in decision-making, and the absence of a direct, causal relationship between the organisation and its social surround (chapter 4, sections 4.2.2, 4.2.3).

As stand-alone comments there does not appear to be a direct correlation between them, but when taken collectively, these dimensions appear to mirror NDM themes (chapter 2, section 2.2). For example, the findings suggest that when physicians' are faced with a regulatory compliance decision-making event various contextual influences kick-in comprising instinct, intuition, prior experience, the use of formal procedures, applied thinking and reasoning to a greater/lesser extent (chapter 4, section 4.3.2). Analysis suggests that the physicians construct a mental image of the current event via pattern matching the situation's primary causal factors against schematic memory structures built from intuition, gut instinct, prior knowledge and expertise which echoes the NDM works of Nemeth and Klein (2011), Klein (2008) and Nutt (2008).

Additionally, there are parallels with authors who postulated that medical experts' decision-making changes over time, often relying on instinct, gist processing and pattern recognition (Klein, 2008; Spring 2008, Lorenz *et al*., 2005; Klein, 1997;

Arkes, Dawes and Christensen, 1986). However, disagreement arises about the impact factor of these behaviours. Strong traditionalists advocate that intuitive DM by experts precisely highlights the poor situation that EBM praxis was intended to correct. Such practice is termed *eminence-based medicine*, represented as someone repeating similar blunders, with increasing confidence, over many years (Isaacs and Fitzgerald, 1999). Contrastingly, behavioural theory suggests that intuition should be commended, rather than vilified as mere clinical opinion, because when engaging high-stake scenarios, accomplished clinicians advance further via using intuition in their DM instead of a strategy based more of analytical deliberation (Lorenz *et al*., 2005; Politser, 1981).

Within PPD, the findings suggest that DM is not traditional or behavioural but some form of pulsing hybrid where contextual features (such as situational data, organisation objectives, clinical expertise, experience, instinct, company procedures) are considered, picked and used, as and when needed. DM appears to echo dual processing and NDM (chapter 2, sections 2.1, 2.2) given the fluctuating way physicians make and take decisions in this environment using intuition, experience, pattern matching and mental processing (Klein, 1997). However, this contrasts sharply with clinical DM research which has mainly concentrated on whether to perform medical procedures on patients using either traditional positivistic-systematic perspectives or a behavioural humanist-intuitive approach (Reyna, 2008; Thompson, 1999). In PPD, it appears that physicians recognise that each compliance situation requires a different DM approach, but possess sufficient skills to adjust and combine methods, where needed. This fluctuating DM approach suggests physicians can lose focus on holistic patient care and echoes the work of Elwyn *et al*. (2014). Furthermore, despite published NDM paradigm and models being presented (chapter 2, section 2.1) this research suggests that PPD physicians are neither aware of them, nor are using them. The physicians are conscious that they utilise prior knowledge, skills, experience and intuition to comprehend and integrate situational cues and data into some form of dynamic, cognitive representation of the situation they are trying to evaluate (chapter 4, section 4.1). However, the mechanism how this occurs is invisible, unknown and can even be unconscious to them. Contrary to using a specific DM model, it appears that each physician consciously seeks data from a variety of themed influences then, undertakes some

personal mental DM diagnosis for regulatory compliance. These themes appear to be drawn from key DM models (chapter 2, sections 2.1, 2.2) with the findings suggesting that NDM dimensions are wrapped in a dual processing frame. This could explain how intuition and conceptual thinking impacts the effects of experience and data analysis within physician DM in context. However, there are relatively few open literature reports that provide empirical study evidence that illustrate and analyse how NDM links to medical DM for physicians working in non-medical environments (Christ, 2014; Reyna, 2008; Klein, 2008; Reyna, 2004; Klein, 1997).

5.2.1 Case for a conceptual framework for physician decision-making in PPD

The empirical findings illustrate that the PPD physicians' DM shares some similarities and parallels with NDM from other fields. Firstly, although depicted as a communicative theory (chapter 2, section 2.2), NDM is useful for sociological analysis, that focuses on cognitive DM as it transpires in real-world, changing and complicated settings, with data collected from descriptions and analysed using categorisations (Zsambok and Klein, 2014; Nemeth and Klein, 2011; Klein, 2008; Nutt, 2008; Salas and Klein, 2001; Zsambok, 1997; Orasanu and Connolly, 1993).

Secondly, NDM and dual processing suggest that decision-making occurs across a cognitive continuum starting with intuition, passing through a quasi-rational cognitive stage, then ending in analysis (Reyna; 2008 a,b; Hammond, 1998, 1996, 1993). This research suggests that PPD physicians assess regulatory compliance DM similarly via a situational spectrum: using instinct and intuition to recognize patterns of cues developed from their prior contextual experiences; memory; combining subject awareness with simulation to generate cognitive representations of the environment, then selecting action courses under time constraints, with significant ramifications, and insufficient data mirroring the work of Wu, Davis and Bell (2012), Klein (2008, 1997); Repovš and Baddeley (2006); and Benner (1984).

Thirdly, the author suggests that these findings indicate that the physician assertions and perceptions (chapter 4) can be combined with dual process modeling and elements of NDM identified during literature research (chapter 2), to create a new and novel framework for regulatory compliance decision-making. Namely, via use of specific NDM models and themes, comprising the following components:

CCT where decision-making fluctuates across a spectrum (Hamm, 1998, 1988a; Hammond et al., 1987). The **Endsley** (1997) approach which highlights where analytical DM processing utilises situation assessment of environmental information to construct a mental representation of some type. The **SRK model** which depicts cognitive DM control layers where task and levels of performance correlate with declining familiarity with environmental scenarios (Rasmussen, 1993, 1986, 1983). The **RPD model**, which describes how intuition and mental processing can be used to generate a cognitive representation of the environment, by accounting for how individuals react given time constraints, insufficient data, and changing environmental influences. The decision-maker makes a form of diagnosis by actively searching for an explanation of the diverse cues. Mental models are then used to evaluate goals, actions, and plans by critiquing and modifying the representation until it fits the environmental information (Klein, 2008; 1998; Roth, 1997). The **RM Model**, where metacognitive skills (identifying key situational assessments, checking for completeness and consistency, generating alternatives when excess conflicting information is encountered) supplementing recognition processes in decision events involving novel situations (Cohen, Freeman and Thompson, 1997).

However, although each NDM model utilises distinct types of cognitive activity, no naturalistic model has been proposed for physician's to use in non-medical environments (Chapter 2). Additionally, since no single model of physician decision-making has been universally accepted, this research suggests that blending NDM themes could align with authors who have called for new ways to tackle contextual DM in healthcare settings (Christ, 2014; Gund *et al*., 2012; Lipworth, Strong and Kerridge, 2012; Légaré *et al*., 2011; Milkman, Chugh and Bazerman, 2009; Stacey *et al*., 2010; Nutt, 2008).

5.2.2 New conceptual decision-making framework integrating DM themes

Literature review and the research findings show that PPD physicians have no formal decision mechanism but use a variety of means to make and take compliance decisions. To help plug this gap, a new conceptual decision-making framework, illustrated in figure 5.2, has been constructed by synthesizing the key DM components identified during the literature search (chapter 2) and integrating the views of the PPD physicians gleaned from the empirical findings (chapter 4).

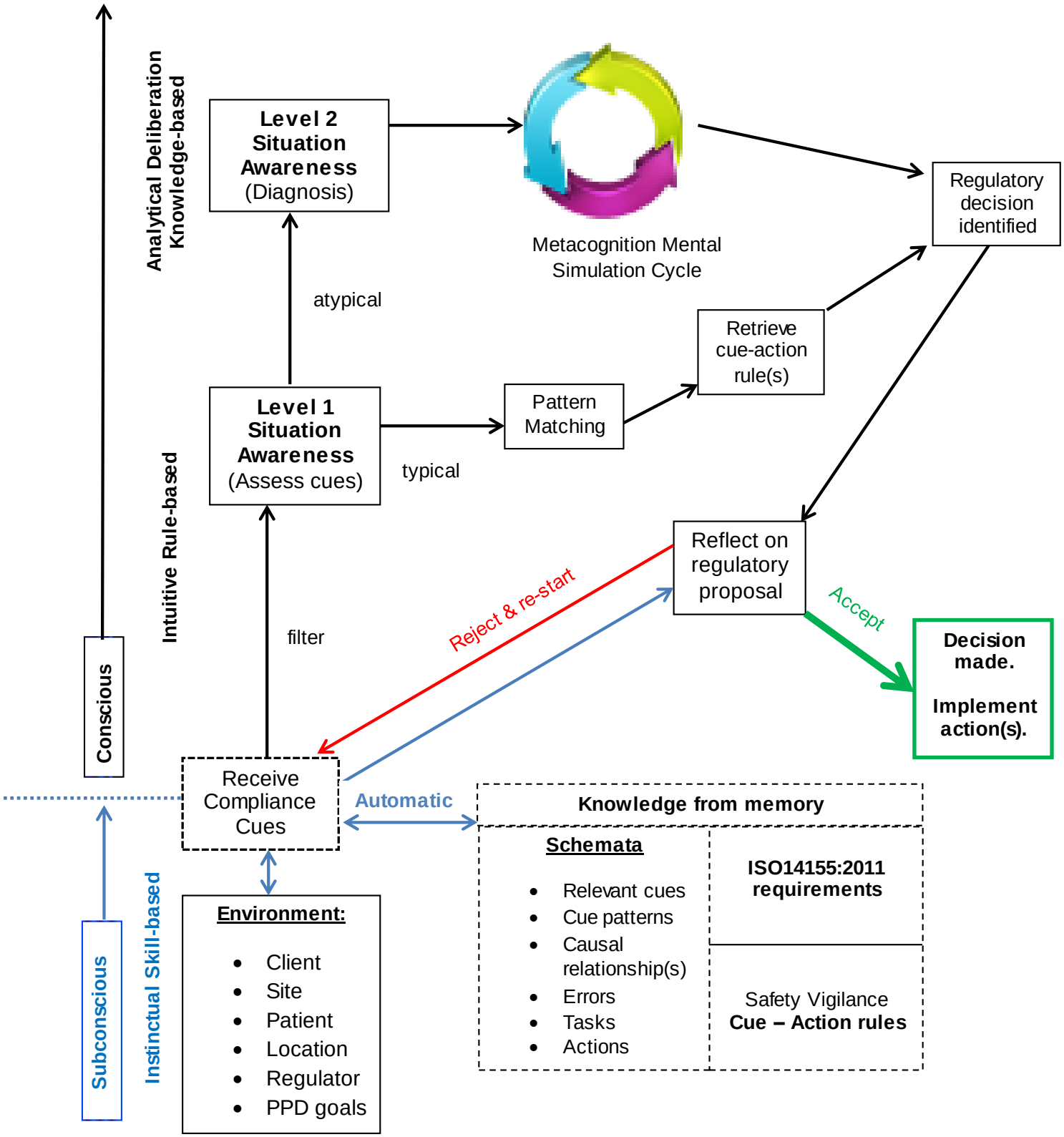

Figure 5.2: New physician decision-making framework integrating DM themes synthesized by author referencing prior works (Schweizer, 2012; Klein, 2008; Cohen, Freeman and Thompson, 1997; Endsley, 1997; Gordon and Gill, 1997; Rasmussen, 1993; Noble, 1993; Hammond *et al.*, 1987; Rumelhart, 1980; Minsky, 1977) and empirical data.

In figure 5.2 the NDM paradigm features heavily in this framework as it emphasizes two physician DM traits: expertise and ability (Kahneman and Klein, 2009; Hodgkinson and Starbuck, 2008). Firstly, it guides the physician to remember prior experience via clues in new scenarios and, secondly, to observe and move clues from past participation in unrecognised situations to help construction, consider and reflect on new ideas for the current position (Kahneman and Klein, 2009).

In this study the conceptual NDM framework focuses on situational assessment, instinct, intuition and a reasoned approach to physician DM as described during the empirical research findings (chapter 4). The framework's foundation is the SRK model with its three control layers based on skill, rule and knowledge (Rasmussen, 1986, 1993). Data is gathered from two sources: the environment (lower left) and from the physician's memory (middle section at figure base) and subsequently enters the decision-making processing that occurs in the physician's mind.

The environmental component covers internal PPD influences such as company versus departmental considerations, people, process and procedural concerns (chapter 4, section 4.6). Additionally, the environmental component covers potential external decision-making influencing factors such as client, site, patient and regulator considerations (chapter 4, section 4.6.2).

The memory schemata is compiled from schema theories which reject the atomistic view of mental processing that suggests the world ultimately consists of logical facts or atoms that cannot be broken down any further (Brewer and Nakamura, 1984). It maintains that some phenomena cannot be accounted for by simply joining together smaller theoretical constructs, and so larger theoretical entities, such as conditional reasoning, are needed to deal with these phenomena (Schweizer, 2012, Reason, 1990). The physicians' responses indicate that memory knowledge within PPD's vigilance department consists of many facets, including compliance decision-making types, planning activities for ISO14155:2011, proactive consideration of errors, organisational goals and objectives, various cue-action rules for the department as well as prior experience of similar scenarios, patterns and relationships (chapter 4, sections 4.3, 4.4 and 4.5). So, when considering DM compliance in this context an overall regulatory compliance consideration was deemed appropriate.

Furthermore, the subconscious consideration is based on the work of two influential theorists, Minsky (1977) Frame Theory and Rumelhart (1980) Schema Theory, who developed the building blocks of cognitive storage and processing with essentially similar ideas. Minsky (1977) was primarily concerned with the way schemata guided encoding and storage of information via pattern recognition, whereas Rumelhart (1980) worked on text comprehension, memory for stories, the embedded nature of schemata and the relationship between old and new knowledge. Common to both theories is the notion that high-level knowledge structures contain information slots which contain a certain data types. If the current environmental input fails to provide specific data to fill the slot then they take on default assignments. This is akin to falling back on stereotypical positions derived from past values and experiences.

Once the information enters the framework (in figure 5.2) it is then processed at one of three layers: instinctual skill-based processing, intuitive rule-base processing, or knowledge-base analytic processing depending on the decision maker's prior experience of the subject and their assessment of the situation. This follows Noble (1993) and the SRK model (Rasmussen, 1983) via referencing its structure, levels and terminology (chapter 2, figure 2.4).

When physician decision makers have high skill-task experience, they will convert knowledge information and influencing environmental data instantly at the skill-base performance level. Interpretation and integration of clues, or constructing alternative options is not needed, since DM occurs via reaction to all influencing factors at an subconscious and automatic level. Execution is controlled by pure stimulus-response linkages refined at the neurological layer. Since behaviour is attention specific, resources are minimal given there is no demand on cognition. This follows the instinctual and automatic decision-making approach of seasoned experts when presented with familiar scenarios (Christ, 2014; Zsambok and Klein, 2014, Zsambok, 1997; Roth, 1997; Rasmussen, 1993a, 1993b, 1983).

Figure 5.2 shows that subconscious mental processing (solid blue lines) occurs automatically via receipt of situation assessment of the environment and memory cues of the influencing variables. The dotted blue line (left hand side of figure 5.2) depicts the interface where DM transitions from subconscious to conscious. It is adapted from clinical contexts where the process of subconscious and conscious DM

has been analyzed using decision theory. Specifically it follows Morris (2011) who suggested that subconscious decisions involve an automatic process akin to numerical computation whereas conscious decisions involve individual experiences indicating personal behaviours are governed by genetic rules but modified by environmental influences. Crossing the line is a blend of System 1 and System 2 dual processing concept (chapter 2, section 2.1) combined with CCT oscillation and SRK leaps (chapter 2, section 2.2).

When physicians are aware of a scenario, but have little prior experience, they can process data and function across an intuitive rule-base layer. In this context intuition starts with subliminal understanding or knowing without conscious recourse to thought, observation or reason but develops into rational thought with increasing DM complexity. DM begins with level 1 situation awareness where some active cognitive processing is required, as the decision-maker filters data, applies discretion, responds to signals and signs by considering a variety of cues and principles, controlled and governed by rules and reason. This point develops Rasmussen's (1983) SRK model by incorporating elements from RPD model (Klein, 2008), Noble (1993) and Endsley's (1997) approach to decision-making, by involving situation assessment, utilising business procedures as well as referencing pattern matching and intellectual intuition. As the physician's assess the information, the cues trigger retrieval of appropriate cue-action rules from memory, through stored past experience associations, which indicate the desired goal and specific action sequence to be executed (Gordon and Gill, 1997).

However, if rule-based intuitive processing does not provide a satisfactory decision, or situation is atypical or novel, the decision process can move upwards in the framework to a more detailed and reasoned analytical process via a mental simulation cycle. This is knowledge-based analysis. It begins with level 2 situation awareness and involves creation of a constructed understanding of the situation, including the compilation of causal stories, mental models and/or tentative diagnosis using a metacognition mental simulation cycle. Essentially this is a heavy analytical processing cycle using conceptual information.

Meta-cognition starts with the Endsley (1995) model but escalates to the RM model (Cohen, Freeman and Thompson, 1997) to confirm the results of the recognition

process and improve understanding of the novel and/or atypical situations. Here pattern perception is insufficient, as no recognizable order fits the presenting scenario, and decision makers have not got rules saved from prior experiences to reference. The meta-cognition cycle follows Peirce (1997) three-stage exploration process comprising deduction, induction and abduction. This is where the decision maker designates meaning to clues and assimilates them into a conscious mental representation of what is occurring, processes the data with respect to goals in memory then runs cognitive simulations in evaluating an action plan. Arduous data retrieval from memory and subsequent analysis supports DM and problem planning actions (Christ, 2014; Klein 2008; 1997, Orasanu and Connolly, 1993).

Furthermore, if the situation is difficult, complex and time allows, the decision maker can repeat evaluative mental simulations, searching the environment for further data to explore alternative scenarios, actions or plans under consideration. In this way the cognitive simulation is used to create notions about supplementary clues which could explain why physicians seek confirming evidence. This is an essentially similar process to physicians undertaking clinical diagnosis (chapter 2, section 2.1).

In NDM modeling emotion and reflection feature prominently but, in contrast to many NDM models, some PPD physicians indicated that emotion is not an influencing factor in this environment. However, the use of reflection does appear to add value (chapter 4, section 4.1.3). The findings suggest that the final decisions need stage-gate consideration; either passing to the implementation phase, or returning to mental simulation and re-evaluation of the DM process. Essentially, reflection in this context is acting as a stop/go check and ratification mechanism for the decision-making event and is depicted on the right side of figure 5.2.

This DM framework should cater for all physician approaches, ranging from those who pause and consider multiple options, to those who generate only one explanation or scenario, generate one overall action to be taken (i.e. decision) and plan the sequence of steps to carry out the action. However, if the scenario, action or plan fails to meet minimum criteria, for example via false mental model(s), or if the decision is heavily affected by time constraints or errors, then the physician can generate a new scenario by running through the cycle again (rejection red line in figure 5.2). Whatever choice is ultimately selected, it is executed (green line figure

5.2), and the physician can subsequently monitor the environment to determine whether, or if, additional changes need to occur via further situational assessment.

Finally, the layers serve to characterize physicians with differing degrees of experience of therapeutic area or presenting study information. So, an expert should be able to move quickly between the three levels depending on familiarity with the scenario, task or situation. However, when a new regulatory change arises, lack of familiarity with the presenting symptoms can move an expert back to another level. This accounts for the physicians' comments and CCT model that indicate decision-making as an oscillating spectrum pulsing between instinct and analysis.

In summary, although the NDM models were presented individually (in chapter 2), when combined with the research findings (in chapter 4), they collectively appear to indicate that physicians use several pathways to comprehend and integrate situational cues, knowledge and environmental influences into a dynamic frame of the situation they are trying to evaluate or diagnose. This new framework (figure 5.2) was constructed by author and synthesizes elements of prior DM works from literature review (chapter 2) with empirical findings (chapter 4). It incorporates subconscious and conscious dual processing, naturalistic themes and the use of reflection as a stage-gate review for shaping physician regulatory compliance decision-making. This allows the physician to assess a descriptive discretionary decision path, make a determination, then either pass to the implementation phase, or re-run the mental simulation to further evaluate the DM process, if required.

5.3 SITUATION AWARENESS

In this research situational awareness comprises the interplay between how PPD physicians make regulatory compliance decisions in clinical research, the new ISO14155:2011 requirements for medical devices, and what influences DM in this context. The findings indicate that the application, emphasis and significance of PPD physician DM varied considerably depending on the regulatory requirements, required skills, organisational role, assigned duties and vigilance perspectives. However, the research findings show that situational awareness is the catalyst for acquiring sufficient environmental, regulatory and expert knowledge required for

taking an informed decision for subsequent utilization within the compliance DM framework, as illustrated in figure 5.2.

This suggests that in this context regulatory compliance decisions can essentially occur at one of three situational hierarchical levels: firstly, the operational level (for service execution); secondly, at the tactical level (for design, establishment, maintenance and improvement); and thirdly, at the strategic level (for significant organisational regulatory compliance decisions based on company goals and objectives). However, as there is no formal DM process, nor decision aids used in PPD, the physician DM influences and approaches can potentially affect the compliance status of the organisation (chapter 4, section 4.3).

From the physicians' responses two distinct situational DM perspectives emerged. Firstly, a senior group of physicians, comprising a small number of highly experienced leaders, primarily immersed in strategic business decision-making phenomena such as corporate strategy, regulatory positioning, client engagement, financial discussions, productivity, competitiveness and marketing. These doctors occupy the highest PPD organisational levels, such as departmental head, and engage mainly with the board of directors, CEO and other functional executive departmental leads (aka C-suite), tending to only interact occasionally with other physicians and vigilance staff at the tactical level. For them, ISO14155:2011 compliance DM concerned assessing its impact on the whole company but this was viewed as an occasional, collaborative and delegated activity with data gathered from many sources (chapter 4, section 4.3). This can be summed up as follows:

".... positions at the executive level are obviously carrying an enormous amount of autonomy but rarely are any of these decisions taken in isolation." Moffat,1

"…. there aren't many people in our organisation who've got the full spectrum of experience that equates with a product development lifecycle …. running controlled clinical trials in the pre-approval arena, commercialisation of product, single market versus global scale, then the post-approval commitments." Torridon,8

Although ultimate regulatory compliance DM responsibility resides with the Chairman and CEO, compliance DM at executive level was viewed as complex, laboured, fragmented, opinionated, client-focused and time bound, but ad hoc. Although sympathetic to scoping issues, the main physician criticisms of the DM approach concerned lack of direction, timeliness of response and DM variability leading to potential unplanned, undesired and out-of-control compliance related events which would then take time, money and resource to help correct (chapter 4, section 4.1).

