Development and Validation of a Generic Instrument for Assessing The Quality of Decision-Making

A thesis submitted in accordance with the conditions
governing candidates for the degree of

DOCTOR OF PHILOSOPHY

in

CARDIFF UNIVERSITY

Presented by

Ronan Donelan

December 2013

DECLARATION

This work has not previously been accepted in substance for any degree and is not concurrently submitted in candidature for any degree.

Signed .....*Candidate*

Date.....17th APRIL 2014.....

STATEMENT 1

This thesis is being submitted in partial fulfilment of the requirements for the degree of PhD.

Signed .....*Candidate*

Date.....17th April 2014.....

STATEMENT 2

This thesis is the result of my own independent work/investigation, except where otherwise stated. Other sources are acknowledged by explicit references.

Signed .....*Candidate*

Date.....17th April 2014.....

STATEMENT 3

I hereby give consent for my thesis, if accepted, to be available for photocopying and for interlibrary loan, and for the title and summary to be made available to outside organisations.

Signed .....*Candidate*

Date.....17th April 2014.....

ACKNOWLEDGMENTS

I am indebted to my supervisors, Prof Sam Salek and Prof Stuart Walker for their advice, guidance and encouragement throughout the preparation of this thesis. Both have provided several years of guidance and support to help in the delivery of this research. Both are pioneering in their professional research and the overall healthcare area. They have both been generous in sharing their expertise, experience and wisdom.

I would like to say a special “Thank you” to all the interviewees who kindly gave up time during their busy workloads. All were very accommodating, supportive and encouraging, for which I am truly grateful.

I would also like to thank the staff at the Welsh School of Pharmacy and Pharmaceutical Services, in particular Ms Helen Harron and Ms Justine Jenkins for their support and encouragement.

To Ross and Ava, thank you for your love and patience and I apologise for the lost holidays and weekends. We will make up for them.

Finally, I dedicate this thesis to my beautiful and ever-supportive wife, Gemma. She has been my rock in all aspects and has provided unfailing support on this professional, educational and challenging life-journey.

CONTENTS

ABSTRACT

Decision-making *per se* can be regarded as part art and part science in the development of new medicines. In the area of pharmaceutical development, decision-making plays a pivotal role in the continuation or the termination of further development or withdrawal of medicinal products. The decisions made at each stage have a direct impact on all stakeholders namely, pharmaceutical companies, regulators, payers and patients. What is lacking at present is a qualified understanding of the subjective decision-making approach, influences, behaviours and other factors which impact the decision-making of individuals and organisations involved in the delivery of new medicines. The aim of this study was, therefore, to develop and validate a generic instrument for appraising the quality of decision-making.

Semi-structured interviews were carried out with 29 key decision-makers from the pharmaceutical industry, regulatory authorities and contract research organisations (CROs). They were invited to discuss all aspects, including their perception of decision-making and its role in drug development and regulatory review; decision making within their organisation; awareness and use of decision-making techniques; and impact and monitoring of decisions. Thematic analysis was carried out using NViVO 8 © software. A preliminary 94-item instrument was developed from the themes and the sub-themes that emerged from the interviews. Content validity was assessed using qualitative and quantitative data from an expert panel involving six key decision makers. A separate international cohort of 120 individuals working in the pharmaceutical industry, regulatory authority or CROs was recruited for factor analysis to reduce items. A further 78 individuals completed the final version of the QoDOS for construct validity and reliability.

Most individuals interviewed were male (55% - n=16) and their level of experience ranged from 7 to 35 years. 32 themes and 90 sub-themes of aspects of decision-making were identified from the interviews. The median numbers of themes reported by experts was 6 (range = 1-10). The key themes included: quality and validity of the data;

political, financial, competitor and reward influences; analytical and logical approach; overconfidence in own judgement; plunging in or procrastinating with decision-making; impact analysis of decisions; education and awareness of evolving decision-making techniques; and SWOT and alternate outcome planning. Relationships between the themes were identified.

A 94-item generic instrument for assessing the quality of life decision-making, Quality of Decision-Making Orientation Scheme (QoDOS) ©, with a 5-point Likert response scale was developed. The content validity panel's rating of each item on a 4-point scale for the 4 attributes showed "strongly agreed" or "agreed" (88%) with an ICC value of .89 (CI = 0.56 – 0.99) suggesting a high agreement between the panel members' responses. This led to the reduction of 20 items and addition of two items as a result of cross-referencing with the qualitative data. Thus, the 76 items (version 2) emerged from content validation. Factor analysis produced a 47-item measure with four factors. The QoDOS showed high internal consistency (n = 120, Cronbach's alpha = 0.89), high reproducibility (n = 20, ICC = 0.77) and a mean completion time of 10 minutes. 10 hallmarks of "Good Decision-Making Practice" (GDMP) were identified.

The QoDOS is a valuable addition to the decision-making tool box of drug developers and regulators and has the potential to fill the missing gap of the entire process which is building quality into the lifecycle of medicine. The identification of ten hallmarks and generation of a framework for GDMP are also important contributions of this study to the field.

LIST OF ABBREVIATIONS

ANOVA: Analysis of variance

BEMA: Benchmarking of European Medicines Agencies

BIA: Biotechnology Industry Association

BRAT: Benefit Risk Action Team

BRR: Benefit Risk Ratio

CAQDAS: Computer assisted qualitative data analysis software

CDER: Centre for Drug Evaluation and Research

CIRS: Centre for Innovation in Regulatory Science

CMC: Chemistry, Manufacturing and Controls

EFPIA: European Federation of Pharmaceutical Industry Association

EMA: European Medicines Agency

EPAR: European Public Assessment Report

EU: European Union

EuNetHTA: European Network for Health Technology Assessment

FDA: Food and Drug Administration

FDA BRF: FDA Benefit Risk Framework

GRP: Good Review Practice

HTA: Health Technology Assessment

ICC: Inter-correlation coefficient

ICH: International Conference on Harmonisation

IDMC: Individual decision-making competence

IDMS: Individual decision-making style

IMI: Innovative Medicines Initiative

IQR: Interquartile range

KOL: Key Opinion Leader

KMO: Kaiser Meyer-Olkin

KPI: Key Performance Indicator

MAA: Marketing Authorisation Application

MCDA: Multi-criteria Decision Analysis

MHRA: Medicines and Healthcare products Regulatory Agency

MTMM: Multi-Trait Multi Methods

NBE: New Biological Entity

NCE: New Chemical Entities

NDA: New Drug Application

ODMA: Organisational decision-making approach

ODMC: Organisational decision-making culture

PhRMA: Pharmaceutical Researcher Manufacturers Association of America

PRAC: Pharmacovigilance regulatory advisory committee

PrOACT-URL: Problem, Objectives, Alternatives, Consequences, Trade-offs, Uncertainty, Risk and Linked decisions framework

PROTECT: Pharmacoepidemiological Research on Outcomes of Therapeutics by a European ConsorTium

QALY: Quality Adjusted Life Years

QoDOS: Quality of decision-making orientation scheme

R&D: Research and development

ROI: Return on investment

SME: Small and Medium Enterprise

SOP: Standard Operating Procedure

SPC: Summary of Product Characteristics

SPSS: Software Package for Statistical AnalySis

SWOT: Strengths, Weaknesses, Opportunities, Threats

UMBRA: Unified Methodologies for Benefit Risk Assessment

UK: United Kingdom

GLOSSARY OF TERMS

ANOVA: Analysis of Variance, which tests for significant mean differences in the variables among multiple groups.

Advisory committee: An expert committee that advises the regulatory authority on the safety, quality and efficacy of medicinal products for human use.

Approval: The approval of a product by a regulatory authority, signified by the granting of a product licence.

Assessment report: This report describes the assessment of the medicinal product and states the reasons for the conclusions. It explains why a marketing authorisation and each of the proposed indications have been approved or rejected and details the benefit-risk considerations for the product. This document also serves as an audit trail and should be sufficiently detailed to allow for secondary assessment by other Member States experts.

Assessment template: A standard document or a form used to record data required by the quality system of the review process.

Bartlett's test of sphericity: Statistical test used in the analysis of variance.

Benefit: The positive results of a given treatment for an individual or a population. (i.e. efficacy, convenience, or even quality of life)

Benefit-risk assessment: A formal way to analyse benefit and risk consequences and their balances from a set of actions and to make choice among actions when risk aversion and preferences are specified.

Bias: Any error that creeps into the data. Biases can be introduced by the researcher, the respondent, the measuring instrument, the sample, and so on.

Category scale: Analyses done to detect cause-and-effect relationships between two or among more variables.

Centralised procedure: The Centralised Procedure is used when a marketing authorisation covering the entire EU region is applied for. A marketing authorisation application is submitted to the European Medicines Agency. A single evaluation is carried out through the Committee for Medicinal Products for Human Use (CHMP). If the Committee concludes that quality, safety and efficacy of the

medicinal product is sufficiently proven, it adopts a positive opinion. This is sent to the European Commission to be transformed into a single market authorisation valid for the whole of the European Union.

Checklist: An informational aid to guide evaluators in determining when qualitative methods are appropriate for an evaluation inquiry.

Clinical section of the dossier: This section consists of the clinical study reports including documentation on the clinical trials performed on the product. This information is provided in Module 5 of the Common Technical Document.

Coding: The analytic process through which the qualitative data that you have gathered are reduced, rearranged, and integrated to form theory.

Concurrent validity: Relates to criterion-related validity, which is established at the same time the test is administered.

Conjoint Analysis: A multivariate statistical technique used to determine the relative importance respondents attach to attributes and the utilities they attach to specific levels of attributes.

Construct validity: Testifies to how well the results obtained from the use of the measure fit the theories around which the test was designed.

Content analyses: An observational research method that is used to systematically evaluate the symbolic contents of all forms of recorded communication.

Content validity: Establishes the representative sampling of a whole set of items that measures a concept, and reflects how well the dimensions and elements thereof are delineated.

Continual improvement: Ongoing activities to evaluate and positively change activities, processes and the quality system to increase effectiveness. This term is frequently used interchangeably with continuous improvement.

Convergent validity: that which is established when the scores obtained by two different instruments measuring the same concept, or by measuring the concept by twp different methods, are highly correlated.

Correlational analysis: Analysis done to trace the mutual influence of variables on one another.

Cronbach's alpha: is a coefficient of internal consistency.

Deductive reasoning: the application of a general theory to specific case.

Descriptive statistics: statistics such as frequencies, the mean, and the standard deviation, which provide descriptive information about a set of data.

Development stage: The phase of the research and development encompassing all activities between drug candidate selection and approval.

Discriminant analysis: a statistical technique that helps to identify the independent variables that discriminate a normally scaled dependent variable of interest.

Discriminant validity: that which is established when two variables are theorised to be uncorrelated, and the scores obtained by measuring them are indeed empirically found to be so.

Effectiveness: Is the extent to which an intervention does more good than harm when provided under the usual circumstances of health care practice.

Efficacy: Is the extent to which an intervention does more good than harm under ideal circumstances.

European public assessment report (EPAR): The European Public Assessment Report is prepared at the end of every centralised evaluation process to provide a summary of the grounds for the opinion in favour of a marketing authorisation as taken by the Committee for Human Medicinal Products (CHMP). The EPAR is derived from the assessment of the documentation submitted by the applicant and the scientific discussions undertaken by the CHMP during the evaluation process. The European Medicines Agency makes the EPARs available to the public after deletion of commercially confidential information. Furthermore, the EPARs are updated throughout the life cycle of the product to reflect changes to the original terms and conditions of the marketing authorisation.

External validity: the extent of generalisability of the results of a casual study to other field settings.

Factor analysis: is a statistical method used to describe variability among observed, correlated variables in terms of a potentially lower number of unobserved variables called factors.

Face-to-face interview: information gathering when both the interviewer and interviewee meet in person.

Face validity: an aspect of validity examining whether the item on the scale, on the face of it, reads as if it indeed measures what it is suppose to measure.

Framework: structured stepwise approach to perform a task.

Good review practice (GRP): GRP is a documented best practice that discusses any aspect related to the process, format, content, and/or management of a product review. GRPs are developed to provide consistency to the overall review process of new products, as well as to improve the quality, efficiency, clarity, and transparency of reviews and review management.

Health Technology Assessment: This is the term used for the assessments made by government and insurance reimbursement agencies, hospital formulary committees and other bodies representing the payers for healthcare and medicines.

Inductive reasoning: a process where we observe specific phenomena and on this basis arrive at general conclusions.

Integrated quality management: is the understanding and effective direction of an organisation, resulting in the best possible management decisions, so that the needs and expectations of all stakeholders and partners are satisfied by the optimum use of all resources.

Interitem consistency reliability: a test of the consistency of responses to all the items in a measure to establish that they hang together as a set.

Internal consistency: homogeneity of the items in the measure that tap a construct.

Interrater reliability: the consistency of the judgement of several raters on how they see a phenomenon or interpret the activities in a situation.

Interviewing: a data collection method in which the researcher asks for information verbally from the respondents.

Key performance indicators (KPIs): KPIs are quantifiable measures that indicate relative performance in relationship to a target goal.

Kaiser-Meyer Olkin: a test to assess the appropriateness of using factor analysis on data.

Likert Scale: an interval scale that specifically uses the five anchors of strongly disagree, disagree, neither disagree nor agree, agree, and strongly agree.

List of questions: A consolidated list of questions provided by the regulatory authority identifying major objections and / or other concerns identified during a review.

Literature review: the documentation of a comprehensive review of the published work from secondary sources of data in the areas of specific interest to the researcher.

Marketing Authorisation: Legal approval granted to a company by a national authority to market a medicinal product in that particular market.

Marketing Authorisation Application: An application submitted by a company to support the regulatory approval for a medicinal product in a country/region. In the US this could also mean a New Drug Application (NDA).

Measurement: A process of establishing the correspondence between a property and a number system.

Methodology: The system of methods and principles used in a particular discipline.

Multiple regression analysis: a statistical technique to predict the variance in the dependent variable by regressing the independent variables against it.

Multitrait-multimethod matrix is an approach to examining Construct Validity**.**

New Active Substance: A chemical, biological or radio pharmaceutical substance that has not been previously available for therapeutic use in humans.

NVivo: a qualitative data analysis computer software package designed for qualitative researchers working with very rich text-based and/or multimedia information, where deep levels of analysis on small or large volumes of data are required.

Non-clinical section of dossier: This section consists of the non-clinical study reports and tests covering the pharmacology, pharmacokinetics and toxicology of the drug. This information is included in Module 4 of the Common Technical Document.

Objectivity: interpretation of the results on the basis of data analysis, as opposed to subjective or emotional interpretations.

Parsimony: efficient explanation of the variance in the dependent variable of interest through the use of smaller, rather than a larger number of independent variables.

Peer review: Peer review means an additional evaluation of an original assessment carried out by an independent person or committee. Peer review can occur either

during assessment of a dossier or at sign-off. Peer review can be internal or external.

Population: the entire group of people, events, or things that the researcher desires to investigate.

Preference values: A quantitative measure of the extent to which an outcome achieves an objective, as judged by an individual or group.

Principal component analysis: a statistical method of analysis which involves finding the linear combination of a set of variables.

Problem definition: a precise, succinct statement of the question or issue that is to be investigated.

QoDOS: Quality of decision-making orientation scheme.

Qualitative study: research involving analysis of data/information that are descriptive in nature and not readily quantifiable.

Quality assurance: Planned and systematic activities implemented in a quality system that provide confidence that quality requirements are fulfilled.

Quality audit: It involves the assessment of any designated process or activity to obtain objective evidence that the existing requirements have been met (for example, effective and efficient implementation of processes and resources). Quality audits can be internal or external.

Quality control: Quality control is operational techniques and activities that are used to fulfil requirements for quality. It involves techniques that monitor a process and eliminate causes of unsatisfactory performance at all stages of the quality cycle.

Quality section of dossier: This section of the dossier consists of chemical-pharmaceutical and biological information for chemical active substances and biological medicinal products. This information is provided in Module 3 of the Common Technical Document.

Quality policy: Overall intentions and direction of an organisation related to quality as formally expressed by top management.

Quality system: The organisational structure, responsibilities, procedures, processes and resources for implementing quality management.

Quantitative: involving considerations of amount or size; capable of being measured.

Questionnaire: a pre-formulated written set of questions to which the respondent records the answers, usually within rather closely delineated alternatives.

Registration: This term is also known as marketing authorisation.

Regression analysis: used in a situation where one or more metric independent variable(s) is (are) hypothesised to affect a metric dependent variable.

Relative efficacy: the extent to which an intervention does more good than harm under ideal circumstances compared to one or more alternative interventions.

Reliability: attests to the consistency and stability of the measuring instrument.

Research: an organised, systematic, critical, scientific inquiry or investigation into a specific problem, undertaken with the objective of finding answers or solutions thereto.

Review: This term is also known as assessment in which the assessors review the dossier in terms of the quality, safety and efficacy of the submitted data.

Review outcome: The result of the regulatory review in terms of whether or not a licence was granted by the authority for marketing the product.

Rigour: the theoretical and methodological precision adhered to in conducting research.

Risk: The negative results (adverse outcomes) of a given treatment for an individual or population in terms of probability of occurrence having considered the magnitude of severity.

Risk-benefit balance: An evaluation of the positive therapeutic effects of a medicinal product in relation to any risk relating to the quality, safety or efficacy of the medicinal product as regards patients' health or public health. A marketing authorisation will be refused if the risk-benefit balance is not considered to be favourable.

Risk management plan: It is a set of pharmacovigilance activities and interventions designed to identify, characterise and manage risks relating to a medicinal product. It consists of an overview of the safety profile of the product, a pharmacovigilance plan and a risk minimisation plan.

Sample: a subset or subgroup of the population.

Sample size: the actual number of subjects chosen as a sample to represent the population characteristics.

Scale: a tool or mechanism by which individuals, events, or objects are distinguished on the variables of interest in some meaningful way.

Scientific advice: Advice provided to companies on the conduct of various tests and trials necessary to demonstrate the quality, safety and efficacy of the medicinal product. The advice covers scientific issues related to the proposed future development of the product.

Scientific assessment: Review of the dossier in terms of safety, quality and efficacy of the data submitted.

Scree (Catrell's) plot: A visual plot in descending order of magnitude of the eignevalues of a correlation matrix which presents the relative importance of the factors.

Self-assessment: This is a carefully considered evaluation resulting in an opinion or judgement of the effectiveness and efficiency of the organisation and the maturity of the quality management system. Self-assessment is usually performed by the organisation's own management.

Spearman's test: is a nonparametric measure of statistical dependence between two variables.

Standard operating procedures (SOPs): SOPs are written documents that describe in detail the routine procedures to be followed for a specific operation, analysis or action.

Submission: The submission of a regulatory dossier to apply for a licence to market the product.

Summary of Product Characteristics (SPC): The SPC is a document that forms an intrinsic and integral part of the marketing authorisation application. The SPC is a summary of the dossier and sets out the agreed position of the medicinal product as distilled during the course of the assessment process. The SPC is the basis of information for health professionals on how to use the medicinal product safely and effectively.

SWOT: A business approach to identify Strength, Weakness, Opportunities, Threats of a situation

Validation process: The process whereby a regulatory authority verifies that all parts of the submitted dossier are present and complete and suitable to be assessed as part of the assessment and registration process.

Validity: evidence that the instrument, technique, or process used to measure a concept does indeed measure the intended concept.

Variable: anything that can take on differing or varying values.

Variance: Indicates the dispersion of a variable in the data set, and is obtained by subtracting the mean from each of the observations, squaring the results, summing them, and dividing the total by the number of observations.

Utility: A subjective measurement that describes a person's or group's preference (satisfaction, risk attitude, etc.).

Value function: A function which convert the input data (parameters) in all criteria into preference value or utility for the options under evaluation.

Value judgement: A subjective assessment for appropriateness of values or utility in a decision-making problem.

Weight: Scaling constants assigned to criteria such that the units of scaled preference values across all criteria are equal.

LIST OF FIGURES

LIST OF TABLES

CHAPTER 1

General Introduction

BACKGROUND

"***From vision to decision, Pharma 2020".....***was the title of the PWC pharmaceutical strategy report issued in late 2012. The opening paragraph of the report states "Pharma's future has never looked more promising – or more ominous. Major scientific, technological and socioeconomic changes will review the industry's fortunes in another decade, but capitalising on these trends will entail making crucial decisions" (PWC, 2012). There is constant discussion, debate and published material on the current and future productivity projections of pharmaceutical industry research and development (R&D). At present, there are several formidable internal and external factors that are facing the industry including items such as increasing stakeholder pressures. These include the current patent expiration, the market dynamics, the in-licensing/out-licensing of assets, the outsourcing of complete R&D activities to service providers and the emergence of non-ICH countries as being key players in the delivery and the demand for pharmaceutical products. So, in regard to the changing pharmaceutical arena, it begs the question, will pharma improve the quality of its decision-making in the future and therefore aim to make its future more promising rather than more ominous?

The development of a new drug from molecule to market is a complex stepwise process that is dependent on multiple and expert input, knowledge and decision-making by a wide range of specialists in various fields. Within the pharmaceutical industry, these come from differing functional areas and comprise individuals with specialised training and expertise in areas such as: synthetic chemistry, manufacturing, non-clinical pharmacology and toxicology, biostatistics, clinical operations, data management, project management, medical affairs, regulatory affairs, benefit/risk pharmacovigilance, management teams, health economics, commercial and legal affairs. Within the regulatory agencies, the expertise of the individuals will have a particular focus on areas such as: chemistry/pharmaceutical and manufacturing controls, non-clinical pharmaco-toxicology, clinical expertise in differing therapeutic areas, biostatistics, pharmacovigilance, regulatory affairs and legal affairs. More recently we are also seeing a growing involvement of agency personnel with expertise in areas such as cost-

effectiveness, pharmacoeconomics and their interaction with Health Technology Assessment (HTA) agencies and patient platform groups.

Rapid advances in drug development such as the use of modelling and simulation, adaptive clinical trials, specific target therapy properties of drug candidates and a greater appreciation of benefit/risk assessment are now common within the drug development programme of New Chemical Entities (NCEs) and New Biological Entities (NBEs). The traditional 'Go/No-go' stage gates are still dominant within the delivery and maturation of new medicines. The science and dynamic evolution of development approaches are new challenges to pharmaceutical companies and regulatory authorities, but both are adapting to the changes (Eichler et al., 2008; Eichler et al., 2012). The drug development arena has inherent high risks and uncertainties associated through each stage of development (Pritchard et al., 2003). The decisions made will dictate the continuation or the termination of a candidate drug and thus limit patients' access to new medicines (Pritchard et al., 2003; Eichler et al., 2008; Chung-Stein, 2011; Colwrick et al., 2011; Eichler et al., 2012). In the regulatory review and the HTA component of the evaluation of new medicines, ever increasing efforts are seen to improve the decision-making process as it is recognised to be in the interest of all stakeholders. The latest MHRA/ Biotechnology Industry Association expert committee report has again highlighted the need for improvement in the regulatory decision-making process (MHRA, 2013).

PHARMACEUTICAL DEVELOPMENT DECISION-MAKING CHALLENGES

Industry

Several decision-making frameworks are available to aid quality decision-making and in particular in the benefit-risk assessment of medicines in the post-approval setting. Quality of decision-making remains a fundamental issue which has a direct impact on all stakeholders (Walker et al., 2007; Mattes et al., 2010) and it is appreciated that "quality" is a difficult concept to define and a difficult parameter to establish and monitor (Lumpkin, 2000).

Pharmaceutical organisations operate in a business environment in which different dynamics and forces are present such as: competitors, governmental regulations, investors, payers and patients. Each plays a significant role in the company's performance by presenting opportunities and imposing threats on Research and Development, manufacturing, clinical and commercial activities. Ironically, although innovative drugs with novel mechanisms of action are attractive to all stakeholders, they also bring the penalty of being unpredictable with unknown risk (Pritchard, 2008). It is therefore in the interest of all stakeholders, that there is an effort to improve decision-making by "dropping the loser" and "supporting the winner" and thus achieve minimum time-to-market. The 2009 European Commission report on the European pharmaceutical sector confirmed the decline of new chemical entities reaching the market and identified some of the company practices possibly contributing to this decline. The report also highlighted the need to address the fragmented decision-making within regional/local Member State regulatory agencies and emphasised that this should be addressed at a local level (ECORYS, 2009).

Within pharmaceutical R & D, the 'Go or No-Go' decisions are based on judgements made by a group of individual health experts with varying background knowledge and experience (Pritchard et al., 2003; Sarac et al., 2012). Decisions are often made based on insufficient or incomplete data, a high degree of uncertainty, time pressure, financials and often in a competitive environment. As drug candidates mature through the R&D processes, the stakeholder groups will tend to include more external regulatory influences and market forces in their decision-making. High quality or optimised decision-making should be considered a cornerstone for effective drug development and life cycle maintenance. The industry has developed many decision-making analysis techniques including qualitative, quantitative and semi-quantitative approaches to try to aid the decision-making process. These techniques include frameworks, value-trees, modelling, simulations and other platforms which aim to provide a systematic and transparent approach to decision-making.

Regulatory

The remit of regulatory agencies is to protect public health. However, the regulatory authorities are increasingly being challenged to find the appropriate balance between the need for rapid access to new medicinal products and at the same time to ensure comprehensive data on their benefits and risks (Breckenridge and Walley, 2008; Eichler et al., 2008; Breckenridge et al., 2010; Eichler et al., 2012). The regulators' dilemma is that of balancing access to market against the requirement for as complete as possible data package prior to licensing as outlined in the European Medicines Agency's (EMA) draft roadmap to 2015 (EMA, 2011b). This dilemma is also compounded by the increasing novelty, complexity and speciality of some clinical development programmes and subsequent regulatory review is becoming an increasing challenge (Eichler et al., 2012). The challenges and the importance of the decision-making process for the regulatory authorities is illustrated by the risk of failure or error in any of the numerous decisions taken by the authority (Jefferys, 2000).

Regulatory agencies are actively working on improving the benefit-risk balance model by focussing on three major aspects for improvement: ensuring a consistent decision-making approach, providing a better rationale for the outcome of the benefit-risk decision-making review and improving communication with the various stakeholders (EMA, 2010; EMA, 2011a; IMI-EFPIA, 2013a). The EMA is actively supporting other areas within the licensing review which could be improved, such as facilitating more continuous dialogue during the assessment of a marketing authorisation, providing additional transparency of the decision-making undertaken and the outcome of the scientific review as summarised in the EU EPARs. It is also aiming to achieve the right balance of protection of commercial confidentiality of proprietary information (EMA, 2010a). Continuous benefit-risk assessments throughout a medicine's lifecycle and other strategies such as staggered-licensing of new medicines in certain situations are discussed in the EMA roadmap (EMA, 2011b). Other initiatives including the option to seek joint scientific advice from CHMP and HTA Agencies from EuNetHTA, has been well received by industry and Authorities (EMA, 2013b). These joint meetings may help to identify and develop the best clinical development programme and registration

strategy that should satisfy the safety, quality and efficacy requirements of the MAA submission and in addition the pharmacoeconomic demands of potential payers. An example of another initiative which is facilitating transparency on safety/benefit expectations of medicines is the establishment of the PRAC advisory meetings (since 2012) which is helping better define expectations of new MAAs (EMA, 2013b).

Other initiatives such as the EU benchmarking system, are helping to achieve a strengthening of the quality assurance systems in place at the level of all EU regulatory authorities (EMA, 2011b). The EU Benchmarking of European Medicines Agencies (BEMA) programme has the following broad aim to 'contribute to the development of a world-class medicines regulatory system based on a network of agencies operating to best practice standard'. BEMA is based on the assessment of the systems and processes in individual agencies against a set of indicators which have been agreed in the following areas: management systems, assessment of marketing authorisation applications, pharmacovigilance (drug safety) activities and inspection services (HMA, 2013). Regulatory Agencies have also recognised and established the importance of a strong Integrated Quality Management (IQM) system (FDA, 2006; FDA, 2009; MHRA, 2009). Integrated management is the understanding and effective direction of an organisation, resulting in the best possible management decisions, so that the needs and expectations of all stakeholders and partners are satisfied by the optimum use of all resources (MHRA, 2009). Linked to the integrated management approach and benchmarking initiatives, the regulatory agencies issue regular performance metrics. These metrics provide a valuable insight into outputs from the regulatory agencies and include information on new approvals, review timelines, clinical trial activities, inspection reports and orphan product designations.

Good review practice (GRP) systems are now present within many regulatory agencies and are helping to add transparency and a systematic approach to the regulatory review (FDA, 2005; FDA, 2006; Dash and Jones, 2010; Molzon et al., 2011; TGA, 2013). The US FDA and EMA have invested considerably over recent years in a quality system which is aimed to be integrated, agency-wide and risk-based in order to control, assure and improve the effectiveness of the regulatory processes (FDA, 2009; EMA, 2011b).

Pharmaceutical organisations also need to ensure that they establish good regulatory practices and that these are being applied. Methods for monitoring and assessing quality procedures should be sought with a view to continuous improvement (Korteweg, 2002; Walker, et al., 2007). It is appreciated by all stakeholders that improved transparency in the decision-making on new medicines and their life cycle will be of benefit to all (Korvivk, 2008).

Decision-Making Issues for The Individual

Decision-making within medicines development and the regulatory review is made at an organisational as well as an individual level. Decision-making is a subjective value assessment and judgement and can be regarded as being part science and part art (Milkman et al., 2008; Kahneman, 2012; Wethey, 2013). This subjective decision-making style represents the combination of how an individual interprets and understands stimuli and the general way in which he chooses to respond to them. It is linked to an individual's education, knowledge, ability, culture and motivation, their value orientation and tolerance for not having valid and reliable information before making a decision. Decision-making is usually considered to be the result of cognitive processes leading to the selection of a course of action between several alternatives (Dhami, 2003; Westaby et al., 2010; Kahneman et al., 2011). It represents a rational or irrational reasoning or emotional process based on prior knowledge as well as individual assumptions based on normative perspectives, which is held by that individual and no other person is privy to that decision-making process. It is this notion that underpins the importance of decision-conferencing where individuals share their normative standards to reach a shared decision.

The act of decision-making is a multi-stage multi-criteria process which should be utilised in 'Go/No-Go' processes. The elements of risk and reward depend on the information available and the individual's outlook in regard to acceptable risk and reward levels. It is also important to appreciate that decision-making is not a linear and predictive process, but rather a non-linear and evolving one. A person's behaviour is an important factor in an individual's decision-making and it is influenced by their

environment (Kahneman, 2012). Successful decision-making can be expected to require a thorough understanding and appreciation of the environment in which that decision will be carried out. Without such an understanding, it is impossible to assess the probable consequences that may result (Messicks and Bazerman, 1996). Thus, the decision environment as defined by the collection of information, alternatives, values, and preferences available at the time of the decision (Harris, 2012), will be of importance for the actual decision process. Therefore, an ideal decision environment would include all possible information, which is accurate and clear and addresses every possible alternative (Ivanona and Gibcus, 2003; Milkman et al., 2008; Harris, 2012; Wethey, 2013). However, in real world medicines development this ideal position is rarely the case in which safety and efficacy evidence is dynamic and development timelines are compressed.