Contrastingly, physicians in tactical roles had an active and sustained interest in ISO14155:2011 from a compliance management perspective but also as a means to improve quality and operational performance. These doctors are situated at the upper echelons of the vigilance department but interact on a daily operational basis with the extended safety team on many client studies at various levels, but rarely with the C-suite. However, the findings revealed that although compliance with this new standard was expected, PPD possesses a mature quality management system where company policies and procedures directly guide the compliance status. Although not explicitly stated, the implication appears to be that the QMS acts as a governance mechanism for DM compliance within the company. However, the QMS was borne out of compliance with pharmaceutical and clinical trial legislation and the new medical device requirements could potentially conflict (chapter 4, section 4).

For these physicians ISO14155:2011 compliance was clear and mandatory, characterized by a set of functional stages comprising tactical planning, trial documentation, study oversight, analysis and reporting against set time deadlines. Although similar to pharmaceutical clinical trial processing, the physicians indicated that they could be involved in any of ISO14155:2011 stages, although primarily responsible for engaging in decision-making at the planning and document management stages and in clinical evaluations (chapter 4, section 4.1). This differs from pharmaceutical trials where physicians are engaged in specific tasks such as medical writing and review of serious adverse event cases. Other perceptions from this group included a pro-active and systematic consideration of people and process issues, environmental features and error minimization when it came preparing for departmental compliance with the standard (chapter 4, sections 4.2, 4.3, 4.4).

5.4 NEW FRAMEWORK FOR ISO14155:2011 COMPLIANCE

The main objective of this thesis was to ascertain how PPD physicians made regulatory compliance decisions, but another underlying research driver was to ascertain how the physicians perceived compliance with ISO14155:2011. Although many physicians were ambivalent on DM and disagreed on the most appropriate approach, there was broad consensus about what physicians must do to meet regulatory compliance pertaining to safety, quality and efficacy of conducting medical device trials in humans. This is illustrated in a new framework in figure 5.3 developed from the physicians' empirical assertions. The research findings indicate that three overlapping situational components influenced both context and physician decision-making directly: firstly awareness of the external standard driving change - ISO14155:2011; secondly, PPD: the clinical research organisation affected by the change, particularly the safety vigilance department; and thirdly, the influencing factors impacting physician decision-makers affected by the change (chapter 4, sections 4.2, 4.3, 4.4 and 4.5).

All physicians were well aware of the pending regulatory change and some had a broad understanding of the requirements. This was surprising given the study data was collected some months after initial publication of the requirements and the information was only beginning to surface on industry webpages. However, many of the physicians had routines, contacts, access to training materials and/or information sources that kept them abreast of regulatory developments (chapter 4, section 4.3.1)

Despite PPD physicians operating at different levels within the company the findings show that all physicians clearly understood that ISO14155:2011 is a new compliance standard for conducting and performing medical device clinical investigations. The majority were also aware that the ISO standard specified some general requirements designed to protect screened patients. The key features being ensuring scientific handling of trial explorations and assisting sponsor companies, clinical monitors, ethics committees, investigating doctors, regulatory authorities and notified bodies affected by medical device compliance scrutiny (chapter 4, sections 4.3 and 4.4). The wealth of perceptions and understandings about what constitutes compliance

with the legislative process for compliance with ISO14155:2011 (chapter 4, sections 4.5 and 4.6) enabled the construction of the compliance framework in figure 5.3.

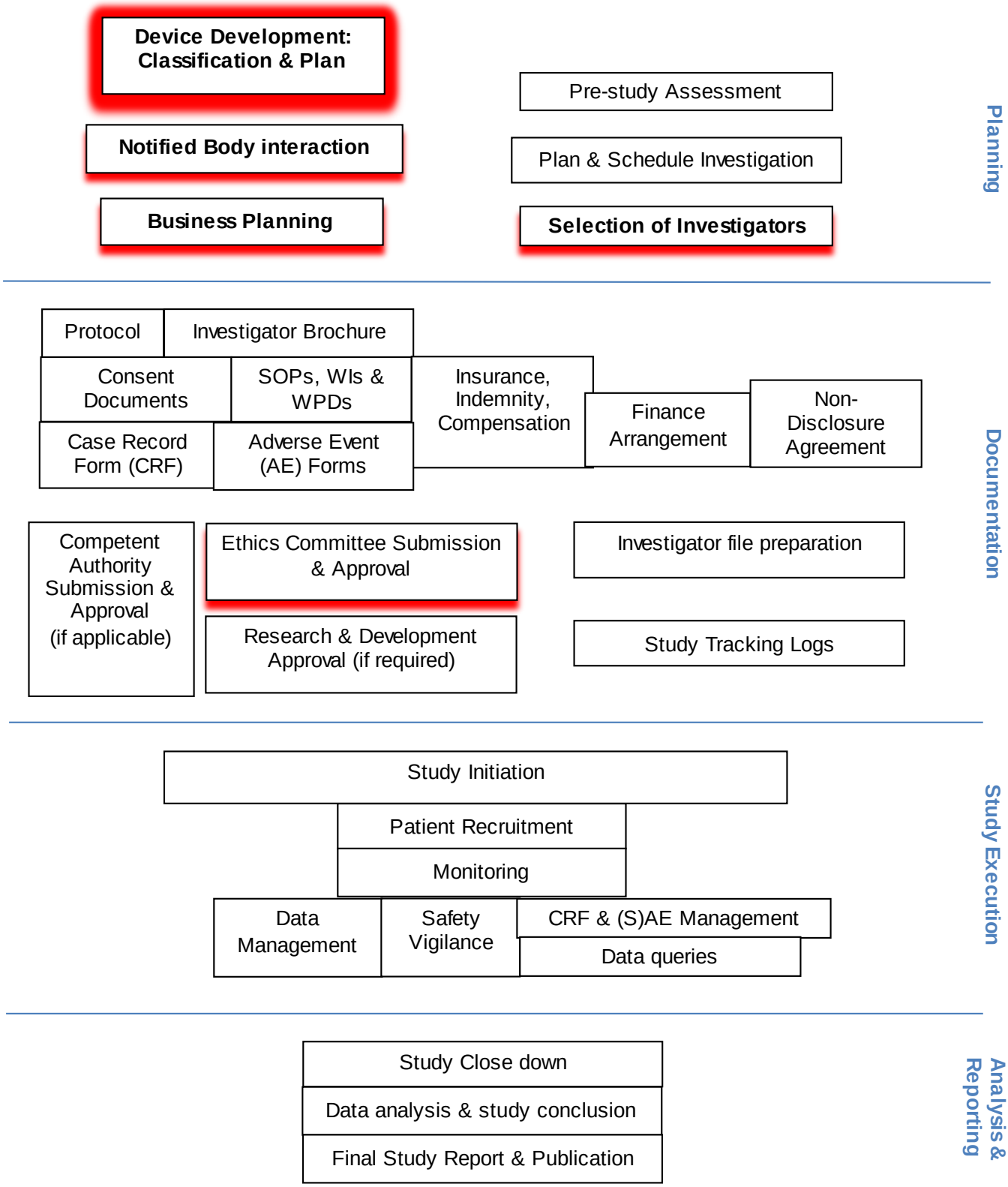

Figure 5.3: Medical device clinical investigation framework for ISO14155:2011 compliance highlighting key themes and decision-making points

Although there was general consensus among the physician responses that compliance with ISO14155:2011 was mandatory, there was an acceptance that any change needed to be assessed. This was to evaluate the requirements but also fit into the existing quality management structure, by identifying key interactions and functionality for continual improvement, whilst allowing corporate regulatory strategy, PPD decision-making and organisational flexibility to be maintained (chapter 4, sections 4.1, 4.2, 4.3, 4.4).

Galligan (1996: 3) argued that the mandatory nature of compliance had to recognise and adopt a “social paradigm" for understanding legislative processes. This research not only utilises empirical study and interpretation of the way that legislation “really works”, as Galligan argued, but uses insights from social science disciplines in analysing and making sense of the convoluted and complex environment of medical device clinical research “to penetrate and comprehend social reality at levels which are beyond simple common sense” (Galligan 1996: 3). Therefore, this research proposes that a medical device clinical investigation framework for ISO14155:2011 compliance can be constructed from the physician’s perspectives, dividing requirements into four distinct layers covering planning, documentation, study execution, analysis and reporting. Each layer is depicted in figure 5.3 with associated narrative descriptions in the following sub-sections.

5.4.1 Planning

The first layer in the compliance framework for ISO14155:2011 (figure 5.3) is planning. This is essential because medical devices regulations mandate that products are safe, effective, have the highest level of patient safety, but also not so stringent innovation and competitiveness in the sector is stifled (Kramer, Xu and Kesselheim, 2012; Smith, 2012; Cuffman and Redberg, 2011). The research findings show that PPD is a service provider that ‘operates in the GxP environment’, balancing ‘alternative positions and points of view’ based on contextual knowledge, past experience and information at that moment in time, but be able to ‘influence the process’ aligned to ‘business strategy’ (chapter 4, sections 4.1 and 4.4). However balancing the regulatory compliance elements with organisational know-how is tricky and challenging.

Planning commences (figure 5.3, top left hand box) with physicians' advising on device development and classification. Here the physicians' experience of clinical trial context, pharmaceutical compliance environments, coupled with expertise in medical devices regulations, can help the client with planning product development decisions, particularly when determining which of the three European medical device directives applies then navigating through study compliance decisions and overlaps with the clinical trial directive and ISO14155:2011 (chapter 4, section 4.4.2).

Additionally each directive defines specific requirements that medical devices must fulfil if they are to be approved and receive CE marking, so the physicians appear to use their skills, knowledge and experience to advise on business planning actions, interactions with the selected notified body, or using their technical experiences helped clients determine their conformity assessment route via risk assessment and device classification advice. This can be summed up in the following quotation

"…. class III devices need a certified quality system and a design dossier, but class IIa/b products only need quality system and technical file. Understanding the similarities and differences between AIMDD, MDD, and IVDD helps classify devices into classes I, IIa, IIb or III based on their level of risk to patient and intended purpose, but ISO14155 now means clinical evaluation is required." Ochil,6

Furthermore, physician involvement in core medical monitoring components is also needed which can cover selection of trial investigators, overseeing eligibility criteria, essential safety and performance requirements for the products, as well as reviewing the clinical data essentials, lab results and interfacing with ethics committees (chapter 4, sections 4.3 and 4.4). Other planning activities include compliance preparation, study scheduling and pre-study assessment decisions at other levels too, such as establishing communication channels, compiling CE marking applications, overseeing submissions to competent authorities and authoring post-market study notifications. It appears that these activities can run in parallel or sequentially through the planning layer. Essentially this means that PPD physicians see their role expanding as this legislative change gets implemented, given the need to span the full spectrum of ISO14155:2011 compliance activities. Most physicians suggest it will be applicable to all medical device classifications with their

engagement fluctuating, as and when necessary, depending on the decisions to be made (chapter 4, sections 4.1, 4,2, 4.3 and 4.4).

5.4.2 Documentation

The second layer of the ISO14155:2011 compliance framework comprises documentation. The research findings illustrate that the physicians viewed documentation and document management as the most critical and essential component for providing written objective evidence to demonstrate compliance with the standard. The strength of feeling regarding documentation was a surprising finding. So, the researcher explored this dimension further by asking each physician to indicate what documents were perceived as compliance requirements. The output from this line of questioning appears in appendix G.

Annex E of ISO14155:2011 lists documents that companies must write, approve and use to demonstrate their compliance with the standard split into two sections: essential clinical investigation documents and other important documents (Smith, 2012; International Organisation for Standardisation, 2011). However, although the majority of the physicians were aware of this requirement, few had referenced the Annex E listing, many had never seen it, and some were unaware of it. No physician could re-create the list of twenty documents in Annex E exactly. Of the nine essential documents, and eleven important ones, only seven were successfully identified by all physicians. They included four essential types covering the investigator brochure, clinical investigation plan, case report form and ethics committee approval; and three important documents comprising the informed consent form, PPD operational documents and training records. Despite this apparent lack of awareness this was an unsurprising result given physicians' use similar document types in pharmaceutical trials and many of these functions are covered under the auspices of the PPD quality management system. The documents least identified were site selection report and device tracking logs most likely given they are new requirements within the standard.

Those physicians who came closest to replicating the complete list were functional whereas those with the biggest knowledge gaps occupied strategic roles. The functional physicians listed many more essential documents, policies and procedures than their executive counterparts in the C-suite, possibly due to their

greater understanding of the subject, of specific operational complexities, or being more up-to-date with other pieces of legislation. However, the strategic physicians were more likely to pick up the business related documents such as financial contracts and insurance certification.

Overall these findings suggest that, irrespective of role and the lack of training on this subject, the physicians possessed a strong perception of the essential and important document types needed for ISO14155:2011 compliance. It appears that the physicians were most likely using a combination of existing and/or prior knowledge when drawing up their lists but any compliance gaps could be easily remedied by referencing the standard directly. The main document types have been added to the framework documentation layer in figure 5.3.

5.4.3 Study Execution

Having approved documentation, policies and procedures in place only forms part of the compliance requirements for ISO14155:2011. When it comes to study execution, analysis and reporting, there was general consensus that PPD's centralized enterprise data and analytics approach leverages overlapping system and process synergies when processing clinical trials' data, irrespective of trial type, and that the company was well covered in this area. This is the third framework layer for ISO14155:2011 compliance and can be summed up as follows:

"…. In today's devices market, high-quality data and the insights gained from analytics of that data are critical for decision-making, competitive differentiation and the delivery of improved business outcomes. PPD has advanced its clinical data capability during the last three years, through new systems and application upgrades such as PPD CTMS, Preclarus and adaptive intelligent monitoring, but more can always be done to advance data quality, standardization and integration." Ochil,7

The majority of respondents indicated that addressing the core elements for execution of a medical device clinical trial was essential to cover the specific requirements of the standard. This included study set-up, initiation, patient recruitment, clinical site monitoring, data management as well as safety vigilance. These are depicted in figure 5.3. Although these activities were perceived to be

'*necessary overhead'* and '*just part of doing the job'*, some physicians perceived these elements to be little different from existing trial compliance interactions given they were broadly similar to pharmaceutical study processing. However, some functional physicians suggested that identifying how and where the specific nuances of the standard requirements should fit within PPD's vigilance department and the existing QMS was important. In this regard there was some additional commentary around potential advancements, such as undertaking a risk-based gap analysis to identify any specific ISO14155:2011 compliance nuances via mode of action / study design queries or evaluating how outcomes were measured, identified, addressed and controlled, as a means to improve (chapter 4, section 4.5). Others suggested that newly contracted medical device studies following ISO14155:2011 could be distinguished as full service awards involving co-working with other PPD functional areas, such as Data Management and Clinical Operations, where multiple touch points occur on common documents, such as case report forms, adverse event paperwork, study closure actions and final study reports. In this regard figure 5.3 suggests that increased physician input would potentially make them more visible to the wider members of the PPD study team, extending workload, influence and DM capabilities internally but also externally via additional client engagement.

5.4.4 Analysis and Reporting

The fourth layer of the ISO14155:2011 compliance framework is considering the study close-out requirements comprising study conclusion, issuance of final study report and its subsequent publication. These activities are also essentially similar to pharmaceutical trial requirements and are depicted in figure 5.3.

Finally, the red highlighted boxes (figure 5.3) illustrate the choice points where physician regulatory DM occurs for compliance with the main ISO14155:2011 requirements steps. Namely, medical device development, notified body interaction, business planning, selection of investigators and ethics committee submission and approvals. The importance of these areas seems to stem from the fact that physicians are actively engaged in peer discourse and debate relating to these sub-division topics. Their opinion is actively sought by others either as part of collaborative decision-making involving multi-disciplinary, cross-functional groups

and/or, in some cases, because the PPD physician acts as the primary decision-maker for that compliance topic (chapter 4, section 4.3.2).

5.5 CHAPTER SUMMARY

This study has found that in the clinical research context PPD physicians subconsciously apply an individual blend of instinct, knowledge, experience and intuition with conscious mental processing, diagnosis evaluation and reflection when making compliance related situational decisions. Although physician DM is viewed as ad hoc, personal, non-proceduralised and inconsistent, compliance decisions are not made in an irresponsible manner. However, there is a clear need to maintain flexibility and adaptability in PPD physicians' regulatory compliance DM as industry regulations continue to appear, requiring PPD to consider change, combined with an urgency to absorb knowledge rapidly, but react accordingly. This contrasts with established pharmaceutical companies where measured compliance DM changes to both product development and service application occur more slowly over time.

The primary output from this research is a cognitive decision-making framework (figure 5.2), built from elements of naturalistic and medical decision-making concepts. It blends intuition, experience and skill with analytical reasoning into a cyclical envelope incorporating contextual characterisations of knowledge structures, company processes, reflection and various internal and external influences on the PPD physicians making regulatory compliance decisions for clinical trials. The secondary research output is the construction of a framework for compliance with ISO14155:2011 requirements (figure 5.3), built from physicians' perceptions and assertions that identifies key "*acts that turn information into action*" (Eddy, 2005:9).

In addressing these new medical device industry requirements this study has involved exploring decision themes using an interpretive philosophy to gather data empirically from physician contextual experiences in a clinical research environment. The richness of the data was dependent on the interaction betwixt the researched and the researcher. From an author's viewpoint four key features emerged from the findings: firstly, physician decision-making in non-medical settings is complicated and fluctuates across a spectrum involving the subconscious and conscious mind where the experts' mental models can influence decisional practice. Secondly, using

an alternative methodology helped highlight the adaptive decision-making approaches as well as highlighting the various influencing factors on the physicians. Thirdly, the findings provided a means to construct a suitable framework to meet the compliance requirements for ISO14155:2011 from physicians' assertions. Finally, it has allowed PPD physician decision-makers to be seen, not as intellectually singular, but operating in a social realm overflowing with bewildering variables and inhabited with many industry players, where interaction co-jointly decides DM process and outcome, following Spring (2008); Patel, Kaufman and Arocha (2002).

The findings have led the researcher to consider, adjust and develop four naturalistic concepts and blend with medical decision-making themes for application to the clinical research vigilance environment. This has resulted in the construction of two new conceptual frameworks to aid both physician decision-making and compliance with ISO14155:2011. The first framework (figure 5.2) builds on existing decision themes in literature but utilises empirical assertions to potentially guide physician decision-making in context. The second framework (figure 5.3) interprets the physician perceptions to compile a discretionary roadmap for compliance with ISO14155:2011 in medical device trials. The author suggests that each framework could perhaps mutually reinforce the other such that, taken together, they form a moderate, but not insignificant, advance in helping PPD physicians make informed, collaborative, discretionary decisions to potentially influence contextual compliance related work in this clinical research department. However, in doing so, an important consideration will be the need to balance the regulatory compliance requirements with PPD's business objectives, existing quality management system as well as client contractual commitments.

CHAPTER 6 : SUGGESTIONS AND RECOMMENDATIONS

6.0 CHAPTER INTRODUCTION

This research has developed two regulatory compliance decision-making frameworks for use in the clinical research environment. The first expands decision theory by combining naturalistic and medical DM concepts with physicians' empirical perceptions to aid making regulatory compliance decisions in context (chapter 5, figure 5.2). The second introduces a potential roadmap for compliance with ISO14155:2011 requirements for medical device trials (chapter 5, figure 5.3). This chapter synthesizes the empirical findings (chapters 4 and 5) and reflects on the contribution of this work on the decision-making field.

6.1 FINDINGS IN LIGHT OF DECISION - MAKING LITERATURE

This thesis covers how PPD physicians perceive regulatory compliance decision-making in a clinical research setting. The findings show that PPD physicians have no formal regulatory compliance decision mechanism but use a variety of means to make and take decisions based on medical reasoning, personal expertise and experience intertwined with business management practices.

Within the clinical research context DM involves PPD physicians forming an individual impression of a presenting situation by blending instinct, intuition, knowledge, skills and experience with reasoned thinking and analysis when taking regulatory compliance decisions. This hybrid DM approach involves gathering data from various sources, such as internal and external environments, memory, prior learning and experience, ethical behaviour and engaging with peers and colleagues (chapter 4) then assessing impressions subconsciously and consciously (chapter 5). This flexible and fluctuating DM approach appears to be in stark contrast to the majority of published literature, which categorises decision research using normative or descriptive models where one approach suppresses the other (chapter 1, section 1.4), or despite theoretical advances with intuitive-experiential and analytical-reasoning approaches that have divided clinical opinion and prevented adoption (chapter 2, section 2.2).

However, the findings are consistent with literature on other levels. Firstly, in that there is no single theory, format or approach available that can be applied and used as a generic framework to medical DM in context (Tonelli, 2011, Mäki, 2009; Baron, 2008). Secondly, explanations regarding the fundamental mechanics of human comprehension, conceptual reasoning and DM involve multiple inputs comprising science, art, intuition, gut instincts, evidence, knowledge, experience, analysis and interpretation (Reyna, 2008a,b; Woolever, 2008).

In this research the primary output is a cognitive decision-making framework (chapter 5, figure 5.2), built from elements of naturalistic models, medical DM and physician assertions, that utilises physicians' prevalent knowledge, personal experience and perceptions with various internal and external workplace influences for making regulatory compliance decisions. This takes into account situation awareness, distinguishes between implicit and explicit cognitive processing by splitting NDM into three layers based on skill, rules and knowledge (chapter 5, sections 5.2 and 5.3). The secondary research output is the construction of a framework for compliance with ISO14155:2011 built from physicians' compliance perceptions and impressions of the medical device compliance requirements (chapter 5, figure 5.3). It divides the standard's compliance requirements into four distinct sections covering planning, documentation, study execution, analysis and reporting (chapter 5, section 5.4). Additionally, this research appears to plug a literature gap as these conceptual frameworks, presented in chapter 5, appear to bridge intelligence gleaned from research study and types of knowledge needed by a physician to make a decision (Tonelli, 2011; 2006). Essentially, construction of these frameworks follow Ochs (1998) and Ketner (1995) who indicated that structures identified abductively are no more favoured orders or credible re-constructions, but practical (re-) arrangements of a reality.

This thesis also appears to align with authors who indicated that professional clinical practice decisions are individual and should be explored by focussing on social psychology theories (Mohan *et al*., 2012; Grol *et al*., 2007; Eccles *et al*., 2006; Michie *et al*., 2005; Connor and Sparks, 2005). Additionally, review of literature suggested that study of social cognitive and subjective influences on physician DM in context could offer a means to address decision challenges faced by physicians working

outside of direct medical practice (chapter 2). In this study, this involved exploring physician roles that did not directly involve patient care using an interpretative investigative enquiry viewed through a naturalistic decision-making lens (chapter 3). Four NDM themes, gleaned from literature review, enabled an exploration of decision-making approaches, regulatory and organisational context, situation awareness and decision errors, where the DM categories identified were combined to construct a research frame that shaped the main study (chapter 2, figure 2.4).