Individual Decision-Making Styles:

On a fundamental level, there are four basic decision-making styles: subjective, objective, analytical and non-analytical (Rowe and Bougarides, 1983; Quernk, 2009). Many factors that can influence an individual's approach to decision-making such as:

- Personal biases which are based on a grounded personal belief or faith and include elements such as a person's political leanings or religious choices
- Cognitive bias may be present in the form of a selective search for evidence or a tendency to think in a certain way. Cognitive biases can lead to deviations from a standard of rationality or good judgment
- Selective perception e.g. where a person discounts certain information too quickly and interprets it in the way they want to, rather than looking at the bigger picture. This behaviour results in a person tending to "see things" based on their particular frame of reference and results in a person perceiving what they want in information while ignoring opposing viewpoints (Hammond, 2002; Verma, 2009).
- Information or data overload can result in "paralysis by analysis" from a state of over-analysing or over-thinking a situation so that a decision or action is never taken, in effect paralysing the outcome. A decision can be

treated as over-complicated, with too many detailed options, so that a choice is never made, instead of trying something and changing if a major problem arises. A person might be seeking the optimal or "perfect" solution upfront, and is concerned about making any decision which could lead to a bad outcome, which can result in no decision being made, which in itself could be considered a bad outcome (Ansoff, 1979)

- Anchoring is where a disproportionate weighting is given to the first information received. This high value assignment or anchoring to initial information rather than being receptive to update information and performing a re-evaluation which would deliver a more balanced approach
- Overconfidence, wishful thinking or optimism bias e.g. being over-confident in one's own decision-making. Overly confident about the accuracy of their prediction and considering too narrow a range of possibilities. A major cause of overconfidence is anchoring (Lovallo and Kahneman, 2003; Hammond et al., 2011; Kahneman, 2012)
- Choice supported bias is the tendency of a person to retroactively assign positive attributes to an option or decision that the person made in the past. The person ignores or downplays the negative aspect of the decision made. This bias can arise due a person's previous experience or memories (Hammond, 2002)
- Recent events or semantic priming: remembering and being overly influenced by recent dramatic events
- Groupthink can occur where a group of people may arrive at a consensus decision albeit a bad one. This phenomenon can be caused by the dynamics and strong personalities within a group. This can result in even a group of intelligent people making a poor decision (Von Bergen and Kirk, 1978; McCauley, 1998; Macleod, 2011)
- Authoritative style: where a single person (leader) makes the decision. This decision-making style is useful when the leader possesses all the necessary information and has the required expertise to make the best decision. This

style can be particularly valuable when a fast decision is required. It can also easily result in bad decisions

- Overweighting or underweighting of probability is observed where a person is more concerned about possible "losses than gains" or conversely where the person has not performed a qualified or quantified risk assessment of possible outcomes (Kahneman and Tversky, 1982; Kahneman, 2012)
- Inertia or status quo bias results in a person leaving a decision challenge as is and perpetuating the current situation by putting the decision-making off to later. This later time can be a distant horizon (Samuelson and Zeckhauser, 1988; Hammond et al., 2011)
- Under-estimating inherent uncertainty and over-estimating is the illusion of control and is caused by an under-estimation or lack of appreciation of the potential items or influences which could impact the decision. This can result in a false sense of security and perception that all is in order, whereas in fact the task or decision could be "spinning out of control" (Hammond et al., 2011)
- Confirming evidence is where a person tends to seek out information that supports their instinct or point of view while avoiding information that may contradict it. The confirming – evidence trap affects where or how we go to collect evidence and how we interpret it. Too much weight can be given to supportive information and too little to conflicting information
- Use of intuition of gut-feeling can be regarded as being a sophisticated form of reasoning based on a distillation of wisdom and instinct that one gains from life-experience, exposure to situations in personal and professional-life. It is a subconscious, complex, and quick acting phenomenon. It does appear directly connected to experience, expertise and deep knowledge developed over years (Mintzberg and Westley, 2001).

For individuals involved in drug development, some people who make individual decisions will be risk-prone while others will be risk-adverse on a particular issue (Mussen et al., 2009). Since actual decisions concerning the balance between benefits

and risks are heavily influenced by the values of the decision makers and are difficult to quantify, better methods are needed for quantifying the benefit-risk profile and expressing the values involved in decision-making. The decisions made during drug development and the regulatory review are based on evolving scientific capabilities and clinical judgement. These decisions need to be monitored throughout the life cycle of a medicine. It is also important to appreciate that benefit-risk analysis undertaken by regulators is not based on a precise mathematical equation and is invariably judgemental. Some people might well reach different decisions on another occasion, even when presented with the same data (Hammond, 2002; Milkman K et al., 2008; Verma, 2009; Rawlins, 2011).

Decision-making considerations for the organisation:

The pharmaceutical industry and regulators also appreciate the need for better decision-making practices and for systematic and transparent approaches to be more evident in the delivery of new medicines and industry/agencies and industry/agencies/academia initiatives are being progressed (Guo et al., 2010a, IMI-EFPIA, 2013b). The main area of collaboration between these stakeholders is in the area of benefit-risk assessment and decision-making frameworks. The pharmaceutical industry and the regulatory agencies appreciate the need to incorporate the perspectives of stakeholders in the development of frameworks intended to aid lifecycle evolution of medicines including the regulatory review. Frameworks provide a structured and systematic outline of how to approach a task. In decision-making, they provide the structure and systematic elements and provide transparency at each stage of the decision process and by inference an auditable trail of the basis of the final decision. Frameworks can facilitate consistency; promote reproducibility, reliability, confidence and overall quality in the decision-making process. They can delivery a platform for effective communication amongst all drug development stakeholders (pharmaceutical companies, regulatory agencies, payers, physicians and patients). This effective communication between the industry and regulatory agencies should be iterative in its nature.

Frameworks for Decision-Making

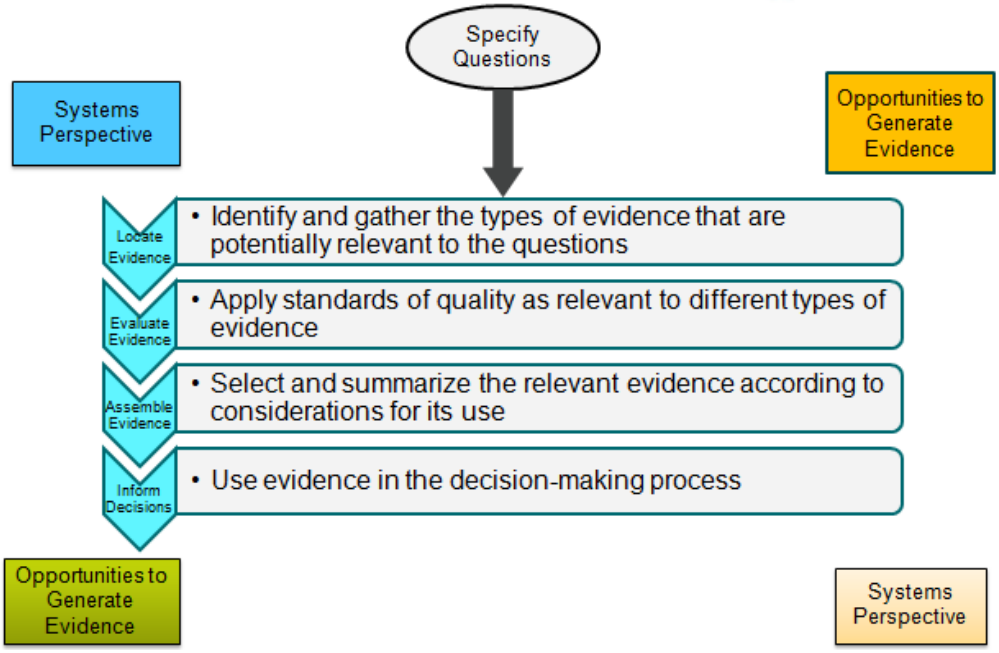
The cornerstones of quality decision-making are: a structured approach, transparency, quality of information and effective communication and use of frameworks capture each of these components in a systematic manner. In general, frameworks are over-arching processes which systematically document important elements of decision-making. They promote the use of a structured and an effective decision-making approach. An effective decision-making process should aim to fulfil the following criteria:

- It focuses on the decision context
- It is logical and consistent
- It acknowledges both subjective and objective factors and blends analytical with intuitive thinking
- It requires only as much information and analysis as is necessary to address the decision context
- It encourages and guides the gathering of relevant information and informed opinion
- It is straightforward, reliable, easy to use, and flexible.

The concept and the recognised benefit of decision-making frameworks is evident across many business disciplines. The fundamental tenets of good framework are as outlined above. Some examples of frameworks used outside of drug development are introduced for reference in Figures 1.1 – 1.3.

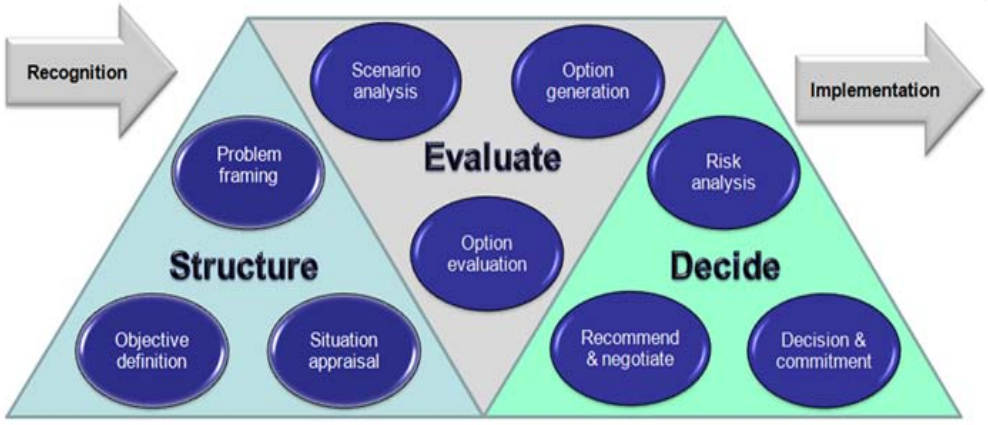
The L.E.A.D. (Locate, Evaluate, Assemble, Decisions) framework process can be used to assemble evidence in a way that is useful to decision makers. The framework recommends a standard systematic template approach that can be used to report results to decision makers, which prompts for 1) a statement of the question, 2) a transparent description of the strategy used to locate the evidence, 3) a table reporting the evidence, and 4) a summary of the evidence organised as answers to the derived questions (Figure 1.1) (Kumanyika et al., 2012).

Figure 1.1: The L.E.A.D decision-making framework



Another framework is the Genesis strategic decision-making process (Genesis, 2013) showing its component elements as outlined in Figure 1.2.

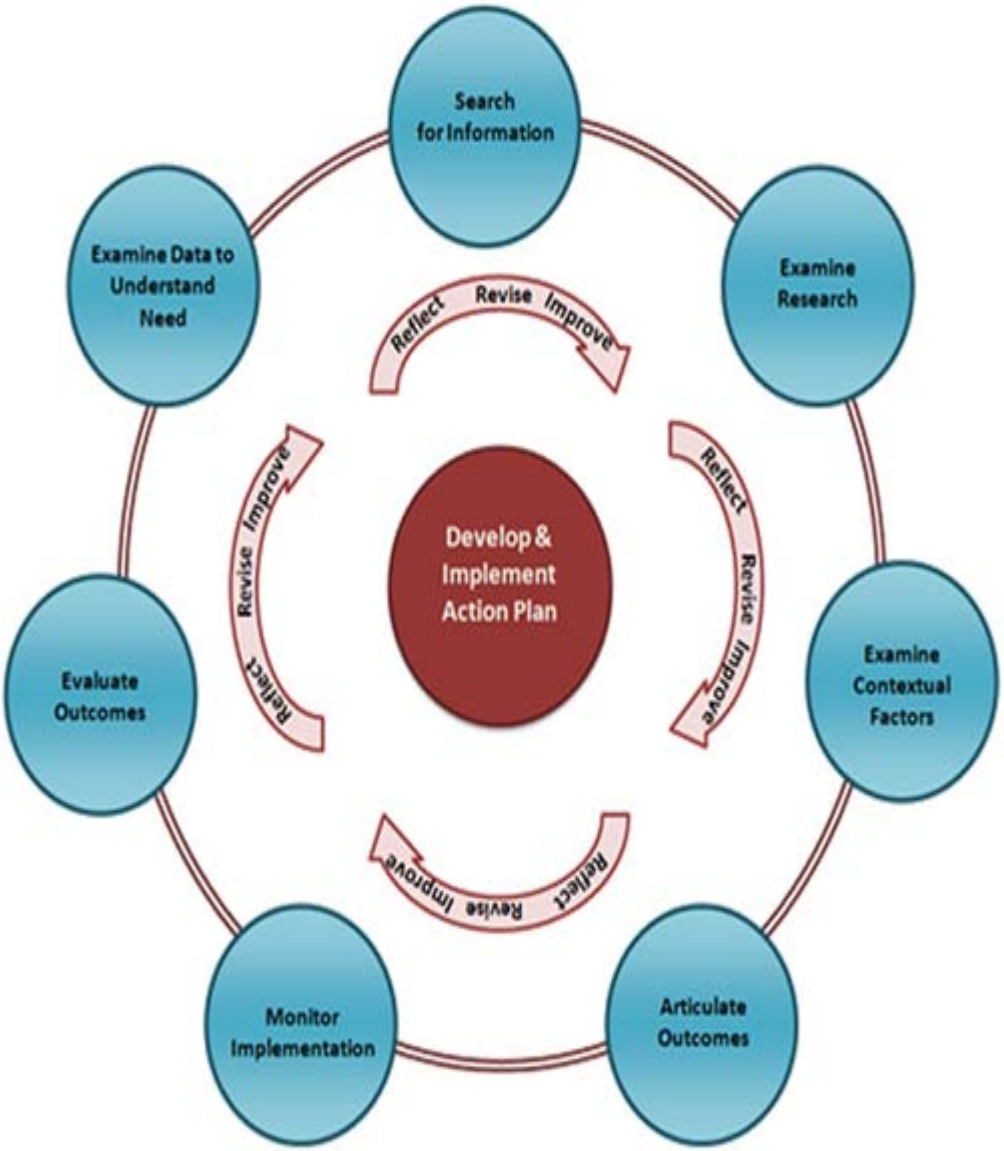
Figure 1.2: Genesis strategic decision-making process



The evidence-based decision-making framework is presented as a circular process aimed at thinking about how decisions can be strengthened at every step in an improvement cycle. Each circle (stage in the cycle) can be considered separately, with revisions and improvements within that circle taking place continually. Although the circles show a progression in decision-making reflecting the typical phases in planning, implementing,

and evaluating a decision, they can also provide a means for reflecting on which areas need more attention after improvement initiatives are underway (Figure 1.3).

Figure 1.3: The Evidence-Based Decision-Making framework



There are other general tools and techniques such as Strengths, Weakness, Opportunities, Threats (SWOTs), the 7-S framework (structure, systems, style, staff, skills, strategy and shared values), Pareto (root cause) analysis, questionnaires, checklists, risk analysis and risk management and decision trees used to support decision-making processes (Van Assen et al., 2009). In regard to the delivery of new

medicines, the EMA and FDA have been supportive of initiates to develop the decision-making frameworks. John Jenkins' (US FDA) conclusion on the regulators perspective on benefit-risk assessment was that "Regulatory risk-benefit decision-making is a qualitative science grounded in quantitative data. Judgment is required in making regulatory risk-benefit decisions and those judgments are influenced by many factors, both extrinsic and intrinsic. Clearly outlining the available data and how decisions (judgments) were made can improve transparency of the decision-making process" (FDA, 2010). He also outlined the desirable properties and attributes of a decision-making framework as being:

- Simple and user-friendly
- Address critical issues
- Capture expert views faithfully
- Represent transparently
- Compatible with quantitative analysis of clinical benefit and safety information
- Facilitate communications (internal and external)
- Broadly applicable

Jenkins described the desired attributes of the framework as being: simple (not simplistic), supports sound expert judgement (not a replacement for it) identifies areas of disagreement and that it captures the decision context.

Decision-making frameworks can be broadly classified into three types: qualitative, semi-quantitative and quantitative (Levitan and Mussen, 2012) Qualitative frameworks are generally templates, grids or visual displays that present the key benefits and risk attributes. They use a process based on internal experts making subjective judgements e.g. on the benefit-risk profile of each product and provide a conclusion. A semi-quantitative framework usually has a qualitative foundation but includes tabular or graphical tools to display and summarise the metrics associated with the key benefits and risks data. The semi-quantitative metrics-collection component requires the use of a

structured or standard working procedure. The decisions made are based on the review of the data results followed by expert judgement. Quantitative frameworks used in benefit-risk assessments for medicines allow for the calculation of a benefit-risk score using weightings, uncertainty calculations and statistical analysis and allows for a benefit-risk balance to be generated. The mathematical component in quantitative frameworks can be expected to require considerable specialised resource and effort. In the end, decisions are again made based on the review of the data results followed by expert judgement. The qualitative frameworks and the insights they deliver are the foundation for additional decision-making that may be performed using semi-quantitative or quantitative methods during and throughout the life cycle of a medicinal product.

The EMA medicines' benefit-risk methodology project is aimed at developing and assessing tools which could be used to aid informed, science-based regulatory decisions. The project has to date consisted of five consecutive work packages. The work packages have and continue to assess the applicability of the following qualitative frameworks: PrOACT-URL, PhRMA BRAT, the 7-step CIRS, the US FDA benefit-risk framework, use of decision tree models and Multi-Criteria Decision Analysis (MCDA) along with other alternative quantitative approaches for assessing the benefit-risk balance (EMA, 2010; EMA, 2010; EMA, 2011a; IMI-EFPIA, 2013b). MCDA can be considered to be the principal foundation in regulatory decision-making for a few existing frameworks namely, the PRoACT-URL, PhRAM's BRAT framework and the 7-step CIRS framework. A short review of the frameworks is presented with special attention being given to the PrOACT-URL technique as it has established proven value in both decision-making at an individual level (personal) and at a professional or business (organisational) level.

PrOACT-URL is a generic decision-making guide and its acronym PrOACT-URL represents the steps of the framework: (1) determine the decision context and frame the ***Pr****oblems*; (2) establish ***O****bjectives* and identify criteria; (3) identify options and ***A****lternatives*; (4) evaluate the expected ***C****onsequences* of the options for each criterion;

(5) assess the ***T**rade-offs* between benefits and risks; (6) report the ***U**ncertainty* in benefits and risks, and assess the impact of uncertainty on the benefit-risk balance; (7) judge the relative importance and the ***R**isk* attitude of the decision maker and assess how this affects the benefit-risk balance; and (8) consider the decision's consistency with other ***L**inked decisions*, both in the past and its impact on future decisions (Hammond, 2002; Hammond et al., 2011).

The PrOACT-URL approach provides a clear outline for a quality decision-making approach. It raises awareness and identification of the known's and unknowns and the intangible aspects relating to the decision situation. The framework helps to transpose the facts, judgement values and an individual's beliefs and feelings into the best possible choice option. The framework is flexible and adaptable and can be used both for professional or business decisions as well as personal decisions. It imbues a systematic sequential approach to the decision challenge. It presents a "divide and conquer" approach by breaking complex or hard decisions into the eight elements outlined. The first five (problem, objectives, alternatives, consequences and tradeoffs) represent the fundamental tenet of the recommended approach. The three remaining elements – uncertainty, risk tolerance and linked decisions, help to clarify decisions in a real-world changing environment (Hammond et al., 2011). The PrOACT-URL approach also provided flexibility and adaptability in that not all of its elements need to be used in a given decision-making situation but it does present a "pick and choose" option to the decision-maker.

Decision tree (and value tree) models incorporate, in diagrammatic displays, decisions (options), subsequent uncertain events, consequences and multiple criteria describing the consequences of a decision. They show these as branching structures, like trees tipped on their sides, with roots (decisions) at the left, and branches to the right showing possible outcomes of the uncertain events, followed by more decisions and a repeated process until a point representing some time in the future when consequences will be apparent. They can be applied to any decision-making scenario. Decision-trees require that preference logic is used in each expansion of the decision-options and implies that

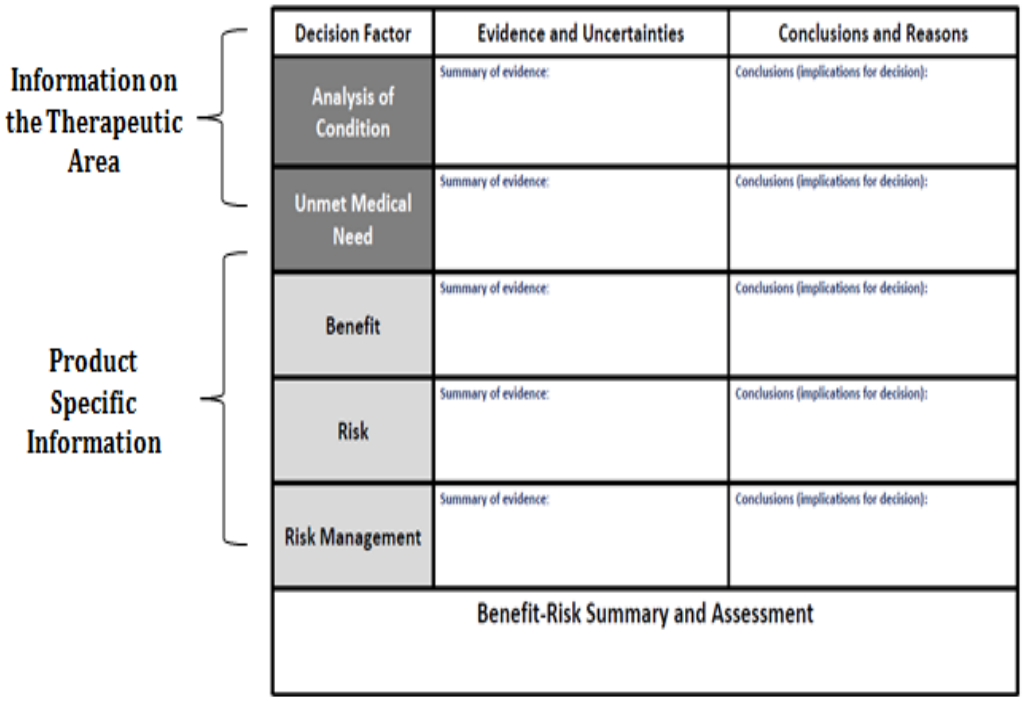
just two quantities are needed for decisions: numbers that express the relative values of possible consequences and numbers showing how likely these consequences are to occur. Multiplying utilities by their associated probabilities and summing those products over all consequences for a given alternative provides an expected utility figure that is a guide to action. The decision-tree approach requires the decomposition of a complex statement into its elements and then assessing probabilities and utilities about the relevant elements and finally reassembling the pieces using the expected utility calculation. That result allows decision-makers to examine their decision preferences and present a logically sound approach to decision-making. One problem with decision trees is that they can expand exponentially as more and more nodes are included, thereby becoming very complex. On the other hand, it is appreciated that if the problem is very complex, unaided human judgement can also be questioned as an acceptable alternative.

The PhRMA BRAT framework standardises and supports the decision-making and communication of a benefit-risk assessment between pharmaceutical companies and regulators through a 6-step process:

Step 1: Define decision context
Step 2: Identify outcomes
Step 3: Identify data sources
Step 4: Customise framework
Step 5: Assess outcome importance
Step 6: Display and interpret key benefit-risk metrics (Coplan et al., 2011).

The US FDA BRF (Benefit-Risk Framework) provides the “big picture” to “tell the story” by summarising evidence and addressing their implications for decision in a table for five decision factors: analysis of condition, unmet medical need, benefit, risk, and risk management and is presented in Figure 1.4 (Frey, 2012).

Figure 1.4: US FDA Benefit-Risk Framework

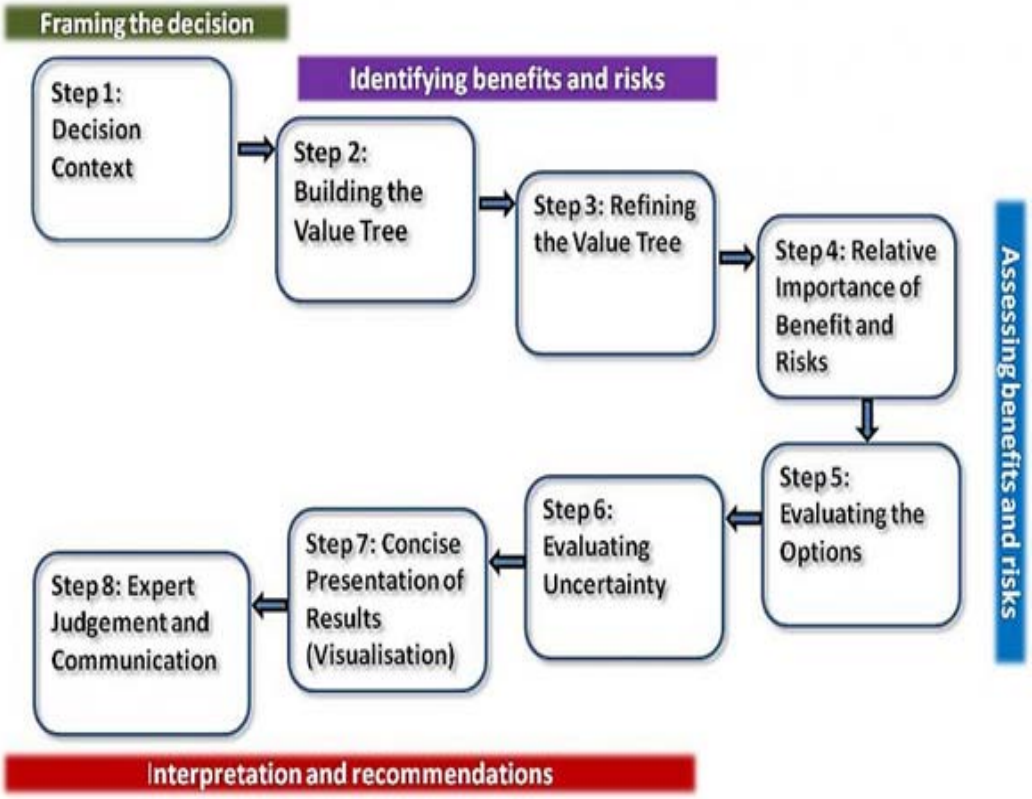


The UMBRA initiative established by CIRS in 2012 aims to provide a platform for the coordinated development of benefit-risk assessment methodologies that can be used internationally during the drug development and regulatory review and post-approval periods. The goals of the programme are to increase the transparency, predictability and consistency with which benefit-risk assessments are conducted. The UMBRA (Unified Methodologies for Benefit-Risk Assessment) framework is aimed at establishing a unified benefit-risk framework with an 8-step common element process addressed in 4-stages shown in Figure 1.5. (CIRS, 2012). The four stages involve:

1. Framing the decision – decision context
2. Identifying benefits and risks – building and refining the value tree
3. Assessing benefits and risks – relative importance of benefits and risks evaluating the options
4. Interpretation and recommendations – evaluating uncertainty, concise presentation of results, and expert judgement and communication.

An attractive element of the UMBRA descriptive framework appears to be its ability to accommodate the perspectives of the pharmaceutical companies, healthcare providers and regulatory agencies.

Figure 1.5: UMBRA benefit-risk framework



Building the benefit-risk toolbox – CIRS workshop report - 2012

The MCDA (Multi-Criteria Decision Analysis) framework is a qualitative and stepwise decision-making process that allows quantification of the overall performance of two or more alternatives. It employs some quantification techniques during the process but the overall framework is qualitative in its nature. It provides an approach and a set of steps, with the goal of providing an overall ordering of options, from the most preferred to the least preferred option. MCDA is a way of looking at complex problems and breaking the problem context into more manageable pieces to allow data and judgements to be brought into the decision task. The elements of the complex problems can be reassembled presenting a coherent overall picture to decision makers. The purpose is to serve as an aid to thinking and decision-making, but not to take the decision. As a set of techniques, MCDA provides different ways of disaggregating a complex problem, of measuring the extent to which options achieve objectives, of weighting the objectives, and of reassembling the pieces (Dodgson, 2009). In benefit-risk assessments, statistical software is regularly used to provide simulation and modelling support to tackle the

complex decision context. As applied to the benefit-risk balance of a drug and its comparators, performance of the alternatives on the favourable and unfavourable effects are judged for their clinical relevance, and all effects are weighted to create a common unit of preference value or utility. Applying an MCDA approach to sum the common units of benefit and risks provides an overall benefit-risk preference value or utility for each alternative, enabling aspects such as the calculation of the difference of the drug against the comparators (Mussen et al., 2009; Tony et al., 2011). The MCDA framework involves:

- Establishing the decision context
- Identifying the options to be appraised
- Identifying objectives and criteria
- 'Scoring' by assessing the expected performance of each option against the criteria. Then assessing the values associated with the consequences of each option for each criterion
- 'Weighting' by assigning weights for each of the criterion to reflect their relative importance to the decision
- Combination of the weights and scores for each option to derive an overall value
- Examining the results
- Performing a sensitivity analysis.

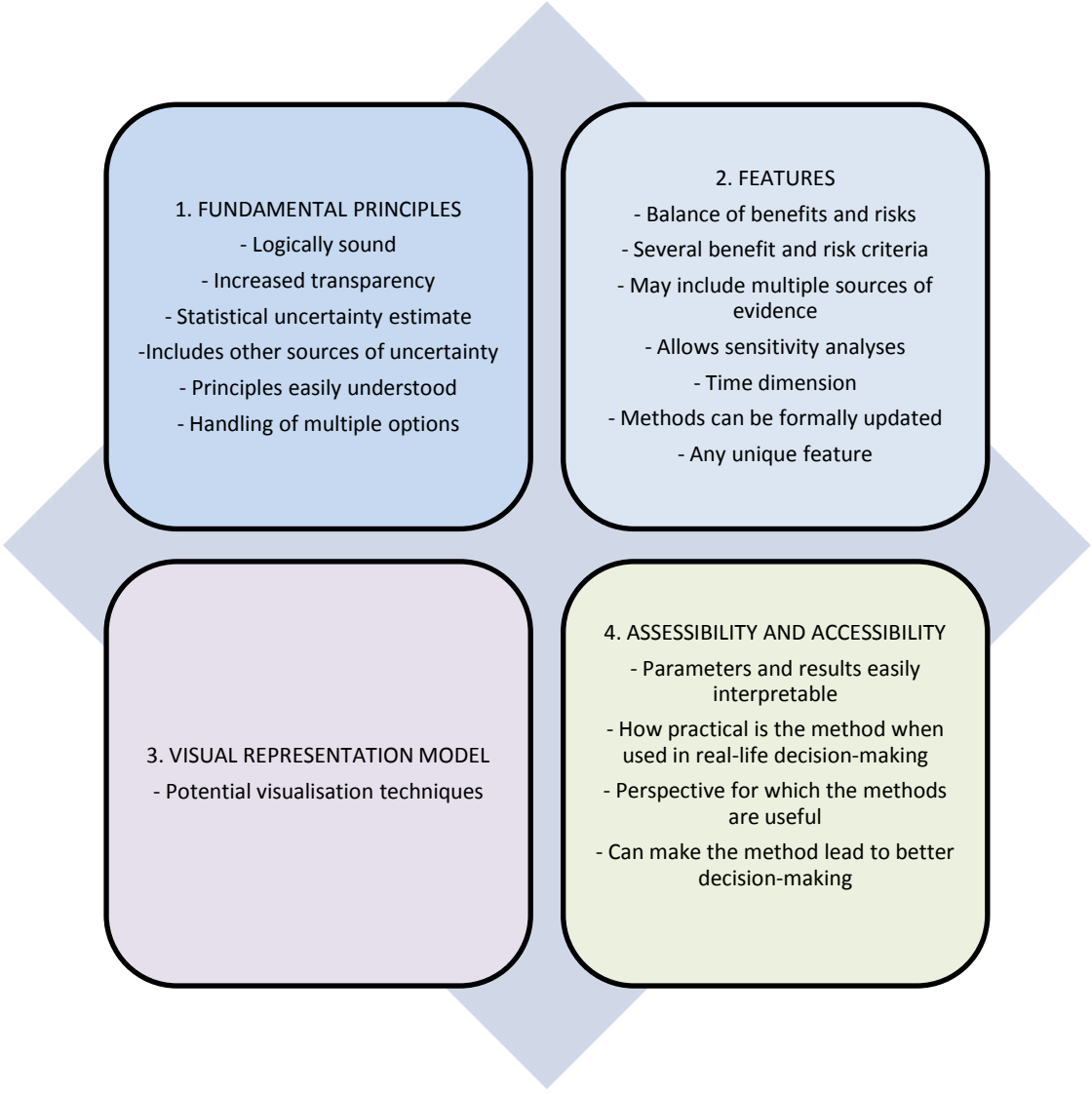
The MCDA approach offers a logical approach which helps to define the problem context, helps decision-makers explore their heuristic values, choices and judgements through structuring and presenting information in a manner that allows them to consider and challenge their considerations. It also identifies a preferred course of action and allows for final decision-making to be based on expert judgement. It is not intended to replace this expert judgement but acts to compliment it. It also gives structure and a step-wise audit trail and transparency to the decision-process. A summary of the comparative characteristics of the PrOACT-URL, PhRMA BRAT, US FDA and UMBRA benefit-risk assessment frameworks is presented in Table 1.1.

Table 1.1 Comparisons of existing benefit-risk assessment frameworks

Frameworks reviewed	Core elements							
	Framing the decision	**Identifying benefits and risks**		**Assessing benefits and risks**			**Interpretation and outcome**	
US FDA	Analysis of conditions and unmet medical needs	Clinical benefits, risks		Evidence and uncertainties				Conclusions and reasons, risk management plans
EMA PrOACT-URL	Nature and framing of the problem	Objectives, favourable and unfavourable effects		Alternatives regarding options to be evaluated and the consequences	Trade-offs and benefit-risk balance	Evaluating uncertainty	Effects table and risk tolerance	Consistency of decisions (linked decisions)
PhRMA BRAT framework	Define decision context	Identify outcomes, extract source data: build value tree	Customise framework: refine value tree	Assess relative importance of different outcomes: weighting or ranking, other stakeholders		Evaluating uncertainty	Display and interpret key benefit-risk metrics and validate results	Decision and communication of benefit-risk assessment
UMBRA Universal benefit-risk framework	**Step 1**	**Step 2**	**Step 3**	**Step 4**	**Step 5**	**Step 6**	**Step 7**	**Step 8**
	Decision context	Building the value tree	Customising the value tree	Weighting of benefits and risks	Scoring the options	Evaluating uncertainties	Concise presentation of results (visualisation)	Expert judgment

The pharmaceutical industry and regulatory agencies agree that frameworks facilitate the provision of quality decisions and transparency. The IMI-PROTECT project (IMI-EFPIA, 2013b) has recommended that frameworks should contain the following four components as shown in Figure 1.6.

Figure 1.6: IMI-PROTECT Evaluation components for evaluation techniques / frameworks



ESFPI/PSI Benefit-Risk Special Interest Group meeting, 2012

In the development and lifecycle of medicines there is still no single framework for decision-making that fulfils the requirements and perspectives of the regulatory and pharmaceutical stakeholders in making and communicating benefit-risk decisions.

Any new decision-making framework should aim to capture a number of key elements and the following builds on the IMI protect initiative (IMI-EFPIA, 2013b):

1. Include the perspectives of the stakeholders by involving them integrally in the qualitative and quantitative development and validation stages of the new framework (or instrument)
2. Have logical soundness and presents coherent dimensions to aid rational thinking
3. Provide a structured and systematic approach
4. Be comprehensive to allow utility in all forms of medicinal products and across all lifecycle stages (e.g. discovery, clinical, registration submission, regulatory review and post-authorisation)
5. Present confidence and acceptability by having undergone due validation resulting in a structured approach that would allow validity checks and an audit trail on stepwise decisions
6. Possess specificity and sensitivity supported by an underpinning statistical perspective
7. Increase transparency in the decision-making
8. Have easily understood principles such as an aim to assess the quality of decision-making
9. Incorporate the value judgements of stakeholders (e.g. individual or organisational)
10. Be derived from and include multiple sources of evidence
11. Allows sensitivity analyses (e.g. use in different populations)
12. Have a time dimension
13. Possess flexibility to be adapted
14. Have the ability for stand-alone use or for combination use with other accepted techniques and/or methodologies e.g. semi-quantitative or quantitative frameworks
15. Present easily interpretable results and facilitate an effective communication of the basis of the decision
16. Add better predictability into the decision-making

17. Be practical in real-life decision-making and easy to use
18. Present a method leading to better decision-making
19. Have a visualisation technique such as a graphical profiling of an individual's decision-making style to promote understanding and communication
20. Have a unique feature such as universality, international attraction and good branding (e.g. memorable brand name).

Benefit-risk assessments and decisions in the development and approval of medicines rely on scientific capabilities and subjective clinical judgements. These decisions need to be monitored during the life cycle of a medicine from drug development to post-marketing and there should be an effective and iterative exchange of information between the different stakeholders. The EMA have provided their opinion and recommend that any quantitative benefit-risk assessment method or approach should have a qualitative framework component. Combinations of such qualitative and quantitative approaches could prove useful (Guo et al., 2010a) and an overarching benefit-risk assessment framework with the capacity to incorporate various quantitative methods would be ideal. A universal overarching framework can be interpreted as a set of principles, guidelines and tools to guide decision-making in organising, understanding, summarising, quantifying and communicating the basis of the decision. Methodologies are tools which assist in conducting the scientific assessment and aid the articulation, communication and visualisation of decisions (Walker, 2011).

Results of a study by Leong *et al.* published in 2013, investigating the need for a universal benefit-risk assessment framework for medicines captured the perspectives of the pharmaceutical industry and the regulatory agencies and showed valuable insights into the current usage of qualitative and quantitative systems. It showed that qualitative systems are employed by both industry and agencies and implied that value and weighting had generally not been applied in benefit-risk assessment. Assigning weights to the different benefits and risks allows transparency, clarification and communication of their relative importance and of the overall basis of the final decision. The absence of fully quantitative systems, values, weights and visualisation tools is recognised as

presenting a challenge to effective communication of decisions to all stakeholders. Having a universal overarching systematic framework for decision-making and benefit-risk assessment in particular, should provide a formal structure for documenting the component processes leading to the final decision and this added transparency will allow all stakeholders to make informed quality decisions (Leong et al., 2013).

Stakeholder Interest in Improved Quality Decision-Making

It is evident from current and joint pharmaceutical industry/regulatory agency activities over the recent years that there is a definite desire by all stakeholders to improve currently used decision-making approaches. Considerable investment of resource and effort is evident on the qualitative, semi-quantitative and quantitative frameworks intended to help in the benefit-risk assessment of medicines. Within all of the frameworks and underpinning techniques, there remains a subjective element of decision-making required at one of the multiple stages of the decision-process. What is not fully transparent is how the subjective decisions in drug development and the regulatory review are made and whether there are influences, behaviours and other latent factors that contribute to the decision-making. These insights into the subjective decision-making element may help to promote better quality decision-making.

To date there is limited information on the quality of decision-making and this prompted the current research. Therefore, the current unknowns are: do these organisations and individuals make good quality decisions? What are the influences and approaches they use in their decision-making? Is there a place for a new framework to further aid decision-making for use throughout the drug development and complete life cycle? What appears to be currently missing from the drug development and review armamentarium is a generic instrument to assess and enable quality decision-making. Such an instrument could also facilitate the development of a decision-making framework to be used beyond just the benefit-risk assessment and it could incorporate the perspectives of the industry and regulatory agencies.

AIM AND OBJECTIVES OF THE STUDY

Aim

The aim of this study is to develop and validate a generic instrument for appraising the quality of decision-making.

Objectives

- Design a framework for the development of a decision-making instrument within drug development and the regulatory review
- Identify decision-making themes from the perspective of the individual and the organisation using qualitative techniques
- Develop a prototype instrument to appraise the quality of decision-making using the outcome of the qualitative techniques
- Determine content validity of the developmental version of the quality of decision-making instrument
- Refine the generic quality of decision-making instrument in the target population using factor analysis
- Development of the final version of the instrument, Quality of Decision-Making Orientation Scheme (QoDOS).

CHAPTER 2

Study Rationale and Methodological Framework

Part 1: STUDY RATIONALE

Chapter one highlighted the paucity of previous research studies investigating the quality of decision-making undertaken by the regulatory agencies and the pharmaceutical industry. Given the importance of global drug development and the societal need for new medicine, it is proposed that information is collected on the decision-making approaches and influences of regulatory agencies and pharmaceutical industry. This will enable:

- Provision of insights into the decision-making approaches and influences of pharmaceutical companies and regulatory agencies
- Generation of an instrument to measure and enable quality decision-making within the drug development life cycle
- Develop an instrument which would allow a visualisation of an individuals and their organisation's decision-making approach which would present an articulation, understanding and clarity on areas for development
- Provide a framework for promoting consistency, transparency and communication of the decision-making approach
- Identification of the hallmarks of good decision-making practice.

The literature review highlighted several past and ongoing initiatives within the pharmaceutical industry and the regulatory agencies (and more recently including academia) aimed at developing decision-making methodologies. Most of these initiatives and aimed at promoting better decision-making and in particular in regard to benefit-risk assessment. Several decision-making frameworks and tools developed to facilitate decision-making were reviewed. It was established that there is no validated and reliable instrument to assess and enable quality decision-making in the drug development and regulatory review, currently available in the public arena. This helped to frame the research question and the research message.

PART 2: METHODOLOGICAL FRAMEWORK

The choice of research approaches depends on the nature of the research question and research objectives (Strauss and Corbin, 1998; Patton 2002). The research method to be used in this investigation into influences, approaches, behaviours and

overall quality of decision-making, will be a mixed-methods approach involving both qualitative and quantitative techniques. In the qualitative research, face-to-face interviews will be conducted with a variety of key opinion leaders (KOLs) from the European Medicines Agency (EMA) and national European regulatory agencies, international pharmaceutical companies and contract research organisations. Quantitative research methods will be for the psychometric evaluation of the instrument and appropriate statistical analyses will be employed for reporting and interpretation of the results. A triangulation of research methodologies will underpin validation of the final generic instrument.

Study Design

The selection of a research design is one of the most important decisions that must be taken into account in order to answer the research questions. A 'research design' is a plan of the procedures for an investigation to be conducted, based on the nature of the research problem or issues being addressed and the researchers personal experience (Creswell, 2003; Meyrick, 2006). The research methodology tells readers how the researcher chooses the available methodology and conducts the various stages of research. It should reflect the overall process, in which the research philosophy, approach, strategy, data collection methods and data analysis are consistent (Saunders, 2009). Such an approach is presented for this research and a description of the planning, evidence gathering, data preparation, analyses, exploration and communication of the research findings and overall conclusion. A mixed-methods approach involving an initial qualitative phase followed by a quantitative will be used in this research study.

Qualitative and Quantitative Research Methodologies

According to Cresswell (2003), qualitative research is an inquiry process of understanding based on distinct and methodological traditions of inquiry that explore a social or a human problem. The researcher builds a complex, holistic picture, analyses words, reports detailed views of informants and conducts the study in a natural setting (Creswell, 2003). It allows us to gain an understanding and to access any latent factors by focusing on the context of people's everyday life (Barbour et al., 2008). Qualitative data consist of items such as: in depth descriptions of circumstances, people, interactions, observed behaviours, events, attitudes, thoughts

and beliefs and include direct quotes from people who have experienced or are experiencing the phenomenon (Strauss and Corbin, 1998; Patton, 2002; Denzin and Lincoln, 2005; Dicicco-Bloom, 2006). These data are gathered using techniques such as focus groups or interviews (Ritchie, 1994; Doyle, 2012).

Qualitative data help researchers understand processes and latent issues, especially those that emerge over time, provide detailed information about setting or context, and emphasise the voices of participants through quotes (Doyle, 2012). Qualitative methods facilitate the collection of data when measures do not exist and provide a depth of understanding of concepts (Strauss and Corbin 1998; Graneheim and Lundman, 2004; Ryan, 2007). To understand the processes or the how and why of a given phenomenon qualitative research provides the necessary in-depth and exploratory tools to achieve a clear picture of the process (Collis, 2009). The overall approach is flexible and evolving and caters for the addition of new information and perspectives. Also, according to Silverman, qualitative research findings from interviews and questionnaires which ask respondents to provide facts, attitudes or experiences, have an important part to play in healthcare (Silverman, 2000).

Quantitative data is any data presented in numerical form such as statistics, percentages, whole numbers, metrics or other such data outputs. It aims to answer typical questions relating to where, what, who, how many and when (Silverman, 2000). The objective of quantitative research is to develop and employ mathematical models, theories and/or hypotheses pertaining to phenomena (Crabtree and Miller, 1999; Silverman 2000).The process of measurement is central to quantitative research because it provides the fundamental connection between the empirical observation and a mathematical expression of quantitative relationships (Silverman, 2000). The approach involves collection and analysis of numerical data answer to answer a research question (Crabtree and Miller, 1999; Moule and Goodman, 2009). Quantitative research and its mathematical output aims to present results in a factual and unbiased manner. The results obtained also allow for an extrapolation from a small population (sample size) to a larger and more generalisable population (Silverman, 2000).

In mixed-methods studies researchers choose to combine different types of research methods. They combine quantitative (e.g. a survey) and qualitative (e.g. an in-depth

interview) research methods, resulting in a combination of statistical and experiential data and findings (Hanson et al., 2005). The mixed-methods pragmatic approach to be used will have an initial qualitative component followed by a quantitative phase. According to DiCicco-Bloom and Crabtree, mixed-methods in which both qualitative and quantitative approaches are integrated in a way that contributes to provide a rich and comprehensive study. Mixed-methods provide rigorous and methodologically sound study designs, with qualitative techniques such as interviews being an integral component of an evolving study process that is responsive to emerging insights, supported by quantitative analyses (Creswell, 2003; Doyle, 2012).

Research purposes are normally categorised as being exploratory, explanatory and descriptive (Creswell, 2003). Exploratory research is undertaken when an issue or phenomenon is poorly understood and little research has been done on it (Creswell, 2003). Normally, an inductive approach is suitable for exploratory purposes to look for patterns and ideas (Collis, 2009), and it is employed in exploratory research to arrive at a set of assumptions on which to base the research design. This approach applies to the current research on the development and subsequent validation of a generic decision-making instrument being undertaken.

Descriptive research is conducted to describe the features of the variables of interest in a situation (Sekaran and Bougie, 2010). A deductive approach is suitable for descriptive research (Sekaran and Bougie, 2010). An explanatory study is used to establish relationships between variables, and both deductive and inductive approaches can be applied to it (Saunders, 2009). As the differences between deductive and inductive research are narrowed down, an approach that combines these two is becoming more widely used (Doyle, 2012). A combined approach can provide a better understanding of a specific research topic rather than two separate ones.

Interpretivism entails that research and reality are inseparable and reality is internal and socially constructed (Remenyi et al., 1998; Denzin and Lincoln 2005). The interpretative paradigm is viewed as qualitative, inductive and subjectivist, while the positivist paradigm is described as quantitative, deductive and objectivist. Interpretivists attempt to understand not only what is happening, but also why it is

happening (Creswell 2003; Denzin and Lincoln 2005). Pragmatists hold the view that it is perfectly possible to work with both philosophies (Saunders, 2009). This approach claims that mixed-methods are possible and highly appropriate within research and provide more comprehensive evidence than one method alone can deliver (Casey et al., 2011; Doyle, 2012). In this research, in order to satisfy the research objectives both qualitative data (which deal with more in-depth and insightful exploration with limited number of interviewees) and quantitative data (which can be collected from wider samples for generalisation) were collected. The philosophical underpinning of pragmatism allows and guides mixed methods researchers to use a variety of approaches to answer research questions that cannot be addressed using a singular method. Mixed methods research is viewed as the third methodological movement and as an approach it has much to offer health and social science research. Its emergence has been in response to the limitations of the sole use of quantitative or qualitative methods and is now considered by many a legitimate alternative to these two traditions. Overall, it can be seen that a mixed-methods pragmatic approach was appropriate and was the approach adopted in this research.

PSYCHOMETRIC PROPERTIES OF A MEASUREMENT TOOL

Psychometrics is the field of study concerned with the theory and technique of psychological measurement, which includes the measurement of knowledge, abilities, attitudes, behaviours and traits. The field is primarily concerned with the construction and validation of measurement instruments such as questionnaires, tests, and personality assessments. It involves two major research tasks, namely: (i) the construction of instruments and procedures for measurement; and (ii) the development and refinement of theoretical approaches to measurement. Psychometric evaluation will be performed on the developmental generic instrument.

In this research, the development of the generic decision-making instrument will have exploratory, descriptive, explanatory and confirmatory purposes. Firstly, this research will be exploratory as there are no currently validated instruments available for assessing the quality of decision-making. This research will employ an inductive approach in the qualitative stage involving the proposed conduct of interviews and subsequent thematic analysis. Secondly, this research will be descriptive, as it will aim to describe any emergent decision-making themes. A deductive approach will

be used in the mixed-method qualitative and quantitative data analyses techniques to test results emergent from the research stages. Thirdly, this research will be explanatory, as it is aimed at establishing the relationships between different decision-making factors and themes which may emerge from the analysis of the results obtained from the different stakeholders. Fourthly, it is hoped to be confirmatory in that it will investigate construct validity and reliability of the generic developmental instrument.

DATA SOURCES AND COLLECTION

MEDLINE, PUBMED and other internet-based search engines were used to perform a systematic literature review to identify methodologies for measuring the quality of decision-making within the drug development arena and the regulatory review. An extensive and systematic literature search was performed to identify such methodologies. These platforms were used to find scientific publications, books, academic conference proceedings. Country specific drug regulatory internet sites were also searched. Key search words included: decision-making (and decision-making), drug development, tool, instrument, validated, risk-benefit, regulatory, pharmaceutical, quality, framework, best-practice and influences. Search inclusion criteria used were 1) only English language publications, 2) with focus on drug development and the regulatory review of drugs and 3) decision-making analysis and techniques. Exclusion criteria included; veterinary-medicine publications, cosmetics, homeopathy, and animal studies. The perspective of the decision-making literature interrogation was not limited to that of any one stakeholder. It is believed that this literature review corroborated the research into the development of a tool to facilitate improved decision-making in the pharmaceutical and regulator target audience.

The literature interrogation helped generate the appropriate framing of the research problem context. This allowed for the rationale of the proposed research approach, the evolution of the research investigation, the proposed methodology, the target study population and the potential target audience that could benefit from the availability of a validated new generic decision-making tool to be identified. In addition to the literature interrogation, direct contact was also made with organisations such as the Cochrane Collaboration, Stanford University, professional

networks specialising in "Decision-Making" and also through the researchers own professional networks to determine if there was a suitable decision-making instrument available in the public domain.

Data Collection Techniques

Qualitative research techniques involving semi-structured interviews, use of expert panels and thematic framing will be used in a complimentary manner to the quantitative techniques which will comprise primarily of several different types of statistical analyses. A tabular summary of the data collection techniques to be employed in the research is presented in Table 2.1

Table 2.1: Overview of the data collection techniques used in the generic decision-making instrument research

Data collection and Analysis Mode	Research Objectives	Thesis Chapter
Semi-structured interviews with Key Opinion Leaders Qualitative research	To identify emergent themes relating to the decision-making research Generate a developmental version of an instrument for measuring the quality of decision-making Generation of a thematic map	3
Qualitative research involving an expert panel /qualitative research	Content validation of the developmental decision-making instrument	4
Qualitative and quantitative research	Factor analysis Item reduction	5
Qualitative and quantitative research	Reliability and construct validity testing of the developmental instrument Identification of the hallmarks of good decision-making practice	6

Decision-Making Instrument: Data Collection Technique

Qualitative and quantitative data collection techniques will be used in this research including interviews with Key Opinion Leader's (KOLs) from the regulatory agencies and pharmaceutical arena. Digital recordings, the NVivo computer relationship database (Bazeley, 2007; Casey et al., 2011) and web-based questionnaires (Richards, 2005). Thematic mapping (Attridge- Stirling, 2001; Braun and Clarke, 2006; Casey et al., 2011), construct validation and triangulation of the

qualitative and quantitative research finding will be used to compound the interpretation of the overall research outcome.

Qualitative Techniques: Semi- Structured Interviews & Questionnaires

There are three recognised different types of interviews: structured, unstructured and semi-structured. Semi-structured interviews strike a balance between a structured interview and unstructured interview. In the semi-structured interviews the questions are open ended and do not limit the respondents/interviewees choice of answers. The purpose is to provide a setting/atmosphere where the interviewer and interviewee can discuss the topic in detail.

The advantages of face-to-face interviews include the flexibility afforded in presenting a series of questions ranging from "closed" to "open", verbal interactions and enhanced assurance on understanding of question asked, It has been shown that individuals are more likely to be interviewed rather than complete a questionnaire, especially when the topic is seen to be interesting and relevant to their own current work (Holstein, 2001; Dicicco-Bloom, 2006). Interviews are also a good method of building rapport and are non-judgemental and can be improved by showing a genuine interest in the responses and appreciation of the time-investment of the interviewee. Semi-structured interviews are generally organised around a set of predetermined open-ended questions or checklist, with other questions emerging from the dialogue between the interviewer and interviewees. Semi-structured in-depth interviews are the most widely used interviewing format for qualitative research and take between 30 minutes to several hours to complete (Dicicco-Bloom, 2006). Semi-structured interviews will be used in this research.

The individual interview technique is also a qualified research data collection method used in new instrument development purposes (Patton, 2002; Patrick et al., 2011a). The main advantages of individual interviews are that they allow face-to-face communication and help to obtain more in-depth and detailed information about an individual's experience. It is also recognised that potential "downsides" to the individual interview approach are: time-sacrifice involved, it may take longer to collect the data, limited to one participant's view at a time; no peer comparison, cost

(e.g. travel, transcription fees) (Patrick et al., 2011b). Individual interviews are ideal for concepts that are sensitive or target populations/people are unlikely to volunteer or share information in a group setting (Patrick et al., 2011b). This is a pertinent consideration for this research in which confidential, sensitive and subjective discussion items will be raised.

Semi-Structured Interview Procedure

In this research, individual face-to-face interviews using a semi-structured interview checklist will be used in the majority of the interviews with the senior decision-makers. Where this is not possible, the interviews will be held by teleconference. The face-to-face interviews should allow for a respect, understanding and rapport to develop between the interviewee and the researcher performing the interviews. It is hoped that the use of this checklist and interviews will provide a free-flowing dialogue and discussion forum between the interviewee and interviewer.

Before the scheduling of any interview, each interviewee will be sent by e-mail a copy of the research outline. This research outline will provide detail on the: research background, research objective, research methodology, informed consent and confidentiality assurance, estimated time needed for the conduct of the interviews, the time window during which interviews are planned, data collection, next steps details in the overall research and inform interviewees that the results of the overall research investigation would be made available in due course. This approach is in line with good research practice (Mathers, 2002; Meyrick, 2006). At the start of all interviews, confidentiality will be assured and a request made to record the interviews.

An Olympus WS-6505 digital high quality voice recorder will be used to record all the interviews with the senior decision-makers. The interview transcripts will form the basis of the qualitative research component (Wellard and McKenna, 2001; Mathers, 2002; Halcomb and Davidson, 2006). The use of audio recording in concept elicitation interviews is well established and helps to fully capture the context and content of each session as well as to produce transcripts that form the data for analysis. Audio recordings facilitate participant anonymity and are generally comfortable for participants, particularly when sensitive topics are being discussed.

Participants are assured of confidentiality and limited use of the recorded materials from their interviews. Recording also frees the interviewer from note taking so that he or she may engage fully with participants (Wellard and McKenna, 2001; Patrick et al., 2011b).

Web-based survey questionnaire platforms will be used during the developmental and validation stages of the generic instrument research. This web-based method involves posting a questionnaire onto a website allowing the respondents to complete remotely (Diem, 2002a). The advantages of this method include: quick responses are possible; it can be inexpensive if the correct software and tools are available; postage is reduced or eliminated; and it is easy for respondents to reply. The Survey-Monkey web-based survey platform will be used in this investigation (Survey Monkey, 2013). The commonly reported techniques aimed at improving questionnaire response rates will be used if needed for each of the questionnaire surveys conducted (Schleyer and Titus K.L., 2000; Diem, 2002b; Boynton, 2004). Data will be collected through the web-based questionnaires and the survey-monkey functionality. All questionnaire returns should be completed directly into the Survey-Monkey database and anonymity and confidentiality will again be respected and assured throughout the data collection, analyses and reporting stages.

Information Sources

The generic developmental instrument will involve gathering information from at least 10 regulatory agencies and more than 60 international pharmaceutical companies.

Study Instruments

As detailed in Chapter 1, there is currently no existing validated instrument available to measure the quality of decision-making within the drug development and regulatory arena. There are many instruments in the medical decision-arena especially relating to quality of life. Many were reviewed for their applicability and value in the current research question and some example instrument articles are referenced (Guyatt, 1993; Pijls-Johannesma et al., 2005; Langham et al., 2008; Ruiz et al., 2008; Rothman et al., 2009; Kriston et al., 2010; Bhatti et al., 2013a; Bhatti et al., 2013b). A tool developed to monitor the Centralised Procedure for submission of

marketing authorisation application (EMA, 2000) was also reviewed but again, the tool was not considered fit-for-purpose to address the research aim relating to the quality of decision-making.

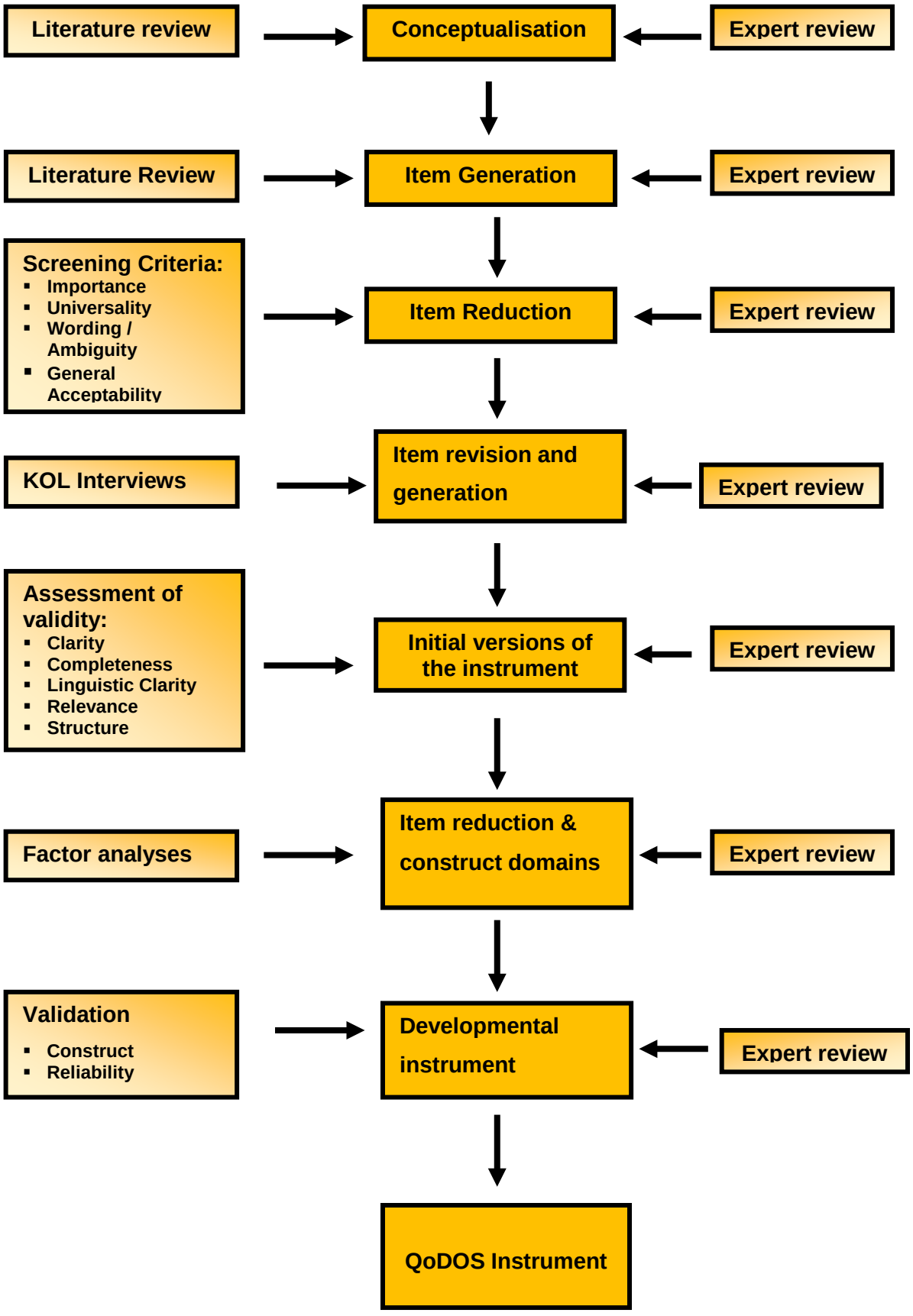
A thorough search of the internet will be performed to investigate many of the web-sites given over to decision-making, decision-analysis and decision-techniques. Some of these sites could be helpful in providing extra dimension considerations to the research question although the sites are not aimed at the drug development or general healthcare arena. It is recognised that the audience for most of these websites appears to quite broad ranging from the "general public" to persons with specific or academic expertise in an area of the decisions sciences or strategic management/ business leadership area (Web, 2012; MindTools, 2013; Government, 2013; Stanford University, 2013; UCI, 2013; Stellenbosch University 2013b).