The findings (chapter 4), and subsequent interpretation (chapter 5), appear to help address questions previously raised on how physicians actually make compliance decisions, integrate their knowledge into practice, and seek alternative options and improvement strategies (Christ, 2014; Tonelli, 2011; Milkman, Chugh and Bazerman, 2009; Milkman, Rogers and Bazerman, 2008; Woolever, 2008). Specifically, the use of dual processing strategy within a flexible NDM framework attempts to illustrate how physicians' contextual DM amalgamates intuition and analysis linked to combining reasoning with interpretation. This draws, and builds, on the published works of some researchers who have expressed niche positions relating to medical and naturalistic decision-making given traditional and behavioural formats do not adequately characterise physician DM processing (chapter 2, sections 2.2 and 2.3).

The new frameworks illustrate that blending NDM core concepts with non-clinical influences is possible and shows regulatory compliance decision-making to comprise the utilization of biomedical and clinical knowledge, physician experience, organisational problem-solving, weighing-up options, balancing risk-benefit and actively reflecting on potential outcomes. Although shared DM was advocated as one potential category advance, the PPD physicians have no direct interaction with clinical trial patients or families, so this factor was not directly applicable. However, patient-related factors were actively considered by the physicians when making clinical trial compliance-related decisions (chapter 4, section 4.4.3). Contrastingly, key contextual themes that impact the physicians' DM appear to be the identification, assessment and consideration of non-clinical influences such as client and regulator factors, organisational role, policy and guidance, as well as physicians' personal characteristics comprising cognition and behaviour in context, (chapter 2, section 2.2). The findings (chapter 4) illustrate that, in this field, environmental influences

impact greatly on the physicians' DM and could be people, process or procedure related involving internal factors (organisational, personal or behavioural) or external factors (ISO14155:2011; client, patient, clinical site(s) and regulatory authorities).

6.2 FINDINGS IN LIGHT OF RESEARCH QUESTION & GOALS

This thesis contends that the study design enabled the research aims (chapter 1, section 1.3) to be answered via four key features that emerged from the findings: firstly, physician decision-making in non-medical settings is complicated and fluctuates across a spectrum involving the subconscious and conscious mind where the expert physicians' mental models influenced decisional practice. Secondly, using an alternative methodology helped highlight that proactive consideration of adaptive decision-making approaches and various impacting factors could influence physicians' DM. Thirdly, the findings provided a means of developing a more suitable description of physician regulatory DM and the compliance requirements for ISO14155:2011 in PPD. Fourthly, it allowed PPD physician decision-makers to be seen, not as intellectually singular, but operating in a social realm overflowing with bewildering variables and inhabited with many industry players, where interaction co-jointly decides DM process and outcome, following Spring (2008); Patel, Kaufman and Arocha (2002).

The research question (chapter 1, section 1.3) was answered given two DM frameworks (chapter 5, figures 5.2 and 5.3) were constructed from the empirical findings, shaped and guided by published decision themes. Furthermore, revisiting the research goals (chapter 1, section 1.3) indicate that all were achieved. Firstly, chapter 2 provides a comprehensive literature examination of decision research in contextual settings, which enabled the author to understand, and critically reflect on, the theory and literature to identify four core DM themes for exploration in the main study. Secondly, these themes, comprising decision-making approach, context, situational awareness and decision error, formed the core of the initial research design framework which subsequently formed the main data gathering and interpretation pillars used to inform and guide the DM narrative in chapters 3, 4 and 5. Thirdly, chapters 3 and 4 demonstrate that understanding, and critically reflecting on, regulatory compliance decision-making and ISO14155:2011 enabled key factors

and parameters to be designed into the study, such that physician perspectives could be identified, articulated, captured, analysed and interpreted. Fourthly, in ascertaining how PPD physicians make regulatory decisions, interpretation of the findings (chapter 5) enabled the construction of two conceptual frameworks for potential use in the PPD vigilance environment: the first illustrating how PPD physicians perceive regulatory compliance decision-making in clinical research and, the second, depicting how to comply with ISO14155:2011 requirements.

Construction of these frameworks appears to align with decision-making authors who have called for contextualising DM approaches via innovative exploration considering medical ethics, evidence based-medicine, engaging with peers and expansion of decision theory (chapter 2, section 2.2). Although the physicians did not use these terms explicitly, the findings illustrate that many of the PPD physicians' engage with these concepts as and when necessary. This implies that these features influenced physicians' decision-making but, as not prescriptive, were only used sporadically (chapter 4).

This study appears to be the first to use decision-making frameworks (chapter 5, figure 5.2 and 5.3) in this manner within the clinical research industry. Although, the frameworks will not detract from physician DM autonomy in PPD they will offer a complementary and discretionary means to structure regulatory DM in context and potentially contribute to practice by providing a compliance guide for ISO14155:2011 within this environment. Each one could also enable PPD to provide new training and learning opportunities for the company physicians, potentially reducing ambivalence and inconsistency of approach to regulatory compliance decision-making in the vigilance department. In addition, the regulatory compliance and physician DM frameworks could also be offered as a PPD service differentiator when bidding for new client studies in the medical device arena.

6.3 RESEARCH LIMITATIONS

The quality of quantitative study is typically appraised for reliability and validity of the research (Aveyard, 2007). This implies that the research design and extent of data collection methods and findings need to be explicitly clarified and stated. However, Horsburgh (2003) expressed concerns about qualitative research being subject to

the same criteria for reliability and validity as quantitative studies, with other authors arguing that qualitative research cannot be assessed using the same quality criteria because the 'measurements obtained' are made via researcher interpretation at research process end point (Lincoln and Guba, 1985:342). So, to address potential limitations in this research the terms 'credibility', 'transferability', 'dependability' and 'confirmability' are used to assess study quality rather than terms such as validity and reliability (Lincoln and Guba; 1985).

As this research process was subjective and qualitative it is open to critique given its limitations can be directed to the following points; namely data gathered from only 18 interviewees yet PPD is an international company with over 12000 employees; novel researcher; biased research; and generalizability of the findings.

Despite PPD's size, use of a purposive sample was due to the bespoke nature of study and small pool of physician decision-makers at top end of the company (n<30). Although access to others was possible and expanding the sample size could have occurred, it would have increased time, logistics and cost in order to accommodate. It is recognised that data density and saturation may not have occurred but it is debatable whether it would have contributed any new evidence to that gathered from the 18 respondents. The sample size used limited the researcher from becoming swamped by data but allowed for an adequate depth / breadth of understanding and exploration of DM themes in sufficient detail to construct the frameworks (chapter 5).

The researcher recognises that bias can take many forms; from researcher through study design, sampling, interviewing, response interpretation and reporting (Pannucci and Wilkins, 2010). In this qualitative study the researcher accepts and acknowledges that some bias was inevitable and that it could have occurred. However, by planning this research on solid academic underpinning, following critical DM literature review, and relating the researched case to broader philosophical positions that cuts across specialisations, (chapters 2 and 3), the impact of bias has been lessened. In addition, by constructing frameworks (chapter 5) that leaves compliance DM flexible and open it caters for physicians from differing backgrounds, facilitating alternative approaches, makes provision for different interpretations and drawing disparate judgments (Denzin and Lincoln, 2011).

As a novel researcher this study could be criticised on the grounds of approach or bias research in that the data was collected by one researcher who works for the company. To counteract these claims some authors have indicated that keeping an accurate trail of the research process, data analysis transparency, and actively working back and forth with the data were key 'truth value' strategies providing the researcher with confidence that research themes development was robust, accurate and open to scrutiny (Lincoln and Guba, 1985:342). Presenting the research design choices, data and an accurate record of the research study process (chapter 3, chapter 4 and Appendices A,B,C,D,E and F) facilitates study transparency, academic qualitative rigour and highlights the credibility and confirmability of the study findings. Therefore this study follows recommendations of Denzin and Lincoln (2011), Cresswell (1998), Boulton and Hammersley (1996), (Cresswell, 1998:3) by showing that 'truth value' strategies were developed from the outset, and upheld over the research process, containing no higher bias against the verification of interviewer's assumptions in a case study versus any alternative enquiry methods.

A link to credibility and confirmability is via use of named DM models, themes and in interviewee response transparency which influenced the research process in terms of data gathered, subsequent analysis and outcomes (Fox, Martin and Green, 2007; Pope and Mays, 2006). Additionally, from a phenomenological perspective reflexivity was used in social construction as it was important to understand the researcher's relationship to theory, research design and how it is co-constructed (Fox, Martin and Green, 2007). Fundamentally the engagement occurred between the researcher and the physician participants. However, it also applies to the research design itself which is a form of co-construction involving the researcher, previous researchers, and the researcher's reading of prior research in order to compile a valid research design (Fox, Martin and Green, 2007). So, this thesis illustrates that an important part of the researcher's reflexivity occurred from deciding the preferred approach, building research design, considering limitations then indicating how they potentially influenced the findings (Cresswell, 2009). Therefore, a crucial aspect of this interpretive phenomenological study was reflexivity given it grasped the social science viewpoint of subjectivity philosophically together with influencing methodologically (Dowling, 2007; Horsburgh, 2003).

A quality study indicator is confirmability and, in this context, the paradigm selected follows suggestions that investigator bias effects are reduced by stating researcher's beliefs and assumptions (chapter 2), providing comprehensive study description to allow integrity of research results to be scrutinised (chapter 3), use of diagrams to demonstrate the audit trail (chapters 1,2,3,4 and 5), recognising flaws in selected study methods and potential effects (chapters 3, 5 and 6) with the entire thesis read as a narrative (Denzin and Lincoln, 2011; Miles and Huberman, 1994).

In this study one could argue that the results (chapter 4) appear credible because the philosophical approach was consistent overall, the main study was carried out according to industry and university ethical principles, and all stages of the study underwent peer review by the researcher's university supervisory team (Lincoln and Guba, 1985). However, this would now require testing by others. On the other hand, dependability requires the researcher to account for a constantly changing context within which research occurs (Thomas, Nelson and Silverman, 2011). In this study, it has been accounted for by the researcher providing an in-depth methodological description, to allow study repetition, utilising overlapping methods (mini-focus groups and semi-structured interviews) to explore physicians' DM approaches and ISO14155:2011 changes impacting the PPD vigilance department, then describing how these changes affected the study design and approach (chapters 2 and 3).

Although Thomas, Nelson and Silverman (2011) postulated that transferability was an indication of whether methodology and/or results could be generalised and applied in other settings; this is open to debate, as transferability is primarily the responsibility of the person generalizing. For example, there are several PPD departments where the compliance frameworks or methodological approach could be potentially used, such as Product Development, Regulatory Affairs and Clinical Operations, where other physicians are employed; or extending the DM framework to other healthcare practitioners; advancing the methods to other legislative compliance scenarios, or widening both frameworks to board level compliance decision-making. However, the two new frameworks presented (chapter 5) may not be generalizable or transferable and only be suitable for this specific vigilance context. Again, only testing by others could confirm or refute this position.

The researcher accepts that abductive reasoning can cause imperfect interpretation and explanations but the uniqueness of this research is in its subjectivity, focus on physician DM in PPD, and innovative use of selective decision theory to construct new regulatory compliance decision-making frameworks for potential use in this context. The strengths are depth and understanding of physician compliance DM in context with high conceptual dependability and confirmability. The weaknesses include bias in stating relationships, potential limited understanding of DM influences in the physician population under study, with statistical significance unknown (Denzin and Lincoln, 2011). In short, given that interpretive phenomenological inquiry was utilised in this research, the underlying message, indeed limitation, is that the social world is multi-faceted, where the individual makes sense of, and constructs, their own reality and that there is no absolute truth (Topping, 2010; Cresswell, 2009).

6.4 CONTRIBUTION TO ACADEMIA & PROFESSIONAL PRACTICE

According to some authors an integral part of a professional doctorate is contributing to practice (Dent, 2002; Bareham, Bourner and Stevens, 2000). This thesis provides a potentially powerful addition to professional practice within the PPD vigilance department given abduction was implicitly, but deliberately, used by the social researcher to explore physician decision-making in an ordered way. This follows Ketner *et al*., (1995) who highlighted that abductive efforts can achieve a research aim by seeking some (new) order, not just the compilation of any structure, but where order discovery corresponds to the data as well as solves the practical problems that arise from them. Although not novel, this approach inferred using two characteristics, namely logic and innovation, but it was a new approach within PPD and in the subject area. Essentially the study strategy and design (chapter 3) was built on a reproducible exploration (i.e. reasonable, rule-governed and methodologically sound approach) but also of innovative character where insight can lead to new and valid knowledge (Peirce, 1992).

The first recommendation is to increase awareness, communicate and recommend the use of the new conceptual physician decision-making framework (chapter 5, figure 5.2) across the PPD book of business. It may require some training on terminology, definitions, and background given its draw on the naturalistic paradigm,

medical DM, and integrating elements such as receipt of cues, intuition, situation awareness and mental simulation. However, this framework illustrates how decision influencing information enters a physician's mind and is processed at one of three levels: automatic skill-based processing, intuitive rule-base processing, or knowledge-base analytical processing, where the route taken is dependent upon the decision maker's prior familiarity over the subject with reflexivity considering the final decision prior to implementation (chapter 5, section 5.2). So, making the wider team aware of these decision-making mechanisms could aid more efficient and better DM across PPD clinical trials in future.

The second recommendation is to implement the newly constructed framework for ISO14155:2011 compliance (chapter 5, figure 5.3) across all medical device clinical trials given that it is built from data gathered from company physicians' perceptions, knowledge, and experience of implementing prior legislative challenges and divides compliance into four distinct contextual sections covering planning, documentation, study execution, analysis and reporting requirements (chapter 5, section 5.4). Again, making the wider team aware of these decision-making mechanisms could aid more efficient and better compliance DM across PPD medical device clinical trials in future.

This thesis also suggests that the theoretical constructed frameworks could help support an improved perception of the regulatory legislative landscape by the company physicians and help facilitate a shared, integrated and informed department response to the compliance issue, thereby making a specific contribution to practice. For example, this study appears to be the first to use decision-making frameworks (chapter 5, figure 5.2 and 5.3) in this manner within the clinical research industry. Although, the frameworks will not detract from physician DM autonomy in PPD they will offer a complementary and discretionary means to structure regulatory DM in context and potentially contribute to practice by providing a compliance guide for ISO14155:2011 within this environment. Each one could also enable PPD to provide new training and learning opportunities for the company physicians, potentially reducing ambivalence and inconsistency of approach to regulatory compliance decision-making in the vigilance department. In addition, the regulatory

compliance and physician DM frameworks could also be offered as a PPD service differentiator when bidding for new client studies in the medical device arena.

Furthermore, an additional contribution could potentially be achieved in other healthcare organisations via transferability and publication of the findings (Thomas, Nelson and Silverman, 2011; Lincoln and Guba, 1985). For example, there may be other CRO safety vigilance departments that could benefit from using similar research methodology to influence practice having been informed of this approach via an academic route. So, utilising academic process could be seen as a guiding influence on this thesis but one where the results and recommendations presented could influence the practice of others. However, this specific methodological approach, namely combining interpretative inquiry using phenomenology, van Manen's methodology, qualitative methods of semi-structured interview and mini-focus groups, framework analysis and abduction, could be deemed to provide competitive advantage and so become part of PPDs intellectual property. Nevertheless, even if this thesis is embargoed and findings unpublished, the researcher still maintains that this work can still provide suggestions for researchers, physician contextual practice and senior business leaders in PPD.

6.5 FURTHER RESEARCH DIRECTION

This research was conducted in a single department of a global clinical research organisation covering two continents. It was designed to provide insight into a single regulatory issue presenting to the departmental physicians and although the research outcomes are two conceptual frameworks, it should be remembered that, both are organisationally and contextually specific. The next steps would be to present each to the department, ascertain their degree of generalisability to the results, potentially implement one, or both, then assess their effectiveness.

This research highlights that a high level of regulatory compliance DM autonomy rests with PPD physicians, particularly in the vigilance department. However, as a multifunctional organisation, PPD physicians also face making efficient and consistent regulatory compliance decisions in parallel with other business areas to facilitate market and client responsiveness. Currently in PPD, regulatory compliance

presents special challenges to departments as decision-making focuses on the unique facets of the requirements on their unit and/or environment. Although this functional autonomy can allow one department to adapt quickly to a shift in their market requirements, promote entrepreneurial zeal within a leadership silo, and/or encourage departmental innovation, it may fail to exploit lessons learned, cross-functional collaboration, opportunities for integration and leveraging synergies across company divisions. Although this could be viewed as a confusing mix of contradictory, but interrelated, strategies, the paradoxical blend seems to reinforce the adaptability of the current PPD business model, organisational resilience and compliance positioning flexibility to clients.

Schwab (2008) indicated that physician DM could be improved via training but the findings (chapter 4, section 4.1.2) indicated that PPD did not train physicians on how to make decisions. Although Baumann, Deber and Thompson (1991) stated that physicians had high confidence levels in their recommendations, other authors illustrated that physicians could be susceptible to overconfidence, biased judgment or conflicts of interest (Greenwood, Coleman and Boozang, 2012; Gorini and Pravettoni, 2011; Schwab, 2008; Henrion and Fischoff ,1986). Implementing the compliance frameworks, based on solid and robust theoretical underpinnings, could be an innovative way forward to help address these potential limitations, and aid DM by reducing uncertainty, avoiding heuristics, framing DM influences and clarifying interpretation of relevant evidence in practice.

Contrastingly one could argue that implementing the new frameworks for physician decision-making and compliance with ISO14155:2011 could help PPD corporate executives move beyond the status quo, reduce inconsistencies, ambiguities and complexities associated with complex regulatory compliance decision-making as well as marketing PPD as having a reasoned approach to DM in future. For example by referencing this research, and assessing for contextual transferability cross-functionally in a parallel timeframe, each framework could be tailored for company use, specific requirements, other departments or clients. One potential research direction could be to apply the DM framework, and/or the methodological approach, to the next pending regulatory change that will impact the PPD business, such as the update to the European clinical trial directive 2001/20/EC due late in 2014. Further

study could determine if they are truly transferable intra- or inter-departmentally or whether further analysis and refinement may be needed. Alternatively, it may be that future interpretivist qualitative research requires the use of alternative means to uncover additional influencing factors in understanding and explaining how physicians think when faced with regulatory compliance issues. However, this assumes an appetite and desire for changing regulatory compliance DM organisationally.

6.6 CHAPTER SUMMARY

The findings indicate there is a clear need for flexibility and adaptability within PPD compliance DM as industry regulations continually appear, requiring the physician decision makers to consider change combined with an urgent need to absorb knowledge rapidly, make decisions and react accordingly. However, decision-making and compliance interpretation in PPD is a radically different situation from established pharmaceutical companies that require specific DM approaches to product, patient and application. Therefore this study provided an opportunity to explore and understand PPD physicians' DM process from within to potentially ascertain new ways of working based on a robust theoretical underpinning.

The study design utilises an alternative academic, philosophical and methodological approach to physician regulatory compliance decision-making versus those currently used in PPD. The approach draws upon a selection of previously published DM themes and blends them with contemporary empirical findings from clinical research to potentially shape future compliance needs. This thesis has involved exploring industry regulatory requirements, medical practice experience and interpretivist philosophy, using a research frame (chapter 2, figure 2.4) allied to qualitative methods to gather empirical data, then analysing and interpreting the findings via a NDM lens within the PPD clinical research vigilance environment. The findings show that rich, deep and meaningful data could be empirically gathered from the physicians via this approach versus those used in the company previously (chapters 3, 4, 5). This has enabled the synthesis of two new conceptual regulatory compliance frameworks to facilitate physician discretionary contextual DM and meeting the requirements of ISO14155:2011 (chapter 5, figures 5.2 and 5.3).

This thesis suggests that the research paradigm selected successfully achieved the study aim and objectives within the time limits of this research, and that the two constructed frameworks could provide practical and relevant support to PPD physicians making regulatory decisions and also to meet the compliance requirements of ISO14155:2011. It would appear that each framework could perhaps mutually reinforce the other such that taken together they form a moderate, but not insignificant, advance in helping PPD physicians make informed, collaborative, discretionary decisions to potentially influence contextual compliance related work in this field. Use of these frameworks could help reduce DM ambivalence, avoid repeating the organisational mistakes of the past, and help improve DM in the PPD vigilance department now and in the future.

The researcher hopes that introducing, implementing and adopting these frameworks will be the next step and provide PPD's vigilance department with a means to guide physician decision-making in context and demonstrate conformity to the essential requirements covered by ISO14155:2011 to regulators and clients alike. These frameworks could act as reference tools to illustrate and shape client and study expectations and set the direction to meet business objectives. When linked to alignment of goals, set by physicians from the top tier of company leadership, they could also potentially guide executive compliance decisions and help provide focus to other department teams. This could be viewed as process enhancement where physician decision-making autonomy is maintained but with flexibility and adaptability enhanced.

REFERENCES:

Abdel-Aleem, S.M. (2009). *Design, Execution and Management of Medical Device Clinical Trials*. John Wiley & Sons. Hoboken, NJ.

Adams, J., Khan, H.T.A., Raeside, R. (2014). *Research Methods for Business and Social Science Students.* (2nd Edition). Sage. New Delhi, India.

Aitken, P., Perahia, D. and Wright, P. (2003). Psychiatrists entering the pharmaceutical industry in the UK. *Psychiatric Bulletin*. 27, 248-250.

Alby, F. and Zucchermaglio, C. (2006). Afterwards we can understand what went wrong, but now let's fix it': How Situated Work Practices Shape Group Decision Making. *Organization Studies.* 27; (7), 943-966.

Allen, P.M. (2006). Evolving Complexity in Social Science. *Complexity and Organization – Readings and conversations.* Routledge. Abingdon. 134-161.

Alper, B.S., White, D.S. and Ge, B. (2005). Physicians Answer More Clinical Questions and Change Clinical Decisions More Often With Synthesized Evidence: A Randomized Trial in Primary Care. *Annals of Family Medicine.* 3; (6), 507-513.

Altmann, G. and Koch, W.A. (editors). (1998). *Systems: New Paradigms for the Human Sciences.* De Gruyter. Berlin.

Alvesson, M. and Deetz, S. (2000). *Doing Critical Management Research*. Sage Publications. London.

Alvesson, M. and Deetz, S. (2006). Critical Theory and Postmodernism Approaches to Organizational Studies. In Clegg, S.R., Hardy, C., Lawrence, T. and Nord, W.R. (Editors). *The SAGE Handbook of Organization Studies.* (2nd Edition). Sage Publications. London. 255-283.

American Society for Testing and Materials. (2014). ASTM Standards for Healthcare Services, Products and Technology. http://www.astm.org/ABOUT/images/Medical_sector.pdf. Accessed 05 February 2015.

Arkes, H.R., Dawes, R.M., and Christensen, C. (1986). Factors influencing the use of a decision rule in a probabilistic task. *Organizational Behavior and Human Decision Processes*. 37, 93-110.

Artman, H. (1998). Coperation and situation awareness within and between time scales in dynamic decision-making. In Waern, I. (Ed.). *Co-operative process management: cognition and information technology.* Taylor and Francis. London, 117-130.

Association of Clinical Research Organizations. (2012). *Home.* http://www.acrohealth.org/ . Accessed 30 September 2013.

Aveyard, H. (2007). *Doing a Literature Review in Health and Social Care. A Practical Guide.* McGraw Hill Open University Press. Maidenhead.

Aveyard, P., Lawrence, T., Cheng, K.K., Griffin, C., Croghan, E., Johnson, C. (2006). A randomised controlled trial of smoking cessation for pregnant women to test the effect of a transtheoretical model-based intervention on movement in stage and interaction with baseline stage. *British Journal of Health Psychology*. 11; (2), 263-278.

Aveyard, P., Massey, L., Parsons, A., Manaseki, S. and Griffin, C. (2009). The effect of transtheoretical model based interventions on smoking cessation. *Social Science and Medicine*. 68; (3), 397-403.

Bainbridge, L. (1988). Types of representation. In Goodstein, L.P., Andersen, H.B., and Olsen, S.E. (Eds.) *Tasks, Errors and Mental Models.* Taylor and Francis. London. 70-91.

Banning, M. (2008). A review of clinical decision making models and current research. *Journal of Clinical Nursing.* 17; (2), 187-195.

Bansal, S.K., Arnold, M. and Garofolo, F. (2010). International harmonization of bioanalytical guidance. *Bioanalysis.* 2; (4), 685-687.

Barbour, R.S. (2001). Checklists for improving rigour in qualitative research. A case of the tail wagging the dog? *British Medical Journal.* 322: 1115-1117.

Baron, J. (2008). *Thinking and Deciding*. (4th Edition). Cambridge University Press. Cambridge.

Barry, D. and Hansen, H. (Eds.). (2008). *The Sage Handbook of New Approaches in Management and Organization*. Sage Publications. London.

Baumann, A., Deber, R. and Thompson, G. (1991). Overconfidence among physicians and nurses: the micro-certainty, macro-uncertainty phenomenon. *Social Science and Medicine.* 32, 167-174.

Bazerman, M.H. and Chugh, D. (2005). Bounded awareness: Focussing failures in negotiation. In Thompson, L. (Ed.), *Frontiers of Social Psychology: Negotiation*. Psychological Press. Hove.

Bazerman, M.H. and Moore, D. (2008). *Judgment in Managerial Decision Making* (7th Edition). John Wiley and Sons. Hoboken, NJ.

Beach, L. R. (1990). Image theory: Decision making in personal and organizational contexts. Wiley. Chichester.

Benner, P. (1984). *From Novice to Expert: Excellence and Power in Clinical Nursing Practice.* Addison-Wesley Publishing. Menlo Park, CA.

Benner, P., (1985). Quality of life: a phenomenological perspective on explanation, prediction, and understanding in nursing science. *Advances in Nursing Science*. 8, 1-14.

Benner, P., Hughes, R.G., and Sutphen, M. (2008). Agency for Healthcare Research and Quality. In Hughes, R.G. (Ed.). *Patient Safety and Quality: An Evidence-Based Handbook for Nurses*. Chapter 6. Rockville, MD.

Benner, P., and Tanner, C. (1987). How expert nurses use intuition. *American Journal of Nursing.* 87; (1), 23-31.

Bensing, J. (2000). Bridging the gap. The separate worlds of evidence-based medicine and patient-centred medicine. *Patient Education & Counseling*. 29, 17-25.

Berkan-Sesen M., Suresh, P., Banares-Alcantara, R., Venkatasubramanian, V. (2010). An ontological framework for automated regulatory compliance in pharmaceutical manufacturing. *Computers and Chemical Engineering.* 34; (7), 1155-1169.

Bernard, W. T. (2002). Beyond inclusion. In Amaratunga, C. (Ed.). *Race, ethnicity, and women's health.* Halcraft. Halifax, NS.

Bernheim, S.M., Ross, J.M., Krumholz, H.M. and Bradley, E.H. (2008). Influence of patients' socioeconomic status on clinical management decisions: a qualitative study. *Annals of Family Medicine*. 6, 53-59.

Bjørk, I.T., and Hamilton, G.A., (2011). Clinical Decision Making of Nurses Working in Hospital Settings. *Nursing Research and Practice.* Article ID 524918. 8 pages. doi:10.1155/2011/524918.

Blaikie, N. (1993). *Approaches to Social Enquiry.* (1st Edition). Polity Press. Cambridge.

Blaikie, N. (2000). *Designing Social Research.* (1st Edition). Polity Press. Cambridge.

Blumer, H. (1962). Society as symbolic interaction. In Rose, A.M. (Ed.). *Human behaviour and social process: An international approach.* Houghton-Mifflin. Boston. 179-192.

Bogner, M. S. (1997). Naturalistic decision making in health care. In Klein, G. and Zsambok, C.E. (Eds.). *Naturalistic Decision Making.* Lawrence Erlbaum Associates. Mahwah, N.J. 61-69.

Borstein, B.H. and Emier, A.C. (2001). Rationality in medical decision making: a review of the literature on doctor's decision-making biases. *Journal of Evaluation in Clinical Practice*. 7, 97-107.

Boulton, D. and Hammersley, M. (1996) Analysis of Unstructured Data in Sapsford, R. and Jupp, V. (Eds.). *Data Collection and Analysis.* Sage. London.

Bowen, J.L. (2006). Educational strategies to promote clinical diagnostic reasoning. *New England Journal of Medicine*. 355; (21), 2217-2225.

Bowling, A. (2009). *Research Methods in Health: Investigating Health and Health Services. (*3rd Edition). Open University Press. Maidenhead.

Bowling, A and Ebrahim, S. (Eds.) (2005). *Handbook of Health Research Methods. Investigation, Measurement and Analysis.* Open University Press. New York.

Bradley, S. (2013). *Rational theory choice: Arrow undermined, Kuhn vindicated*. http://philsci-archive.pitt.edu/10112/ . Accessed 26 April 2014.

Bradley, E.H., Curry, L.A. and Devers, K.J. (2007). Qualitative Data Analysis for Health Services Research: Developing Taxonomy, Themes, and Theory. *Health Services Research*. 42; (4), 1758-1772.

Brannick, M. T., Salas, E. and Prince, C. (1997). Team Performance Assessment and Measurement, Theory, Methods, and Applications. Lawrence Erlbaum Associates. London.

Brajtman, S., (2005). Helping the family through the experience of terminal restlessness. *Journal and Hospice and Palliative Nursing*. 7; (2), 72-81.

Braun, V. (2006). Using thematic analysis in psychology*. Qualitative Research in Psychology,* 3; (2), 77-101.

Brehmer, B. (1990). Strategies in real time decision-making. In Hogarth, R. (Ed.). *Insights in decision making.* Elsevier Science. Amsterdam.

Brewer, W.F., and Nakamura, G.V. (1984). The nature and functions of schemas**. I**n: Wyer, R.S. Jr. and Srull, T.R. (Eds.), *Handbook of social cognition*. Erlbaum. Hillsdale, NJ. 1, 119-160.

Bridle, C., Riemsma, R.P., Pattenden, J., Sowden, A.J., Mather, L., Watt, I.S. and Walker, A . (2005). Systematic review of the effectiveness of healthn behaviour interventions based on the transtheoretical model. *Psychology and Health*. 20, 283-301.

Briss, P., Rimer, B., Reilley, B., Coates, R.C., Lee, N.C., Mullen, P., Corso, P., Hutchinson, A.B., Hiatt, R., Kerner, J., George, P., White, C., Gandhi, N., Saraiya, M., Breslow, R., Isham, G., Teutsch, S.M., Hinman, A.R., and Lawrence, R. (2004). Promoting informed decisions about cancer screening in communities and healthcare systems**.** *American Journal of Preventative Medicine.* 26**,** 67-80.

Brown, R. (1998). *Dynamics within and between groups*. Blackwell, Oxford.

Bruggink, G.M. (1985). Uncovering policy factors in accidents. *Air Line Pilot*. 22-25.

Bruin, W.B., Parker, A.M. and Fischhoff, B. (2007). Individual differences and reasoning: A study on personality traits. *British Journal of Psychology*. 101, 545-562.

Bryant, M. and Cox, J.W. (2013). Beyond Authenticity? Humanism, Posthumanism and New Organization Development. *British Journal of Management*. Article first published online: 10 MAR 2013. DOI: 10.1111/1467-8551.12005.

Bryman, A. and Bell, E. (2007). *Business research methods*. (2nd Edition). Oxford University Press. Oxford.

Buchanan, D. and Huczynski, A. (1997). *Organisational behaviour*. (3rd Edition). Prentice Hall, UK.

Burkle, C.M., Mueller, P.S., Swetz, K.M., Hook, C.C. and Keegan, M.T. (2012). Physician perspectives and compliance with patient advance directives: the role external factors play on physician decision making. *BMC Medical Ethics*. November. 13; (31), 1-9.

Burleson, W., Clark, S.S., Ransford, B., Fu, K. (2012). Design challenges for secure implantable medical devices. In *Proceedings of the 49th Annual Design Automation Conference* (DAC '12). ACM. New York. 12-17.

Cannon-Bowers, J.A. and Salas, E. (2001). Reflections on shared cognition. *Journal of Organizational Behavior.* 22; (2), 195-202.

Carel, H. (2008) *Illness.* Acumen. Stocksfield.

Carnevali, D.L., Mitchell, P.H., Woods, N.F. and Tanner, C.A. (1984). *Diagnostic Reasoning in Nursing*. Lippincot. Philadelphia.

Carroll, J. and Johnston, E. (1992). Decision research: A field guide. *Journal of the Operational Research Society*. 43, 71-72.

Carter, S.M. and Little, M. (2007). Justifying Knowledge, Justifying Method, Taking Action: Epistemologies, Methodologies, and Methods in Qualitative Research. *Qualitative Healthcare Research.* 17, 1316-1328.

Chapman, G.B. and Elstein, A.S. (2000). Cognitive processes and biases in medical decision making. In Chapman G.B. and Sonnenberg, F.A. (Eds.) *Decision Making in Health Care. Theory, Psychology, and Applications.* Cambridge University Press. Cambridge. 183-210.

Chapman, G.B. and Sonnenberg, F.A. (2000). *Decision Making in Health Care. Theory, Psychology, and Applications.* Cambridge University Press. Cambridge.

Charles, C., Gafni, A. and Whelan, T. (1997). Shared decision-making in the medical encounter: what does it mean? (or it takes at least two to tango). *Social Science and Medicine.* 44, 681-692.

Charles, C., Gafni, A., and Whelan, T. (2004). Self-reported use of shared decision-making among breast cancer specialists and perceived barriers and facilitators to implementing this approach. *Health Expert.* 7, 338-348.

Cheung, J. and Hocking P. (2004). The experience of spousal carers of people with multiple sclerosis. *Qualitative Health Research.* 14; (2), 153-166.

Chia, R. (2002). The Production of Management Knowledge: Philosophical Underpinnings of Research Design. In Partington, D. (Ed.). *Essential Skills for Management Research*. (1st Edition). Sage Publications. London.

Christ, T.W. (2014). Scientific-Based Research and Randomized Controlled Trials, the "Gold" Standard? Alternative Paradigms and Mixed Methodologies. *Qualitative Inquiry.* 20; (1), 72-80.

Cioffi, J. (2012). Expanding the scope of decision making research for nursing and midwifery practice. *International Journal of Nursing Studies.* 49; (4), 481-489.

Clewis, R. (2009). *The Kantian Sublime and the Revelation of Freedom*. Cambridge University Press. Cambridge.

Cohen, M.S. (1993). The naturalistic basis of decision biases. In Klein, G.A., Orasanu, J., Calderwood, R., and Zsambok, C.E. (Eds.). *Decision making in action: Models and methods.* 51-99. Ablex. Norwood, NJ.

Cohen, D., J. and Crabtree, B., F. (2008). Evaluative Criteria for Qualitative Research in Health Care: Controversies and Recommendations. *Annals of Family Medicine*. 6; (4), 331-339.

Cohen, L., Manion, L., and Morrison, K.R.B. (2007). *Research methods in education.* (6th Edition). Routledge. London.

Cohen, M.S., Freeman, J.T, and Thompson, B.B. (1997). Training the Naturalistic Decision Maker. In Klein, G. and Zsambok, C.E. (Eds.). *Naturalistic Decision Making.* Lawrence Erlbaum Associates. Mahwah, N.J. 257-268.

Cohen, M.Z., and Omery, A., (1994). Schools of phenomenology: implications for research. In: Morse, J.M. (Ed.), *Critical Issues in Qualitative Research Methods*. Sage Publications. Thousand Oaks, CA.

Collins, R. (1994). *Four Sociological Traditions*. Oxford University Press. New York.

Conner, M. and Sparks, P. (2005). Theory of planned behaviour and health behaviour. In Conner, M. and Norman, P. (Eds.). *Predicting health behaviour*. (2nd Edition). Open University Press. Berkshire. 170-222.

Cook, R.I., and Woods, D.D. (1994). Operating at the sharp end: The complexity of human error. In Bogner, S. (Ed.). *Human error in medicine*. Lawrence Erlbaum Associates. Mahwah, NJ.

Cooke, N.J., Kiekel, P.A., Salas, E., Stout, R., Bowers, C., and Cannon-Bowers, J. (2003). Measuring team knowledge: A window to the cognitive underpinnings of team performance. *Group Dynamics: Theory, Research, and Practice*. 7; (3), 179-199.

Council for International Organizations of Medical Sciences. (2012). *About Us*. http://www.cioms.ch/ . Accessed 30 September 2013.

Corbin, J., and Strauss, A. (1990). Grounded theory research: Procedures, canons, and evaluative criteria. *Qualitative Sociology.* 13; (1), 3-21.

Corcoran, S.A. (1986). Task complexity and nursing expertise as factors in nursing decision making. *Nursing Research*. 35; (2), 107-112.

Creswell, J. W. (1998) *Qualitative Inquiry and Research Design: Choosing Among Five Traditions.* Sage. London.

Creswell, J. W. (2009). *Research design: qualitative, quantitative, and mixed methods approaches*. (3rd Edition). Sage. London.

Creswell, J. W., and Plano Clark, V. L. (2011). *Designing and conducting mixed methods research* (2nd Edition). Sage. Thousand Oaks, CA.

Cristancho, S.M., Vanstone, M., Lingard, L., LeBel, M-E. and Ott, M. (2013). When surgeons face intraoperative challenges: a naturalistic model of surgical decision-making. *The American Journal of Surgery.* 205; (2), 156-162.

Crotty, M., (1996). *Phenomenology and Nursing Research*. Churchill Livingstone, Melbourne.

Cuffman, G.D. and Redberg, R.F. (2011). Medical Devices-Balancing Regulation and Innovation. *New England Journal of Medicine*. 365, 975-977.

Dadds, M. (2008). Empathetic validity in practitioner research. *Educational Action Research*. 16: (2), 279-290.

Dahlbom, B. 1992. 'The Idea that Reality is Socially Constructed,' in Floyd, C. Zullighoven, H. and Budde, R. *Software Development and Reality Construction*. Springer-Verlag. New York. 101-126.

Dacy, D. (2010). Optimizing Package Design for EtO Sterilization. *Medical Device and Diagnostic Industry.* 33; (1), 78-80.

Davies, M.B. (2007). *Doing a successful research project*. Using qualitative or quantitative methods. Palgrave Macmillan. Basingstoke.

Dawson, C. (2010). *Introduction to Research Methods*. How To Books. Oxford.

Dawson, N.V. and Arkes, H.R. (1987).Systematic errors in medical decision making: judgment limitations. *Journal of General Internal Medicine.* 2, 183-187.

De Maeseneer, J., Willems, S., De Sutter, A., Van de Geuchte, I., and Billings, M. (2007). Primary health care as a strategy for achieving equitable care: a literature review commissioned by the Health Systems Knowledge Network.

Denzin, N. and Lincoln, Y. (2003). The Discipline and Practice of Qualitative Research. In Denzin N. and Lincoln Y (Eds). *Collecting and Interpreting Qualitative Materials.* (2nd Edition). Sage Publications. California.

Denzin, N.K. and Lincoln, Y. S. (2011). *The SAGE Handbook of Qualitative Research*. SAGE publications. Thousand Oaks, CA.

De Roy, P.G. (2004). Helsinki and the Declaration of Helsinki. *World Medical Journal*. 50; (1), 9-11.

Dewberry, C., Juanchich, M. and Narendran, S. (2013). Decision-making competence in everyday life: The roles of general cognitive styles, decision-making styles and personality. *Personality and Individual Differences*. 55, 783-788.

Dick, P. (2004). Discourse Analysis. Stories in Organizational Research. In Cassell, C. and Symon, G. (Eds.). *Essential Guide to Qualitative Methods and Analysis in organizational Research.* Sage. London. 203-213.

Dickins, T. E. (2004). Social constructionism as cognitive science. *Journal for the Theory of Social Behaviour.* 34; (4), 333-352.

DiMaggio, P. (1997). Culture and Cognition. *Annual Review of Psychology*. 23, 263-287.

DiMatteo, M. R. (1998). The role of the physician in the emerging health care environment. *Western Journal of Medicine*. 168; (5), 328-333.

Dixon, J.R. (1999). The International Conference on Harmonization Good Clinical practice Guideline. *Quality Assurance: Good Practice, Regulation, and Law.* 6; (2), 65-74.

Donalek, J., (2004). Phenomenology as a qualitative research method. *Urologic Nursing.* 23; (5), 349-354.

Dorner, D. (1987). On the difficulties people have in dealing with complexity. In Rasmussen, J., Duncan, K., and Leplat, J. (Eds.). *New technology and human error*. 97-109. Wiley. Chichester.

Dougherty, M.R.P., Gettys, C.F. and Ogden, E.E. (1999). MINERVA-DM: a memory processes model for judgments of likelihood. *Psychological Review.* 106, 180-209.

Dreyfus, H.L. (1997). Intuitive, Deliberative, and Calculative Models of Expert Performance. In Zsambok, C.E. and Klein, G. (Eds.). *Naturalistic Decision Making*. Lawrence Erlbaum. Malwah, NJ. 17-28.

Dreyfus, S. (1989). In Davis, R. (Ed.). Expert Systems: How far can they go? Part One. *AI Magazine.* Spring. 61-67.

Dreyfus, S.E. (1981). *Formal models vs. human situational understanding: Inherent limitations on the modelling of business expertise.* ORC 81-3. Operations Research Center. University of California. Berkeley, CA.

Dreyfus, H.L., and Dreyfus, S. (1986). *Mind over machine: The powers of human intuition and expertise in the era of the computer.* The Free Press. New York

Drillings, M., & Serfaty, D. (1997). Naturalistic decision making in health care. In. Klein, G. and Zsambok, C.E. (Eds). *Naturalistic Decision Making.* Lawrence Erlbaum Associates. Mahwah, N.J. 71-80.

Drury, J.L. and Darling, E. (2008). A “thin-slicing” approach to understanding cognitive challenges in real-time command and control. *Journal of Battlefield Technology*. 11; (1), 9-16.

Duchon, D., Dunegan, K.J., and Barton, S.L. (1989). *IEEE Transactions on Engineering Management.* 36; (1), 25-27.

Eakin, J.M. and Mykhalovskiy, E. (2003). Reframing the evaluation of qualitative health research: reflections on a review of appraisal guidelines in the health sciences. *Journal of Evaluation in Clinical Practice. Special Issue: Evidence Based Medicine.* 9; (2), 197-194.

Easterby-Smith, M., Thorpe, R. and Jackson, P. (2008). *Management Research.* (3rd Edition). Sage Publications Limited. London.

Eccles, M.P., Hrisos, S., Francis, J., Kaner, E.F., Dickinson, H.O., Beyer, F. and Johnston, M. (2006). Do self-reported intentions predict clinicians' behaviour: a systematic review. *Implementation Science*. 1**,** 28.

Eddy, D. M. (2005). Evidence-based medicine: A unified approach. *Health Affairs.* 24, 9-17.

Edwards, W. (1992). *Utility Theories: Measurements and Applications*. Kluwer Academic, Boston.

Elgen, R.M., Gilchrist, A. and Reisine, T. (2008). An overview of drug screening using primary and embryonic stem cells. *Combinatorial Chemistry and High Throughput Screening,* 11, 566.

Elliott, T. (2005). *Expert Decision-Making in Naturalistic Environments: A summary of Research.* DSTO-GD-0429*.* Land Operations Division, Systems Sciences Laboratory. Defence Science and Technology Organisation. Australian Government Department of Defence.

Elwyn, G., Dehlendorf, C., Epstein, R.M., Marrin, R., White, J. and Frosch, D.L. (2014). Shared Decision Making and Motivational Interviewing: Achieving Patient-Centered Care Across the Spectrum of Health Care Problems. *Annuls of Family Medicine*. 12: (3), 270-275.

Elwyn, G., Edwards, A., Gwyn, R. and Grol, R. (1999). Towards a feasible model for shared decision making: focus group study with general practice registrars. *British Medical Journal*. 319, 753-756.

Elwyn, G., Edwards, A. and Kinnersley, P. (1999). Shared decision-making in primary care: the neglected second half of the consultation**.** *British Journal of General Practice.* 49**,** 477-482.

Elwyn, G., Edwards, A., Kinnersley, P. and Grol, R. (2000). Shared decision making and the concept of equipoise: the competences of involving patients in healthcare choices. *British Journal of General Practice.* 50, 892-899.

Endsley, M.R. (1988). Design and evaluation for situation awareness enhancement. In *Proceedings of the Human Factors Society 32nd Annual Meeting.* Human Factors Society. Santa Monica, CA. 97-101.

Endsley, M.R. (1995). Towards a Theory of Situation Awareness. *Human Factors.* 37; (1), 32-64.

Endsley, M.R. (1997). The Role of Situation Awareness in Naturalistic Decision Making. In Zsambok, C.E. and Klein, G. (Eds.). *Naturalistic Decision Making*. Lawrence Erlbaum. Malwah, NJ. 269-283.

Endsley, M. R., and Bolstad, C. A. (1994). Individual differences in pilot situation awareness. *International Journal of Aviation Psychology.* 4; (3), 241-264.

Epstein, R.M. (2013). Whole mind and shared mind in clinical decision-making. *Patient Education and Counseling*. 90, 200-206.

Epstein, S. (1994). Integration of the cognitive and psychodynamic unconscious. *American Psychologist*. 49, 709-724.

Eriksson, P. and Kovalainen, A. (2008). *Qualitative Methods in Business Research.* Sage Publications. London.