Generic Instrument Development Techniques

Conceptual Model and Hypothesis

The origin of the conceptual framework was an appreciation of the lack of research performed to date investigating the actual quality of decision-making by stakeholders involved in the research, development and delivery of new medicines. An initial six themes were generated for the interview checklist based on value judgments which formed the basis of the qualitative interviews and in turn the construction of the developmental decision-making instrument. The objectives of the conceptual framework were to explore the ways in which individuals (decision-makers) and different companies/organisations manage decision-making and to identify the hallmarks of good decision-making practice. The steps involved in the development of the generic decision-making instrument are presented in Figure 2.1.

Figure 2.1: Development of The Generic Decision-Making Instrument



Psychometric Evaluation of The Study Instrument

As the generic instrument is a new instrument it will be examined to ensure it has adequate measurement properties relevant to decision-making from the perspective of the individual and the organisation. The applicability, practicality, acceptability, as well as four validity aspects of the instrument will be evaluated at several stages through its development (Nunnally and Bernstein, 1994; Simon et al., 2006; NIH, 2012). Qualitative and quantitative research components will be employed in the stepwise development and validation of the instrument.

Validity can be established in several ways and addresses the issue of whether what we are trying to measure is actually measured. Published measures for various concepts usually report the kind of validity that has been established for an instrument, so that the user or reader can judge the "goodness" of the measure (Streiner and Norman, 2008; Bougie, 2010).

Face validity

Face validity simply indicates whether, on the face of it, the instrument appears to be assessing the desired qualities. The criterion represents a subjective judgement based on a review of the measure itself by one or more experts, and rarely are any empirical approaches used (Streiner and Norman, 2008). Face validity will be performed at each stage of the instrument development. Face validity measurement can be considered as a basic and a very minimum index of content validity. In questionnaire and instrument development, each component item is reviewed by a person or team familiar with the target research area and asked to validate whether in their judgement that the questionnaire/instrument content, layout, language and format are appropriate. A positive review and acceptance provides an implicit assessment of face validity.

Content validity

Content validation is an important process whereby a new measuring instrument is examined for its focus and emphasis relating to the target population (Streiner and Norman, 2008; Bougie, 2010). In questionnaire or instrument development, it is used to ensure that the questionnaire includes a representative and adequate set of items to uncover the concepts in the research questions. The more the scale items

represent a related field or domain of the concept being measured, the greater the validity. The use of expert judges to solicit opinions on the suitability of the measure is used to establish content validity. It is a fundamental requirement of instrument validation and also inherently supports construct validity and generalisability of a new instrument. The content validation exercise to be performed will involve a panel of not less than four experts reviewing and providing their feedback on the language clarity, completeness, relevance, and scaling of the developmental instrument items. Quantitative assessment techniques can be used to complement the subjective reviews of the expert panel. The techniques that will be used are: calculation of the Content Validity Index (CVI) and Scale Content Validity Index (S-CVI). In addition, intraclass correlation coefficients (ICC) and reliability (Cronbach's alpha) testing will be determined using SPSS statistical software. Content validation will be described in more detail in Chapter 4.

Criterion-related validity

Criterion-related validity is established when the measure differentiates individuals on a criterion it is expected to predict. There are two types of criterion-related validity; predictive and concurrent validity (Streiner and Norman, 2008) Predictive validity indicates that a future criterion can be replaced by a current measurement on a scale. Concurrent validity refers to a relationship between a predictor variable and a current variable, both of which are assessed at the same time (McDaniel and Gates, 2002. In other words, when testing different individual variables that are known to be different, they should score differently on the results (Sekaran and Bougie, 2010).

Construct validity

Construct validity is concerned with how well the results obtained from the use of a measure fit the theoretical foundations from which it is designed (Meehl, 1955; Trochim, 2006). It associates the practical components of an instrument test score obtained from with some underlying theory of behaviour (Salkind, 2006; Trochim, 2006). Constructs are underlying latent variables which cannot be directly observed but encompass the foundation dimensions of a psychometric instrument. Construct validation contains two validity sub-categories (convergent and discriminant). Convergent validity is the degree to which the concepts that should be related theoretically are interrelated in reality. Discriminant validity is the degree to which

concepts should *not* be related theoretically and are in fact *not* interrelated in reality and is established when two variables which are predicted to be uncorrelated or to have low correlation (Westen and Rosenthal, 2003; Trochim, 2006; MacKenzie et al., 2011). Evidence of construct validity can be presented using a multi-trait-multi-method matrix (MTMM). The MTMM is an approach which examines convergence (evidence that different measurement methods of a construct give similar results) and discriminability (ability to differentiate the construct from other related constructs) (Campbell and Fiske, 1959; Trochim, 1989).

Sensitivity

The sensitivity of the instrument is the ability to measure any degree of change (Streiner and Norman, 2008). Sensitivity assessments will be performed during the development of the generic instrument.

Responsiveness

Responsiveness assesses the ability to measure important change. According to Liang (2000), it is the ability of an instrument to measure a meaningful or clinically important change in a clinical state (Liang, 2000). Patrick and Chiang, view sensitivity and responsiveness as a form of construct validation, assessing the hypothesis that the instrument is capable of detecting meaningful change (Patrick, 2000).

Practicality

The practicality of the study instrument should also be addressed when evaluating the suitability of a measure and this includes considerations such as respondent burden, the cost in administering, mode of administration of the instrument (e.g. interviews or self-administered), the ease with which the measure can be scored and whether it is readily understood (Holstein, 2001; Dicicco-Bloom, 2006).

Reliability

Reliability of a measure indicates the extent to which it is without bias and therefore ensures that consistent measurements across time and various items in an instrument i.e. it helps to assess the "goodness" of a measure (Sekaran and Bougie, 2010). It refers to the extent to which the instrument is measuring consistently and producing

the same result on repeated trials (Higginson, 2001) and assesses that a test is measuring something in a reproducible fashion; it says nothing about what is being measured.

Measures of internal consistency are the most widely used indices of reliability. The reliability coefficient expresses the proportion of the total variance in the measurement which is due to 'true' differences between subjects (Streiner and Norman, 2008).

Thus the formal definition of reliability is

$$\text{Reliability} = \frac{Subject\ Variability}{Subject\ Variability + Measurement\ Error}$$

Reliability is expressed as a number between 0 and 1, with 0 indicating no reliability, and 1 indicating perfect reliability (Streiner and Norman, 2008; Eisinga et al., 2013). Cronbach's alpha coefficient testing is the most popular test of inter-item consistency reliability (Salek et al., 1996; Streiner and Norman, 2008). It measures how united the items are in a test or assessment and is determined by Cronbach's alpha coefficient (Salkind, 2006). Cronbach's alpha testing will be used in the validation testing of the new generic instrument. Internal consistency is also a relative measure of reliability and reflects the scale's ability to differentiate among people. Split-half, parallel (Davidshofer and Murphy, 2005) and Guttman (Davidshofer and Murphy, 2005) reliability testing are also widely used in qualitative psychometric research and will be used in the battery of reliability tests to be performed on the developmental instrument. The internal consistency of measures is indicative of the homogeneity of the items in the measure that tap the construct. In other words, the items should "hang together as a set" and be capable of independently measuring the same concept so that the respondents attach the same overall meaning to each of the items, thus supporting construct validation. This can be seen by examining whether the items and the subsets of items in the measuring instrument are correlated. The internal consistency reliability is a test of the consistency of respondents' answers to all the items in a measure. It presents an estimate of degree of inter-correlation between independent measures of the same concept. The consistency over repeated measures of the same test can be assessed with the Spearman's correlation coefficient and the equivalence of different versions of the same measure can be indexed by a statistical

correlation. The internal consistency, which addresses the relatedness/homogeneity of a single test form, may be assessed by correlating performance on 'two halves of a test', which is termed *split-half reliability*. The value of this Pearson product-moment correlation coefficient for two half-tests is adjusted with the Spearman–Brown prediction formula to correspond to the correlation between two tests (John and Benet-Martinez, 2000b).

Intra-class correlations (ICC) is the ratio of variance of measurements of a given target to the variance of all targets and is a complimentary method for assessing reliability. ICC describes how strongly the items in the same grouping correlate or resemble each other. It is used to assess the consistency, or conformity, of measurements made by multiple observers measuring the same quantity. ICC will be measured as one of the battery of tests performed to evaluate reliability.

Manual Review and Coding of The Transcripts

The transcripts from each of the interviews with the KOL's will form the basis of the qualitative research component of this study. Each resultant interview transcript will be carefully read, reviewed and manually coded for emergent decision-making themes and sub-themes. This will involve a line by line review of the transcripts and particular noteworthy quotations will be noted. The time to manually code the transcripts is expected to take on average three hours per interview script. A standard manual systematic coding approach will be followed comprising of five steps (Ritchie, 1994): familiarisation, identification of a thematic framework, indexing, grouping, mapping and interpretation:

Stage 1: Familiarisation: the process by which the reviewer becomes familiar and then wholly immersed in the transcripts of the data collected. Throughout this process there is a growing awareness of the key ideas and recurrent emergent themes (Basit, 2003).

Stage 2: Identification of a thematic framework: this occurs after familiarisation with the data set and when the emerging themes are recognisable. The themes and sub-themes emerge as those that have been expressed by the participants and form the basis of a thematic framework. Following the identification of the thematic

framework, the themes and subthemes can be refined. Refining a thematic framework is not an automatic or mechanical process, but involves both logical and intuitive thinking. It involves making judgments about meaning, about the relevance and importance of themes and about implicit connections between ideas (Ritchie, 1994).

Stage 3: Indexing: is the process of assigning portions, phrases or sections of the data to a particular theme or sub-theme heading. This data management step assists with the more formal allocation of themes and sub-themes into defined theme groupings.

Stage 4: Grouping is the arrangement of the indexed themes and sub-themes under a specific heading. The naming of the theme heading is an important process and naming is best done using the language of the interviewees as closely as possible, because the names of the concepts represent the perspectives of interviewees and not that of the developers. This naming approach will be followed for emergent decision-making themes.

Stage 5: Mapping and interpretation: Mapping involves the linkage of the emergent theme outputs to allow an interpretation and analysis of key emergent characteristics. This analysis should be able to provide a schematic diagram of the event/phenomenon emergent themes thus guiding interpretation of the overall data set (Ritchie, 1994). It is at this mapping and interpretation stage that the objectives of the qualitative analysis are identified in terms of defining concepts, theme associations, thematic mapping, providing explanations as well as helping to developing future strategies.

Data management, processing and analysis

Data Management

Interviews will be transcribed into Word format. The transcription of the individual interviews from the audio-recording to Word format is expected to take on average eight hours per interview script. The transcripts will be transferred into the qualitative software package NVivo 8 for data management and processing.

The computer software package NVivo 8, will be used to analyse all the interview data and support thematic evolution and coding (Richards, 2005; Bazeley, 2007). NVivo is a specialist package developed solely as a computer aided qualitative data analysis system (CAQDAS) and is recognised globally as a reputable tool for managing and supporting this type of analytical work (Richards, 2005). It will be used to organise, transcribe data, facilitate coding, to perform analyses and assess inter-coder reliability. The NVivo functionality does not assign codes to the data and manual subjective coding will be required in this research (Richards, 2005; Bazeley, 2007).

NVivo has two principal benefits: efficiency (time burden of manual approach) and transparency (NVivo facilitates the maintenance of a clear audit trial). NVivo is a type of database known as a 'relational database' which facilitates the linking of all relevant imported data (audio and transcripts). It allows a researcher to map out a project, set up frameworks, organise ideas and establish a range of queries and themes. The functionality allows for non-numerical and/or unstructured data to be organised and analysed. In turn, the software allows for the classification, sorting and arrangement of information; examination of relationships in the data; and combination of analysis with linkage to themes and concepts using a "Node and Node Tree approach" coding approach. The Node approach identifies trends, themes and allows cross-examination of information in various ways. This type of database facilitates linking all relevant data generated during the data gathering and importation process. The NVivo system enables the researcher to also add notes to transcript imports.

Data Processing

The NVivo 8 software will also be used for data processing. NVivo 8 provides a "tree branch", that is, a hierarchal nodal-coding system for emerging themes and links to their main category (conceptual core domain). A colour coding system in this software allow for large amount of text data to be organised in a consistent standard manner. This data text being meticulously analysed word-by-word and line-by-line from the large body of the verbatim transcription text. Subsequently, all the interview transcripts data will be combined in order to build a broader picture of different emerging aspects of decision-making themes. Various decision-making

themes that emerge will be coded and grouped into core decision-making categories. A thematic map of the emergent themes will be generated which should allow a holistic visualisation of the research subject themes and sub-themes.

Coding Framework and Content Analysis

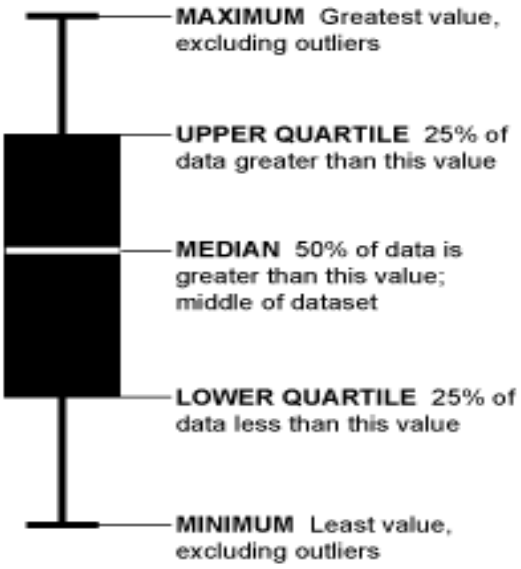
The interview transcript information obtained will be qualitatively coded into nodes, major categories and domains. Thereafter, it will be analysed, summarised and quantified in the form of numbers and percentages to provide statistical meaning to the data.

Quantitative techniques: Data processing and analyses Used on The New Generic Instrument

Data processing and statistical analysis will be carried out using Microsoft Excel and SPSS for the QoDOS development instrument research. Various descriptive statistics techniques will be used in the analyses, interpretation and reporting of quantitative data. Descriptive tables and bar charts, spider plots and "Box and Whisker plots" will also be used to illustrate key features in the distribution of data. The Box-and-Whisker plot graphically describes the shape and characteristics of the distribution of comparative data. It is a valuable tool for presenting the distribution of related datasets. A general guide to interpreting a Box-and-Whisker plot is presented in Figure 2.2 (Salek et al., 1996; Zuckerman, 2006).

A spider graph (also known as a radar chart) is a graphical method of displaying multivariate data in the form of a two-dimensional chart of quantitative variables represented on axes starting from the same point. The relative position and angle of the axes is typically uninformative. They are used in profiling quality improvement programmes and performance metrics (Basu, 2004; Zuckerman, 2006).

Figure 2.2: Guide to interpreting a Box-and-Whisker plot



Statistical programming and descriptive statistics will be employed in the exploratory and confirmatory factor analyses and construct validation. Descriptive statistics apply transformations of the obtained data into a form which can provide the characteristics of large sets of data. The descriptive statistics to be used in the research include Cronbach's alpha (reliability), Kaiser Meyer-Olkin (KMO), Barlett's test of Sphericity, Scree plots, Spearman Rank Correlation Coefficient, intraclass correlation coefficient (ICC) techniques, ANOVA, discriminatory, convergent and regression analysis.

Cronbach's alpha determinations will be used to measure the internal consistency reliability of the evolving developmental instrument and this testing will also provide supportive evidence for the retention and deletion of the items during a planned factor analysis (Pallant, 2005; Petter, 2007; Streiner and Norman, 2008). Scree plots provide a useful and easily interpretable impression of the number of factors within each extraction result. Factor rotation will be performed using the Varimax technique and Kaiser-Meyer-Olkin (KMO) and Bartlett's test of sphericity measurements will be taken to demonstrate that adequate sampling is being performed for each extraction stage (Field, 2009). Reliability testing using intraclass correlation coefficient (ICC) techniques will be used to evaluate inter-rater scores.

Hallmarks of Good Decision-Making Practice

It is hoped that the insights gained during the development and validation of the generic instrument could also facilitate the identification of the hallmarks of quality decision-making. It is anticipated that the decision-making themes that emerge from the qualitative interviews and corroborated by quantitative research may allow for best practice recommendations and approaches to be generated. If these hallmarks of good decision-making practice do emerge from the research then an attempt will be made to transpose them into a new decision-making framework. The framework would present a systematic and structured approach to decision-making.

SUMMARY

- A detailed outline of the systematic development approach of the generic decision-making instrument is provided including the conceptual phase, interview stage, item generation phase, content validation, web-based questionnaires conducted, factor-analyses, item reduction, construct validation, and reliability testing of the new instrument
- The various qualitative methodologies and techniques that will be used in the research have been described
- Methodological choices relating to interviews, transcriptions, database management, data processing, data reporting, data analyses and data interpretation have been evaluated and detailed
- The different types of psychometric properties that will be tested with the new instrument were discussed
- The various quantitative methodologies and statistical techniques proposed to be used in the generation, processing and interpretation of output results from the various research components have been evaluated and detailed
- The secondary study outcome, relating to potential identification hallmarks of good decision-making and creation of a new framework for quality decision-making has been detailed.

CHAPTER 3

Development of a Generic Decision-Making Tool: Qualitative Study

INTRODUCTION

Decision-making among the regulators of medicines and members of the pharmaceutical industry is driven by various factors. Regulators must adhere to a remit to positively impact public health whilst remaining mindful of precedents and adhering to laws, regulations and policies (Eichler et al., 2008; Breckenridge et al, 2011). Pharmaceutical industry members, on the other hand, are motivated by the need to predictably and transparently develop medicines that will fulfil patients' needs and regulatory requirements whilst delivering profit to shareholders (Breckenridge and Woods, 2005; PWC, 2012).

The challenges to medicines development for both regulators and industry have been well documented and include increasing dossier complexity, the need for expedited approval timing, escalating costs in the face of constraints on capital, patent expiries, dwindling pipelines and stakeholder scrutiny with resulting demands for access, proven value, productivity and return on investment (PWC, 2012). Any support for quality decision-making in the face of these sometimes conflicting drivers and challenges would benefit all stakeholders (Walker et al., 2007).

Decision-making *per se,* can be regarded as being part science and part art, with *art* in this case being the subjective human component within the decision-making process. This subjective decision-making style reflects the combination of how an individual perceives and comprehends stimuli and the general manner in which he or she chooses to respond to it. It is linked to an individual's knowledge, ability, motivation, their value orientation and tolerance for ambiguity (Kahneman, 2012). Decision-making is usually considered to be the result of cognitive processes leading to the selection of a course of action among several alternatives (McDermott, 2008). It also represents a rational or irrational reasoning or emotional process based on prior knowledge as well as a person's individual assumptions. In a normative perspective, decision-making deals with the logics and rationality of the outcome related to the individual or collective choice made.

In another sense, decision-making may be regarded as the result of problem-solving processes, which ends in an assumed rational choice (Kahneman, 2003; Kahneman,

2012). In most specialist or science-based professions, decisions are commonly made, continuously or at points or gates in the development of a specific product or service. In the pharmaceutical industry, decision-making involves making judgments on specific scientific data sets on the development of a novel molecule or pharmaceutical in order to take appropriate actions in respect to company objectives (Pritchard et al., 2003).

By its very nature, drug development has many inherent risks and effective decision-making is required to successfully deliver new medicines. In the drug development arena, decisions commonly have to be made based on insufficient data, a high degree of uncertainty, time pressure, significant economical stakes, and often in a competitive environment where several stakeholders are competing to be first on the market with their specific drug candidate (Pritchard et al., 2003; Chung-Stein, 2011). (Pritchard et al., 2003, Chung-Stein, 2011). Other potential factors such as the nature of the sponsor organisation and target patient characteristics of the treatment indication add increasing variability to the outcome such that different decision-makers could make different decisions faced with the same set of criteria (Kostopoulou and Wildman, 2004).

Investigation into the decision-making approaches of individuals and organisations involved in medicines research and delivery may provide useful insights into how both the person and the company make decisions. This enhanced understanding may facilitate a clearer understanding of decision-making approaches and this in-turn may help to identify or enable better decision-making practices for both the individual and the organisation. A structured systematic research study may help reveal determinants of the decision-making process as well as providing research participants with a structured reflection on their own decision-making style and approach. This enhanced understanding may also help them to improve their future decisions.

At a fundamental level, there are four basic decision-making styles: subjective, objective, analytical and non-analytical, with numerous academic sub-styles such as directive, analytical, conceptual and behavioural (John and Benet-Martinez, 2000a; Kahneman, 2012). Linked to these styles, numerous qualitative, semi-quantitative

and quantitative decision approaches have evolved such as the PROACT-URL and Multi-Criteria Decision Analysis (Guo et al., 2010b; EMA, 2013a; Leong et al., 2013). Frameworks are recognised as being helpful in decision-making and several are being developed on an ongoing basis.

The overall aims of this study were to develop a generic questionnaire instrument to assess and enable higher quality decision-making. The research question being, "could the development and availability of a decision-making instrument, enrich the quality of decision-making by individuals and organisation stakeholders from the medicines development arena". The aim of this initial qualitative component of the research was to investigate fundamental considerations as to how individuals and organisations working in the drug delivery arena manage decision-making.

METHODS

Research Design and Methodological Framework

The overall research was exploratory and descriptive in nature. Since there are no well-established theoretical frameworks for determining the "quality of decision-making" and as limited research has been conducted on the component factors, an inductive approach exploring the research question was followed. The initial qualitative stage involved the conduct of semi-structured interviews. Thematic analyses of the output from the interviews delivered in-depth insight into decision-making themes and considerations. The research consisted of the quantification and analysis of decision-making outputs. The content analysis performed, provided a systematic way of identifying and organising relevant data into meaningful information on decision-making.

Conceptual Model and Hypothesis

A conceptual framework is used in research to outline possible courses of action or to present a preferred approach to an idea or thought. Conceptual frameworks (theoretical frameworks) are a type of intermediate theory that attempt to connect to all aspects of enquiry (e.g. problem definition, purpose, literature review,

methodology, data collection and analysis). Conceptual frameworks can act like maps that give coherence to empirical enquiry. It is hoped that such a thematic map could be generated for decision-making domains as part of this qualitative research. Thematic maps can also ease the tension between human judgement and statistical analysis in qualitative research (Trochim, 1989; Attridge-Stirling, 2001).

The conceptual framework presented in this research is that the quality of decision-making could be enriched by the use of a generic decision-making instrument. This would initially involve an exploration of the decision-making approaches of senior decision-makers and the regulatory agencies or organisations in which they are employed. This exploration may lead to a better understanding of how these individuals and their organisations manage decision-making. In turn, this understanding could facilitate the development of an appropriate generic questionnaire for use in decision-making considerations of individuals and organisations.

The origin of the conceptual framework was an appreciation of the lack of research performed to date investigating the quality of decision-making of stakeholders involved in the research, development and delivery of new medicines. An expert panel met and identified six decision-making items based on value judgments, to be researched in the study. The six items formed the basis of the initial interviews and in-turn the construction of the generic instrument. These six items were:

- General understanding or perception of decision-making
- Decision-making within the drug development arena
- Decision-making within the regulatory review
- Decision-making within their organisation
- Awareness and use of decision-making techniques
- Impact and monitoring of decisions.

The underpinning principles of the conceptual framework were as follows:

- Identification of the decision-making themes relevant to the research question

- Improvement in the quality of regulatory submissions and reviews by improving the decision-making approach and techniques employed within the drug development process and regulatory review
- A final research output being the delivery of an instrument to people working within the pharmaceutical arena and regulatory agencies. The instrument could be used by them as a convenient tool with inherent generalisable properties to monitor and improve quality decision-making in routine and challenging decision-making situations.

Choice of Sample and Design of Interview Checklist

The initial operational phase of the qualitative research involved the conduct of semi-structured interviews with experienced decision-makers employed within the pharmaceutical arena and regulatory agencies. The participants were appropriate as it reflected a sub-set of the intended target population (pharmaceutical industry and regulators) to be further investigated in a follow-on research study. The criteria adopted for recruitment of the study were:

- Individuals employed in a senior position of authority within a regulatory agency or pharmaceutical industry organisation
- Having more than five years experience in a managerial role
- Located in either the EU or USA
- English language speaker
- Willingness and availability to participate in a 45 – 90 minute interview.

A six-item checklist detailed previously was designed for semi-structured interviews. Content validation was performed on the developmental instrument by an expert panel (Denzin and Lincoln, 2005; Hayes et al., 1995). The content validation exercise ensured that the construction and format of the questionnaire allowed information relevant to the purposes of the study and the target population to be obtained with appropriate reliability and validity. The language, redundancy, formulated questions, terminology, format and layout of the questionnaire were reviewed and agreed by the expert panel. It adhered to appropriate best approach recommendations (Patrick et al., 2011a; Patrick et al., 2011b).

In advance of all interviews, a copy of the research study outline was sent by e-mail to each of the prospective interviewees. This research outline provided details on the background, objectives, methodology, voluntary consent, anonymity and confidentiality assurance, estimated time needed for the conduct of the interviews, the time-window during which interviews were planned, data collection and the next steps in the overall research. Mention was included that the results of the overall research investigation would be made available to the interviewees in due course. A copy of the research outline given to participants is provided in Appendix I.

Data Collection

Each interview was audio-recorded and in-turn transcribed verbatim into Word format within 1-week of the conduct of the face-to-face interview whenever possible. The transcription of the individual interviews from the audio-recording to Word format took eight hours on average per interview script. Thematic coding on each transcript was performed using the NVivo8 relational database (Bazeley, 2007) and by manual review and coding.

Computer Assisted Coding of The Interview Transcripts

The proprietary relational database NVivo8 was used in the computerised coding exercise (Bazeley, 2007). NVivo8 software and functionality allowed for the interview transcripts to be analysed and for the identification and quantification of emergent decision-making themes and sub-themes. The functionality of NVivo8 automatically facilitated the following: coding of similar themes (thematic coding), identification of a thematic framework, indexing of the emergent themes and subthemes and grouping of the themes under category headings, comparison and quantification (frequencies) of emergent data to be generated. This automated coding approach was complimentary to the manual coding also performed on the transcripts.

Manual Review and Coding of The Transcripts

Each interview transcript was carefully read, reviewed and manually coded for emergent decision-making themes and sub-themes. This involved a line by line review of the transcripts and identification of the decision-making themes. Particular quotations from the interviewees were noted. The time to manually code the transcripts took on average three hours per interview script. A standard manual

coding approach was followed comprising of five steps (Ritchie, 1994); familiarisation, identifying a thematic framework, indexing, grouping, mapping and interpretation.

Overall, all the information obtained by the interview techniques described was qualitatively coded into themes and sub-themes and quantified in the form of numbers and percentages for ease of interpretation.

RESULTS

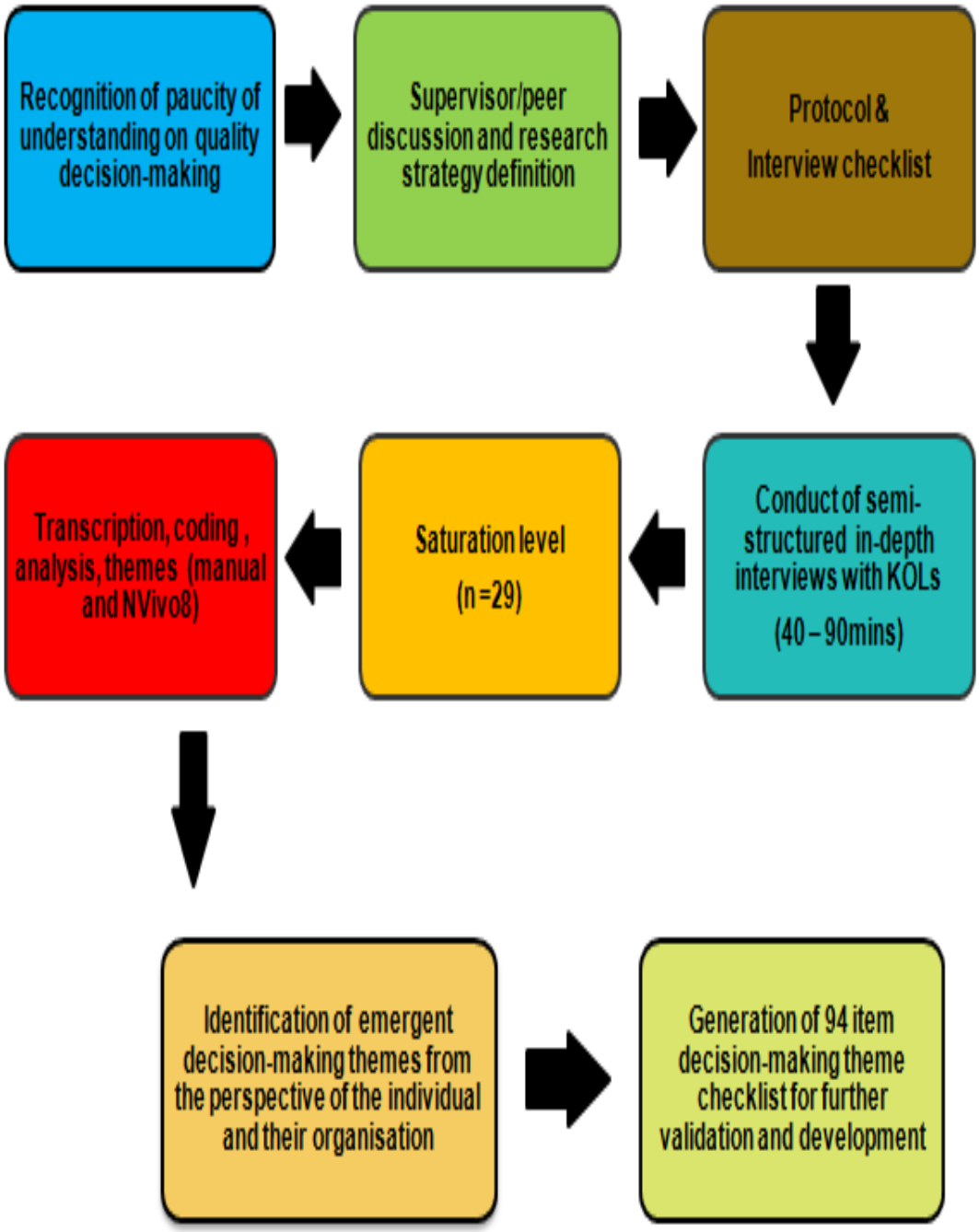
The interviewees who participated were all at a managerial or senior executive level within their respective organisations. The interview checklist captured socio-demographic details of the interviewees such as; their name, their job role, the organisation in which they are employed and the number of years of experience they have within pharmaceutical development or within regulatory agencies. The interviewees were from European Medicines Agency (EMA), Medicines Human Regulatory Agency (MHRA), Irish Medicines Board (IMB), EU and US Pharmaceutical companies and US Contract Research Organisations. A summary of the demographics of the study participants is presented in Table 3.1.