European Directive 2001/20/EC. (2001). *Clinical Trials Practice Directive. Official Journal of the European Communities*. http://www.eortc.be/services/doc/clinical-eu-directive-04-april-01.pdf . Accessed 24 April 2014**.**

Fadde, P.J. and Klein, G.A. (2010). Deliberate performance: Accelerating expertise in natural settings. *Performance Improvement*. 49; (9), 5-14.

Falzer, P.R., & Garman, D.M. (2009). A conditional model of evidence based decision making. *Journal of Evaluation in Clinical Practice.* 15, 1142-1152.

Falzer, P.R., & Garman, D.M. (2010). Contextual decision making and the implementation of clinical guidelines: An example from mental health. *Academic Medicine.* 85, 548–555.

Falzar, P.R. and Garman, D.M. (2012). Image Theory's counting rule in clinical decision making: Does it describe how clinicians make patient-specific forecasts? *Judgment and Decision Making*. 7; (3), 268-281.

Fan, X., Sun, S., McNeese, M. and Yen, J. (2005). Extending the recognition-primed decision model to support human-agent collaboration. *Proceedings of the fourth international joint conference on Autonomous agents and multi-agent systems.* 945-952.

Faunce, T.A. and Jefferys, S. (2007). Whistleblowing and Scientific Misconduct: Renewing Legal and Virtue Ethics Foundations. *Journal of Medicine and Law.* 26; (3), 567-584.

Faunce, T.A. and Nasu, H. (2009). Normative Foundations of Technology Transfer and Transnational Benefit Principles in the UNESCO Universal Declaration on Bioethics and Human Rights. *Journal of Medicine and Philosophy.* 0, 1-26.

FDA. (2015). US Food and Drug Administration. Reprocessing Re-useable Medical Devices. http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/ReprocessingofReusableMedicalDevices/default.htm. Accessed 31 January 2015.

Fish, D. and Coles, C. (1998). *Developing Professional Judgement in Health Care. Learning through the critical appreciation of practice*. Butterworth-Heinemann. Oxford.

Fishbein, M. (2008). A reasoned-action approach to health promotion. *Medical Decision Making*. 28; (6), 834-844.

Fishbein, M.and Ajzen, I. (2010). *Predicting and changing behavior: The Reasoned Action Approach*. Taylor and Francis. New York.

Fischhoff, B. (2008). Assessing adolescent decision-making competence. *Developmental Review.* 28, 12-18.

Fischhoff, B. (1988). Judgment and decision making. In Sternberg, R.J. and Smith, E.E. (Eds.). *The psychology of human thought.* Cambridge University Press. Cambridge, NY. 150-187.

Fischhoff, B. (1982). Debiasing. In Kahneman,D., Slovic, P. and Tversky, A. (Eds.) *Judgment Under Uncertainty: Heuristics and Biases*. Cambridge University Press. Cambridge. 422-444.

Fischhoff, F.E., and Johnson, S. (1997). *Organisational decision-making*. Cambridge University Press. Cambridge.

Flin, R., Youngson, G. and Yule, S. How do surgeons make intraoperative decisions. *Quality and Safety in Health Care.* 16, 235-239.

Food and Drug Administration. (2014). *Overview of Device Regulation*. http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/default.htm . Accessed 26 August 2014.

Fotis, N. and Bix, L. (2006). Sample Size Selection Using Margin of Error Approach. *Medical Device and Diagnostic Industry.* 28; (10), 80-89.

Fox, M., Martin, P. and Green, G. (2007). *Doing Practitioner Research*. Sage Publications. London.

Franklin, M.I. (2012). *Understanding Research: Coping with the Quantitative-Qualitative Divide.* Routledge. London and New York.

Freeman, R.E., Wicks, A.C., and Parmar, B. (2004). Stakeholder Theory and "The Corporate Objective Revisited". *Organization Science.* 15; (3), 364-369.

Fu, K. and Blum, J. (2013). Controlling for cybersecurity risks of medical device software. *Communications. ACM.* 56; (10), 35-37.

Furber, C. (2010). Framework analysis: a method for analysing qualitative data. *African Journal of Midwifery and Women's Health*. 4; (2), 97-100.

Gabriel, Y. and Griffiths, D.S. (2004). Stories in Organizational Research. In Cassell, C. and Symon, G. (Eds.). *Essential Guide to Qualitative Methods and Analysis in organizational Research.* Sage. London. 114-126.

Gale, J. and Marsden, P. (1985). Diagnosis: Process not Product. In Sheldon, M., Brooke, J. and Rector, A. (Eds.). *Decision making in General Practice.* Stockton Press. New-York. 59-90.

Galligan E. (1996). Case notes. *Irish Planning and Environmental Law Journal.* 3; (4), 180-188.

Galotti, K. M. (2002). *Making decisions that matter: How people face important life choices.* Lawrence Erlbaum Associates. Mahwah, NJ.

General Medical Council. (2015). Working with Doctors. Working for Patients. http://www.gmc-uk.org/education/continuing_professional_development/cpd_guidance.asp. Accessed 29 January 2015.

George, L., Kaempf, G.L., Klein, G., Thorsden, M.L., and Wolf. S. (1996). Decision making in complex naval command-and-control environments. *Human Factors.* 38, 220-231.

Gill, S.L. and Lambert, M.J.. (2004). Life Cycle of Physician Executives. Life-cycle phases for physician executives provide order in turbulent environment. *Healthcare Executives*. 19; (1), 42-43.

Glaser, B. (2001). Doing grounded theory. *Grounded Theory Review.* 2, 1-18.

Godin, G., Bélanger-Gravel, A., Eccles, M. and Grimshaw, J. (2008). Healthcare professionals' intentions and behaviours: A cognitive systematic review of studies based on social cognitive theories. *Implementation Science*. 3, 36.

Goodstein, L.P., Andersen, H.B., and Olsen, S.E. (1988). *Tasks, Errors And Mental Models.* Taylor and Francis. London.

Gordon, S.E. and Gill, R.T. (1997). Cognitive Task Analysis. In Zsambok, C. and Klein, G. (Eds.). *Naturalistic Decision Making*. Lawrence Erlbaum Publishers. Mahwah, NJ. 131-140.

Gordon, J., Markham, P., Lipworth, W.L., Kerridge, I.H., Little, M. (2012). The dual nature of medical enculturation in postgraduate medical training and practice. *Medical Education.* 46; (9), 894-902.

Gore, J., Banks, A., Millward, L., and Kyriakidou, O. (2006). Naturalistic Decision Making and Organizations: Reviewing Pragmatic Science. *Organizational Studies*. 27; (7), 925-942.

Gorini, A. and Pravettoni, G. (2011). An overview on cognitive aspects implicated in medical decisions. *European Journal of Internal Medicine*. 22, 547-553.

Grant, S. and van Zandt, T. (2009). Expected Utility Theory. In Anand, P, Pattanaik, P.K. and Puppe, C. (Eds.). *The hand-book of rational and social choice.* Oxford University Press. Oxford. 21-68.

Greenwood, K., Coleman, C.H., Boozang, K.M. (2012). Toward Evidence-Based Conflicts of Interest Training for Physician-Investigators. *Journal of Law, Medicine and Ethics.* Fall. 40; (3), 500-510.

Griffen, J.P., Posner, J. and Barker, G.R. (Eds.). (2013). *The Textbook of Pharmaceutical Medicine.* (7th Edition). BMJ Books. John Wiley & Sons. Chichester.

Griffen D., Shaw P. and Stacey R. (2006). *Evolving Complexity in Social Science. Complexity and Organization – Readings and conversations*. Routledge. Abingdon. 162-184.

Grol, R., Bosch, M., Hulscher, M., Eccles, M. and Wensing, M. (2007) Planning and studying improvement in patient care: the use of theoretical perspectives. *Milbank Quarterly.* 85, 93-138.

Groopman J. (2007). *How Doctors Think*. Houghton Mifflin. Boston.

Guba, E. G. and Lincoln, Y. S. (1994). Competing paradigms in qualitative research. In Denzin, N. K. and Lincoln, Y. S. (Eds.). *Handbook of qualitative research.* Sage. London. 105-117.

Guerrier, M., Légaré, F., Turcotte, S., Labrecque, M. and Rivest, L-P. (2013). Shared Decision Making Does Not Influence Physicians against Clinical Practice Guidelines. *PLoS ONE*. 8; (4), 1-7.

Gummesson, E. (2000). *Qualitative Methods in Management Research*. (2nd Edition). Sage Publications. Thousand Oaks, CA.

Gund, A., Lindecrantz, K., Schaufelberger, M., Patel, H., and Sjöqvist, B.A. (2012). Attitudes among healthcare professionals towards ICT and home follow-up in chronic heart failure care. *BMC Medical Informatics and Decision Making*. 12**,** 138.

Hafferty, H.W. (2006). Professionalism - The Next Wave. *New England Journal of Medicine.* 355; (20), 2151-2152.

Hagens, V., Dobrow, M.J., and Chafe, R. (2009). Interviewee Transcript Review: assessing the impact on qualitative research. *BMC Medical Research Methodology*. 9, 47.

Hajjaj, F.M., Salek, M.S., Basra, M.K.A. and Finlay, A.Y. (2010). Non-clinical influences on clinical decision-making: a major challenge to evidence-based practice. *Journal of the Royal Society of Medicine*. 103, 178-187.

Hamm, R.M. (1988a). Clinical intuition and clinical analysis: Expertise and the cognitive continuum. In Dowie, J. and Elstein, A. (Eds). *Professional judgment: A reader in clinical decision making.* Cambridge University Press. Cambridge. 78-105.

Hamm, R.M. (1988b). Moment-by-moment variation in experts' analytic and intuitive cognitive activity. *IEEE Transactions on Systems, Man, and Cybernetics.* 18; (5), 757-776.

Hamm R.M. (1998). Clinical intuition and clinical analysis: expertise and the cognitive continuum. In Dowie, J. and Elstein, A. (Eds.). *Professional Judgement: A Reader in Clinical Decision-making.* Cambridge University Press. Cambridge. 78-105.

Hamers, J.P.H., Huijer Abu Saad, H., and Halfens, R.J.G. (1994). Diagnostic process and decision making in nursing: a literature review. *Journal of Professional Nursing.* 10; (3), 154-163.

Hammersley, M. (1989). *The dilemma of qualitative method: Herbert Blumer and the Chicago tradition*. Routledge. London.

Hammond, K.R. (1993). Naturalistic decision making from a Brunswickian viewpoint: Its past, present, future. In Klein, G. A., Orasanu, J., Calderwood, R. and Zsambok, C.E. (Eds.). *Decision making in action: Models and methods*. Ablex. Norwood, NJ. 205-227.

Hammond, K.R. (1996). *Human Judgment and Social policy: Irreducible Uncertainty, Inevitable Error, Unavoidable Injustice*. Oxford University Press. New York.

Hammond, K.R. (1998). Judgment and decision making in dynamic tasks. *International Journal of Information Technology and Decision Making*. 14, 3-14.

Hammond, K.R., Hamm, R.M., Grassia, J., and Pearson T. (1987) Direct comparison of the efficacy of intuitive and analytic cognition in expert judgement. *IEEE Transactions on Systems, Man and Cybernetics*. 17, 753–770.

Hansen, J.T. (2000). Psychoanalysis and Humanism: A Review and Critical Examination of Integrationist Efforts With Some Proposed Resolutions. *Journal of Counseling and Development*. 78; (1), 21-26.

Hansen, J.T. (2009). On Displaced Humanists: Counselor Education and the Meaning-Reduction Pendulum. *The Journal of Humanistic Counseling, Education and Development.* 48; (1), 65-76.

Hardy, D. and Smith, B. (2008). Decision making in clinical practice. *British Journal of Anaesthesia.* 9, 19-21.

Hassouneh-Phillips, D., (2003). Strength and vulnerability: spirituality in abused American Muslim women's lives. *Issues in Mental Health Nursing*. 24, 681-694.

Hatch, M.J. and Cunliffe, A.L. (2006). Organization Theory. (2nd Edition). Oxford University Press. Oxford.

Henrion, M. and Fischoff ,B. (1986). Assessing uncertainty in physical constants. *American Journal of Physics*. 54, 791-798.

Herfield, C. (2013). *Axiomatic Choice Theory Traveling between Mathematical Formalism, Normative Choice Rules and Psychological Measurement, 1944-1956.* Center for the History of Political Economy at Duke University. CHOPE Working Paper No. 2013-11. http://hope.econ.duke.edu/sites/default/files/Herfeld_Working%20PaperCHOPE_Axiomatic%20Choice%20Theory%20Traveling.pdf . Accessed 26 November 2013.

Herbert-Croteau, N., Brisson, J. and Pineault, R. (2000). Review of organisational factors related to care offered to women with breast cancer. *Epidemiologic Reviews*. 22, 228-238.

Hodgkinson, G.P. and Starbuck, W.H. (2008). *The Oxford handbook of organizational decision making.* Oxford University Press. Oxford.

Holloway, I. and Freshwater, D. (2007). Vulnerable story telling: narrative research in nursing. *Journal of Research in Nursing*. 12; (6), 703-711.

Holloway, I. and Freshwater, D. (2009). *Narrative Research in Nursing.* Blackwell Publishing. Oxford.

Holloway, I., and Wheeler, S., (2010). *Qualitative Research in Nursing and Healthcare.* (3rd Edition). Wiley-Blackwell. West Sussex.

Hope, R.A. (1998). Ethics and law for medical students: the core curriculum. *Journal of Medical Ethics.* 24; (3), 147-148.

Hope, T., Savulescu, J. and Hendrick, J. (2003). *Medical Ethics and Law: The Core Curriculum.* Churchill Livingstone. London.

Horsburgh, D. (2003). Evaluation of qualitative research. *Journal of Clinical Nursing*. 12; (2); 307-312.

Hu, J., and Liden, R. C. (2011). Antecedents of team potency and team effectiveness: An examination of goal and process-clarity and servant leadership. *Journal of Applied Psychology.* 96, 851-862.

Hughes, J. (1990). *The Philosophy of Social Research*. (2nd Edition). Longman. London.

Hung, S.Y., Ku, Y.C. and Chien, J.C. (2012). Understanding physicians' acceptance of the Medline system for practicing evidence-based medicine: a decomposed TPB model. *International Journal of Medical Informatics*. 81, 130-142.

Hutchins, E. (1996). *Cognition in the wild.* (2nd Edition). MIT Press. Cambridge, MA.

International Conference on Harmonization. (2015). ICH Harmonization for better health. http://www.ich.org/home.html . Accessed 29 January 2015.

International Organization for Standardization. (2011). *ISO 14155:2011. Clinical investigation of medical devices for human subjects - Good clinical practice*. https://www.iso.org/obp/ui/#iso:std:iso:14155:ed-2:v1:en . Accessed 04 June 2014.

ISO13485:2003. Medical Devices - Quality Management System - Requirements for regulatory purposes. http://www.iso.org/iso/iso_catalogue/catalogue_tc/catalogue_detail.htm?csnumber=36786 Accessed 31 January 2015.

Isaacs, D. and Fitzgerald, D. (1999). Seven alternatives to evidence based medicine. *British Medical Journal*. 319, 1618.

Jackson, E. (2013). *Medical Law: Text, Cases and Materials*. (3rd Edition). Oxford University Press. Oxford.

James, K. and Vinnicombe, S. (2002). Acknowledging the Individual in the Researcher. In Partington, D. (Ed.). *Essential Skills for Management Research* (1st Edition). Sage Publications. London.

Janis, I.L. (1972). *Victims of Groupthink: A psychological study of foreign policy decisions and fiascos*. Free Press. New York.

Janis, I.L., and Mann, L. (1977). *Decision-making: a psychological analysis of conflict, choice and commitment*. Free Press. New York.

Jenkins, H.M. (1985) A research tool for measuring perceptions of clinical decision making. *Journal of Professional Nursing*. 1; (4), 221-229.

Johnston, B.M., Milligan, S., Foster, C. and Kearney, N. (2011). Self-care and end of life care - patients' and carers' experience a qualitative study utilising serial triangulated interviews. *Supportive Care in Cancer.* 20; (8), 1619-1627.

Jones, P.E., and Roelofsama, P. (2000). The potential for social contextual and group biases in team decision-making: biases, conditions and psychological mechanisms. *Ergonomics*. 43, 1129-1152.

Joseph, G.M. and Patel, V.L. (1990). Domain knowledge and hypothesis generation in diagnostic reasoning. *Medical Decision Making.* 10; (1), 31-46.

Joseph, S., Beer, C., Clarke, D., Forman, A., Pickersgill, M., Swift, J., Taylor, J., Tischler, V. (2009). Qualitative Research into Mental Health: Reflections on Epistemology. *Mental Health Review Journal*. 14; 1, 36-42.

Kahneman, D. and Klein, G. (2009). Conditions for intuitive expertise: A failure to disagree. *American Psychologist.* 64; (6), 515-526.

Kampf, G.L., and Klein, G. (1994). Aeronautical decision making. The next generation. In Johnston, N., McDonald, N., and Fuller, R. (Eds.). *Aviation psychology in practice.* 223-254. Avebury Technical. Hants, England.

Kasi, P. (2009). *Research: What, Why and How? A Treatise from researchers to Researchers.* (1st Edition). AuthorHouse. Bloomington.

Kelly, D.,F., Magill, G. and ten Have, H. (2013). *Contemporary Catholic Health Care Ethics*. (2nd Edition). Georgetown University Press. Washington, DC.

Kelson, M., Akl, E.A., Bastian, H., Cluzeau, F., Curtis, J.R. et al. (2012). Integrating Values and Consumer Involvement in Guidelines with the Patient at the Center: Article 8 in Integrating and Coordinating Efforts in COPD Guidance Development. An Official ATS/ERS Workshop Report. *Proceedings of the American Thoracic Society*. 9, 262-268.

Klein, G. (1997). The Recognition-Primed Decision (RPD) Model: Looking Back, Looking Forward. In Klein, G. and Zsambok, C.E. (Eds.). *Naturalistic Decision Making*. Lawrence Erlbaum Associates. Mahwah, N.J. 285-292.

Klein, G. (1997a). *Making Decisions in Natural Environments.* (Special Report 31): Research and Advanced Concepts Office, U.S. Army Research Institute for the Behavioral and Social Sciences.

Klein, G. (1998). *Sources of power: How people make decisions*. MIT Press. Cambridge, MA.

Klein, G. (2008). Naturalistic decision making. *Human Factors*. 50, 456-460.

Klein, G.A. (1989). Recognition-primed decisions. In Rouse, W.B. (Ed.), *Advances in man-machine systems research.* JAI Press. Greenwich, CT. 5, 47-92.

Klein, G.A. (1993). A recognition primed decision (RPD) model of rapid decision making. In Klein, G.A., Orasanu, J., Calderwood, R., and Zsambok, C.E. (Eds.). *Decision-making in action: Models and methods.* Ablex. Norwood, NJ. 138-147.

Klein, G.A., Calderwood, R. and Clinton-Cirocco, A. (1986). Rapid decision making on the fire ground. In *Proceedings of the Human Factors Society 30th Annual Meeting.* Human Factors Society. Santa Monica, CA. 576-580.

Klein, G. and Klinger, D. (1991). Naturalistic Decision Making. *Human Systems IAC Gateway*. 2; (1), 16-19.

Klein, G. A., Orasanu, J., Calderwood, R. and Zsambok, C. E. (Eds.). (1993). *Decision Making in Action: Models and Methods*. Ablex Publishing Corporation. Norwood, NJ.

Klein, G., Phillips, J.K., Rall, E.L. and Peluso, D.A. (2007). A Data-Frame Theory of Sensemaking. In Hoffmann, R.R. (Ed.). *Expertise out of Context. Proceedings of the Sixth International Conference On Naturalistic Decision Making.* Lawrence Erbaum Associates. New York.

Kim, Y. (2011). The Pilot Study in Qualitative Inquiry. Identifying Issues and Learning Lessons for Culturally Competent Research. *Qualitative Social Work.* 10; (2), 190-206.

Kitson, A., Harvey, G. and McCormack, B. (1998). Enabling the implementation of evidence based practice: a conceptual framework. *Quality in Health Care.* 7,149-158

Kohn, L.T., Corrigan, J.M. and Donaldson, M.S. (2000). *To err is human: building a safer health system.* Institute of Medicine. National Academy Press. Washington, DC.

Koliadis, G., Desai, N.V., Narendra, N.C. and Ghose, A.K. (2010). Analyst-Mediated Contextualization of Regulatory Policies. *Services Computing.* IEEE International Conference. July. 281-288.

Kordeš, U. (2009). The Phenomenology of Decision Making. *Interdisciplinary Description of Complex Systems.* 7; (2), 65-77.

Kramer, D.B., Xu, S. and Kesselheim, A.S. (2012). Regulation of Medical Devices in the United States and European Union. *New England Journal of Medicine.* 366, 848-855.

Kravitz, R.L., Duan, N. and Braslow, J (2004). Evidence-based medicine, heterogeneity of treatment effects, and the trouble with averages. *Milbank Quarterly*. 82, 661-687.

Krueger, R.A. and Casey, M.A. (Eds.). (2000). *Focus Groups: A Practical Guide for Applied Research.* Sage. London.

Kuhn, T. (1992). *The Structure of Scientific Revolutions.* (3rd edition). University of Chicago Press. Chicago.

Kushniruk, A.W. (2001). Analysis of Complex Decision-Making Processes in Health Care: Cognitive Approaches to Health Informatics. *Journal of Biomedical Informatics*. 34; (5), 365-376.

Kvale, S. (1996). *Interviews: An Introduction to Qualitative Research Interviewing*. Sage. Thousand Oaks, California.

Lamm, H. (1988). A review of our research on group polarisation: eleven experiments on the effects of group discussion on risk acceptance probability estimation and negotiation positions. *Psychological Reports*. 62, 807-813.

Langridge, D. (2007). *Phenomenological Psychology: Theory, Research and Method.* Pearson Prentice Hall. London.

Lauri, S. and Salanterä, S. (2002). Developing an instrument to measure and describe clinical decision making in different nursing fields. *Journal of Professional Nursing.* 18; (2), 93-100.

Lawton, J., Jenkins, N., Darbyshire, J., Farmer, A., Holman, R., Hallowell, N. (2011). Challenges of maintaining research protocol fidelity in a clinical care setting: a qualitative study of the experiences and views of patients and staff participating in a randomized controlled trial. *TRIALS.* 12, 108.

Lawton, J., Jenkins, N., Darbyshire, J., Farmer, A., Holman, R., Hallowell, N. (2012). Understanding the outcomes of multi-centre clinical trials: A qualitative study of health professional experiences and views. *Social Science and Medicine.* 74; (4), 574-581.

Leana, C.R. (1985). A partial test of Janis's groupthink model: effects of group cohesiveness and leader behaviour on defective decision-making. *Journal of Management.* 11, 5-17.