Table 3.1: Socio-Demographics of study participants

Organisation, number of participants and gender	Job Title Range	Years of Experience
Regulatory Agency (n = 9, 6M/3F)	Group Head – Head of Agency	9 – >35 years
Pharmaceutical Company (n=10, 5M/5F)	Manager – Global Function Head	8 - >35 years
CRO (n=10, 5M/5F)	Manager – Global Function Head	7 - >30 years

The objectives of the conceptual framework are to explore the ways in which individuals (decision-makers) and different organisations manage decision-making. The conceptual framework and methodology used in this qualitative research are outlined in Figure 3.1.

Figure 3.1: Qualitative development of a generic decision-making tool



Conduct of Semi-Structured Interviews

A total of 29 semi-structured interviews were conducted investigating the decision-making approaches and considerations of the study participants and their organisations. The semi-structured interviews were conducted between September 2011 and January 2012. The interviews on average lasted around 50 minutes.

In the qualitative interviews, the emergent theme saturation level was achieved after completion of 29 interviews. No additional decision-making themes were seen to emerge from the 27th, 28th or 29th interview performed and the 29th was the final interview conducted. Analyses of the decision-making themes and sub-themes evident in the interview transcripts were performed using NVivo8 and its automated thematic coding functionality. Manual review and subjective evaluation of apparent themes and associated coding of these emergent items were also performed. The NVivo8 automated coding and the manual evaluations of the transcripts from the interviews with the senior regulatory and industry key opinion leaders provided quantified outputs and valuable insights into the decision-making approaches of the study participants and that of their organisation.

NVivo8 Relational Database Thematic Coding

NVivo8 thematic output provided details of emergent decision-making themes and sub-themes from the transcripts data set. Information on the prevalence of what was cited (number of times referenced in the data-set themes and sub-themes) and also by how many of the 29 person participants was recorded (Table 3.2). Here, the number of citations made by an individual included those relating to one or more of the sub-themes. This results in the total number of citations not being the same as the sum-total of all sub-theme citations due to the possibility of overlapping of citations in a case where a person made more than one reference to that theme/sub-theme.

Table 3.2: Emergent themes and sub-themes from the NVivo8 analysis

Theme	Sub-Theme	Citations*	Individuals**
1.Analytical		**31(Total)**	**19 (Total)**
	Analytical Tools	20	13
	SOP's Templates - Stepwise Procedures	23	14
2. Benefit Risk		**52 (Total)**	**13 (Total)**
	Critical Understanding of issue or decision	10	6
	Mitigation approach	2	2
	Qualitative approach	11	7
	Quantitative approach	20	9
	Structured approach	19	7
3. Champions		**19 (Total)**	**17 (Total)**
	Champion as Project leader	19	17
4. Consensus		**41(Total)**	**24(Total)**
	Consensus is the normal goal targeted	29	22
	Cultural considerations with consensus approach.	3	3
	Weaknesses related with trying to reach consensus	12	7
5. Critical nature of the decision		**10 (Total)**	**7 (Total)**
	Clear understanding of the impact of the decision	9	7
	Effective communication and comprehension	1	1
6. Culture		**54 (Total)**	**25 (Total)**
	Autocratic	8	5
	Disciplined governance	13	9
	Global Culture	10	7
	Hierarchical	23	12
	Innovative & ability to challenge & recommendations	1	1
	Portfolio therapeutic specialisation	1	1
	Traditional conservative	8	6
7. Decision-making		**43 (Total)**	**10 (Total)**
	Analytical in approach	7	7
	Defined relationships	5	3
	Objective approach	9	7
	Structured approach to decision-making	23	10
	Subjective approach	14	6
8. Drug development portfolio & differentiation		**26 (Total)**	**21 (Total)**
	Understanding of drug development	25	21
	Understanding of portfolio management	19	12

*****The number of items listed in the dataset

**Number of interviewees who mentioned a specific theme or sub-theme

Table 3.2: Emergent themes and sub-themes from the NVivo8 analysis cont'

Theme	Sub-Theme	Citations	Individuals
9. Engagement		**24 (Total)**	**19 (Total)**
	Engagement linked to understand of task	10	7
	Stakeholders	14	13
10. Experience		**23 (Total)**	**14 (Total)**
	A person's inexperience & associated risk	3	2
	Talent, track record & professional experience	22	14
11. Enhancements		**49 (Total)**	**13 (Total)**
	Decision Criteria	1	1
	Extrinsic factors e.g. patient choice	8	7
	Impact analysis	5	5
	Qualification of the decision makers	2	2
	Qualitative approach	2	2
	Quantitative approach	7	4
	Structured approach	7	5
	Successful communication & clarity of language	6	4
	Training & awareness	1	1
	Understanding of critical nature of issue	8	5
12. Facilitators		**26 (Total)**	**25 (Total)**
	Facilitators are not used in the organisation	12	12
13. Facilitators are used on rare or exceptional occasions		**5 (Total)**	**5 (Total)**
	External facilitators are used	1	1
	Internal facilitators are used	4	4
14. Facilitators are used routinely in the organisation		**3 (Total)**	**3 (Total)**
	External facilitators are used	0	0
	Internal facilitators are used	0	0
15. Framework		**15 (Total)**	**7 (Total)**
	Framework templates	9	5
	Structures approach to decision-making	11	5
16. Human factors and considerations		**43 (Total)**	**29 (Total)**
	Experience and maturity of decision-making	5	5
	Gut feeling intuition	39	28
17. Individual		**25 (Total)**	**10 (Total)**
	Human or personal factors	16	5
	Preferred approach	13	5
18. Mechanisms and procedures		**30 (Total)**	**8 (Total)**
	Standard mechanisms or procedures	30	8

*****The number of items listed in the dataset

**Number of interviewees who mentioned a specific theme or sub-theme

Table 3.2: Emergent themes and sub-themes from the NVivo8 analysis cont'

Theme	Sub-Theme	Citations	Individuals
19. Metrics and benchmarks		**33 (Total)**	**25 (Total)**
	Benchmarking is not used	2	2
	Benchmarking is used	33	23
20. Milestones		**12 (Total)**	**7 (Total)**
	Milestones employed in the decision-making	12	7
	Milestones not used	1	1
21. Poor quality decisions		**25 (Total)**	**22 (Total)**
	Bad decisions experienced	1	1
	Escalation of commitment	25	22
22. Quality		**24 (Total)**	**7 (Total)**
	Lack of quality	0	0
	Quality enhancements	9	5
	Quality factors	16	5
23. Review or impact analysis		**15 (Total)**	**9 (Total)**
	Retrospective impact analysis and lessons	10	7
	Review steps or time-outs employed	6	3
	Review steps during a decision-making task	6	3
24. Situation		**29 (Total)**	**14 (Total)**
	Differing situations require different approaches	28	14
25. Strategy		**22 (Total)**	**14 (Total)**
	Appreciation of preferred outcome	1	1
	Organisation strategy	22	14
26. Subjective		**43 (Total)**	**17 (Total)**
	Approach to the decision-making	37	14
	Human factors & considerations	17	8
27. Team or group		**116 (Total)**	**27 (Total)**
	Advantages of team based decision-making	29	20
	Decision made on team basis	70	26
	Disadvantages of team based decisions	17	15

*****The number of items listed in the dataset
**Number of interviewees who mentioned a specific theme or sub-theme

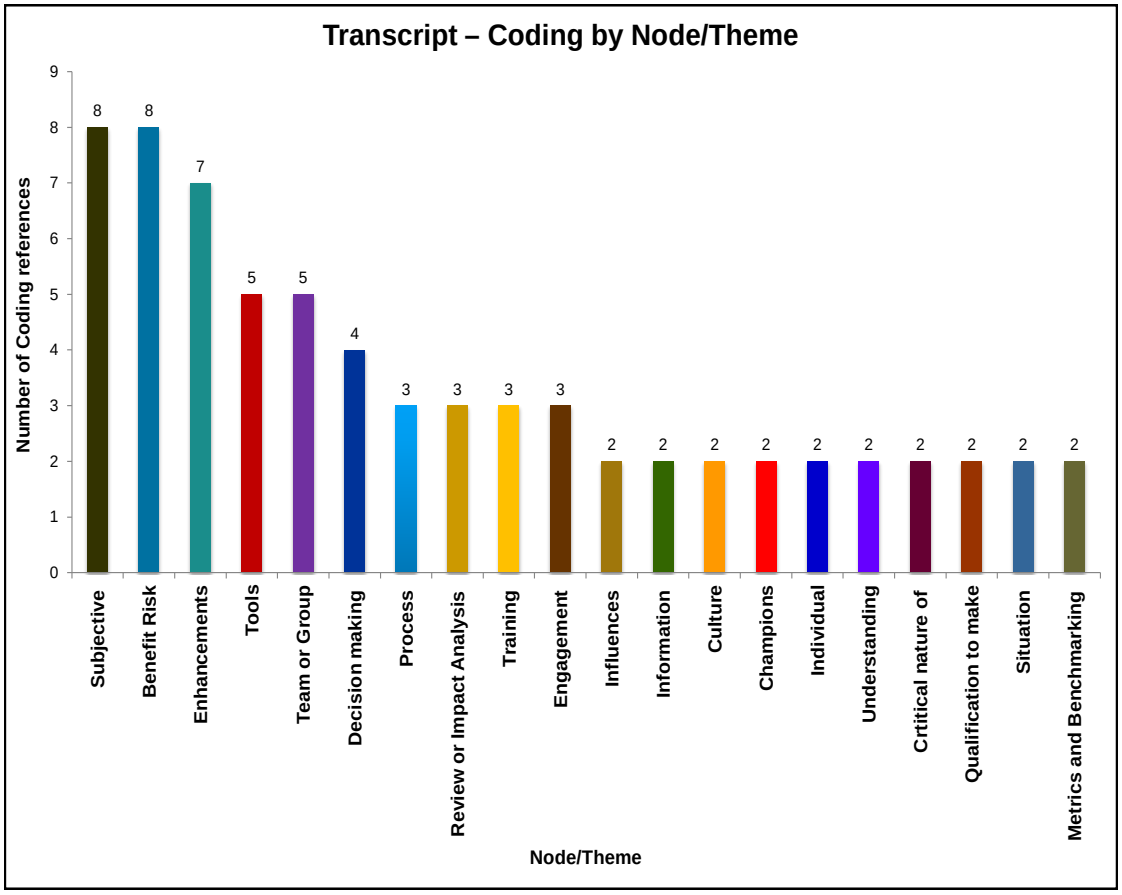
Table 3.2: Emergent themes and sub-themes from the NVivo8 analysis cont'

Theme	Sub-Theme	Citations	Individuals
28. Process		**45 (Total)**	**23 (Total)**
	Standard approach or process not employed	0	0
	Standard processes	45	23
29. Tools		**53 (Total)**	**20 (Total)**
	Awareness	5	5
	Unawareness	35	11
	Usage of tools	5	4
	Usage of tools in decision-making	4	4
30. Training		**47 (Total)**	**24 (Total)**
	No training received	53	24
	Perceived benefit of training	11	9
	Training received	2	1
31. Understanding		**28 (Total)**	**13 (Total)**
	Background & task	10	8
	Science or issue in question	7	6
	Understanding of expectations	12	7
32. Influences		**69 (Total)**	**20 (Total)**
	Competitors	1	1
	Human nature	1	1
	Incentives rewards penalties	14	6
	Money /costs /politics	18	11
	Origin of project	15	6
	Patients expediting delivery of medicines	4	4
	People & talent	4	3
	Precedents	14	7
	Regulatory & legal	11	6
	Stakeholder motivation	20	17
	Strategic fit	8	6
	Timelines	2	2

*****The number of items listed in the dataset
**Number of interviewees who mentioned a specific theme or sub-theme

The NVivo8 decision-making thematic analyses provided data for both the individual interviewees and for 29 person study participants. An illustrative example of the NVivo8 output for an individual from the study is provided in Figure 3.2.

Figure 3.2: Example NVivo8 data output for an individual interviewee



Automated NVivo8 and Manual Review and Evaluation of The Interview Transcripts

The automated thematic coding resulted in the identification of 32 emergent decision-making themes and more than 90 sub-themes from the interview transcripts. A manual content analysis and subject evaluation of the interview transcripts was also performed and this produced a complimentary list of decision-making themes from the study participants transcripts.

Validation of The NVivo Output

The validation of the NVivo output i.e. consolidation of the 32 themes and sub-themes and manual content analysis of the interview transcripts, resulted in the identification and emergence of 19 overarching decision-making themes. The manual review and coding approach was performed as detailed (in Chapter 2) i.e. familiarisation, thematic framework identification, indexing and grouping of the decision-making themes. Following the familiarisation and complete immersion into

the transcribed narrative outputs from the interviews, 32 themes were identified and further consolidated into the following 19 overarching themes given below:

1. Quality and validity of data
2. Time considerations
3. Organisational, hierarchical and cultural influences
4. Analytical and logical approach
5. Qualification and experience in previous decision-making
6. Subjective and personal considerations
7. Political, financial, competitor and reward influences
8. Precedents for similar previous decisions
9. Perpetuating previous decision-making mistakes
10. Plunging in or procrastination with decision-making
11. Clear understanding or lack of understanding of the decision in question
12. Overconfidence in own judgement
13. Group successes and group failures
14. SWOT and alternate outcome planning in decision-making
15. Impact analyses of decisions
16. Decision-making audit trail
17. Education and awareness of evolving decision-making techniques
18. Individual versus Corporate decision-making
19. Quantitative frameworks.

An illustration of the relationship between these 19 decision-making themes and the themes and sub-themes identified in Table 3.2 is as follows: ‘Clear understanding or lack of understanding of the decision in question (Number 11 from list above) with Table 3.2 “Critical nature of the decision” (item 5) and “Critical understanding of issue or decision” (Subtheme of item 2), “Understanding of critical nature of issue” (Sub-theme of item 11).

The approach adopted by which the sub-themes were grouped into themes for each of the resultant 19 decision-making domains is expanded below accompanied by relevant supportive example verbatim quotes from the study participants.

Quality and Validity of Data

The expectation and need for good quality, reliable data on which a person can make a decision was raised in the majority of interviews. This theme encompassed items such as reliability and validity of the source data and trustworthiness of the information provided on which to base a decision. The need for valid and ideally high quality data of suitable integrity was evident. The theme of what constitutes a "quality" decision and the challenge with defining *quality* in this context was also apparent.

"Valid data is a fundamental requirement for good decision-making"....Regulatory Agency

"You need to be able to trust the data you are being asked to review and upon which you are being asked to make a decision".....Pharmaceutical Company

Time Considerations

The reality of having to make timely or real-time decisions was raised in several interviews as was the need to adhere to "review timelines". The Regulatory Agency personnel also specifically advised that there is an obligation for them to work to defined review timeframes. In addition, Regulatory Agency personnel also advised that on occasion, they need to make fast decisions. Items which have a spontaneous safety concern, need quick action and timely/quick decision-making. The sub-theme of workload and time sacrifice/time allocation for making decisions was raised. The challenge of needing to be able to "multi-task" on several projects was raised. This multi-tasking impacts the time allowance or tolerance that can be allocated to individual decision-making exercises.

"We have a public health remit and there are times when we need to make a decision in a rapid manner. Sometimes we do not have all the background information available but still we need to make that decision".....Regulatory Agency

Organisational, Hierarchical and Cultural Influences

Several themes emerged relating to the philosophy and organisational approach to decision-making. Items such as cultural influences, in particular in the larger

organisations were raised. The use of scientific committees was mentioned by all the regulatory agency interviewees. From an industry perspective, the formal requirement for decision-making to be escalated upwards to the appropriate management executive empowered with the actual decision-making was apparent.

"In larger companies, you have more stakeholders in place and therefore it is important to know the decision-making approach because there is likely to be more of a commonality of opinions. Political astuteness is also vital in a large Pharma organisation".....Pharmaceutical Company

Analytical and Logical approach

The use of frameworks to assist with the decision-making process and the use of analytical and step-wise decision-making approaches were apparent. The potential that such approaches may add transparency to the decision-making process was raised.

"A quantitative assessment and analytical procedures will improve transparency in decision-making"…..Regulatory Agency

"A general best-practice framework for decision-making within the drug development arena or in the regulatory review would comprise an awareness of the implications of decision-making and the need to approach decision-making in a logical manner"....Pharmaceutical Company

Qualification and Experience in Previous Decision-Making

Bias based on a person's previous experience in decision-making was apparent. It was clearly evident that past experience in the decision-making arena and exposure to similar challenges in the past are important factors for both individuals and organisations. In addition, the theme of qualification of the decision-maker to make those decisions (scientific, strategic, benefit/risk...etc.) was raised. The academic qualifications complimented by practical "on the job" experience were cited as being important. The theme of "intuition" and "gut-feeling" also overlapped with the theme of Qualification. It was apparent that this intuition/gut-feeling appears to also develop with a senior decision-makers' increasing experience. This intuition/gut-

feeling theme was captured under the "overconfidence" theme discussed later on in this section.

"What makes one person out to be a good decision-maker? What qualifies that person to make decisions? Is it scientific or professional training? How much does a person require, in order for that person to make better decisions? It is a subjective matter and worth investigating".....Pharmaceutical Company

Subjective and Personal Considerations

Personal preferences relating to the subjective interpretation of the decision-making task in question and the personality of the decision-maker were apparent. The individual human element of a person's beliefs, the values important to that person and their preferred approach to decisions were evident.

"I like to review all the available background information before starting on the decision-making exercise".....Pharmaceutical Company

Political, Financial, Competitor and Reward Influences

Internal and external factors that impact on decision-making were evident. Items were apparent which were considered somewhat outside of the control of the decision-maker but which did impact the decision-making. Considerations such as go/no–go decisions based on financial sales predictions, return on investment (RoI) and continuation of a project because of some internal or external political considerations were raised. The concept of "reward" for achieving milestones and the impact this has on decision-making emerged from the industry but not from the agency representatives.

"A lot of go/no-go decisions are based on political reasons. We do not always like to say this is the case but in reality it is".....Pharmaceutical Company

"Everyone monitors the competition in drug development".....Pharmaceutical Company

Precedents for Similar Previous Decisions

Previous precedent emerged as a decision-making theme. Precedents in terms of traditional drug development or drug-class considerations were apparent from the perspective of both the agency and industry personnel. In addition, the need and desire for consistency was evident in regard to drug approvals.

"Previous approvals in that therapy area are always reviewed during our assessment".....Regulatory Agency

"We have a standard proven approach to internal decision-making. This is what we follow".....Pharmaceutical Agency

Perpetuating Previous Decision-Making Mistakes

Repeated mistakes or lack of learning from previous experience, or not applying "lessons learned" were apparent. The challenge of following a previous unsuccessful course of action which has a high probability of a negative outcome was evident.

"We are all guilty of this but at least we recognise our errors" .....Pharmaceutical Company

Plunging-in or Procrastination with Decision-Making

The impact of procrastination and the inability of a person to make a decision at a suitable time were apparent. The potential for information or data "overload" relating to a decision which could result in a decision not being made, or being postponed or leading to a request for even more information was evident. The polar theme, where a person may make a snap-decision without having suitable salient facts was raised. The "plunging-in" was also linked with the potential theme of self over-confidence relating to the perspective of both the individual and the organisation.

"The good assessor will make a regulatory decision and make a good recommendation, the poor assessor will sit on the fence and write a report and say it is up to the advisory committee".....Regulatory Agency

"Paralysis by analysis is resulting in the death of creativity".....Pharmaceutical Company

Clear Understanding or Lack of Understanding of the Decision in Question

The need to clearly understand the context of the decision that one is being asked to make was apparent. The use of appropriate language and instruction in communicating what a decision-maker is being asked to do was evident.

"People need to understand what they are being asked to do and also the factors involved in the decision that they are being asked to make".....Pharmaceutical Company

Over-Confidence in Own Judgement

Several themes relating to both over-confidence and use of "intuition / gut-feeling" emerged. Over-confidence and use of intuition were not seen in a negative context but merely one that needs to be appreciated, managed and balanced.

"Intuition and gut-feeling have a place but it is often an educated gut-feeling and educated intuition in decision-making. It is not something that you are born with. It comes about with the experience of the job environment over 10, 20, 30 years"... ...Pharmaceutical Company

"We might say that decision-making is all science and that it is all quantitative and it is all black and white, it is not. The very sophisticated blend of intuition or gut-feeling comes into good decision-making practice as well".....Regulatory Agency

Group Successes and Group Failures

The use of teams or groups for several aspects of decision-making was apparent. The use of scientific advice committees by regulatory agencies, internal steering committees and executive committees emerged. In addition, the pros and cons of aiming for consensus approach on important decisions were raised. The theme of using tools such as "facilitators" and decision-conferencing to facilitate decision-making emerged. The dynamics of a group decision-making approach and the challenge to terminate such a decision-making exercise being conducted by a group was also apparent.

"Project teams can be very possessive and defensive of their baby (project) which can make it a very challenging situation when tough decisions need to be made on the continued viability of the project"..... Pharmaceutical Company

*"Sometimes you are better just to go with a more extreme decision rather than a compromise one, and this will mean that some people may be unhappy. I am not sure that aiming to reach consensus always is a good thing or always results in the best decision.....*Regulatory Agency

SWOT Analyses and Alternate Outcome Planning in Decision-Making

The use of identifying the strengths, weaknesses, opportunities and threats, within the decision-making framework emerged from the study. The need to identify the pros, cons and the options relating to a decision and to have contingency considerations in place for a decision outcome were apparent.

*"We routinely use SWOTs, they are what we used during our restructuring exercise".....*Regulatory Agency

*"You always need a back-up plan, SWOTs and contingency planning should always be part of decision-making".....*Pharmaceutical Company

Impact Analyses of Decisions

The value in identifying good decision practices adopted as well as bad decision practices was apparent. The need and value of reviewing and examining the impact of decision-making outcomes is also important. With hindsight, could or should a different approach have been adopted for a particular task?

*"It is important that organisations look back at the decisions they made 10 years ago and review whether in hindsight, these were good or bad decisions"...*Pharmaceutical Company

*"We should all take time to perform impact analyses and try to learn from the good and the bad".....*Regulatory Agency

Decision-Making Audit Trail

The value of maintaining an audit trail for important decisions was apparent. The step-wise path of the decision exercise undertaken relating not only to major Go/No-Go decisions but also those decisions which may need to be reviewed or examined at a later date emerged. Transparency in the process and the potential for better predictability in future judgments were linked to having a record / audit trail of previous successes.

"Transparency, the justification for decisions, and understanding why a decision has been made need to be documented, it is good practice".....Regulatory Agency

Education and Awareness of Evolving Decision-Making Techniques

The value and benefit of receiving training in the science of decision-making and also on the tools and techniques that are currently available to facilitate decision-making were identified.

"It is important that we are trained in decision-making. We also need understanding and practical application of the tools which can assist our decision-making. So, I think it should be part of people's ongoing professional training".....Pharmaceutical Company

"Modelling and simulation is becoming ever more the norm in drug development. One of the challenges we have, is in keeping pace with advancements in drug development and the models employed in decision-analysis".....Regulatory Agency

Individual Versus Corporate Decision-Making

The different decision-making approaches of the individual compared with that of the organisation were apparent. The challenge with understanding how the individual and the organisation reach their decisions was evident.

"There is a difference between the corporate decision-making process and that of the individual. For example, we have a good understanding of how a committee makes a

decision but we do not necessarily understand how individuals on that committee have made their own position or decision".....Regulatory Agency

"We need to have a better understanding on how an individual reaches their own conclusion this is particularly important in regard to benefit-risk decision-making".....Regulatory Agency

Quantitative Frameworks

The value of assigning weightings (relative importance) to the decision-making exercise in situations such as benefit-risk assessments and the transparency that such a quantitative weighting process could bring to a decision was evident.

"The concept of weighting is a nice framework for benefit-risk decision-making".....Regulatory Agency

"I am a firm believer in quantitative assessment to improve transparency in decision-making.…...Regulatory Agency

Thematic Map

A secondary objective of the qualitative investigation was to generate a thematic map of the decision-making themes that emerged from the study. Thematic networks are web-like illustrations that summarise the main themes constituting a piece of research. The thematic mapping network technique is a robust and sensitive tool for the systematisation and presentation of qualitative analyses (Trochim, 1989, Attridge-Stirling, 2001, Braun and Clarke, 2006). In instrument development, maps can help with structural conceptualisation to articulate the expected relationships between constructs that are being measured and are a tool for defining the conceptual domains (Marquart, 1989; Davis, 1989). The thematic map generated from the study is presented in Figure 3.3.

Figure 3.3: Thematic map of decision-making themes from the qualitative research

Decision-Making Results from the Perspective of The Individual and The Organisation

In addition to the composite results obtained for the 29 participants, unique results for each individual participant were also generated in the NVivo8 system. However, it should be noted that assurance was provided to the interviewees that confidentiality would be respected and that results which could identify an individual or their organisation would not be presented. Therefore, limited presentation of source

individual interviewee results are provided in this thesis. The individual commentary in the form of the verbatim quotes from individuals' interview transcripts is intended to provide valuable insights into the perspective of the individuals who volunteered to participate in this research.

The consolidated output of the qualitative research comprised the identification of almost 100 themes and sub-themes relating to decision-making approaches. This combination of the automated and manual subjective thematic coding results was used to form the basis for the decision-making instrument which would be subjected to further development and validation. A total of 94 items were agreed for inclusion in the first version of the instrument. The further development and validation of the instrument is reported in Chapters 4 – 6. A copy of the 94-item checklist including the rating scale used on each items is presented in Appendix III.

DISCUSSION

The goal of this qualitative research study was to investigate and gain insight into the decision-making approaches used by the Pharmaceutical Industry and Regulatory Agency decision-makers, in their professional work. This goal was successfully achieved. In addition, the identification and application of the decision-making themes which emerged from the research should enable the generation of a generic developmental decision-making instrument.

The qualitative research approach involved the conduct of semi-structured interviews with a variety of key opinion leaders from the EMA, national European regulatory agencies and international pharmaceutical industry. These interviews generated valuable insights into the decision-making approaches both from the perspective of the individual and their organisation. The interviewees were engaged and supportive of the study and were accommodating with their time-sacrifice and flexibility to participate in the interviews. The beneficial and advantageous approach of face-to-face interviews is well documented and this was the case also in this study (Holstein, 2001). It is also noteworthy, that the interviews allowed for respect, understanding, rapport and relationship-building to develop between the interviewee and the researcher performing the interviews.

The complimentary combination of the NVivo8 and the manual thematic coding helped to detail a wide-spectrum of decision-making components and emergent themes from the study. It was evident that this coding process did not deliver the same amount of subjectivity as generated by the manual review of the interview transcripts. However, the combination of both the automated computerised NVivo8 system and the subjective manual evaluation of the interview transcripts did ensure that all decision-making themes contained within the interviews were explored. Almost 100 decision-making themes and sub-themes were apparent from the data analyses. This allowed for the generation of a 94-item developmental version of the instrument which will form the basis for a larger sample-size and more powerful research investigation into the decision-making approaches of individuals and their organisations.

Of particular note, some of the decision-making themes that emerged from the interviews may be somewhat surprising bearing in mind that most of the study participants worked in a highly regulated working environment where regulations, directives, SOPs and other guidance documents are the norm. Some particularly important themes and decision-making aspirations received from the study participants are detailed below:

The desire for enhanced transparency, consistency and predictability within the decision-making approaches used by individuals, committees and organisations overall.

The use of intuition or “gut-feeling” in the decision-making process of individuals even though they are working in an evidenced based and systematic drug development environment. This intuition was seen as a positive attribute which matures and appears to become more beneficial and accurate, the longer the individual has been working in his or her profession. Linked with intuition was the assertion that for many individuals, the more experience gained in their professions, the higher the quality of their decision-making and the easier the decision-making process is for them. The experienced professional is less likely to procrastinate over a decision and appears to have a greater appreciation of the consequences of the decision-making process that they are being asked to make. An area of contention linked with experience was that

of, “what qualifies an individual to be a good decision-maker in a given situation?” Academic, clinical or professional qualifications linked with the subjective personality and astuteness of the individual emerged as important facets for being a “good decision-maker”.

The recognition of the value of training in the science of decision-making and a greater understanding and appreciation of the tools available to support decision-making was echoed by many of the study participants. Simple tools such as SWOTs and decision-trees were routinely used by some people, while some other participants advised they never employ such techniques. There appears to be a lack of training offered within the profession (Agency and Industry) but it was the belief of many that they and their organisation would benefit from such training.

Ensuring an understanding of the decision-context, determining the internal and external influences which might be relevant to the decision being asked, awareness of one’s own personal decision-making preferences, appreciation of previous similar and most importantly, the validity and integrity of the information that one is being asked on which to base the decision were key items that emerged from the interviews.

Other items such as re-evaluating as new information becomes available, reviewing the impact of decisions made and applying “lessons learned” to new projects and decisions were thought to be beneficial. The pros and cons of group decision-making and seeking a consensus approach were raised along with the potential value of assigning quantitative weightings within a step-wise decision-making approach while at the same time, ensuring that there is a audit record trail maintained of each decision-step.

The simple thematic map generated captured the decision-making themes that emerged from the qualitative research. It is appreciated that thematic mapping can help to ease tension between quantitative and qualitative measurements by combining statistical analysis and human judgements. The main strength that mapping offers in the validity exercise of an instrument is that it allows relationships to emerge and these emergent categories are more data driven than they are in a traditional content analysis. The thematic map can help in formalising a choice in a syntax/context

relationship (Jackson and Trochim, 2002). The generated thematic map can also contribute to the construct validation of the developmental instrument. Construct validity refers to how operationalisations in research reflect the theoretical constructs they are supposed to reflect. In determining if there is construct validity, researchers should have an idea of the interrelationships among constructs (Jackson and Trochim, 2002).

The decision-making themes discussed in this chapter were not the conclusive list of considerations which were volunteered by individuals during the qualitative research. However, the items raised by the study participants did provide supportive justification and validation of the research being performed. This study has demonstrated that the area of decision-making in the medicinal product development and life cycle is under-researched. The potential benefits of improved decision-making within both the drug development arena including the regulatory review would benefit all concerned stakeholders. Improved and better quality decision-making could be expected to expedite the delivery of new medicines. These improvements could be initiated by individuals and organisations, having a better fundamental understanding of the principles and themes of decision-making.

Overall, this study has achieved its aim of exploring decision-making from the perspective of the individual and the organisation working in the drug development arena. The detailed content analysis in the research produced vital information for the development of a novel concept for a decision-making instrument. Decision-making themes and considerations have emerged which can be incorporated into a generic 94-item decision-making checklist which will undergo further content validation, field testing and refinement. The supportive engagement of the participants involved in this study is also positive endorsement of the value of this research.

SUMMARY

- This chapter provided information about how data was collected for the conceptualisation and development of a decision-making tool
- Twenty-nine interviews were conducted with senior decision-makers from regulatory agencies and the pharmaceutical industry to investigate how they manage decision-making at an individual and/or organisational level
- NVivo8 qualitative software was used for managing the large quantity of data and for content analysis
- Thematic coding of the interview transcripts was performed using NVivo8 and manual content analysis which resulted in an enhanced understanding and appreciation of the decision-making considerations and identified thirty-two themes from the perspective of the of individual and their organisation
- The emergent decision-making themes and commentaries volunteered by the study participants provided evidence of the need for a more systematic approach to decision-making within the regulatory and pharmaceutical environment
- Positive endorsement of the study was received from the study participants which provided further impetus and validity to the continuation of the development of a generic decision-making instrument
- A 94-item decision-making theme checklist was generated

CHAPTER 4

Development of a Generic Decision-Making Tool: Content Validation

INTRODUCTION

Content validation helps to examine whether the measurement tool possesses the right emphasis and focus for the concept being measured and the target population. This evaluates whether a scale has enough items and covers each of the domains being measured. The items of a new instrument should be relevant and representative of the target population and/or construct (Streiner and Norman, 2008). Content validation is a primary validation step which helps to compliment, endorse and increase the probability of obtaining high construct validation in the development of an instrument (Denzin and Lincoln, 2005).

The process of establishing content validity of an instrument by using a panel of experts to determine the suitability of an instrument or questionnaire items is a well established procedure in instrument development. The opinion and judgement of experts to modify or remove items from a developmental instrument helps to ensure the appropriateness of such a tool. The opinion of the experts is also sought to verify that the scale is appropriate for the intended purposes. (Strauss and Corbin, 1998; Streiner and Norman, 2008). Haynes et al (1995), defined content validity as: "the degree to which elements of an assessment instrument are relevant to and representative of the targeted construct for a particular assessment purpose" (Hayes et al., 1995). Instrument content validation is a process which may encompass both "quantitative" and "qualitative" approaches and is a vital part of the overall instrument validation process. Items should be reviewed and judged by a panel of experts using an assessment scale covering item relevance, representativeness, specificity and clarity. The use of these content validation expert panels may help to eliminate early items which if left in the questionnaire might be "outliers" at a later stage of analysis and which could contribute to spurious or incorrect study findings (Hayes et al., 1995).

In this validation exercise, the content validity was evaluated by a complimentary triangulation of methods to ensure appropriate reliability and validity of the 94-item developmental version of the decision-making instrument.

METHODS

The 94-item developmental version of the decision-making instrument was carefully reviewed for the four attributes of: language clarity, completeness, relevance, and scaling. These item attributes are well established in the content validation investigation of new instrument development (Norusis, 1993; Graneheim and Lundman 2004; Pallant, 2005; Simon et al., 2006; IBM, 2011; Patrick et al., 2011a; Bhatti et al., 2013b).

The content validity of the 94-item developmental version of the instrument was carried out in two separate stages, i.e. an initial qualitative stage followed by a quantitative stage. In the qualitative assessment, the expert panel members were asked to review and make comment on the developmental version of the instrument. In the quantitative part, the panel members were asked to complete a formalised scale to assess each item and the instrument as a whole. The results from the qualitative and quantitative parts were used to make changes to the 94-item developmental version to ensure that items were relevant and appropriate to the decision-making construct.

The 94-item developmental version of the instrument was initially examined for content validation by a team of six experts. Their task was to review the instrument and to use their subjective judgement to rate each of the 94-items using a 4-point Likert scale (strongly agree, agree, disagree and strongly disagree) for its language clarity, completeness, relevance and scaling (Denzin and Lincoln, 2005; Bougie, 2010; Bhatti et al., 2013b). The experts were encouraged to suggest appropriate changes as necessary in order to develop an instrument which could accurately measure what was intended to be measured. The identification, communication and selection of the independent expert panel were performed in an appropriate manner. The six member panel “quorum” was in line with best practice reported in the literature (Lynn, 1986; Polit, 2006).

Part I: Qualitative Assessment

A six member expert panel of experienced and senior decision-makers from the regulatory agencies and pharmaceutical and CRO industry carried out the content

validation. The pharmaceutical (two) and Clinical Research Organisation (two) panel members were all experienced professionals at advanced managerial level and all with more than seven years experience (7 – 30 years). The regulatory agency experts (two) were experienced "Assessors" with more than seven years Regulatory Agency experience. All of the experts considered themselves experienced and experts in 'decision-making'.

Procedure

All of the expert panel members were initially contacted either by a face-to-face meeting or by telephone to determine their willingness and availability to participate in the validation exercise. Following their agreement, they were all sent by email, additional background on the research, a copy of the developmental questionnaire and instructions on how to complete it (a copy of each is provided in Appendices II and III).

Each expert member participated in two ways: firstly, by individually completing the 94-item development questionnaire and the rating of each item using a 4-point scale. Secondly, by participating in an all panel round-table discussion meeting once all six feedback forms had been analysed.

The rating guidance given for assessing each of the 94-item development questionnaire using a 4-point scale for its language clarity, completeness, relevance and scaling is as follows:

Language Clarity: The sentence and wording should be clear, understandable, straightforward and simple. Completing the questionnaire should not require reading skills beyond that of a 12-year-old to avoid missing values and unreliable answers.

Completeness: The sentence structure should be complete not broken and should end properly.

Relevance: Each item should be relevant to the subject area and target population.

Scaling: Panel members should rate the scaling system as to whether or not the response options fit the statements/item on the 4-option scale.

Part II: Quantitative Assessment

In the quantitative stage, the completed questionnaires from each of the six panel members were transposed from Word format questionnaires into Excel. Excel results were generated for each individual panel member as well as the composite panel. The results from these scores were used to generate the relevance scale which was computed using Content Validity Index (CVI), Scale Content Validity Index (S-CVI), using Excel. Intraclass correlation coefficients (ICC) and reliability (Cronbach's alpha) measurement were determined using SPSS statistical software. It is appreciated that there are very different opinions in the literature about whether Kappa measurement versus the ICC technique is better for inter-rater reliability. For non-quantitative data (categorical/nominal), the kappa coefficient is the techniques of choice. The ICC is more appropriate and better than the kappa technique for analysing data obtained from ratings using any scale (e.g.1 to 10) (Bhatti et al., 2013a; Bhatti et al., 2013b) and it was used for the qualitative phase to measure the level of agreement (inter-rater reliability) among the panel of judges.

RESULTS

The results of the content validity are presented in two parts; quantitative and qualitative. The quantitative results are those obtained directly on the questionnaire feedback rating forms. The qualitative results comprise the comments made by individual panel members and also the outcomes of discussions at the expert panel meeting. The changes made to the 94-item developmental version of the questionnaire are discussed taking into account both the quantitative and the qualitative components.

The completed questionnaire feedback forms with the comments from each expert panel member were returned in advance of a pre-scheduled expert panel meeting. At this meeting, a summary of the background and framework of the research project was outlined for the expert panels in line with good practice (Terwee et al., 2007). The panel meeting reviewed the composite feedback received from all panel

members and following panel discussion, resulted in the reduction/removal of several items from the 94-item instrument. In addition, some changes were made to the language of some items. The panel also provided their opinion on the time sacrifice needed for "time-to-complete" the questionnaire.

Part I: Quantitative Assessment

The results for the quantitative assessment were based on the returned questionnaire feedback forms (n=6). The results for each of the four rating criteria: language, clarity, completeness, relevance and scaling were analysed. Each of the six judges rated the 94 items. The feedback results of each of the six individuals are summarised in Table 4.1.

Table 4.1: Summary of percentage rating results given by each expert rater

	Expert 1	***Expert 2***	***Expert 3***	***Expert 4***	***Expert 5***	***Expert 6***
Strongly Agree	86%	22.%	57%	50%	32%	74%
Agree	6%	61%	36%	37%	50%	20%
Disagree	6%	14%	7%	13%	17%	5%
Strongly Disagree	2%	3%	0%	0%	1%	1%
Combined Strongly Agree/Agree	92%	83%	93%	87%	82%	94%
Strongly disagree/disagree	8%	17%	7%	13%	18%	6%

Language Clarity

When the judges were asked whether the items showed good language clarity, there were 385 ratings (68.3%) for strongly agree, 93 (16.5%) for agree, 68 (12.1%) for disagree and 14 (2.5%) for strongly disagree. Three (0.5%) were missing (not completed) and were not included in the analysis. A sum of 85% was obtained for the "strongly agree/agree" scores suggesting that the expert panel agreed with the clarity of the language.

Completeness

The rating of the items for completeness revealed that there were 213 ratings (37.8%) for strongly agree, 259 (45.9%) for agree, 80 (14.2%) for disagree and 8 (1.4%) for strongly disagree. Four (0.7%) were missing and not included in the analysis. A sum

of 84% was obtained for the ”strongly agree/agree” scores suggesting the experts agreed on the completeness of the scale.

Relevance

When the judges were asked whether the items were relevant, there were 183 ratings (32.4%) for strongly agree, 292 (51.8%) for agree, 77 (13.6%) for disagree and 7 (1.2%) for strongly disagree. Five (0.9%) were missing and not included in the analysis. A sum of 84% was obtained for the “strongly agree/agree” scores suggesting the experts agreed on the relevance of the scale.

Scaling

With regard to scaling, there were 399 ratings (70.7%) for strongly agree, 158 (28%) for agree, 2 (0.4%) for disagree and 0 (0%) for strongly disagree. Five (0.9 %) were missing and not included in the analysis. A sum of 99% was obtained for the ”strongly agree/agree” scores suggesting the experts agreed on the scaling of the scale.

A tabular summary of the judges’ ratings of the 94 items across the four content validation criteria is presented in Table 4.2

Table 4.2: The judges’ ratings (n=6) of the 94 items across four criteria

Judges’ response option	Language Clarity	Completeness	Relevance	Scaling
Strongly agree	385 (68.3%)	213 (37.8%)	183 (32.4%)	399 (70.7%)
Agree	93 (16.5%)	259 (45.9%)	292 (51.8%)	158 (28%)
Disagree	68 (12.1 %)	80 (14.2%)	77 (13. 6%)	2 (0.4%)
Strongly Disagree	14 (2.5%)	8 (1.4%)	7 (1.2%)	0 (0%)
Missing	3 (0.5%)	4 (0.7%)	5 (0. 9%)	5 (0.9%)
Strongly Agree / Agree	476 (84.8%)	472 (83.7%)	475 (84.2%)	557 (99%)
Strongly Disagree/Disagree	82 (14.6%)	88 (15.6%)	84 (14.9%)	0 (0.0%)

Of the 94-items, the items which had the most number of "Disagree and Strongly Disagree" ratings emerged from the results and were discussed during the expert panel meeting. Twenty such items emerged and will be discussed in the next section.

Content Validity Index

In addition to the subjective testing performed on the developmental instrument, the additional content validation tests of: content validation index (CVI) and the content validity of the whole scale (S-CVI) were applied to the qualitative data (Polit, 2006).

$$\text{CVI} = \frac{\text{Number of items on which expert raters Agreed}}{\text{Total number of expert raters}}$$

The CVI and S-CVI have been used in healthcare research for the determination of content validity in the development of multi-item scales rated by multiple expert raters (Polit, 2006). There is a general agreement about the calculation of the CVI. A panel of content validation experts is asked to rate each scale item in terms of its relevance to the underlying construct. These items are typically on a four point scale to avoid having a neutral and ambivalent midpoint although a five or three point scale may be used (Lynn, 1986). A requirement of CVI is that a minimum of three expert raters are involved in the rating exercise and twice this amount was used in the validation exercise. The CVI can be calculated on an item level (I-CVI) and scale level (S-CVI). The item content validity index (I-CVI) is calculated as a level of agreement between a panel of judges for each individual item i.e. the proportion of experts who rate it as content valid. It is calculated by the number of experts giving a positive rating ("strongly agree" or "agree" in the case of the developmental instrument) divided by the number of experts (n=6), therefore calculating the proportion of judges in agreement about relevance" (Polit, 2006).

Individual Items

The range of the CVI is from -1.00 to +1.00, with +1 indicating perfect item-objective relevancies. The minimum acceptable I-CVI value for items varies depending on the number of judges involved but a minimum value of 0.70-0.8 is recommended (Lynn, 1986). For the validation exercise, a minimum value of 0.8 was used. Items with an index of less than 0.8 were discarded from the measure to

improve its validity. Of the 94-items, a total of 20 items had an I-CVI of less than 0.8. These items were:

- My decision-making is in line with that of the organisation
- I am "engaged" in my decision-making
- My organisation is engaged in its decision-making
- Training in the science of decision-making would benefit me
- My organisation would benefit from training in the science of decision-making
- I quantify the cost implications of my decision-making
- My organisation quantifies the cost implications of its decision-making
- I consult with colleagues before making a decision
- In my organisation, consultation with colleagues is encouraged in decision-making
- My decision-making is quantifiable
- My organisation's decision-making approach is quantifiable
- My organisation questions the integrity of its decision-making
- My decision-making is balanced
- My organisation’s decision-making is balanced
- I qualify the cost implications of my decision-making
- My organisation qualifies the cost implications of its decision-making
- My over-optimism results in me underestimating the outcome of a decision
- My organisation's over-optimism results in underestimating the outcome of a decision
- I systematically analyse how I make decisions
- Decision-making within my organisation is systematically analysed.

The twenty items with an I-CVI value of less than 0.8 were complimentary evidence of those items observed by the subjective review of the 94-items with the highest number of “strongly disagree /disagree” ratings.

Overall Instrument (94-items)

The scale content validity index (S-CVI) is defined as “the proportion of total items judged content valid” (Lynn, 1986). For the developmental instrument this would be the number of “strongly agrees” and “agrees” and is calculated by the average of the

I-CVIs (Polit, 2006). The S-CVI for the 94-item developmental instrument was calculated as 0.85, which is an acceptable value to suggest the scale is content valid.

Statistical Testing of Agreement

The 94 items of the developmental version of the instrument were rated on a 4-point ordinal scale for four different content validation criteria by six judges. It is important to establish the inter-rater reliability between the ratings given by the expert panel. This will indicate the level of consistency between the panel of judges and whether the data produced by the judges' ratings can be relied upon.

The most commonly used measures of agreement for quantitative data (the rating results) are the Intraclass Correlation Coefficient (ICC). This was appropriate due to the type of rating method/scale used (ordinal scale) in the questionnaire assessment. SPSS 20 statistical software was used to calculate the ICC and the reliability of the results from the six ratings by determination of Cronbach's alpha. The ICC analysis between all six raters showed an ICC of 0.894 ($p<0.0001$. CI=0.561 to 0.993), indicating a high level of agreement between the six raters for the four criteria (language, scaling, relevance and completeness) and supporting the content validity of the items chosen for the developmental version of the instrument.

The Cronbach's alpha reliability measurement of the six-rater sample results was 0.91, indicating a high level of reliability and further endorsement of content validity for the developmental instrument.

Part II: Qualitative Assessment

The results from the questionnaire feedback forms ("written feedback") were collated and discussed at the expert panel meeting. The members of the panel participated in free and open discussion which resulted in consensus recommendation on retaining 74 items and the removal of 20 items from the 94-item developmental instrument. Editorial language changes were recommended to some of the 74 remaining items. In addition, two further items were added giving a total of 76-items.

The items chosen by the panel for removal were all those that had been identified in as having a CVI of less than 0.8 and discussed previously. In addition, to the CVI and S-CVI testing performed, the subjective test of "Face validity" was also performed by the expert panel. Face validity is an intuitive type of validity in which the experts provided their feedback on whether the developmental instrument actually appears to reflect the concept that it is intended to measure. It indicates that the items that are intended to measure a concept, do, on the face of it, look as though they measure the concept (Patton, 2002; Denzin and Lincoln, 2005; Bougie, 2010). It is considered a basic and minimum index of content validity (Streiner and Norman, 2008). All six raters provided their positive opinion that the developmental instrument does appear to measure the "decision-making" concept and this face validity further helped to provide useful support for the instrument development process.

Revisions to The Original Developmental Instrument

The expert panel meeting was interactive and constructive. All of the panel members actively participated and aired their opinions while at the same time allowing and agreeing on consensus recommendations on revisions to the instrument. Twenty items were removed from the original 94-item developmental version of the instrument (Version 1) and the majority of these were done so by clear consensus and did not warrant much panel discussion. However, three of the 20 items which were removed did require notable discussion time as there was originally no clear consensus on whether to retain or to remove them. These items were:

- Training in the science of decision-making would benefit me
- My organisation would benefit from training in the science of decision-making
- I systematically analyse how I make decisions.

As part of a lengthy panel review and discussion, the final consensus was to remove these three items. In addition, the panel recommended the re-wording of six of the 74 retained items as presented in Table 4.3.

Table 4.3: Item wording changes recommended by the expert panel

Original item wording	Revised item wording
I use tools which facilitate my decision-making	I use tools e.g. modelling or decision trees which facilitate my decision-making
I understand the instructions before making a decision	I understand the context of the decision I am being asked to make
My organisation re-evaluates its decision-making as new information becomes available	My organisation re-examines its decision-making as new information becomes available
In my decision-making, I perpetuate the same mistakes as made in the past	In my decision-making, I make the same mistakes as made in the past
In my organisations decision-making, it perpetuates the same mistakes as in the past	In my organisations decision-making, it makes the same mistakes as made in the past
I communicate effectively the decisions I make	I effectively communicate the decisions I make

The expert panel also recommended the addition of two new items to the developmental instrument. These were:

- *My decision-making approach in practice tends to focus on discussions rather than actual decisions*

- *Decision-making in my organisation tends to be final and not open to reinterpretation or discussion*

Following the expert panel meeting, the output and recommendations of the expert panel to the developmental instrument were reviewed and it was agreed to incorporate the changes to the developmental instrument. This resulted in the 76-item developmental instrument that would then undergo further psychometric testing. During the expert panel meeting, the panel advised that 30 – 40 minutes would be a time estimate needed to complete the revised 76-item questionnaire, based on their experience of completing the original 94-item questionnaire.

Branding of The Decision-Making Instrument

The expert panel were introduced to the proposed brand name of "QoDOS" (Quality of Decision-Making Orientation Scheme) assigned to the instrument and advised that the proposed name was "strong and appropriate" for the decision-making instrument.

A copy of the post-content validation 76-item QoDOS developmental instrument (Version 2) is presented in Appendix IV.

DISCUSSION

The content validation of the developmental version of the decision-making instrument was an essential process for it to be fit-for-purpose. The design of the process was in line with best practice recommendations reported in the literature for content validation of a new instrument i.e. qualitative and quantitative components, use of a multi-expert panel, structural element assessment of the scale by evaluating language clarity, completeness, relevance and scaling in addition to overall face-validity assessment.

The inclusion of panel experts from the three different disciplines (regulatory agency, pharmaceutical industry and CRO) was reflective of the proposed final target audience for the decision-making instrument. The heterogeneity of the panel members provided extra robustness to the content validation exercise being evaluated. The panel experts were all experienced professionals with many years of experience in decision-making. All of the panel members were supportive and participated actively in the two stage review process (questionnaire completion and expert panel meeting).

The use of I-CVI, S-CVI, ICC and reliability measurements provided complimentary and quantitative statistical support for the overall robustness of the content validation. The statistical evaluation and the triangulated qualitative assessment of the expert panel resulted in changes being made to the original developmental instrument and resulted in a shortened version.

Overall, the expert consensus was that the content of the developmental version of the instrument was straight forward and appropriate in relation to the specific decision-making concepts and was relevant to the target population. This agreement among the expert panel members was reassuring and encouraging. It also provided confidence that the outcome of this stage was satisfactory in terms of establishing content validation and proof-of-concept of the shortened developmental version and

supported further psychometric testing of the instrument through item reduction using factor analyses. The resulting 76-item instrument was given the name, "Quality of Decision-making Orientation Scheme" with the abbreviation "QoDOS". The expert panel opinion was that this was an appropriate and strong acronym for the decision-making instrument.

SUMMARY

- The 94 items resulting from the quantitative study (Chapter 3) were reviewed for language clarity, completeness, relevance and scaling. Content validation was performed on the original 94-item developmental version of the instrument using a panel of six experts
- Qualitative and quantitative methods were used in the content validation study
- The scale content validity index of 0.85 suggested that the content validity of the scale was high
- The test of agreement between raters (ICC) was 0.89 ($p<0.0001$. CI=0.561 to 0.993), indicating a high level of agreement between the raters
- The expert panel review resulted in the reduction of the original 94 items to 76 items (QoDOS Version 2)
- Content validity and the sub-component of face-validity was successfully evaluated and the developmental instrument deemed fit-for-purpose and suitable for further item reduction investigation
- The brand name 'QoDOS' (Quality of Decision-making Orientation Scheme) was assigned to the instrument.

CHAPTER 5

Development of The QoDOS:
Factor Analysis

INTRODUCTION

Factor analysis is a statistical technique used to analyse, investigate and identify the relationships between a set of variables (items) measured or observed, in particular for those with similar concepts (Cattell, 1978; Floyd, 1995; Bhatti et al., 2013b). It is used to help confirm the grouping of the instrument items that have been based on subjective opinion through use of mathematical modelling. A factor is a group of items that may be said to belong together (Hazard, 2011). Factor analysis is widely used to reduce a large number of correlated variables to a more manageable number, and is regularly used to reduce the number of items in questionnaires. The use of factor analysis is not designed for testing hypotheses or for judging whether one group is significantly different to another (Pallant, 2005). It is a statistical technique used to identify a relatively small number of factors that can be used to represent relationships among a set of many interrelated variables. In other words it allows for a large number of individual scale items and questions to be refined and reduced to a smaller number of derived items (Pallant, 2005; Field, 2009; Bhatti et al., 2013b). For the purposes of this current research, factor analysis was used to reduce the number of items in the current 76-item developmental QoDOS instrument and also to identify underlying factors within the reduced set of items.

Factor analysis is an established approach used in the development of new instruments in various research areas and in particular for those with a psychometric or a Quality of Life component (Fayers and Hand, 1997; Nedert et al., 2001; Fredheim et al., 2007; ESPRINT Group., 2007; Coyne Karin S., 2012). Factor analysis was employed to refine the QoDOS (Version 2) prior to its full scale psychometric evaluation. This psychometric evaluation included construct validity, responsiveness, reliability and interpretability testing.

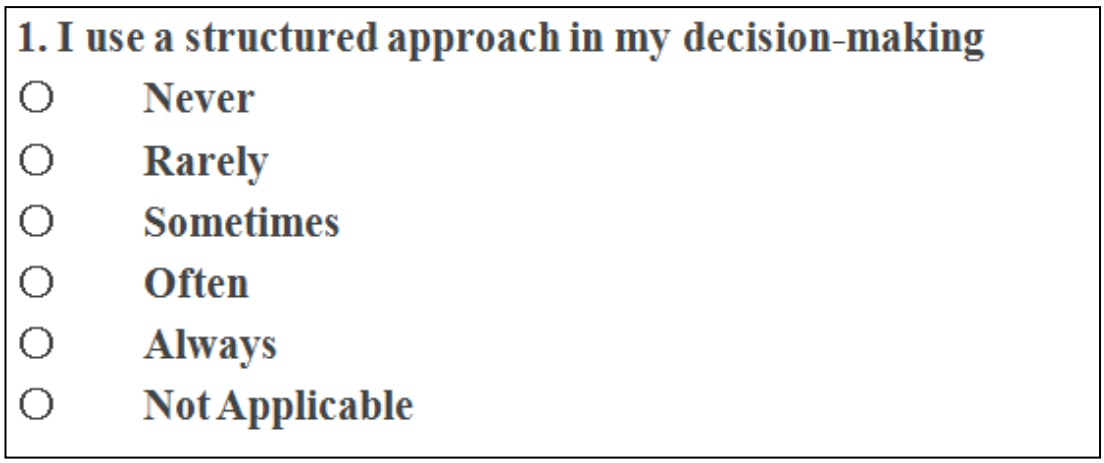
METHODS

There were two distinct research component phases involved in the factor analysis and item reduction of the 76-item QoDOS instrument (Version 2) as detailed in Chapter 4. These phases were as follows:

Component phase 1: Conduct of a research study survey using the QoDOS instrument in a large sample population to investigate the decision-making approach of individuals and their respective organisations. Each prospective participant was contacted in advance and provided with background information on the research project and given assurance on anonymity and confidentially on all research related materials. The same confidentiality commitment as detailed previously in Chapter 3 was provided to all would-be participants.

Survey Monkey was used for the issuance of the QoDOS (Version 2) questionnaire to all participants and in-turn for the automatic compilation of completed questionnaire returns. A 100% response rate was achieved and this can be expected to be due to the functionality within Survey Money which requires that a questionnaire must be fully completed before it can be sent into its central database. It will not accept data from partially completed questionnaires. The Survey Monkey question structure used a Likert response format as exemplified in Figure 5.1.

Figure 5.1: Survey Monkey Likert format used in the research



The time-window for the issuance and completion of the QoDOS developmental survey was July 2012 to October 2012.

Survey Monkey and Excel were used in the quantitative analysis of this component of the research. An Excel database was used to compile the completed questionnaires received from each of the research participants. The functionality of the Excel database facilitated the data management and interpretation of the study results. The

combined Survey Monkey survey and Excel functionality allowed for the generation of results in various formats including spider graphs, bar charts and 'Box and Whisker' plots for the research sample data.

Component phase 2: The quantitative data generated in Component 1 research was transposed into statistical format ready for factor analysis and item reduction.

Data Capture, Processing and Analyses (Component Phase 2)

Data processing and statistical analyses were performed using the well established methodology involving SPSS 20 statistical software for Windows (Norusis, 1993; Pallant, 2005; IBM, 2011).

Exploratory factor analysis (EFA) using the "principle component analysis" was performed using SPSS20 statistical software. EFA is used to investigate whether there is any correlation among a set of items and to identify the dimensions or factor structure of the new measure and to can be used to reduce items (Fayers and Hand, 1997; Pallant, 2005). It can also be used to support construct validation of new instruments (Bhatti et al., 2013b). For the QoDOS (Version 2), EFA was used to explore the underlying structure, to reduce the number of items (inappropriate ones that may not contribute to the underlying factors) and to support its appropriateness (construct validity).

Using the SPSS 20 software, a correlation and component matrix was created for the dataset. Descriptive statistical techniques were used to measure the Kaiser-Meyer-Olkin (KMO) measure (which comparatively measures the magnitudes of the observed correlation coefficients to the magnitudes of the partial correlation coefficients) and Bartlett's test of sphericity for adequate sampling. A multi-step factor analysis was performed and Scree plots were generated at each extraction stage. The Scree plots provided a useful, easily interpretable impression of the number of factors within each sequential extraction result. Factor rotation was performed using the Varimax technique and Kaiser-Meyer-Olkin (KMO) and Bartlett's test of sphericity measurements were measured at each extraction stage. Reliability testing was performed by measuring Cronbach's alpha to measure the internal consistency and intraclass correlation coefficient (ICC) to evaluate inter-rater

reliability. The Cronbach's alpha testing also provided supportive evidence for the retention and deletion of the items during the factor analysis (Pallant, 2005; Petter, 2007; Streiner and Norman, 2008).

The following steps and rules were applied during the factor analysis:

1. Reliability test (Cronbach's alpha) of items was carried out before at each factor analysis step.

2. Factor analysis was performed on the remaining items.

3. *Analysis criterion:* Only factor loadings of $\geq$ 0.4 were progressed. Items which failed to load on any component were removed. Items with "corrected items-total correlation" (factor loadings) values <0.4 were deemed not to be discriminating well / poorly fitting and were removed. As a rule of thumb, the eigenvalue of 0.32 is considered to be a minimum loading for an item (Costello and Osborne, 2005) but in this study, due to the large number of variables, a value of 0.4 was assigned and considered appropriate to represent strong correlation.

4. Items which loaded on multiple components with not much difference between values (weak complex variables) were removed. However, items with significantly higher loading were retained.

5. Further factor analysis was carried out to see whether or not the remaining items with a similar concept fitted together under the appropriate corresponding components.

6. Successive factor analyses were carried out to examine the difference (similarities, number of items removed and the types of items removed).

7. Items were retained of removed based on their loading score. A table was generated showing the ranking of items based on loading scores. This was used to decide which items should be deleted and which should be retained for additional analysis. This assessment on whether to retain or remove an item was performed

simply by “eyeballing” the ranked included in the table. Items were deleted, retained, merged or rephrased on statistical, conceptual and philosophical grounds.

8. After the final analysis, any item that did not conceptually fit in the final extracted components was manually moved to ones that were more appropriate and meaningful to that component. This allowed for a logical ordering of concepts to be generated.

RESULTS

Study Participants

Six hundred individuals were contacted and invited to participate in the study. A total of 130 responded, of which 120 were evaluable. This included 76 from the EU and US pharmaceutical industry, 19 from the regulatory agencies (European Medicines Agency, Danish Agency, Irish Medicines Board, UK MHRA, Singapore Ministry of Health and the UAE Ministry of Health), 23 from CROs (EU and US) and two from academia. The research results obtained from the 120 evaluable participants provided insights into decision-making from the perspective of the individual and also that of the organisation in which they were/are employed. The results also allowed for comparisons to be made across the three main organisations that participated in the study i.e. the Regulatory Agencies, Pharmaceutical Companies and CROs.