Lee A., Joynt, G.M, Lee, A., K., T., Ho, A.,M.,H., Groves, M., Vlantis, A.C., Ma, R.,C.,W., Fung, C.,S.,C., and Aun, C.,S.,T. (2010).Sing Illness Scripts to Teach Clinical Reasoning Skills to Medical Students. *Family Medicine*. 42; (4), 255-261.

Légaré, F., Moher, D., Elwyn, G., LeBlanc, A. and Gravel K. (2007). Instruments to assess the perception of physicians in the decision-making process of specific clinical encounters: a systematic review. *BMC Medical Informatics and Decision Making.* 7; (30), 1-16.

Légaré, F., Stacey, D., Pouliot, S., Gauvin, F.P., Desroches, S., Kryworuchko, J., Dunn, S., Elwyn, G., Frosch, D., Gagnon, M.P., Harrison, M.B., Pluye, P., Graham, I.D. (2011). Interprofessionalism and shared decision-making in primary care: a stepwise approach towards a new model. *Journal of Inter-Professional Care*. 25; (1), 18-25.

Lerner, J. and Keltner, D. (2000). Beyond valence: Toward a model of emotion specific influences on judgment and choice. *Cognition and Emotion*. 14, 473-494.

Lerner, J.S. and Keltner, D. (2001). Fear, anger, and risk. *Journal of Personality and Social Psychology*. 81, 146-159.

Lewis, S., Glenton, C. and Oxman, A. (2009). Use of qualitative methods alongside randomized controlled trials of complex healthcare interventions: methodological study. *British Medical Journal.* 339; (10), 1136.

Lewis, J.L. and Sheppard, S.R.J. (2006). Culture and communication: can landscape visualization improve forest management consultation with indigenous communities? *Landscape and Urban Planning.* 77; 291-313.

Lieberman, J. D., Krauss, D. A., Kyger, M., and Lehoux, M. (2007). Determining dangerousness in sexually violent predator evaluations: cognitive-experiential self-theory and juror judgments of expert testimony. *Behavioral Sciences and the Law.* 25; (4), 507-526.

Lim, B. C., and Klein, K. J. (2006). Team mental models and team performance: A field study of the effects of team mental model similarity and accuracy. *Journal of Organizational Behaviour.* 27, 403-418.

Lincoln, Y.S. and Guba, E.G. (1985). *Naturalistic Inquiry.* Sage. Beverly Hills, CA.

Lincoln, Y. and Guba, E. (2000). Paradigmatic controversies, contradictions, and emerging confluences. In N.K. Denzin and Y.S. Lincoln (Eds.). *Handbook of Qualitative Research.* Sage. Thousand Oaks, CA.

Linstead, S. (1993). From Postmodern Anthropology to Deconstructive Ethnography. *Human Relations*. 46; (1), 97-120.

Lintern, G. (2010). A Comparison of the Decision Ladder and the Recognition-Primed Decision Model. *Journal of Cognitive Engineering and Decision Making.* 4; (4), 304-327.

Lipshitz, R. (1993a). Decision making in three modes. *Journal for the Theory of Social Behavior*. 24, 47-66.

Lipshitz, R. (1993b). Converging themes in the study of decision making in realistic settings. In Klein, G. A. Orasanu, J., Calderwood, R and Zsambok, C.E. (Eds.). *Decision making in action: Models and methods***.** Ablex. Norwood, NJ. 103-137.

Lipshitz, R. (1997). Naturalistic Decision Making Perspectives on Decision Errors. In Zsambok, C. and Klein, G. (Eds.). *Naturalistic Decision Making*. Lawrence Erlbaum Publishers. Mahwah, NJ. 151-160.

Lipshitz, R., and Ben Shaul, O. (1997). Schemata and Mental Models in Recognition-Primed Decision Making. In Zsambok, C. and Klein, G. (Eds.). *Naturalistic Decision Making*. Lawrence Erlbaum Publishers. Mahwah, NJ. 293-303.

Lipshitz, R., Klein, G., Orasanu, J. and Salas, E. (2001). Focus article: Taking stock of naturalistic decision making. *Journal of Behavioural Decision Making.*14, 331-352.

Lipshitz, R., & Strauss, O. (1997). Coping with uncertainty: A naturalistic decision-making analysis. *Organizational Behavior and Human Decision Making Processes.* 69, 149-163.

Lipworth, W.L., Kerridge, I.H. and Day, R.O. (2013). Formulating an ethics agenda for drug development, regulation and utilization. *Therapeutic Innovation and Regulatory Science.* 47; (1), 46-49.

Lipworth, W.L., Kerridge, I.H., Little, M., Gordon, J. and Markham, P. (2012). Meaning and value in medical school curricula. *Journal of Evaluation in Clinical Practice.* 18; (5),1027-1035.

Lipworth, W.L., Little, M., Markham, P., Gordon, J. and Kerridge, I.H. (2013). Doctors on status & respect: qualitative study. *Journal of Bioethical Inquiry.* 10; (2), 205- 207.

Lipworth, W.L., Strong ,K. and Kerridge, I.H. (2012). Medical Ethics. In Bowden, P. (Ed.), *Applied Ethics: Strengthening Ethical Practices.* (1st Edition). Tilde University Press Australia. Australia. 107-118.

Liu, S.T., Nemeth, J.M., Klein, E.G., Ferketich, A.K., Kwan, M.P., Wewers, M.E., (2012). Adolescent and adult perceptions of traditional and novel smokeless tobacco products and packaging in rural Ohio. *Tobacco Control*. doi:10.1136/tobaccocontrol-2012-050470.

Lorenz, K.A., Ryan, G.W., Morton, S.C., Chan, K.S., Wang, S., and Shekelle, P.G. (2005). A qualitative examination of primary care providers' and physician managers' uses and views of research evidence. *International Journal of Qualitative Health Care*. 17, 409-414.

Maisel, W.H. and Kohno, T. (2010). Improving the Security and Privacy of Implantable Medical Devices. *New England Journal of Medicine*. 362; (13), 1164-1166.

Mak, Y., and Elwyn, G., (2003). Use of hermeneutic research in understanding the meaning of desire for euthanasia. *Palliative Medicine*. 17, 395-402.

Mäki, U. (2009). Economics Imperialism: Concept and Constraints. *Philosophy of the Social Sciences.* 39; (3), 351-380.

Makoul, G., Arntson, P. and Schofield, T. (1995). Health promotion in primary care: physician-patient communication and decision making about prescription medications. *Social Science and Medicine.*1241-1254.

Makoul, G., and Clayman, M.L. (2006). An integrative model of shared decision making in medical encounters. *Patient Education and Counseling.* 60, 301-312.

Manktelow, K. and Jones, J. (1987). Principles from the psychology of thinking and mental models. In Gardiner, M., and Christie, B. (Eds.). *Applying cognitive psychology to user-interface design.* Wiley. Chichester. 83-117.

Martin, R.M. (1978). A Clinical Model for Decision Making. *Journal of Medical Ethics*. December. 4; (4), 200-206.

McCauley, C. (1989). The nature of social influence in groupthink: compliance and internalisation. *Journal of Personality and Social Psychology*. 57, 250-260.

McConnell, C.R. (2011). *Case Studies In Health Care Supervision*. (2nd Edition). Jones and Bartlett Publishers. Sudbury, MA.

McEachan, R.R.C., Conner, M., Taylor, N.J. and Lawton, R.J. (2011). Prospective prediction of health-related behaviors with the Theory of Planned Behavior: a meta-analysis. *Health Psychology Review.* 5; (2), 97-144.

McKeown, R.E., Reininger,B.M., Martin, M., and Hoppmann, R.A. (2002). Shared decision making: views of first year residents and clinic patients. *Academic Medicine.* 77, 438-445.

McKinlay, J.B., Potter, D.A. and Feldman, H.A. (1996). Non-medical influences on medical decision-making. *Social Science and Medicine*. 42; 950, 769-776.

McMurray, A. J., Pace, R. W., & Scott, D. (2004). *Research: A commonsense approach*. Thomson Social Science Press. Southbank, Victoria, Australia.

McNaughton, D.A. and Rawling, J.P. (2007). In Ashcroft, R.E., Dawson, A., Draper, H. and McMillan, J.R. (Eds.). *Principles of Health Care Ethics*. (2nd Edition). John Wiley and Sons. Chichester.

McNeil, B.J., Pauker, S.G., Cox, H.C., Jr., and Taversky, A. (1982). On the elicitation of preferences for alternative therapies. *New England Journal of Medicine.* 306, 1259-1262.

McWhinney, I.R. (1997). *A Textbook of Family Medicine.* (2nd Edition). Oxford University Press. Oxford, New York.

Means, B., Salas, E., Crandall, B. and Jacobs, T.O. (1993). Training decision-makers for the real world. In Klein, G., Calderwood, R. and Zsambok, C. (Eds.). *Decision-making in action: models and methods*. Ablex. Norwood, NJ. 306-326.

Medicines and Healthcare Products Regulatory Agency. (2014). *How we regulate devices.* http://www.mhra.gov.uk/Howweregulate/Devices/Legislation/index.htm . Accessed 26 April 2014.

Merriam, S. (2009). *Qualitative research: A guide to design and implementation.* Jossey-Bass. San Francisco, CA.

Michie, S., Johnston, M., Abraham, C., Lawton, R., Parker, D. and Walker, A. (2005). Making psychological theory useful for implementing evidence based practice: a consensus approach. *Quality and Safety in Health Care.* 14, 26-33.

Milkman, K., L., Chugh, D. and Bazerman, M.H. (2009). How Can Decision Making Be Improved? *Perspectives on Psychological Science*. 4; (4), 379-383.

Milkman, K., L., Rogers, T. and Bazerman, M. (2008). Harnessing our inner angels and demons: What have we learned about/want/should conflict and how that knowledge can help us reduce short-sighted decision-making. *Perspectives on Psychological Science.* 3, 324-338.

Minsky, M. (1977). Plain talk about neurodevelopmental epistemology. Proceedings of the Fifth International Joint Conference on Artificial Intelligence. Boston. MA. In Winston, P., and Brown, R. (Eds.), 1979. *Artificial Intelligence.* Volume 1. MIT Press. Boston.

Montaño, D.E. and Kasprzyk, D. (2008). Theory of reasoned action, theory of planned behaviour, and integrated behavioural model. *Behavior and Health education: Theory Research and Practice*. (4th Edition). Jossey Bass, SF. 105-172.

Moore, D. and Lowenstein, G. (2004). Self-interest, automaticity, and the psychology of conflict of interest. *Social Justice Research*. 17; (2), 189-202.

Morris, J.A. (2011). The conscious mind and its emergent properties; an analysis based on decision theory. *Medical Hypotheses*. 77; (2), 253-257.

Morse, J.M., Barrett, M., Mayan, M., Olson, K., Spiers, J. (2002). Verification strategies for establishing reliability and validity. Qualitative Research International *Journal of Qualitative Studies.* 1, issue 2.

Mosier, K.L. (1997). Myths of Expert Decision Making and Automated Decision Aids. In Zsambok, C. and Klein, G. (Eds.). *Naturalistic Decision Making*. Lawrence Erlbaum Publishers. Mahwah, NJ. 319-330.

Moule, P. and Goodwin, M. (2009). *Nursing Research: An Introduction.* Sage. London.

Mulholland, J. (1995). Nursing, humanism and transcultural theory: the 'bracketing-out' of reality. *Journal of Advanced Nursing*. 22; (3), 442-449.

Murray E., Charles, C., and Gafni, A. (2006). Shared decision-making in primary care: Taioring the Charles et al. model to fit the context of general practice. *Patient Education and Counseling.* 62; (2), 205-211.

Murray, E., Pollack, L., White, M., and Lo, B. (2007). Clinical decision-making: physician's preferences and experiences. *BMC Family Practice.* 8; (10), 1-10.

Nemeth, C. and Klein, G. (2011). The Naturalistic Decision Making Perspective. In: Cochrane, JJ. (Ed.). *Wiley Encyclopedia of Operations Research and Management Science.* John Wiley and Sons. New York.

Nirmalanandhan, V.S. and Sittampalan, G.S. (2009). Stem cells in drug discovery, tissue engineering, and regenerative medicine: emerging opportunities and challenges. *Journal of Biomolecular Screening.* 755.

Noble, D. (1993). A model to support development of situation assessment aids. In Klein, G., Orasanu, J., Calderwood, R., and Zsambok, C.E. (Eds.). *Decision-making in action: Models and methods*. Ablex. Norwood, NJ. 287-305.

Norman, G. (2006). Building on experience - the development of clinical reasoning. *New England Journal of Medicine*. 355; (21), 2251-2252.

Nussbaum, M.C. (1999). Virtue Ethics: A Misleading Category? *The Journal of Ethics*. 3; (3), 163-201.

Nutt, P.C. (2002). *Why Decisions Fail: Avoiding the Blunders and Traps that Lead to Debacles.* Barrett-Koehler. San Francisco, CA.

Nutt, P.C. (2008). Investigating the Success of Decision Making Processes*. Journal of Management Studies.* 45; (2), 425-455.

O'Connor, A.M., Llewellyn-Thomas, H.A. and Flood, A.M. (2004). Modifying unwarranted variations in health care: shared decision making using patient decision aids. *Health Affairs.* Millwood. Supplement Variation: VAR63-72.

Okasha, S. (2011). Theory choice and social choice: Kuhn versus Arrow. *Mind*. 477, 83-115.

Ollis, S., Button, B., and Fairweather, M. (2005). The influence of professional expertise and task complexity upon the potency of the contextual interference effect. *Acta Psychologica*. 118; (3), 229-244.

Orasanu, J., and Connolly, T. (1993). The reinvention of decision making. In Klein, G. A., Orasanu, J., Calderwood, R. and Zsambook, C.E. (Eds.), *Decision Making in Action: Models and Methods.* Ablex Publishing Corporation. Norwood, NJ. 3-20.

Orasanu, J., Martin, L., and Davidson, J. (2001). Cognitive and contextual factors in aviation accidents: decision errors. In Salas, E. and Klein, G. (Eds.). *Linking expertise and naturalistic decision-making.* Lawrence Erlbaum Associates. Mahwah, NJ. 209-243

Palmer, C.R. (2002). Ethics, data dependent designs and the strategy of clinical trials: time to start learning-as-we-go? *Statistical Methods in Medical Research*. 11, 381-402.

Pannucci, C.J. and Wilkins, E.G. (2010). Identifying and Avoiding Bias in Research. *Plastic and Reconstructive Surgery.* 126; (2), 619-625.

Paris, C.R., Salas, E. and Cannon-Bowers, J. A. (2000). Teamwork in multi-person systems: A review and analysis. *Ergonomics.* 43, 1052-1075.

Passaro, P.D., Cole, H.P., and Wala, A.M. (1994). Flow Distribution Changes in Complex Circuits: Implications for Mine Explosions. *Human Factors.* 36; (4), 745-756.

Patel, V.L., Kaufman, D.R. and Arocha, J.F. (2002). Emerging paradigms of cognition in medical decision-making. *Journal of Biomedical Informatics*. 35, 52-75.

Peirce, C,S. (1997). Pragmatism as a principle and method of Right Thinking. In Turrisi, P.A. (Ed.). *The 1903 Harvard lectures on Pragmatism by Charles Sanders Peirce State*. University of New York Press. Albany, NY.

Perry, C. (2011). A structured approach to the journey of doctoral research. *International Journal of Organisational Behaviour.* 6; (1), 1-12.

Pfeffer, J. and Sutton, R. (2000). *The Knowing-Doing Gap*. Harvard Business School Press. Boston, MA.

Pharmaceutical Product Development. (2014) http://www.ppdi.com/Therapeutics.aspx . Accessed 09 January 2015.

Pharmaceutical Product Development. (2010). Delivering results for our clients, driving value for our shareholders. 2010 Annual Report.

Pharmaceutical Product Development. (2009). *Ahead of the Curve. Delivering results for our clients, driving value for our shareholders.* PPD 2009 Annual Report.

Phillips, N. and Hardy, C. (2002). *Discourse Analysis: Investigating Processes of Social Construction*. Sage. London.

Plano Clark, V.L. (2010). The Adoption and Practice of Mixed Methods: U.S. Trends in Federally Funded Health-Related Research. *Qualitative Inquiry*. 16; (6), 428-440.

Pojman, L.P. and Fieser, J. (2009). Virtue Theory. *Ethics: Discovering Right and Wrong* (6th Edition). Wadsworth. Belmont, CA. 146-169.

Polit, D. F., Beck, C. T., and Hungler, B. P. (2001). *Essentials of Nursing Research: methods, Appraisal, and Utilization*. (5th Edition). Lippincott. Philadelphia.

Polit, D. F., Beck, C. T. (2008). *Nursing Research: Generating and Assessing Evidence for Nursing Practice*. (8th Edition). Lippincott, Williams and Wilkins. Philadelphia, PA.

Polit, D.F. and Hungler B.P. (1999). *Nursing research: Principles and methods*. (6th Edition). Lippincott. Philadelphia.

Politser, P. (1981). Decision Analysis and Clinical Judgment. A Re-evaluation. *Medical Decision Making*. 1; (4), 361-389.

Polkinghorne, D., (1983). *Methodology for the Human Sciences*. SUNY press. Albany.

Pope, C., and Mays, N., (2006). Qualitative methods in health research. In: Pope, C., and Mays, N., (eds). *Qualitative research in health care*. (3rd Edition). Blackwell Publishing. Oxford.

Porter, R. (1997). *The Greatest Benefit to Mankind: A Medical History of Humanity*. WW Norton and Co., New York.

Postmes, T. and Lea, M. (2000). Social processes and group decision-making: anonymity in group decision support systems. *Ergonomics*. 43, 1252-1274.

Prochaska, J., O. (2008). Decision making in the transtheoretical model of behavior change. *Medical Decision Making*. 28; (6), 845-849.

Prochaska, J., O. and Velicer, W., F. (1997). The Transtheoretical Model of Health Behavior Change. *American Journal of Health Promotion.* 12; (1), 38-48.

Raber, J.H. (2010). The Formulary Process from a Risk Management Perspective. *Pharmacotherapy.* 30; (6), 2.

Racher, F., (2003). Using conjoint interviews to research the lived experience of elderly rural couples. *Nurse Researcher*. 19; (3), 60-72.

Rahman, M. (2009) Understanding naturalistic decision making under life threatening conditions. *Proceedings of the 9th International Conference on Naturalistic Decision Making.* The British Computer Society. Swindon. 121-128.

Rakover, S.S. (2002). Reconstruction of Past Events from Memory: An Alternative to the Hypothetico-Deductive (H-D) Method. *Behavior and Philosophy*. Center for Behavioral Studies, Cambridge. 30, 101-122.

Rasmussen, J. (1983). Skill, rules and knowledge: signals, signs and symbols, and other distinctions in human performance models. *IEEE Transactions on Systems, Man and Cybernetics.* 13, 257-266.

Rasmussen, J. (1993a). Deciding and Doing: Decision making in natural contexts. In Klein, G. A., Orasanu, J., Calderwood, R. and Zsambok, C.E. (Eds.). *Decision making in action: Models and methods.* Ablex. Norwood, NJ. 158-171.

Rasmussen, J. (1993b). *Perspectives on the concept of human error*. Paper presented at the Conference on Human Performance and Anesthesia Technology. March. New Orleans, LA.

Reason, J. (1990). *Human error*. Cambridge University Press. Cambridge, England.

Remenyi, D.,Williams, B., Money, A., and Swartz, E. (1998). The case study. In Remenyi, D. (Ed.), *Doing research in business and management: An introduction to process and method*. Sage. London.

Repovš, G. and Baddeley, A. (2006). The multi-component model of working memory explorations in experimental cognitive psychology. *Neuroscience*. 139, 5-21.

Reyna, V.F. (2008a). Theories of Medical Decision Making and Health: An Evidence-Based Approach. *Medical Decision Making*. 28; (6), 829-833.

Reyna, V.F. (2008b). A theory of medical decision making and health: fuzzy-trace theory. *Medical Decision Making*. 28; (6), 850-864.

Reyna, V.F. and Brainerd, C.J. (2011). Dual processes in decision making and developmental neuroscience: A fuzzy-trace model. *Developmental Review*. 31; (2-3), 180-206.

Ribeill, Y.J. (2013). Discovery of new medicines. In Griffen, J.P., Posner, J. and Barker, G.R. (Eds.). *The Textbook of Pharmaceutical Medicine*. (7th Edition). BMJ Books. John Wiley & Sons. Chichester.

Ritchie, J. and Lewis, J. (Editors). (2003). *Qualitative Research Practice. A Guide for Social Science Students and Researchers*. Sage Publications. London.

Ritchie, J., Spencer, L., and O'Connor, W. (2003) Carrying out qualitative analysis. In Ritchie, J. and Lewis, J. (Eds.) *Qualitative research practice: A guide for social science students and researchers*. Sage. London, Thousand Oaks, New Delhi.

Ross, L., Greene, D., and House, P. (1977). The false consensus effect: an egocentric bias in social perception and attribution process. *Journal of Experimental and Social Psychology*. 13, 279-301.

Ross, K.G., Klein, G., Thunholm, P., Schmitt, J.F. and Baxter, H.C. (2004). The Recognition-primed decision model. *Military Review*. LXXIV; (4), 6-10.

Roth, E.M. (1997). Analysis of Decision Making in Nuclear Power Plant Emergencies. An Investigation of Aided Decision Making. In Zsambok, C. and Klein, G. (Eds.). *Naturalistic Decision Making*. Lawrence Erlbaum Publishers. Mahwah, NJ. 175-182.

Rothwell, P.M. (2005). Treating individuals 2. Subgroup analysis in randomised controlled trials: importance, indications, and interpretation. *Lancet.* 365; (9454), 176-186.

Rumelhart, D.E. (1980). Schemata: The building blocks of cognition. In Spiro, R.J., Bruce, B.C. and Brewer, W.F. (Eds.). *Theoretical issues in reading comprehension*. Erlbaum. Hillsdale. NJ.

Sabatier, V., Mangematin, V., and Rouselle, T. (2010). From Recipe to Dinner: Business Model Portfolios in the European Biopharmaceutical Industry. *Long Range Planning.* 43, 431-477.

Sade, R.M. (2007). Report of the Council on Ethical and Judicial Affairs. *The American Medical Association. CEJA Report 10-A-07*. http://www.ama-assn.org/resources/doc/ethics/x-pub/ceja_10a07.pdf . Accessed 12 July 2013.

Salas, E., and Fiore, S. M. (2004). *Team Cognition: Understanding the factors that drive process and performance*. American Psychological Association. Washington.

Salas, E., Muñiz, E. J. and Prince, C. (2001). Situation Awareness in Teams. In Karwowski, W., (Ed.). *International Encyclopaedia of Ergonomics and Human Factors*. Taylor and Francis Ltd. London.

Salas, E. and Klein, G. (Eds.). (2001). *Linking expertise and naturalistic decision making.* Lawrence Erlbaum. Mahwah, NJ.