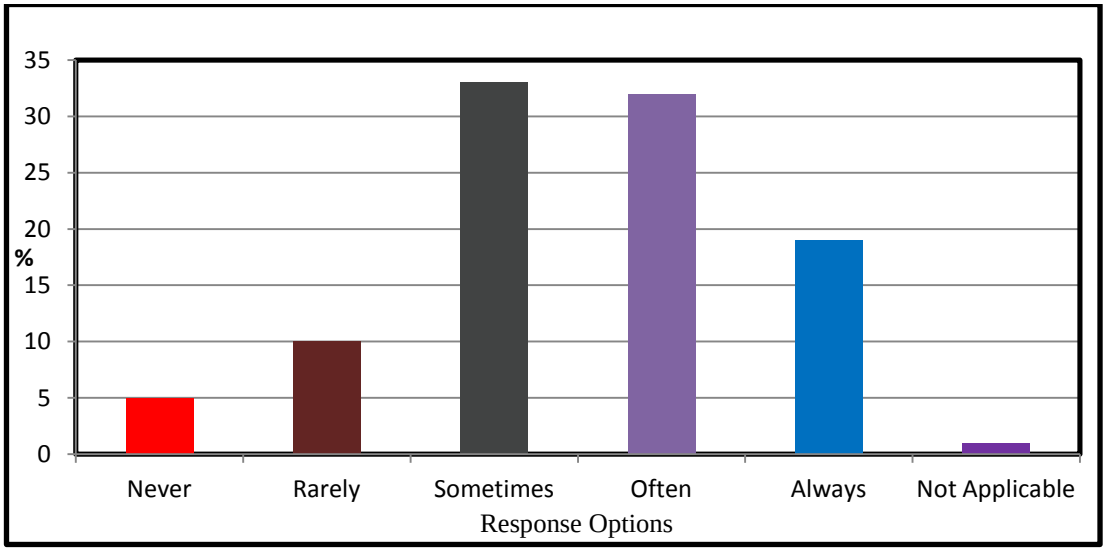
Organisation and Individual Related Item Responses

Composite results for the 120 person research sample were generated for each of the 76-items in the developmental questionnaire. The results provided a quantitative response rate to the Likert scale ratings used in the questionnaires for each item. It was possible to separate the composite results into two distinct categories: those responses which were answered from the perspective of the Organisation and those which were responded to from the perspective of the Individual.

A selection of four organisational related item responses and four individual related item responses are presented in Figures 5.2 – 5.8 respectively for reference and example purpose.

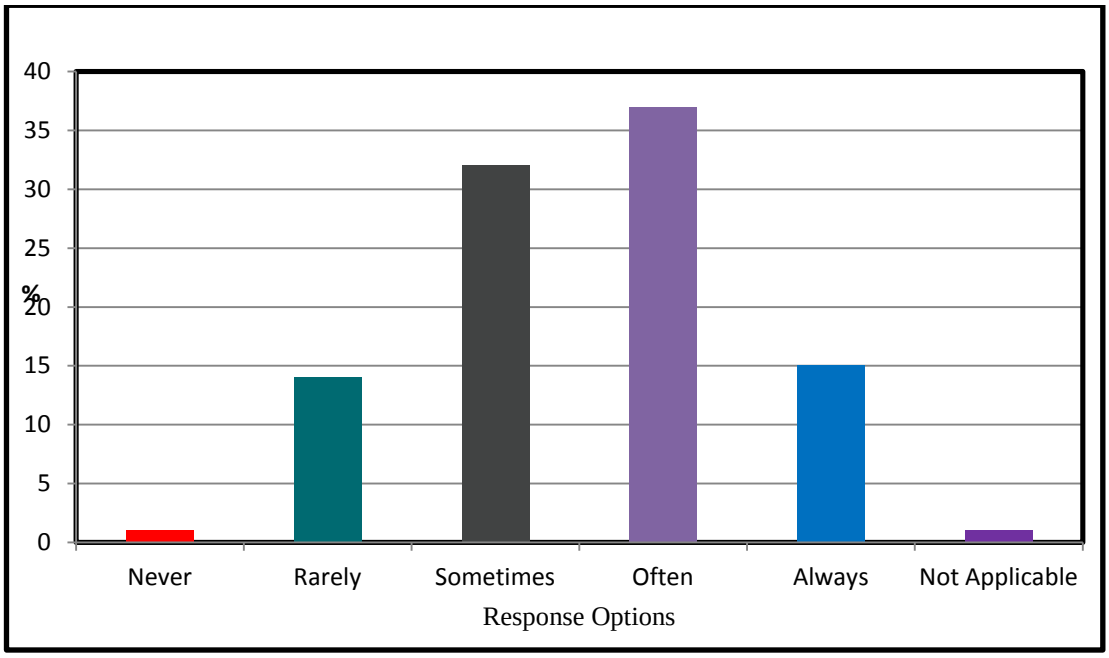
A structured approach to decision-making (Figure 5.2) appeared to be routine practice in approximately 50% of cases (always/often), 33% on a "sometimes" basis and rarely or never up to 15% of occasions.

Figure: 5.2: My organisation uses a structured approach in its decision-making



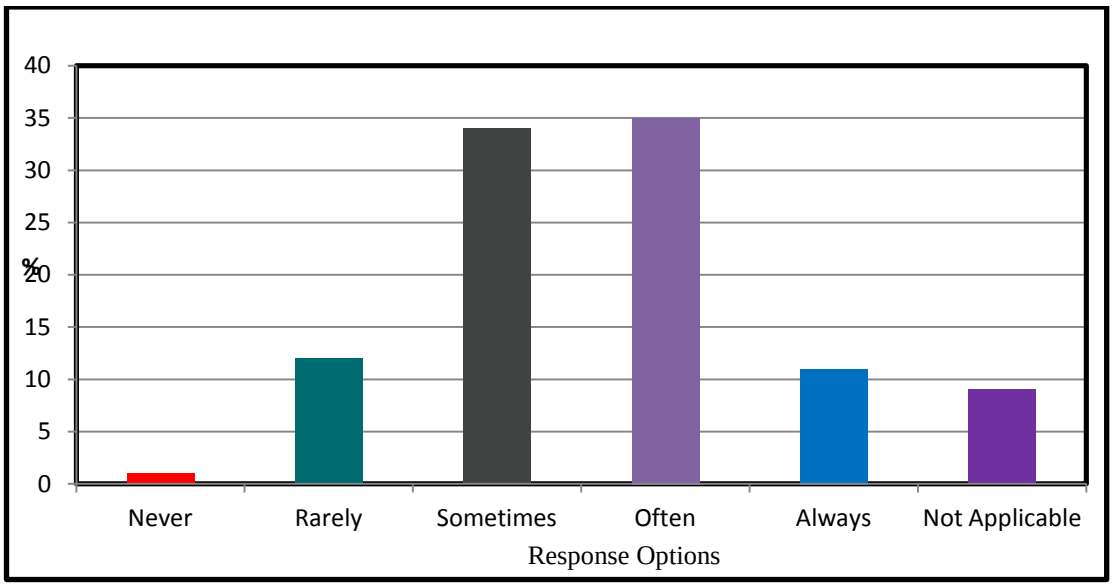
Re-evaluation of decision-making with the availability of new information (Figure 5.3) appears to be standard practice in 15% of cases and an often/sometimes basis for an additional 70%. It appears not to be the standard approach in about 15% of decision-making exercises.

Figure 5.3: My organisation re-examines its decision-making as new information becomes available



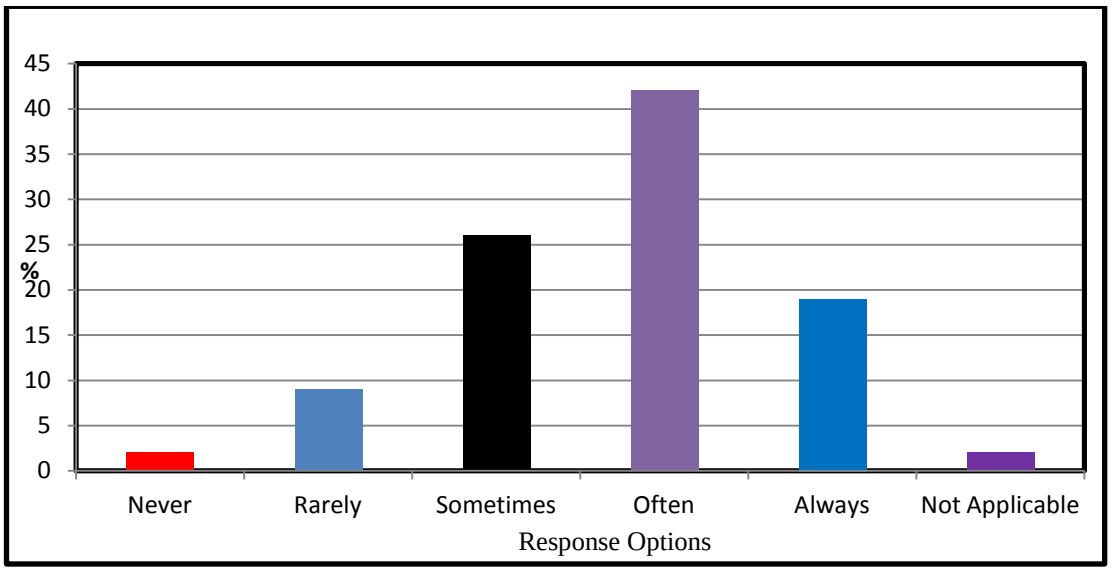
It would appear that organisations only consistently review the probability of success in their decisions in just over 10% of cases. It appears to be rarely/never performed in around 12% of occasions. This could infer that organisations are either not familiar with the advantages of re-examination as it appears not to be used on a standard basis (Figure 5.4).

Figure 5.4: My organisation quantifies the probability of success in its decision-making



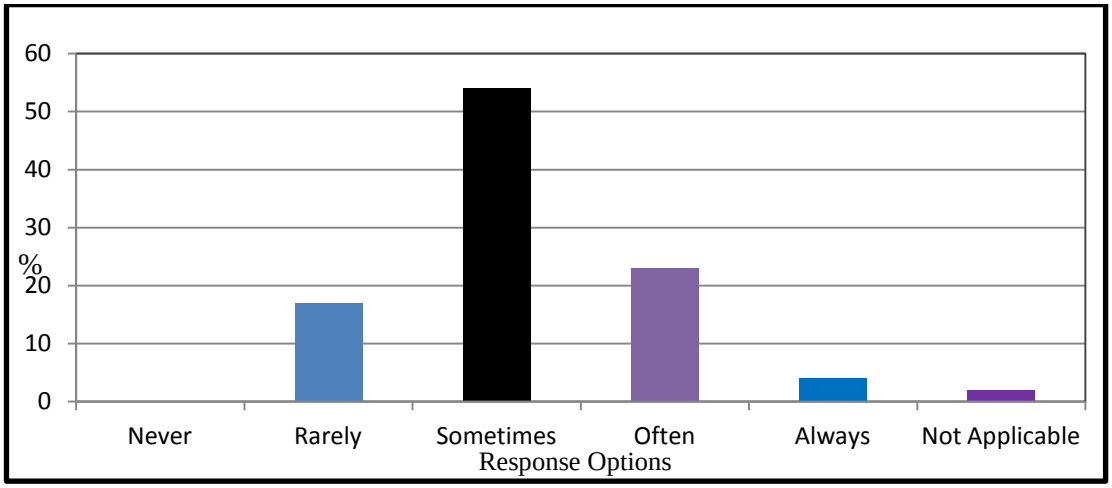
Organisations appear to perform a relatively routine assessment of the impact of the decision-making. It appears not to be performed in 10% of cases (Figure 5.5).

Figure 5.5: My organisation evaluates the impact of its decisions



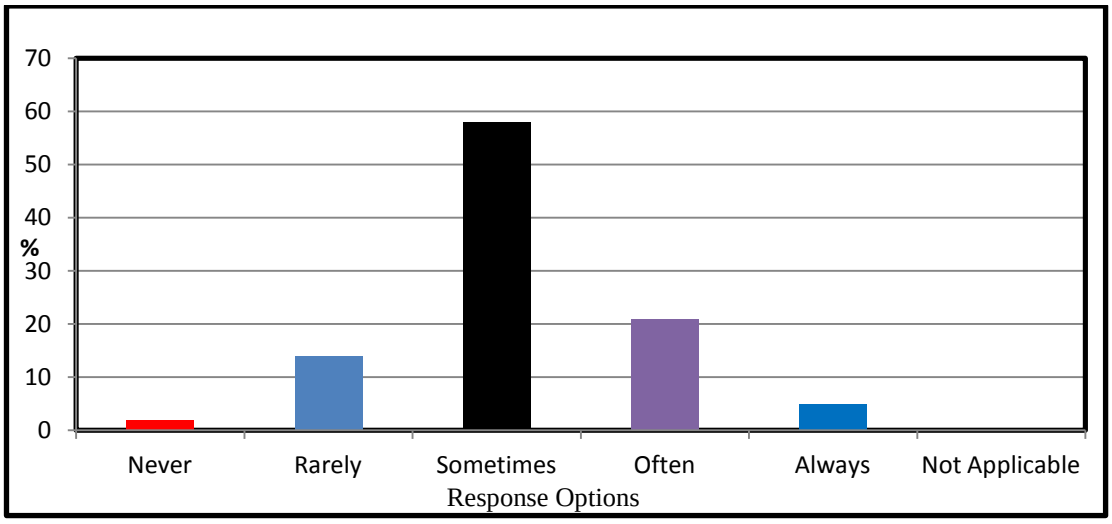
From the perspective of the individual it appears that the majority of individuals (around 85%) felt as though they could make better decisions ranging from a sometimes to an always basis (Figure 5.6).

Figure 5.6: I feel that I could make better quality decisions



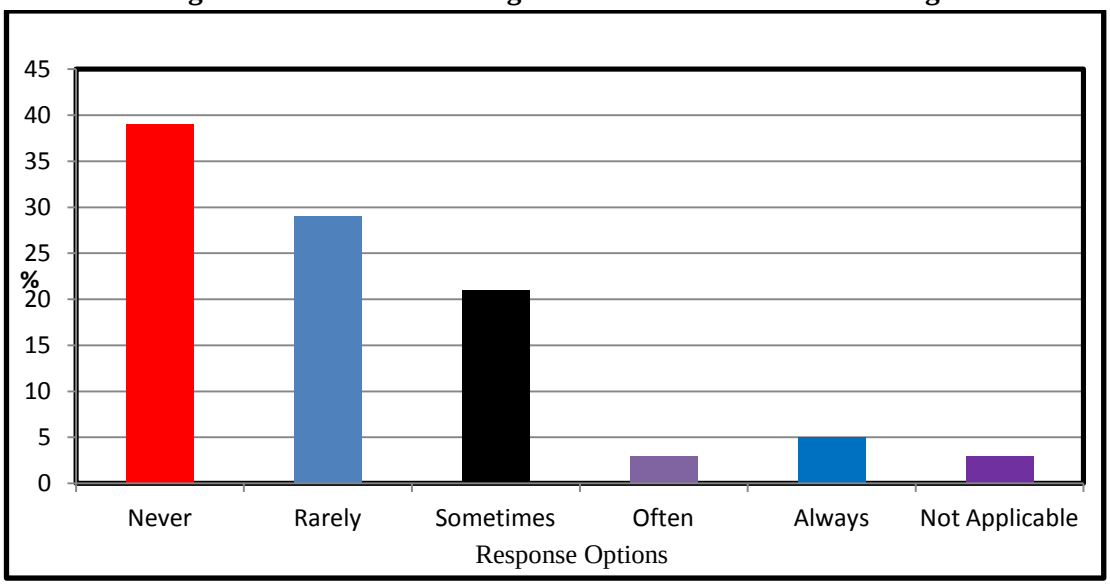
The use of intuition as a standard practice appears to be the case in around 25% of people. Less than 15% appear to use it only on a 'rarely/never' basis and 75% on a 'sometimes/often' basis. It is recognised that different situation will call upon different decision-making approaches but still this is an interesting finding considering the background of the individuals and the evidence based medicines arena.

Figure 5.7: I use intuition or "gut-feeling" in my decision-making



More than 35% of persons who participated in the research advised that they had not received any training in the science of decision-making. Less than 10% of persons advised that they received training on often/always basis (Figure 5.8). This is an interesting and somewhat disappointing finding when one considers the evolving and innovated nature of drug development and the regulatory review and the increasing convergence of industry and regulators in effective delivery of new drugs.

Figure 5.8: I receive training in the science of decision-making



The collection of all the item response data in Excel format allowed for the quantification of the response metrics per response option for each of the organisations. A tabular summary of the response metrics for the organisations is given in Table 5.1.

Table 5.1: Response metrics for individuals from the three organisations*

	Regulatory Agencies (n=19)	**Pharmaceutical Companies (n=76)**	**CROs (n=23)**
Never	99 (6.9%)	203 (3.5%)	63 (3.6%)
Rarely	242 (16.8%)	934 (16.2%)	278 (15.9%)
Sometimes	378 (26.2%)	2030 (35.1%)	608 (34.8%)
Often	367 (25.4%)	1768 (30.6%)	537 (30.7%)
Always	225 (15.6%)	714 (12.4%)	221 (12.7%)
Not Applicable	133 (9.2%)	127 (2.2%)	40 (2.3%)

* The results of the Academics (n=2) were excluded in the metric and statistical analyses due to such low participant numbers.

The percentage of "Affirmative" responses received from the individuals from the three organisations was 67% (Regulatory Agencies), 78% (Pharmaceutical companies) and 78% (CROs).

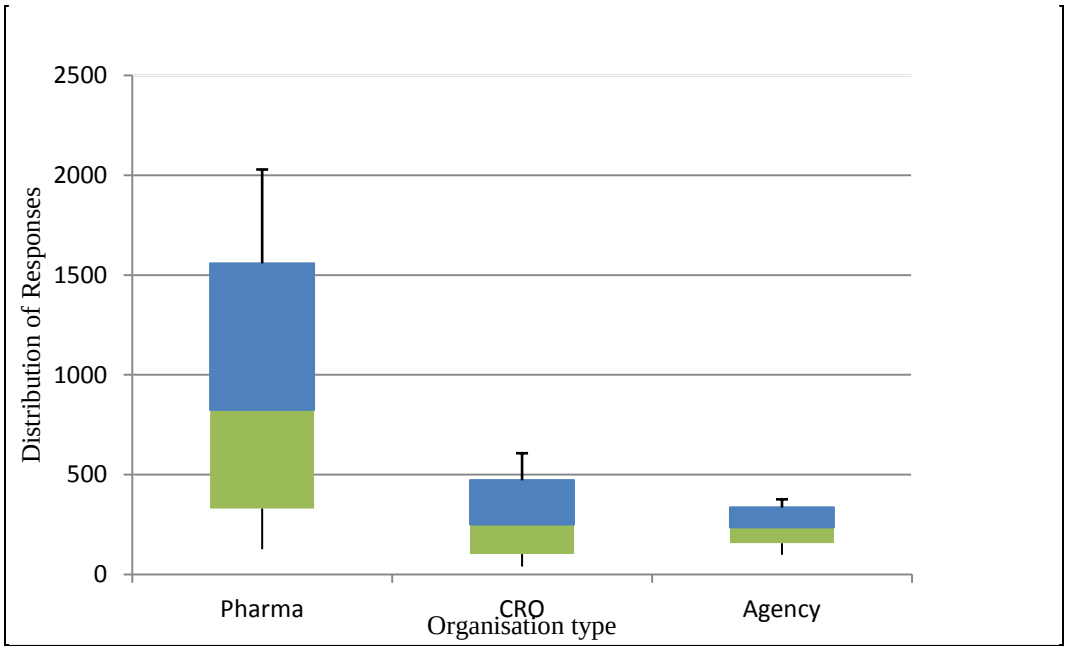
Comparative statistical analyses were performed on the organisation data to generate items such as correlation information and comparative "box and whisker" plots on the distribution of the data. The correlation coefficients for the associations between the results of the organisations were high as shown in Table 5.2.

Table 5.2: Correlation coefficients for the three organisations

	Regulatory Agencies (r, $p<0.001$)	Pharmaceutical Companies (r, $p<0.001$)	CROs (r, $p<0.001$)
Regulatory Agencies	-	0.98	-
Pharmaceutical Companies	0.98	-	0.99
CROs	0.98	0.99	-

Comparative 'box and whisker' plots of the three different organisation results were generated. The plots were generated using Minimum, 25%, Median, 75% and the Maximum of the datasets (Figure 5.9). A 'Box and Whisker' plot presents summary information about the distribution of the data or results. It plots the minimum, the 25^{th} percentile, the median, the 75^{th} percentile and the maximum results and scores that are far removed from the rest (outliers). Fifty per cent of the results are within the coloured boxed areas. The length of the box corresponds to the inter-quartile range (IQR) which is the difference between the 75% and 25% percentiles. The IQR is an established technique used for enabling comparisons to be made among several groups of data. In addition to distribution or spread of results, they also give information on the central tendency of the data set (Sekaran and Bougie, 2010). The Box-and-Whisker plots present a visualisation of the distribution in responses between the organisations and the close comparison between the CRO and the Agency distribution is noteworthy.

Figure 5.9: Box and Whisker plot for the distribution of the results from the three organisations



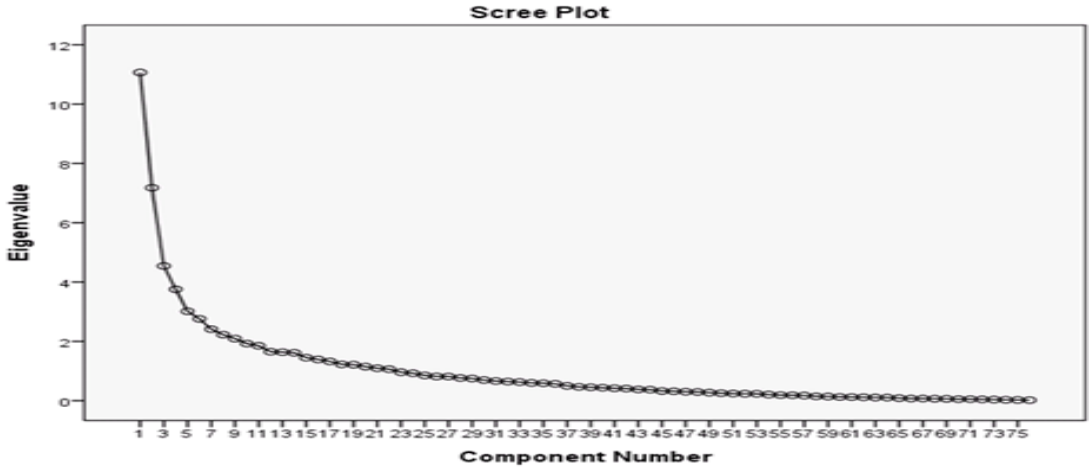
Statistical Factor-Analysis

The 76-item QoDOS (Version 2) contained questions relating directly to the decision-making approach adopted by "organisations" (Regulatory Agencies and Pharmaceutical Industry) and that used by "Individuals" (from within the Regulatory Agencies and Pharmaceutical Industry). Eight different SPSS analyses approaches were attempted on the 76-item instrument using SPSS 20. The approaches investigated the use of PCA, item reduction, Scree plots, KMO, Bartlett's Sphericity testing, statistics descriptive techniques, ICC and several different rotation techniques. The factor analyses did not result in satisfactory item convergence of item reduction. In the draft instrument, the questions were presented in a composite manner and not separated on the basis of whether the question item related to the "Individual" or the "Organisation".

Factor Analysis of The Composite 76-item Instrument

The factor-analysis attempted on the 76-item instrument, commenced with generation of a Scree plot. A rule-of-thumb in interpreting Scree plot outputs is that the "bend in the elbow" or "point of inflexion" is indicative of the number of latent factors within the item set. The Scree plot for the 76 items inferred the presence of nine or ten latent factors (Figure 5.10).

Figure 5.10: Scree plot for the 76-item composite instrument



The Cronbach's alpha for the 76-items instrument was 0.861 which inferred good reliability (Pallant, 2005). As indicated in Table 5.3, the KMO which measured the adequacy of the proposed factor analysis for the 76 items was 0.553. This KMO result was above the 0.5 threshold of acceptability, although it did infer that the sample size was "mediocre" in nature (Pallant, 2005; Field, 2005). Bartlett's test of sphericity tests whether the correlation matrix is an identity matrix, which would indicate that the factor model is inappropriate.

Table 5.3: KMO and Bartlett's Test results for 76 items

Kaiser-Meyer-Olkin Measure of Sampling Adequacy	0.553
Approx. Chi-Square	6007.891
Significance ('p')	0.0001

Organisation Versus Individual Factor Analysis Methods

Following the unsuccessful factor analysis attempts and item reduction of the 76-item QoDOS developmental instrument, the items were separated into two groups depending on whether the item related to organisational or individual level decision-making. This split the 76 items into two separate blocks, one containing 35 organisational items and the other 41 individual related items. The two blocks were given the coding nomenclature d1 – d76 in the SPSS procedural analysis approach with d1 – d36 comprising the Organisational level items and d37 – d76 the individual level items (Table 5.4). This in essence, produced two new distinct domains of the QoDOS instrument. One for Organisational related items (d1 – d36 (excluding d15, which was an organisational item)) and another one for Individual related items (d37 –d76).

Table 5.4: Mapping and separation of the 76 QoDOS items to their organisational level (35) and individual level (41) items

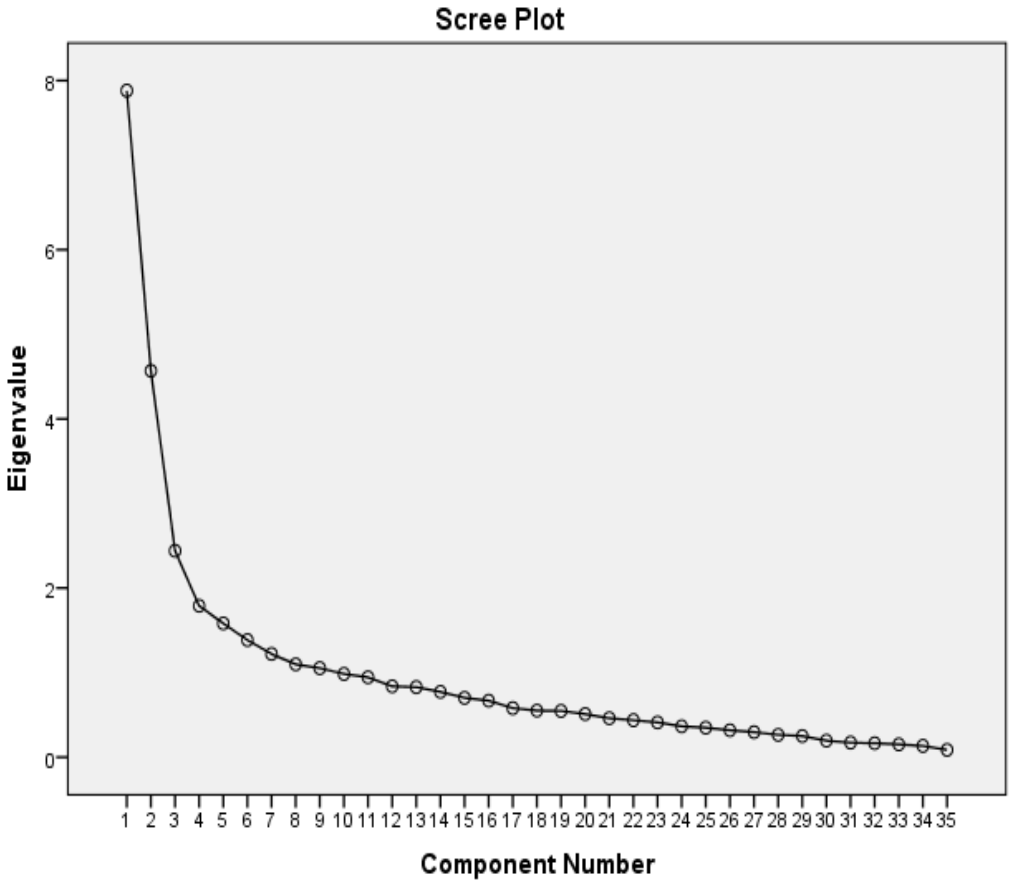
Organisation level items			Individual level items	
Q2	d1		Q1	d37
Q4	d2		Q3	d38
Q6	d3		Q5	d39
Q7	d4		Q13	d40
Q8	d5		Q15	d41
Q9	d6		Q16	d42
Q10	d7		Q18	d43
Q11	d8		Q19	d44
Q12	d9		Q21	d45
Q14	d10		Q22	d46
Q17	d11		Q24	d47
Q20	d12		Q25	d48
Q23	d13		Q26	d49
Q28	d14		Q27	d50
Q31	d16		Q29*	d15
Q33	d17		Q30	d51
Q35	d18		Q32	d52
Q37	d19		Q34	d53
Q39	d20		Q36	d54
Q41	d21		Q38	d55
Q48	d22		Q40	d56
Q49	d23		Q42	d57
Q51	d24		Q43	d58
Q53	d25		Q44	d59
Q54	d26		Q45	d60
Q56	d27		Q46	d61
Q58	d28		Q47	d62
Q60	d29		Q50	d63
Q63	d30		Q52	d64
Q65	d31		Q55	d65
Q68	d32		Q57	d66
Q70	d33		Q59	d67
Q72	d34		Q61	d68
Q74	d35		Q62	d69
Q76	d36		Q64	d70
			Q66	d71
			Q67	d72
			Q69	d73
			Q71	d74
			Q73	d75
			Q75	d76

*Q29 (my procrastination has resulted in a negative outcome) was assigned inadvertently as out of sequence "d" reference number but this did not impact the analyses.

Factor Analysis of The Organisational Related Items

A 12-step factor analysis was performed on the 35 organisational related items using SPSS 20. This helped to explore the underlying structure of the 35 items, to confirm appropriateness (construct validity) and to further develop the instrument by reducing inappropriate items that did not contribute to underlying domain factors of the instrument. Reliability testing using Cronbach's alpha and ICC were measured along with KMO and Barlett's testing. Scree plots were generated at each factor analysis stage. The Scree Plot for the 35 Organisational related items is presented in Figure 5.11 and inferred the presence of six or seven latent factors for the 35 items.

Figure 5.11: Scree plot of the 35 organisational level items



The reliability statistics performed resulted in a Cronbach's alpha of 0.776 for the 35 Organisational items which was a satisfactory robust result. As indicated in Table 5.5, the KMO for the 35 Organisation item solution was 0.743 and was satisfactory. The Bartlett's test result obtained rejected the hypothesis (at $p \geq 0.0001$) that the

correlation matrix is an identity matrix. This supported the appropriateness of the factor model.