Salmela, S., Poskiparta, M., Kasila, K., Vahasarja, K. and Vanhala, M. (2009). Transtheoretical model-based dietary interventions in primary care: a review of the evidence in diabetes. *Health Education Research*. 24; (2), 237-252.

Saunders, M., Lewis, P., and Thornhill, A. (2009). *Research Methods for Business Students.* (5th Edition). FT Prentice Hall. London.

Sayre, J. (2000). The Patient's Diagnosis: Exploratory Models of Mental Illness. *Qualitative Health Research.*10; (1), 71-83.

Scharf, C. (2012). *Repudiating Feminism: Young Women in a Neoliberal World*. Ashgate Publishing. Farnham.

Scheffler, S. (1988). *Consequentialism and Its Critics*. Oxford University Press. Oxford.

Schraagen, J.M., Militello, L.G, Ormerod, T. and Lipshitz, R. (2008). *Naturalistic Decision Making and Macrocognition*. Ashgate Publishing. Aldershot.

Schutz, A. (1962). In Natanson, M. (Ed.). *Collected papers I: The problem of social reality.* (3rd Edition). Martinus Nijhoff. Netherlands.

Schwab, A.P. (2008). Putting cognitive psychology to work: Improving decision-making in the medical encounter. *Social Science and Medicine*. 67, 1861-1869.

Schwandt, T.A. (1994). Constructivist, interpretivist approach to human inquiry. In Denzin, N.K.. and Lincoln, Y.S. (Eds.) *Handbook of qualitative research*. Sage Publications. Thousand Oaks, CA. 118-137.

Schwandt, T. A. (2001). *Dictionary of qualitative inquiry.* (2nd Edition). Sage. Thousand Oaks, CA.

Schweizer, M. (2012). *Comparing Holistic and Atomistic Evaluation of Evidence*. MPI Collective Goods Preprint, 2012/21. http://dx.doi.org/10.2139/ssrn.2184242 Accessed 11 January 2013.

Sekaran, U. and Bougie, R. (2010). *Research Methods for Business: A Skill Building Approach.* (5th Edition). John Wiley and Sons. Hoboken. Chichester, NJ.

Shaban, R. Z. (2005). Theories of judgment and decision-making: a review of the

theoretical literature. *Journal of Emergency Primary Health Care*. 3, 1-2.

Shotter, J. (1990). Wiggenstein and and Psychology: on our 'Hook Up' to Reality. *Royal Institute of Philosophy Supplement*. 28, 193-208.

Simon, H.A. (1957). *Models of man*. Wiley. New York.

Simon, H.A. (1983). *Reason in human affairs*. Stanfor University Press. Stanford. CA.

Smith, F. (2012). A Review of the ISO14155:2011 Standard for Conducting Medical Device Clinical Trials. *QUASAR.* April; 119, 10-13.

Smith, J.A., Flowers, P. and Larkin, M. (2009) *Interpretative Phenomenological Analysis. Theory, Method and Research.* Sage. London.

Spiegelberg, S.H., Deluzio, K.J., Muratoglu, O.K. (2003). *Extractable residue from recalled Inter-Op acetabular shells.* 49th Annual Meeting of the Orthopaedic Research Society.

Spring, B. (2008). Health decision-making: lynchpin of evidence-based practice. *Medical Decision Making.* 28; (6), 866-874.

Stacey, D., Légaré, F., Pouliot, S., Kryworuchko, J., and Dunn, S. (2010). Shared decision making models to inform an interprofessional perspective on decision making: a theory analysis. *Patient Education and Counseling*. 80; (2), 164-172.

Stanovich, K.E. and West, R.F. (2000). Individual differences in reasoning: Implications for the rationality of debate. *Behavioral and Brain Sciences*. 23, 645-665.

Starfield, B. (2006). Threads and yarns: weaving the tapestry of comorbidity. *Annals of Family Medicine*. 4, 101-103.

Staw, B.M. (1976). Knee-deep in the Big Muddy: A Study of Escalating Commitment to a Chosen Course of Action. *Organizational Behavior and Human Performance.* 16; (1), 27-44.

Stevenson, F.A. (2003). General practitioner's views on shared decision making: a qualitative analysis. *Patient Education Counseling*. 50, 291-293.

Stout, R. J., Cannon-Bowers, J. A., Salas, E., and Milanovich, D. M. (1999). Planning, shared mental models, and coordinated performance: An empirical link is established. *Human Factors.* 41, 61-72.

Strauss, A. and Corbin, J. (2008). *Basics of Qualitative Research*. (3rd Edition). Sage. Newbury Park, CA.

Stroebe, W. and Diehl, M. (1994). Why groups are less effective than their members: on productivity losses in idea generating groups. In Stroebe, W., and Hewstone, M. (Eds.). *European Review of Social Psychology*. Wiley, Chichester. 271-303.

Suresh, P. and Basu, P.K. (2008). Improving Pharmaceutical Product Development and Manufacturing: Impact on Cost of Drug Development and Cost of Goods Sold of Pharmaceuticals. *Journal of Pharmaceutical Innovation*. 3; (3), 175-187.

Swallow, V., Lambert, H., Santacrose, S.,and Macfadyen, A. (2011). Father and mothers developing skills in managing children's long-term medical conditions: how do their qualitative accounts compare? *Child: Care, Health and Development.* 37, (4), 512-523.

Tamayo-Sarver, J.H., Dawson, N.V., Hinze, S.W., Cydulka, R.K., Wigton, R.S. and Baker, D.W. (2005). Rapid Clinical Decisions in Context: A theoretical model to understand physician's decision-making with an application to racial/ ethnic treatment disparities. *Research in the Sociology of Healthcare*. 23, 183-213.

Thewlis, J. (Ed.) (1973). *Concise Dictionary of Physics*. Pergamon Press. Oxford.

Thomas, J., Harden, A., Oakley, A., Oliver, S., Sutcliffe, K., Rees, R., Brunton, G., Kavanagh, J. (2004). Integrating qualitative research with trials in systematic reviews. *British Medical Journal.* 328, 1010.

Thomson, C. and Dowding, D. (2002). Clinical Decision Making and Judgement in Nursing. Churchill Livingstone. London Tversky, A. and Kahneman, D. (1981). The framing of decisions and the psychology of choice. *Science.* 211, 453-458.

Tierney, S., Elwers, H., Sange, C., Mamas, M., Rutter, M.K., Gibson, M., Neyses, L. and Deaton, C. (2011). What influences physical activity in people with heart failure? A qualitative study. *International Journal of Nursing Studies*. 48; (10), 1234-1243.

Tonelli, M.R. (2006). Integrating evidence into clinical practice: an alternative to evidence-based approaches. *Journal of Evaluation in Clinical Practice.* 12; (3), 248-256.

Tonelli, M.R. (2011). Integrating clinical research into clinical decision making. *Annali Dell Istituto Superiore di Sanita*. 47; (1), 26-30.

Topping, A., (2010). The Quantitative-Qualitative Continuum. In Gerrish, K., and Lacey, A., (Eds). *The Research Process in Nursing*. (6th Edition). Wiley-Blackwell. West Sussex.

Towle, A. and Godolphin, W. (1999). Framework for teaching and learning informed shared decision making. *British Medical Journal.* 319, 766-771.

Traynor, M. (2009). Humanism and its critiques in nursing research literature. Journal of Advanced Nursing. 65; (7), 1560-1567.

Trevino, L.K. (1986). Ethical Decision Making in Organizations: A Person-Situation Interactionist Model. *The Academy of Management Review.* 11; (3), 601-617.

Tuah, N., Amiel, C., Qureshi, S., Car, J., Kaur, B. and Majeed, A. (2011). Transtheoretical model for dietary and physical exercise in weight loss management

for overweight and obsese adults. *Cochrane database of Systematic Reviews*. Oct 5; (10), CD008066. doi: 10.1002/14651858.CD008066.pub2

Tversky, A. and Kahneman, D. (1974). Judgment under uncertainty: Heuristics and biases. *Science*. 185, 1124-1131.

Tversky, A. and Kahneman, D. (1981).The framing of decisions and the psychology of choice. *Science*. 211, 453-458.

Tversky, A. and Koehler, D. (1994). Support theory: a non-extensional representation of subjective probability. *Psychology Review*. 101, 547-567.

Uchitelle, L. (2006). Lure of Great Wealth Affects Career Choices. *New York Times*. November 27.

van Manen, M. (1990). *Researching Lived Experience: Human Science for an Action Sensitive Pedagogy*. Althouse Press. Ontario.

van Manen, M. (1997). *Researching the lived experience: human science for an action sensitive pedagogy*. (2nd Edition). Althouse Press. Ontario.

van Schaik, P., Flynn, D., van Wersch, A., Douglass, A. and Cann, P. (2005). Influence of illness script components and medical practice on medical decision making. *Journal of Experimental Psychology*. 11, 187-199.

Virani, T., Lemieux-Charles, L. Davis, D.A. and Berta, W. (2009). Sustaining Change: Once Evidence-Based Practices Are Transferred, What Then? *Healthcare Quarterly.* 12; (1), 89-95.

Wacker, C., Prkno, A., Brunkhorst, F.M. and Schlattmann, P. (2013). Procalcitonin as a diagnostic marker for sepsis: a systematic review and meta-analysis. *The Lancet Infectious Diseases*. 13: (5), 426–435.

Wainwright, D.W. and Waring, T.S. (2006). The Politics of Information and Communication Technology Diffusion: A Case Study in a UK Primary Health Care Trust. The Transfer and Diffusion of Information Technology for Organizational Resilience. In Donnellan, B., Larsen, T., Levine, L. and DeGross, J. (Eds.). *International Federation of Information Processing*. 206, 71-90.

Wand, Y. and Weber, R. (1993). "On the ontological expressiveness of information systems analysis and design grammars," *Journal of Information Systems.* 3; (4), 217-237.

Wang, K. (2015). China Introduces New Medical Device GMP and GSP Rules. http://www.ropesgray.com/news-and-insights/Insights/2015/January/China-Introduces-New-Medical-Device-GMP-and-GSP-Rules.aspx?utm_source=Mondaq&utm_medium=syndication&utm_campaign=View-Original Ropes and Gray. Accessed 08 January 2015.

Ward, D.J., Furber, C., Tierney, S. and Swallow, V. (2013). Using Framework Analysis in nursing research: a worked example. *Journal of Advanced Nursing.* 69; (11), 2423-2431.

Webb, T., Joseph, J., Yardley, L. and Michie, S. (2010). Using the Internet to promote health behavior change: A systematic review and meta-analysis of the impact of theoretical basis, use of behavior change techniques, and mode of delivery on efficacy. *Journal of Medical Internet Research*. 10; 12(1), e4.

Webb, C. and Kevern, J., (2000). Focus groups as a research method: a critique of some aspects of their use in nursing. *Journal of Advanced Nursing*. 33 (6), 798-805.

Weber, M. (1947). *The Theory of Social and Economic Organization*. Translated by Henderson, A. M. and Parsons, T. The Free Press. Glencoe, IL.

Weick, K.E. (1995). *Sensemaking in Organizations*. Sage Publications. Thousand Oaks, CA.

West, R. (2005). Time for a change: putting the Transtheoretical (Stages of Change) Model to rest. *Addiction*. 100; (8), 1036-1039.

White, J.E., Nativio, D.G., Kobert, S.N. and Engburg, S.J. (1992). Content and process in clinical decision making by nurse practitioners. *Image: The Journal of Nursing Scholarship*. 24; (2), 153-158.

Whitney, S.N., Holmes-Rovner, M. and Brody, H. (2008).Beyond Shared Decision Making: An expanded typology of medical decisions. *Medical Decision Making*. 28, 699-705.

Wiggenstein, L. (2010). In Hacker, P.M.S., and Schulte, J. (Eds.). *Philosophical Investigations.* (4th Edition). Wiley-Blackwell. West Sussex.

Willig, C., (2008) *Introducing Qualitative Research in Psychology. Adventures in Theory and Method.* Open University Press. Maidenhead.

World Health Organization. (2009). *Definition of Terms.* http://www.wpro.who.int/nr/rdonlyres/45b45060-a38e-496f-b2c1-bd2dc6c04c52/0/44definitionofterms2009.pdf . Accessed 24th June 2011.

Woods, D.D., Johannesen, L.J., Cook, R.I., and Sarter, N.B. (1994). Behind human error: cognitive systems, computers and hindsight. *Crew Systems Ergonomics Information Analysis System*. Wright-Patterson AFB. Dayton, OH.

Woolever, D.R. (2008). The Art and Science of Clinical Decision Making. *Family Practice Management.* 15; (5), 31-36.

Woolf, S.H, Chan, E., C., Y., Harris, R., Sheridan, S., L., Braddock, C., H., Kaplan, R., M., Krist, A, O'Connor, A., M., Tunis, S. (2005). Promoting Informed Choice: Transforming Health Care To Dispense Knowledge for Decision Making. *Annals of Internal Medicine.* 143, 293-300.

World Medical Association. (2014). *Handbook of Declarations.* http://www.wma.net/en/30publications/10policies/10about/index.html Accessed 5th July 2014.

World Medical Association. (2013). 64th Assembly. *Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects*. World Medical Association. Fortaleza, Brazil.

Wu, H.W., Davis, P.K., and Bell, D.S. (2012). Advancing clinical decision support using lessons from outside of healthcare: an interdisciplinary systematic review. *BMC Medical Informatics and Decision Making*. 12, 90.

Xia, J., Arrowsmith, C., Jackson, M., and Cartwright, W. (2008). The way finding process relationships between decision-making and landmark utility. *Tourism Management.* 29; (3), 445-457.

Yates, F.J. (2001). "Outsider" impressions of naturalistic decision-making. In Salas, E. and Klein, G.A. (Eds.). *Linking expertise and naturalistic decision-making.* Lawrence Erlbaum Associates. Mahwah, NJ. 9-35.

Yetisen, A. K., Martinez-Hurtado, J. L., da Cruz Vasconcellos, F., Emre Simsekler, M.C., Akram, M.S., Lowe, C.R. (2014). The regulation of mobile medical applications. *Lab on a Chip*. 14; (5), 833-840.

Yin, R.K. (2009). *Case Study Research. Design and Methods*. Fourth Edition. Sage Publications. Thousand Oaks, CA.

Zsambok, C. E. (1997). Naturalistic decision-making: Where are we now? In Zsambok, C.E. and Klein, G. (Eds.), *Naturalistic decision making.* Lawrence Erlbaum Associates Inc.. Mahwah, NJ. 3-16.

Zsambok, C.E., and Klein, G. (Eds.) (2014). *Naturalistic Decision Making*. Psychology Press. New York.

Zuckerman, D. (2011). Medical Device Recalls and the FDA Approval Process. *Archives of Internal Medicine.* 171; **(**11), 1006-1011.

APPENDICES :

Ref	Title	Page:
A	Physician demographics within purposive sample	**196**
B	Dr “Cairngorm” interview transcript	**197**
C	Cairngorm data coding frame with in-vivo comments	**204**
D	Data Coding Frame – Overall summary	**205**
E	Literature influencing data collection questions	**206**
F	Interviewee questionnaire	**208**
G	PPD physician’s perceptions on documents needed for ISO14155:2011 compliance	**210**

APPENDIX A :

Physician demographics within purposive sample

Identifier	Sex	Ethnicity	Nationality	Medical degree	University	Graduated	Registration status	Med Practice (yrs)	CRO (years)	Location
Cairngorm	F	White	British	MB ChB	Cambridge	1981	Active & current	21	10	Cambridge
Campsie	M	White	British	MB ChB	Leeds	1979	Active & current	22	11	Cambridge
Cuillen	F	White	British	MB ChB	London	1985	Active & current	18	10	Cambridge
Galloway	M	White	British	MB ChB	London	1989	Active & current	11	13	Cambridge
Grampian	F	African	American	MD	Alabama	1993	Active & current	10	10	Raleigh
Lammermuir	M	Asian	American	MD	Colorado	1991	Active & current	12	10	Wilmington
Lowther	F	White	American	MD	Florida	1986	Active & current	16	11	Wilmington
Moffat	F	Hispanic	Spanish	LMS	Barcelona	1991	Active & current	10	12	Raleigh
Moorfoot	M	White	American	MD	N Carolina	1992	Active & current	12	9	Wilmington
Munro	F	White	American	MD	Maryland	1985	Active & current	19	9	Wilmington
Ochil	M	Latino	American	MD	Texas	1983	Active & current	18	12	Wilmington
Pentland	M	White	American	MD	N Carolina	1990	Active & current	13	10	Raleigh
Sidlaw - A	F	White	American	MD	S Carolina	1988	Active & current	14	10	Wilmington
Sidlaw - B	F	White	American	MD	N Carolina	1989	Active & current	11	13	Wilmington
Sidlaw - C	F	White	Irish	MB BCh BAO	Dublin	1987	Active & current	16	10	Raleigh
Torridon - A	M	White	British	MB ChB	Brighton	1976	Active & current	21	16	Cambridge
Torridon - B	F	White	British	MB ChB	Edinburgh	1975	Active & current	26	11	Glasgow
Torridon - C	F	White	British	MB ChB	Manchester	1984	Active & current	15	14	Cambridge

Note: Dr "Cairngorm" profile highlighted in yellow. Cairngorm transcript follows in Appendix B, together with subsequent coding frameworks appearing in Appendices C and D respectively.

APPENDIX B: Dr "Cairngorm" transcript, PPD Cambridge office, 16 Sep 2013.

Decision making approach

Q. What are the key decision making areas, or themes, covered by PPD regulatory decision makers?

A. Depends on what the decision is and what it is about. Because I probably make decisions about 100 times a day about various things and they are all totally different. So you've got to know what the question is. A lot of our decisions are around protocol questions so you need to know the protocol. Look at the question and refer to the protocol to make sure that whatever you are saying is in line with the protocol. The trouble is that you really need to understand what the person is asking if asking a protocol question. If it's simple, then I answer. However, it's not always clear what's being asked. Sometimes it takes a little time to do that. So, I look at it, then I'll go do something else for a bit. Coming back to it helps me to really try to think about the subject and think of alternatives. So, for example, I had a compliance decision to make recently which wasn't straightforward & thought it could be one thing or another. Went back & forth between the two as reasons why it could be either one. So, I went away and did other things, came back to it, and then kind of decided.

Q. Does regulatory compliance decision making approaches differ within PPD?

A. I think it would, particularly for checking whether legislation is applicable to our company and department. However, I do not know how other departments address these things.

Q. How do physicians make regulatory judgements and decide on a course of action at PPD?

A. I look at it in the context of the overall patient. If it's something clear cut then just go by the protocol. If decisions is unclear, say reviewing lab data which requires some clinical judgment about whether it is medically relevant or not, I'd look at the data, look at it in the context, consider what possible outcomes could be or scenarios before deciding whether to issue a query about it or not. What risks to patient? What pieces of data are needed for completeness?

Q. What DM tools and techniques are used in PPD to make decisions?

A. We do not really use them in PPD.

Situation awareness

Q. How does context / situation awareness influence problem solving as part of your professional decision making processing?

A. My situation awareness comprises study related medical decisions, or guiding team involvement, rather than focusing on individual subjects. If data is needed I raise queries that go back to the investigating doctor based on my knowledge of the clinical condition. At other times it can be based on a patient's history or through examination of data and findings. So, its diagnosis, treatment then deciding trial management in terms of the clinical investigation, starting with the patient history.

Q. What can you tell me about ISO14155:2011?

A. Well, ISO14155 is a harmonized regulatory standard that defines how companies should conduct and undertake clinical trial investigations of medical devices. It carries several mandatory compliance elements and they are checked by the notified bodies such as BSI.

Q. What decision making factors are needed for compliance with ISO14155:2011?

A. In our department we need to determine if the standard is applicable then a comprehensive and robust plan is put in place that will cover all client and business study needs. This includes research and development activities of the medical device, its subsequent classification, interaction with the regulatory authorities and notified body, business planning, pre-study assessments, planning and scheduling the investigation activities and ensuring appropriate selection of the principal study investigators.

Q. What would you say are the essentials elements of compliance with ISO14155:2011?

A. The clinical trial study documents are absolutely critical. For example the investigator brochure, study protocol, clinical investigation plan, case report form, adverse event form, staff CV, signature log, ethics committee approval, health authority approvals, financial contract, informed consent form, training records, operational documents, lab values and declaration of conformity.

Q. How have you ascertained the requirements for ISO14155:2011?

A. Through the recent RISC meeting where the topic was an agenda item. I am the medical monitors group rep so will take the new information back to the department for relaying to my colleagues at the team meeting.

Q. How does context or situation awareness influence problem solving as part of PPD and your professional decision making process?

A. In the past PPD was really bad at not having context around whatever people want you to do. Particularly when I first started, for the first couple of years, you'd be invited to a meeting but there would never be any context, never be an overall strategy, never be any communication about background to projects, what it was all about, what it was trying to achieve? etc. It was a case of someone starting talking about what they wanted you to do but never any context or background to it. So, it's extremely poor. Today, we have high level company goals to guide us but have to interpret them at department level by picking on things that we know are achievable. However this means having to translate them into something that is understandable. Although the vast majority of what we do supports clinical trials but our name is a misnoma as we have absolutely no involvement with the clinical sites.

Q. How has this way of working affected the PPD approach to decision making?

A. It can be difficult because of the number of moving parts and people having alternate priorities and agendas. Certainly when I was in hospital medicine, it did not seem to be terribly worthwhile in terms of intervention. Let's put it this way - in medicine people tend to get better by themselves but not in surgery. So if you are a GP then you don't need to do anything because people will get better by themselves since not a lot of really useful things take place there. The point of saying this is that whatever you're doing in PPD: a piece of text for this, figures or hours for that – we do the best job for making it up but I'm not sure that it reflects reality per se. However, I do not believe that you can't say we'll do this one

this way. We do try and train people in the base medical tasks to do things in a particular way and answer consistently such as listings, reviews, answering queries or labs.

Unfortunately, we actually do not have the personnel with the experience for so it's kind of making it up a little bit. But it doesn't seem to matter that what we say is speculative. It's not a very good way of working. It's just the culture of the company that you've got to do without any, or that type of, information. Oh well whatever! We'll do this for the time being & then we might change the decision at a later date when you give us some information about it. It's a definite means for improvement. I'm not sure it's possible to improve but it is certainly an opportunity.

Q. How has this way of working affected the department approach to decision making?
A. PPD is particularly bad at not having context around whatever people want you to do. People have their own agendas. So, they simply ask away but see no need to provide any background or justification for it. The thing with PPD is that you've got to decide more quickly and without much context than any other place I've worked. Quality is less important as long as you give an answer received according to people's timeframes but there's not much critique of whatever the deliverable is. For example each bid for medical monitoring services is so different. I might make 100 decisions a day but they are all different and presenting data changes and is all different. However, as a trained medic I'm always looking to see what are the risks to patient. In medicine, everything you do is based on the patient's history and examination of findings. I try to do this in PPD to a certain extent by seeking out what pieces of data are needed for completeness through the overall patient context.

Q. How does prior knowledge affect compliance decision making approach in PPD?
A. Well it's difficult to assess whether people use it or not. Generally yes. But it's more about the process than a peck and the paper pushing part rather than the medical decision making. You just kind of figure out that things will be alright in the end. Which generally is the same in medicine, pretty much, as people get better despite what you do, not because of it often.

Expertise in context

Q. How do you use you past experience to categorise situations and make judgments?

A. It depends on what you are trying to decide about. Whether it is something easy, whether you need to bother other people, whether it is something that you need to think a lot about. Just depends on the question. If I can't decide then it's really helpful to talk to others. If they know something better than I do, whether it's therapeutic area or whatever then I'd go & chat to that somebody. Almost always.

Q. How do individual expert differences affect the decision strategies in PPD?

A. I think it does because people have different interpretations of whatever the question is and so would do different things. Not necessarily that the different things are wrong just that you could approach in different ways. I think that people also come from different perspectives and take different stances on things. So it's often helpful to say what would you do with this problem, in this situation and see what options there are? That's an approach that I use often. It doesn't have to be with other physicians either. Get answers back & then I think "Oh yeah, that's a good idea, I wonder if that would work for me in my situation." I don't have a process. I don't choose it just that one scenario sounds like the best thing to do. If you have options you think which one would be the best, which one would apply the most.

Q. How do expert group differences affect decision strategies at PPD?

A. I don't know. Sometimes you think that's a load of crap! Based on a hunch maybe but I don't know I've never thought about it before. Some things you decide on a hunch, for example, when we are recruiting. That's much more based on instinct than on any decision making. Other times I talk to my peers and discuss projects or cases, either initiated by me or in team calls.

Q. If task-by-task model works & subjective one more open to interpretation, is there a mechanism to discuss the interpretation?

A. Yes. Team meetings, & that sort of thing, where people can bring to the table things they are uncertain about, or have had a dilemma about. Four or five people participate in the discussion such as regional medical monitor, medical monitor, sponsor physician(s).

Q. If split decision how do you decide which way to go?

A. Either be the sponsor person or the lead medical monitor. Normally the sponsor though.

Q. Is there any formula or framework in use within PPD for split decisions?

A. No process. What we do is that people just put their perspectives and arguments forward for doing this one way or the other. Typically decision making is by consensus. However, if no consensus then that's something that we might need to revisit. It is rare that there's no consensus or absolute dichotomy. Someone would speak out, voice an opinion, we consider it and come to a consensus somehow. In more complicated or complex scenarios some things are open to interpretation. When things are subjective it's difficult to ensure everyone doing the same thing, unless very clear directives on a task-by-task, or study-by-study, basis are given.

Q. How do you account for variability in human DM?

A. Well you can't. If you ask three physicians you get four opinions at the best of times. What we do try and do is to have one person overseeing the medical monitors for a particular study. So the lead oversees the regional & study MM & that lead person will check the output whether leads, queries or labs or whatever to make sure we are doing things in the same way.

Q. What themes, tools and areas influence physician decision-making at PPD?

A. Training on the process is the initial thing. Then having the tasks supervised for period of time. The become unsupervised only when they had demonstrated that they were reasonably competent. For each new study that we get there would be period where the lead person trains the other and disseminates medically related and study pertinent information down to them.

Q. Does this apply to case specifics or does it apply to organisational decisions too?

A. Probably a bit of both.

Q. So what's the mechanism to establish competency?

A. Well, it's the lead person reviewing whatever pieces of work they send out and making sure that there is sufficient quality and that the answers are accurate. Then when they have

seen a dozen, or something like that, then they say its fine for that person not to show me all their work before it goes out. The number is entirely arbitrary.

Q. Do you ever make decisions under emotion?

A. I suppose so. Emotion can influence decision-making but I've no experience of that here. PPD don't tend to discriminate or act on it to guide thinking or action. If anyone did then you'd revisit the decision when feeling less emotional.

Q. Do all physicians in the team follow this approach?

A. I don't really know.

Q. Are there any other approaches that you've seen I clinical practice or other roles?

A. I don't know.

Q. How do you build expertise in your current role?

A. For myself? It's trial and error and more based on a hunch than on any decision-making process. However, I do try and check with someone else if it's the right thing. I try and get feedback in advance of deciding, or decide, then get feedback on whether that was a good decision or good thing to do, etc.

Q. Is that something you do regularly?

A. Yeah. I think so.

Q. Do you share that information?

A. Well, probably not. Sometimes, depends on the information. Because if it is role specific then it wouldn't matter. So what I'd commonly do would be to talk with xxxxx and say I did such-and such, what do you think? Seek feedback – that's ok, or you should have done this or that … blah, blah, blah. So that's a really good way of me getting feedback on the decisions I've made and what else I could have considered & done differently. Xxxxx also operates in a similar manner. So, for example, we do feedback on various things.

Q. How do expert physicians influence and shape compliance decision making in PPD?

A. What we do is try and get the story, then make a mental list of what options there would be and then look for information to support them. If we get different answers then we look for different information to support them. It could be that information comes from any source. So, for example, when asked to give a SAE rate for protocols when bidding them, we view the clinical protocol, and decide whether it's simple, short study, blah, blah, blah … so get basic information from the protocol and then think of prior cases or percentage occurrences, such as about 30%, could be a little higher, say 40%, and then I'll go and collect additional pieces of information to support that and then refine my answer so it's as good as can be by looking at internet, prescribing information, other protocols, blah, blah, blah. So you end up trying to refine that number back down to something that is accurate by getting information around it. So, I think that is probably a model for decision making – get story, get basics, formulate some sort of mental list of answers, hypotheses or diagnoses, and then look for information to support or refute them.

Q. Do expert group differences affect decision strategies in PPD?

A. Probably but I haven't time to think about it. The rest of the team are probably the same.

Q. Does your professional training as a doctor influence the decision making approach?

A. Maybe but I don't know whether it's anything to do with training as a doctor, probably more to do with clinical experience and observing others. For example, I take the history first. So that gives you the story. Then do some investigations to get more information from different sources that are more detailed. I try and make a mental list of options and form hypotheses. Then you have chunks of information that would support or refute those hypotheses.

Q. How does cognition and intuition influence your expertise within clinical research?

A. I think there's a case for assessing lots of alternatives when it comes to decision making in clinical trials. That includes knowing instinctively what to do, for example, in trial design rather than ploughing through phase III the whole time. However, it's rare that something is really thought of , or evaluated, from a fully reasoned or considered point of view because normally clients have a fixed idea of what they want before they come to PPD and aren't really open to alternative suggestions. They want to do things their way and that's it. So I think that's a big chunk of it. We don't really need to think of alternatives because the direction is pretty much cast in stone. Strategy is there but all we're really doing is responding to the individual questions and tasks. A little bit of manoeverability is possible but not very much and so expertise can be redundant.

Decision Error

Q. How are decision errors accounted for within the decision making process @ PPD?

A. When something is going wrong then we'll have a team meeting to discuss it. Try and look out what went wrong and any underlying factors. Then, we try to fathom out what are the options for doing something differently. How to evaluate those options as the best ones? So there is a kind of mental process for trouble shooting that way. We don't really do proactive. I suppose in the project team situation there are different scenarios that can be looked at, such as different options at project team level whether you bring more sites on, or try & focus on the sites you have got, or that sort of thing

Q. Is the trouble shooting process is efficient?

A. I think it's pretty efficient because the speed at which this company moves is phenomenal in terms of successfully trouble shooting things. Quickly deciding on alternatives and then implementing them is something we are really good at. However, it's difficult because lots of times we've not seen good decisions from sponsors but that doesn't bother me in the slightest. They can make their own mistakes. I wouldn't argue against them unless it impacted on PPD. How it affects their work is their problem.

Q. So if a client makes a call and it negatively impacts on you or your team what would you do?

A. We would normally try and talk them out of it using cost as a driver. We say that we can do that if you want but that will cost extra. It does not seem to be a typically successful strategy though. Client makes a decision and sticks to it. It's steadfast and not usually changed. Because we're their servants. You don't take advice from your cleaning lady at home, do you? So they don't really take advice from us!

Q. How are decision errors categorised within the decision making process @ PPD?
A. My feeling is that we tend to take not necessarily the easiest option, but the most straightforward option based on current knowledge or knowledge from past experience. Group past experience or individuals past experience within the group, but we tend to do things the same way and not look to the future much. It is effective but doesn't necessarily give you anything innovative or out of the ordinary.

Q. Where and when can expert decision errors occur within the decision making process @ PPD?

A. I don't know if it is poor decision making, or not, or things are just very vague. For example, doctors are assigned to client programs but no one really decides what that means and how that's going to be operationalized. A lack of context, wide understanding of what that means to be in a specific client alliance, linked to vague expectations and unclear requirements is frustrating. PPD people do not understand their roles and what that means because it is not really made clear to them. So it's hardly surprising errors occur.

Q. What error factors impact the decision making process @ PPD?

A. That's the trouble. It's extremely badly organised and not communicated to the rest of the organisation although in RFI innovative proposals are sometimes discussed.

Q. When decision errors occur how are they identified and addressed?

A. Usually an internal call of some description alerting me to a project problem. It all sounds great in theory but actually in practice no one knows what they are doing, the clients are never happy, we end up working for free a lot of the time because their expectations as a client are something that we cannot match.

Q. What resources exist in PPD to avoid decision errors?

A. None. I assign resources once error notifications appear on my desk. It does astonish me actually that people talk about doing stuff right first time but people do not know what their role is, or what they are supposed to be doing and that it is not really communicated. There is no shared understanding. Project managers should do that but maybe they do not understand either. Then you receive negative feedback such as clients aren't very happy with you because you are not doing this, or a situation has occurred here. But how are we supposed to know what we're meant to do? That's at the senior director level. People who are in charge of client programs expect everyone to be able to know what they're supposed to be doing without them communicating it. It's all very badly done.

Q. Could errors influence ISO14155 decision making compliance?

A. Assessing for errors is really about conducting a business impact assessment and determining the risks involved. Decide what that means and how that's going to be operationalised, set expectations and communicate, so shared understanding. Then interpret ISO14155 to determine its applicability, scope and impact on our business.

Footnotes:

- Red text depicts four core DM concepts identified from literature review (chapter 2).
- Yellow highlighted text shows in-vivo segments identified for framework analysis coding (see Appendix C).

APPENDIX C: Cairngorm data coding frame with in-vivo comments

Decision making issues

In-Vivo Segment	Key issue	Transcript code	Aug thesis ref	Feb thesis ref
more based on a hunch than on any decision-making process	Intuition	Cairngorm, 5	chapter 4, p. 87	chapter 4, p. 93
if you ask 3 physicians, you get 4 opinions at the best of times	Process & procedure	Cairngorm, 4	chapter 4, p. 88	chapter 4, p. 94
some things are open to interpretation. When subjective it's difficult to ensure everyone doing the same thing, unless very clear directives on a task-by-task, or study-by-study, basis are given	Process & procedure	Cairngorm, 4	chapter 4, p. 88	chapter 4, p. 94
I take the history first. So that gives you the story. Then do some investigations to get more information from different sources that are more detailed. I try and make a mental list of options and form hypotheses. Then you have chunks of information that would support or refute those hypotheses.	Reasoned approach	Cairngorm, 6	chapter 4, p. 89	chapter 4, p. 95
rare that there's no consensus, or absolute dichotomy, Someone will speak out, voice an opinion, we consider it and come to a consensus somehow.	Second opinion	Cairngorm, 4	chapter 4, p. 92	chapter 4, p. 98
emotion can influence decision-making but I've no experience of that here. PPD don't tend to discriminate or act on it to guide thinking or action. If anyone did then you'd revisit the decision when feeling less emotional.	Emotion	Cairngorm, 5	chapter 4, p. 93	chapter 4, p. 99
it's not always clear what's being asked. Sometimes it takes a little time to do that. So, I look at it, then I'll go do something else for a bit. Coming back to it helps me to really try to think about the subject and think of alternatives.	Reflection	Cairngorm, 1	chapter 4, p. 93	chapter 4, p. 99
do not really use them in PPD.	Decision tools	Cairngorm, 1	chapter 4, p. 95	chapter 4, p. 101
it carries several mandatory compliance elements and they are checked by the notified bodies such as BSI.	Understand ISO14155	Cairngorm, 1	chapter 4, p. 103	chapter 4, p. 109
conducting a business impact assessment and determining the risks involved. Decide what that means and how that's going to be operationalised, set expectations and communicate, so shared understanding. Then interpret ISO14155 to determine its applicability, scope and impact on our business.	Plan for ISO14144	Cairngorm, 8	chapter 4, p. 104	chapter 4, p. 110
if the standard is applicable then a comprehensive and robust plan is put in place that will cover all client and business study needs. This includes research and development activities of the medical device, its subsequent classification, interaction with the regulatory authorities and notified body, business planning, pre-study assessments, planning and scheduling the investigation activities and ensuring appropriate selection of the principal study investigators.	Plan for ISO14155	Cairngorm, 2	chapter 4, p. 104	chapter 4, p. 110
PPD is particularly bad at not having context around whatever people want you to do. People have their own agendas. So, they simply ask away but see no need to provide any background or justification for it.	People	Cairngorm, 3	chapter 4, p. 110	chapter 4, p. 116
it doesn't seem to matter that what we say is speculative.	Client view	Cairngorm, 3	chapter 4, p. 113	chapter 4, p. 119
as a trained medic I'm always looking to see what are the risks to patient. In medicine, everything you do is based on the patient's history and examination of findings. I try to do this in PPD to a certain extent by seeking out what pieces of data are needed for completeness through the overall patient context.	Patient view	Cairngorm, 3	chapter 4, p. 113	chapter 4, p. 119
you just kind of figure out that things will be alright in the end. Which generally is the same in medicine, pretty much, as people get better despite what you do, not because of it often.	Patient view	Cairngorm, 3	chapter 4, p. 113	chapter 4, p. 119
Absolutely no involvement with the clinical sites.	Clinical sites	Cairngorm, 2	chapter 4, p. 114	chapter 4, p. 120
you've got to decide more quickly and without much context than any other place I've worked. Quality is less important as long as you give an answer received according to people's timeframes but there's not much critique of whatever the deliverable is.	DM criticism	Cairngorm, 3	chapter 4, p. 117	chapter 4, p. 123

APPENDIX D: Data Coding Frame – Overall summary

The data coding frame that summarizes regulatory compliance decision-making core concepts, dimensions and key issues, as discoursed by the purposive sample of PPD physicians during interviews, is illustrated below. Cairngorm's contribution to key issues, identified from in-vivo segments (highlighted in yellow within Appendix B) and highlighted in green text (Appendix C), is outlined in green text in the right hand column of the Appendix D table below.

Each of the four core concepts (as illustrated in chapter 2, figure 2.4 following literature review) are depicted in the left hand column of table below. Each core concept has been sub-divided into dimensions and key issues. The key issues are gleaned from the physician assertions gathered during each interview. Dimensions were built via the data framework analysis (see chapter 4, tables 4.2, 4.3, 4.4 and 4.5) with the final output being a tabulated summary (chapter 4, table 4.1), and replicated below, that highlights the links between dimensions and key issues presented.

Core concept	Dimension	Key issues
Decision-making	At PPD Physician approaches Physician influences Types and tools	No formal model; C-suite versus department; Physician involvement. Instinct; intuition; reasoned thought; hybrid method(s) & skillset(s). Individual versus Group DM; Emotion; Reflection; Criticism Strategic, tactical, transactional Some versus none.
Decision error	Correction Effectiveness Improvement measure(s) Error prevention	Identify, confirm, react and fix. Check that fix works. Lessons learned so get better. How to stop errors occurring?
ISO14155:2011 compliance	Awareness Understanding Planning Study execution Analysis & reporting	Info source: internal vs. external. Clarity, interpretation & impact. What is needed? Who to engage? How & who to do it? Check, act & execute.
Situational awareness	ISO14155:2011 impact PPD implications Environmental influences	Compliant decision-making factors. Company vs. vigilance department; People; Process; Procedure. Client; Patient; Clinical site; Regulatory Authority.

APPENDIX E: Literature influencing data collection questions

How do decision making principles guide physicians' compliance with ISO14155 for running medical device clinical trials? (Smith, 2012; Hajjaj *et al*., 2010; Klein, 2008; Kvale, 1996)

- **DM modeling**

Question	Reference source(s)
How are / what the DM approaches, aids or tools used in clinical practice? In PPD? Expand (for more detail).	Nemeth & Klein, 2011; Klein, 2008
What are the key decision making areas, or themes, covered by regulatory decision makers at PPD?	Hajjaj *et al*., 2010; Lipshitz *et al.,* 2001;
Does DM differ within PPD projects & departments? If yes, explain.	Hardy and Smith, 2008; Klein, 1998
Does DM approach differ within between individual decision makers? If yes, explain.	Lipworth, Kerridge and Day, 2013
How do physicians make regulatory judgments and decide on a course of action @ PPD?	Guerrier *et al*., 2013; Gill and Lambert, 2004

- **Situation Awareness**

Question	Reference source(s)
How does context / situation awareness influence problem solving as part of your professional decision making processing?	Bensing, 2000; Endsley, 1997
Explore how does this process work at PPD? If not, why? Other factors?	Cohen, Freeman & Thompson, 1997
How have you ascertained the requirements for ISO14155:2011?	Smith, 2012
How has this knowledge affected the organisational / departmental / individual DM approach for compliance with ISO14155:2011	Lipworth *et al*., 2012; Klein, 2008
What are the key DM factors needed for compliance with ISO14155:2011? How comply? What is needed?	Smith, 2012; Spring, 2008

- **Expertise**

Question	Reference source(s)
How do you use your past experience to categorise situations and make judgments?	Hafferty, 2006
How do individual expert differences affect decision strategies in PPD	Norman, 2006
How do expert group differences affect decision strategies @ PPD?	Bowen, 2006
How does your professional training, skills and experience influence your decision-making approach	Christ, 2014; Starfield, 2006; Rothwell, 2005
How do expert groups influence and shape decision-making @ PPD?	Woolever, 2008
What themes, factors, tools, areas influence expert DM groups (physicians) @ PPD?	Groopman, 2007
How does cognition & intuition influence your expertise?	Lipshitz, 1997

- **Decision error**

Question	Reference source(s)
How are decision errors accounted for within the decision-making process @ PPD?	Jones & Roelofsma, 2000
How are decision errors categorised within the decision-making process @ PPD?	Orasanu, Martin & Davidson, 2001
Where and when can expert decision errors occur in the decision-making process @ PPD?	Martin & Davidson, 2001; Woods *et al.,* 1994
What error factors impact the decision-making process @ PPD?	Lipshitz, 1997
When decision errors occur how are they identified and addressed?	Dreyfus & Dreyfus, 1986
What resources do PPD have in place to avoid decision errors?	Rettinger & Hastie, 2001; Lipshitz *et al*., 2001
What errors could influence ISO14155 DM compliance	Smith, 2012; Lipshitz & Ben Shaul, 1997; Cook & Woods, 1994

APPENDIX F: INTERVIEWEE QUESTIONNAIRE

Data collection questions:

How do decision making principles guide physicians' compliance with ISO14155 for running medical device clinical trials?

- **DM modeling**

Question	Semi-Structured Interview	Mini Focus Group
How are / what the DM approaches, aids or tools used in clinical practice? In PPD?	**X**	**X**
Expand (for more detail).	**?**	**?**
What are the key decision making areas, or themes, covered by regulatory decision makers at PPD?	**X**	**X**
Does DM differ within PPD projects & departments? If yes, explain.	**X**	**X**
Does DM approach differ within between individual decision makers? If yes, explain.	**X**	**X**
How do physicians make regs judgments and decide on a course of action @ PPD?	**X**	**X**

- **Situation Awareness**

Question	Semi-Structured Interview	Mini Focus Group
How does context / situation awareness influence problem solving as part of your professional decision making processing?	X	X
Explore how does this process work at PPD?	X	X
If not, why? Other factors?	X	X
How have you ascertained the requirements for ISO14155:2011?	X	X
How has this knowledge affected the organisational / departmental / individual DM approach for compliance with ISO14155:2011	X	X
What are the key DM factors needed for compliance with ISO14155:2011? How comply? What is needed?	X	X

- **Expertise**

Question	Semi-Structured Interview	Mini Focus Group
How do you use your past experience to categorise situations and make judgments?	X	X
How do individual expert differences affect decision strategies in PPD	X	X
How do expert group differences affect decision strategies @ PPD?	X	X
How does your professional training, skills and experience influence your decision-making approach	X	X
How do expert groups influence and shape decision-making @ PPD?	X	X
What themes, factors, tools, areas influence expert DM groups (physicians) @ PPD?	X	X
How does cognition & intuition influence your expertise?	X	X

- **Decision error**

Question	Semi-Structured Interview	Mini Focus Group
How are decision errors accounted for within the decision-making process @ PPD?	X	X
How are decision errors categorised within the decision-making process @ PPD?	X	X
Where and when can expert decision errors occur in the decision-making process @ PPD?	X	X
What error factors impact the decision-making process @ PPD?	X	X
When decision errors occur how are they identified and addressed?	X	X
What resources do PPD have in place to avoid decision errors?	X	X
What errors could influence ISO14155 DM compliance	X	X

APPENDIX G: DOCUMENTS FOR ISO14155:2011 COMPLIANCE

As described by the PPD company physicians during data collection sessions.

Documentation / Source	Campsie	Cairngorm	Cuillin	Galloway	Grampian	Lammuir	Lowther	Moffat	Moorfoot	Munro	Ochil	Pentland	Sidlaw	Torridon
Investigator Brochure	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖
Study Protocol	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖		✖	✖	
Clinical Investigation Plan	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖
Case Report Form	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖
Adverse Event Form	✖	✖	✖	✖	✖			✖	✖					✖
CV of key staff	✖	✖	✖				✖			✖	✖		✖	
Signature log(s)	✖	✖	✖							✖	✖		✖	
Ethics Committee approval	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖
Notified Body certification	✖				✖		✖		✖		✖			✖
Competent authority approval		✖	✖	✖		✖		✖		✖	✖			✖
Financial contract		✖			✖		✖		✖				✖	✖
Insurance certification	✖		✖		✖		✖		✖	✖	✖	✖	✖	
Informed consent form	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖
Contractual agreement(s)			✖	✖				✖		✖	✖			
Medical device tracking log(s)				✖		✖				✖	✖			
Training records	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖
Site selection report			✖								✖			
Operational documents	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖
Normal laboratory values listings	✖		✖		✖	✖					✖			
Declaration of Conformity	✖	✖	✖		✖	✖		✖		✖	✖			✖