Table 5.5: KMO and Bartlett's test results for 35 organisational item

Kaiser-Meyer-Olkin Measure of Sampling Adequacy	0.743
Bartlett's Test of Sphericity	595
Significance ('p')	0.0001

The ICC Reliability coefficient describes how strongly items in the same group resemble each other. The ICC Reliability coefficient ICC = % of variance in the scores results from "true" variance among subjects. ICC ranges from 0 (no agreement) to 1 (perfect agreement). The "single" measure gives the reliability of the scale that is scored by just one of several raters or at one of several occasions and the "average" " measures provided the reliability of a scale that is made up as the average of the different raters. The average ICC value for the organisational items was above 0.77 which is considered acceptable.

Factor Analysis 1:

This included all 35 organisation-related items. The initial factor analysis performed based on the Kaiser's rule, yielded 9- factors with eigenvalue of at least 1 (Table 5.6). The resultant nine factors were also supported by the subjective interpretation of the Scree plot (factors to "bend in elbow"). Item d23 (Q49) was removed as a result of Analysis 1.

Further automatic step-wise extractions were performed on the 35 items and resulted in five component factors and 21 items. As part of the analysis, some Cronbach's alpha measurements were calculated in addition to KMO to add extra robustness to the statistical analysis. A summary of the additional nine extraction steps and results obtained is presented after Table 5.6.

Table 5.6: Results of factor analysis 1: Total variance explained

Component	Initial Eigenvalues			Extraction Sums of squared loadings	
	Total	% of Variance	Cumulative %	Total	% of Variance
1	7.881	22.516	22.516	7.881	22.516
2	4.569	13.054	35.571	4.569	13.054
3	2.440	6.972	42.542	2.440	6.972
4	1.790	5.113	47.656	1.790	5.113
5	1.582	4.520	52.176	1.582	4.520
6	1.386	3.959	53.135	1.386	3.959
7	1.220	3.487	59.622	1.220	3.487
8	1.098	3.138	62.759	1.098	3.138
9	1.052	3.007	65.766	1.052	3.007
10	0.984	2.813	68.579		
11	0.944	2.698	71.277		
12	0.838	2.395	73.671		
13	0.829	2.367	76.039		
14	0.772	2.206	78.245		
15	0.702	2.006	80.250		
16	0.668	1.909	82.159		
17	0.580	1.656	83.815		
18	0.551	1.575	85.390		
19	0.547	1.562	86.952		
20	0.510	1.458	88.409		
21	0.460	1.314	89.724		
22	0.438	1.250	90.974		
23	0.411	1.174	92.148		
24	0.365	1.042	93.190		
25	0.349	0.998	94.187		
26	0.319	0.911	95.099		
27	0.296	0.847	95.946		
28	0.265	0.756	96.702		
29	0.250	0.713	97.415		
30	0.195	0.557	97.972		
31	0.173	0.493	98.465		
32	0.165	0.470	98.935		
33	0.152	0.433	99.369		
34	0.134	0.384	99.752		
35	0.087	0.248	100.00		

Factor Analysis 2: This resulted in item reduction with the removal of two items; d12 (Q20) and d33 (Q70). The KMO for the resultant 9-factor solution was 0.736.

Factor Analysis 3: This produced a KMO of 0.722 for a 9-factor solution.

Factor Analysis 4: This used a 2-factor analysis and resulted in the removal of two further items; d28 (Q58), d26 (Q54). The resultant KMO was 0.722 for the resultant 9-factor solution.

Factor Analysis 5: This used a 2 factor-analysis and resulted in the removal of three items; d4 (Q7), d34 (Q72), d35 (Q76). The KMO for the resultant 8-factor solution was 0.731.

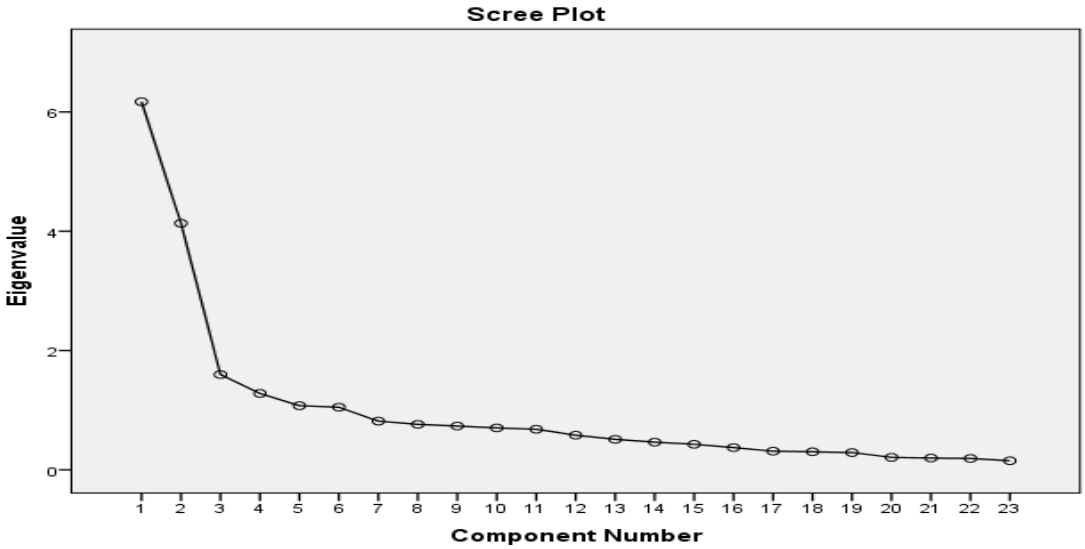
Factor Analysis 6: This resulted in the removal of one further item namely; d10 (Q14). The KMO was 0.749 for the resultant 8-factor solution. The Cronbach's alpha was 0.768.

Factor Analysis 7: This resulted in the removal of three items: d33 (Q17); d31(Q65); and d32 (Q68). With KMO of 0.750 for the resultant 6-factor solution and 23 items. The Scree plot for the 23 item solution is presented in Figure 5.12 and it inferred the presence of six factors.

Factor Analysis 8: This resulted in the removal of one further item namely; d29 (Q60). The KMO was 0.789 for the resultant 6-factor, 22 item solution.

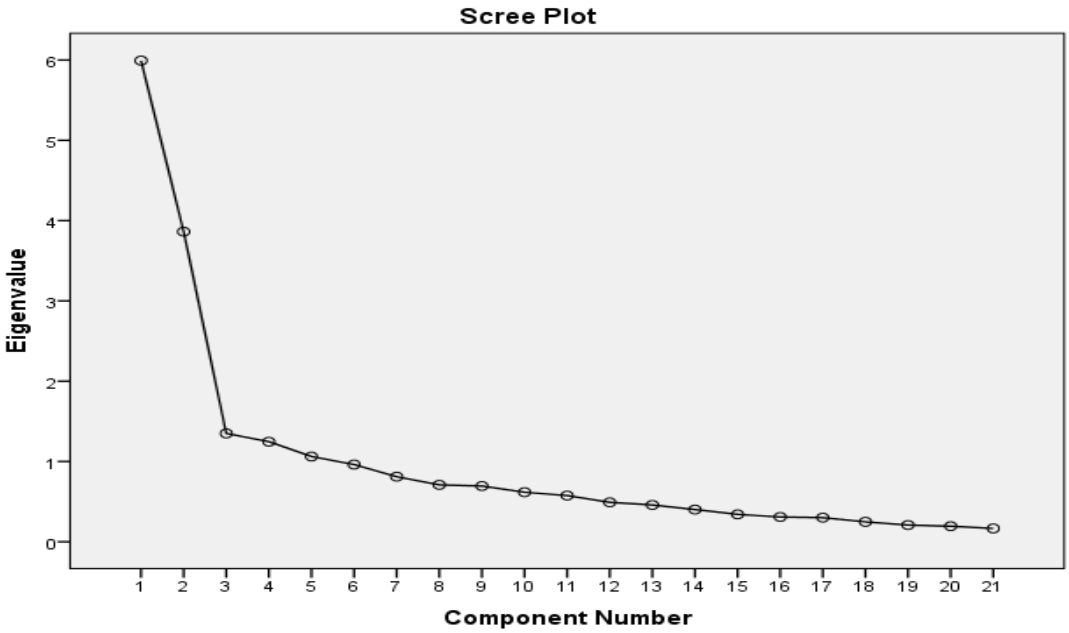
Factor Analysis 9: This resulted in the removal of one further item namely; d7 (Q10). The KMO was 0.802 and the Cronbach's alpha was 0.762 for the resultant 5-factor, 21 item solution.

Figure 5.12: Scree plot for the 23 organisational influence items



Factor Analysis 10: This resulted in a KMO of 0.804 for the resultant 21 item solution. The Scree plot for the 21 item solution is presented in Figure 5.13 and inferred the presence of four factors.

Figure 5.13: Scree plot for the 21 item organisation level influences



The factor analysis performed, reduced the 35 Organisational items to 21 items. Eigenvalues were generated for each of the 21 items (factors). The Scree plot was relatively improved compared to the previous extraction. The eigenvalue loading results showed that most loading was accounted for on five factors, with the majority loading onto two factors as shown in Table 5.7.

Table 5.7: Total variance explained for the 21-item solution

Component	Initial Eigenvalues			Extraction Sums of squared loadings	
(d)	Total	% of Variance	Cumulative %	Total	% of Variance
1	5.993	28.538	28.538	5.992	28.538
2	3.862	18.393	46.930	3.862	18.393
3	1.350	6.427	53.357		
4	1.247	5.936	59.264		
5	1.062	5.056	64.349		
6	0.962	4.582	68.931		
7	0.810	3.859	72.790		
8	0.709	3.374	76.165		
9	0.694	3.306	79.471		
10	0.618	2.941	82.411		
11	0.576	2.741	85.152		
12	0.491	2.338	87.490		
13	0.459	2.184	89.675		
14	0.401	1.911	91.585		
15	0.341	1.624	93.210		
16	0.309	1.470	94.680		
17	0.301	1.432	96.112		
18	0.248	1.180	97.292		
19	0.208	0.992	98.284		
20	0.194	0.923	99.207		
21	0.166	0.793	100.00		

The first five component factors explained relatively large amounts of variance (especially factors one and two) whereas the subsequent factors explained small and reducing amounts of variance. Only the initial two factors had loadings above an eigenvalue of 2.

Rotation Factor Matrix

The component matrix for the 21 extracted variables was rotated using Varimax functionality. This Varimax rotation helped to confirm the initial structure of the scale and delivered a matrix of the factor loadings for each vairable onto each of the two factors. The loading solution showed the variables listed in order of the size of

their factor loadings onto each of the two component factors. Loading values with a unique value of less than 0.4 were supressed. The rotated matrix 2-factor solution for the 21 organisational variables showing the loading of each variable is presented in Table 5.8.

The Varimax rotation maximised the variance of each of the 21 items, so the total amount of variance accounted for was redistributed over the two extracted factors. Overall, the factor analysis on the Organisational items allowed a reduction from 35 to 21 items. The analysis was also discriminatory in nature in that different loadings resulted for the differing constructs which was also supportive of overall construct validity.

Factor Analysis of Individual Related Items

The grouping of the original composite 76-item QoDOS (Version 2) into two blocks, resulted in 41 individual related items in the "individual" block. Factor analysis on the 41 items was performed using SPSS 20. A total of 11 consecutive factor analysis item reduction steps were performed on the 41 individual related items. Reliability testing using Cronbach's alpha and ICC were measured along with KMO and Barlett's testing. Scree plots were generated at each factor analysis stage. The Scree Plot for the 41individual related items is presented in Figure 5.14 and inferred the presence of nine or ten latent factors for the 41 items.

Figure 5.14: The Scree plot for the 41 individual related items

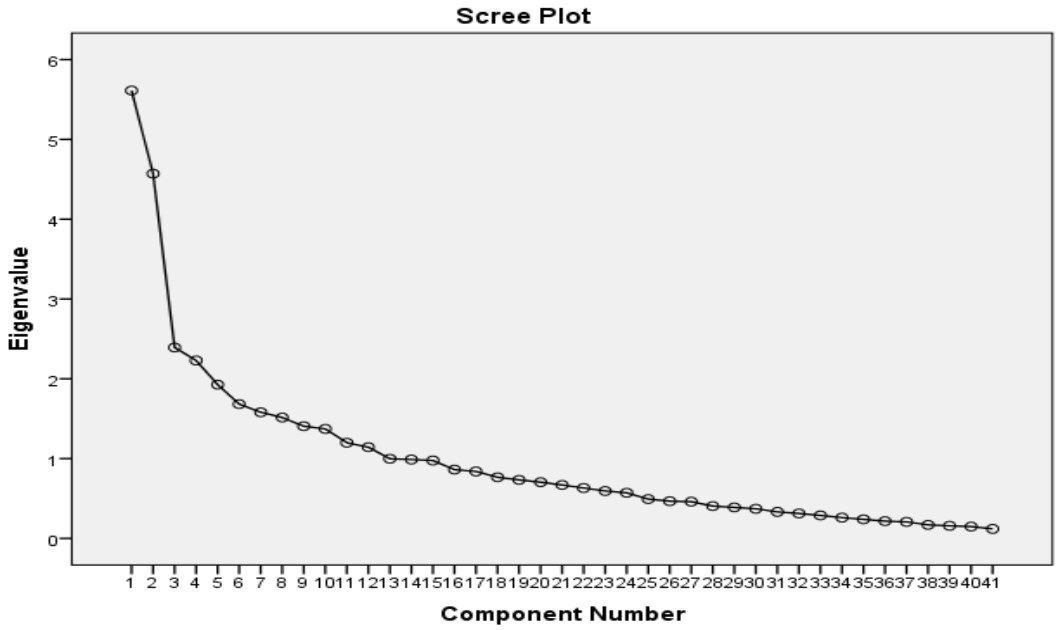


Table 5.8: The organisational item resultant rotated factor loadings (pattern matrix)

		Variable	Factor1	Factor2
My organisation's decision-making is influenced by company politics	Q11	d8	.796	
My organisation has suffered a negative outcome due to slow decision-making	Q31	d16	.719	
In my organisation's decision-making, it makes the same mistakes as made in the past	Q53	d25	.684	
My organisation's decision-making is influenced by vested interest of individuals	Q9	d6	.668	
My organisation's culture has resulted in its inability to make a decision	Q33	d17	.666	-.373
My organisation continues with projects which should be terminated at an earlier stage	Q28	d14	.631	
My organisation's decision-making is influenced by competitors	Q8	d5	.585	.406
My organisation's decision-making is influenced by incentives or penalty payments	Q12	d9	.575	
My organisation underestimates problems which adversely impacts its own decision-making	Q56	d27	.569	
My organisation quantifies the probability of success in its decision-making	Q37	d19	.382	.710
My organisation qualifies the probability of success in its decision-making	Q35	d18		.664
My organisation encourages innovative decision-making	Q63	d30		.637
My company uses a structured approach in its decision-making	Q2	d1		.634
My organisation effectively communicates the decisions it makes	Q74	d35	-.481	.612
My organisation provides clear and unambiguous instructions for decision-making	Q39	d20		.612
My organisation evaluates the impact of the decisions it makes	Q4	d2		.600
My organisation's decision-making approach is transparent	Q41	d21	-.375	.587
My organisation's decision-making is consistent	Q48	d22	-.384	541
My organisation is open to using better alternatives in its decision-making	Q51	d24		.539
My organisation re-examines its decision-making as new information becomes available	Q49	d23	-.488	.537
My organisation's decision-making is influenced by external stakeholder's demands	Q6	d3		.520

The reliability statistics performed resulted in a Cronbach's alpha of 0.809 for the 41 Individual item instrument which was a satisfactory robust result. As indicated in Table 5.9, the KMO for the 41 Individual item solution was 0.645 and was "fair". The Bartlett's test result obtained rejected the hypothesis (at $p \geq 0.0001$) that the correlation matrix is an identity matrix. This supported the appropriateness of the factor model.

Table 5.9: KMO and Bartlett's Test results for the 41 individual items

Kaiser-Meyer-Olkin Measure of Sampling Adequacy	0.645
Bartlett's Test of Sphericity	820
Significance (p)	0.0001

The Intraclass Correlation Coefficient for the 41 individual items were also generated and had an average ICC value of 0.8, which was acceptable. As part of the step-wise factor analyses, some Cronbach's alpha measurements were calculated in addition to KMO to add extra robustness to the statistical analysis. A summary of the additional 11 extraction steps is presented below:

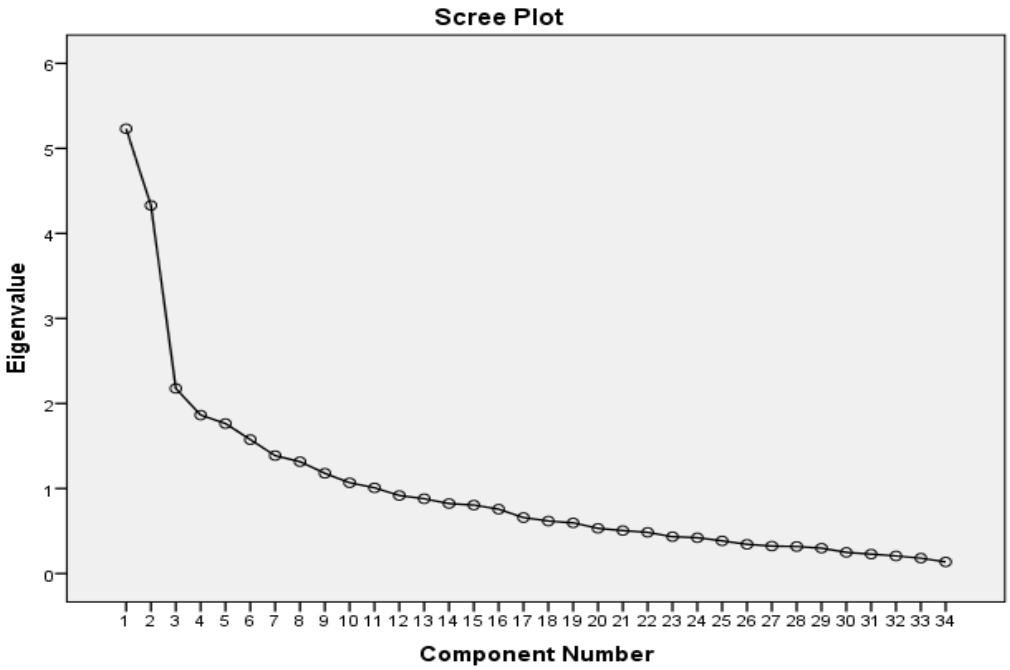
Factor Analysis 1: 41 Individual related items

The initial factor analysis performed based on the Kaiser's rule, yielded 12 factors with an Eigen-value of at least 1. The 12-factor solution was also supported by the subjective interpretation of the Scree plot (factors to "bend in elbow"). Four Items; d74 (Q71), d42 (Q16), d43 (Q18), d61 (Q6) were removed as a result of the first factor analysis. Further automatic step-wise extractions involving 11 reiterations were performed on the remaining items which resulted in 6 component factors and 22 items.

Factor Analysis 2:

This resulted in the reduction of three items: d41 (Q15); d76 (Q75); and d70 (Q64) with KMO value of 0.683 for the resultant 11-factors and 34-item solution. The Scree plot for the 34 item solution is presented in Figure 5.15 and inferred the presence of 12 latent factors.

Figure 5.15: Scree plot for the individual items solution (2nd factor analysis)



Factor Analysis 3:

This resulted in item reduction leading to the removal of one item namely: d72 (Q67). The KMO obtained post-factor analysis three was 0.695.

Factor Analysis 4:

This resulted in the removal of one item namely: d66 (Q57). The KMO obtained post-factor analysis was 0.700 (good) and the Cronbach's alpha of 0.809 (very good).

Factor Analysis 5:

This resulted in the removal of a further one item: d75 (Q73). The KMO obtained post-factor analysis was 0.710 (good).

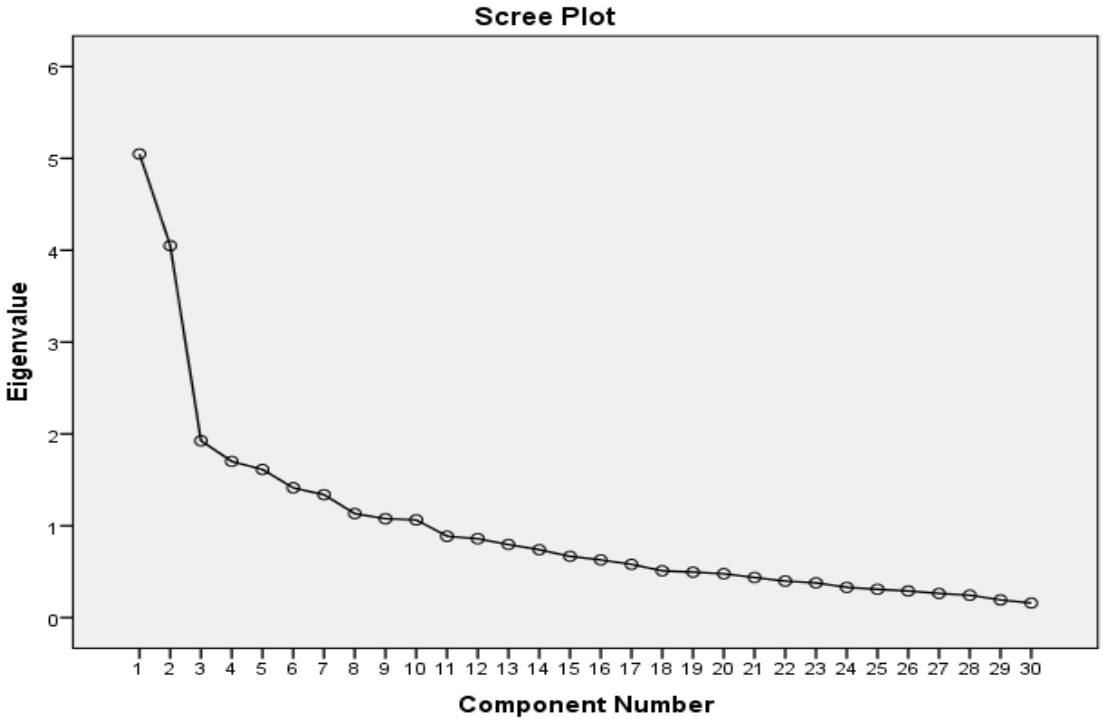
Factor Analysis 6:

This resulted in item reduction of one item namely: d69 (Q62). The KMO obtained post-factor analysis was 0.713 (good).

Factor Analysis 7:

The KMO obtained post-factor analysis seven, was 0.713 (good) and the Cronbach's alpha was 0.803 (good). The Scree plot obtained and presented in Figure 5.16 inferred the presence of four factors.

Figure 5.16: Scree plot for the individual items (7th factor analysis)



Factor Analysis 8:

This resulted in the removal of five items: d40 (Q13): d48 (Q25); d47 (Q24); d63 (Q50); and d38 (Q3). The KMO obtained was 0.713 (good).

Factor Analysis 9:

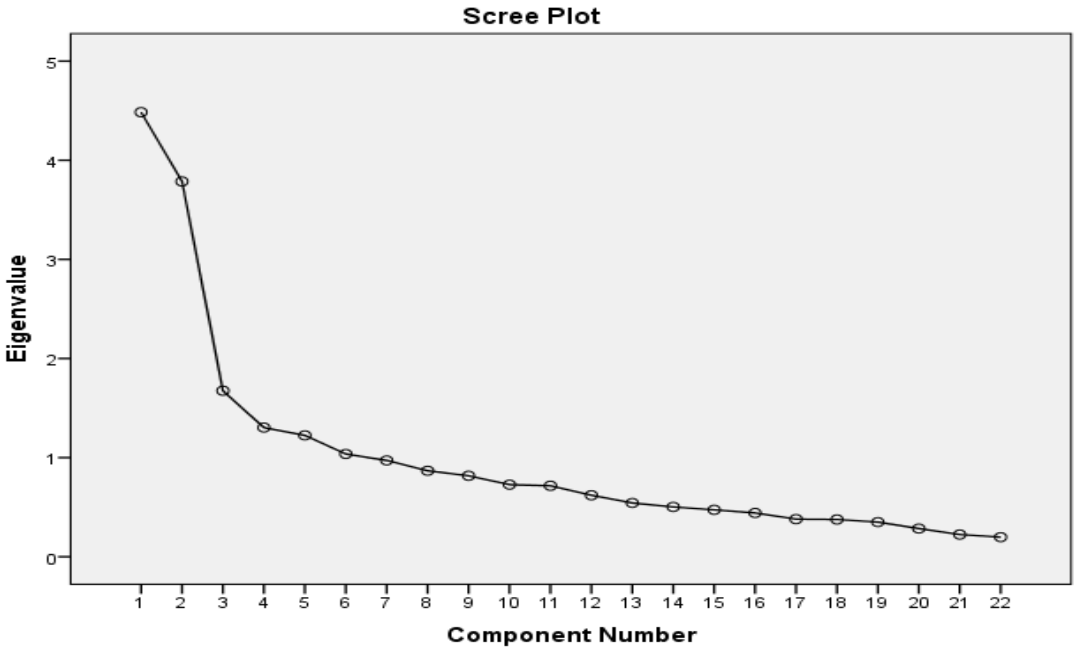
Factor analysis nine resulted in the removal of two items namely: d45 (Q21) and d61 (Q46). The KMO was 0.755 (good) with a Cronbach's alpha of 0.821(good).

Factor Analysis 10:

Factor analysis ten resulted in the removal of a further single item: d44 (Q19). The KMO obtained was 0.765 (good).

Factor Analysis 11: Factor analysis eleven, resulted in no further reduction of items. The KMO obtained was 0.762 (good) and the Cronbach's alpha of 0.796 (good). The Scree plot inferred the presence of at least 6 latent factors, two of which were most dominant. No clear "point of inference / elbow break" was evident in the Scree plot, as presented in Figure 5.17.

Figure 5.17: Scree plot for the individual items (11th factor analysis)



The ICC reliability coefficient results describe how strongly items in the individual item group resemble each other. The average ICC value was 0.796 which is acceptable. The factor analysis performed on the individual items reduced the number of items from 41 to 22. The eigenvalue loading resultant from the final extraction are presented in Table 5.10 showed that a six component factor solution explained relatively large amounts of variance (especially factors one and two) whereas the subsequent factors explained small and reducing amounts of variance. Only the top two dominant factors had loadings above an eigenvalue of 2 (same criteria as applied to the Organisational items).

Rotation Factor Matrix

The component correlation matrix for the 22 extracted variables was rotated using Varimax functionality. The Varimax rotation helped to confirm the initial structure of the scale and delivered a matrix of the factor loadings for each variable onto each of the two dominant factors. The loading solution showed the variables listed in order of the size of their factor loadings onto each of the two component factors. Loading values with a unique value of less than 0.4 were suppressed. The rotated matrix 2-factor solution for the 22 individual variables showing the loading of each variable is presented in Table 5.11.

The Varimax rotation maximised the variance of each of the 22 factors, so the total amount of variance accounted for was redistributed over the two extracted factors. The reduction of the original 41 organisational items to 22 and followed by their loading onto two factors will allow for an individual behaviour title to be allocated to the two factors. The analysis was also discriminatory in nature in that different loadings resulted for the differing constructs which was also supportive of overall construct validity.

Table 5.10: Total variance explained for the 22 item solution

Component	Initial Eigenvalues			Extraction Sums of squared loadings	
d	Total	% of Variance	Cumulative %	Total	% of Variance
1	4.485	20.385	20.385	4.485	20.385
2	3.786	17.208	37.592	3.786	17.208
3	1.675	7.612	45.205		
4	1.303	5.922	51.127		
5	1.225	5.566	56.693		
6	1.037	4.713	61.406		
7	0.972	4.417	65.824		
8	0.867	3.943	69.766		
9	0.817	3.712	73.479		
10	0.727	3.307	76.785		
11	0.716	3.256	80.041		
12	0.620	2.819	82.860		
13	0.542	2.466	85.326		
14	0.502	2.284	87.610		
15	0.473	2.152	89.761		
16	0.441	2.006	91.768		
17	0.380	1.276	93.493		
18	0.376	1.710	95.203		
19	0.349	1.589	96.792		
20	0.284	1.292	98.084		
21	0.224	1.017	99.101		
22	0.198	0.899	100.00		

Table 5.11: The 22 individual related decision-making factors: following item reduction and SPSS extraction

		Variable	Component (Factor)1	Component (Factor)2
My procrastination has resulted in a negative outcome	Q29	d15	.734	
I have experienced "paralysis by analysis" caused by my slow decision-making	Q30	d51	.720	
Emotion is part of my decision-making	Q66	d71	.706	
I have experienced a negative outcome by a decision not being made	Q32	d52	.680	
In my decision-making, I make the same mistakes as made in the past	Q52	d64	.600	
Recent or dramatic events greatly impact my decision-making	Q59	d67	.559	
My decision-making could be improved by assigning weights	Q42	d57	.532	
I continue with projects which should be terminated at an earlier stage	Q27	d50	.522	
I feel that I could make better quality decisions	Q22	d46	.502	
I underestimate problems which adversely impact my decision-making	Q55	d21	.493	
I quantify the probability of success in my decision-making	Q36	d54	.445	.326
I qualify the probability of success in my decision-making	Q34	d53	.441	.312
I understand the context of the decision I am being asked to make	Q38	d55		.741
I consider uncertainty and unknowns in my decision-making approach	Q45	d60		.644
I present contingencies or achievable options as part of my decision-making	Q43	d58		.642
My decision-making is consistent	Q47	d62		.635
My decision-making approach is transparent	Q40	d56		.608
I use a structured approach in my decision-making	Q1	d37		.591
My decision-making is knowledge based	Q69	d73		.529
I understand the importance of the decisions I make	Q5	d39		.509
My professional experience is important when having to make challenging decisions	Q26	d49		.484
I generate a SWOT (strengths, weaknesses, opportunities, threats) analysis in my decision-making	Q44	d59		.482

Factor Analysis Final Output

The factor analysis and item reduction performed on the initial 76-item draft instrument resulted in the emergence of the following list of reduced items for the Organisation and Individual decision-making categories.

Organisational Related Items (21-items):

- My organisation's decision-making is influenced by company politics
- My organisation has suffered a negative outcome due to slow decision- making
- In my organisation's decision-making, it makes the same mistakes as made in the past
- My organisation's decision-making is influenced by vested interest of individuals
- My organisation's culture has resulted in its inability to make a decision
- My organisation continues with projects which should be terminated at an earlier stage
- My organisation's decision-making is influenced by competitors
- My organisation's decision-making is influenced by incentives or penalty payments
- My organisation underestimates problems which adversely impacts its own decision-making
- My organisation quantifies the probability of success in its decision- making
- My organisation qualifies the probability of success in its decision-making
- My organisation encourages innovative decision-making
- My company uses a structured approach in its decision-making
- My organisation effectively communicates the decisions it makes
- My organisation provides clear and unambiguous instructions for decision-making
- My organisation evaluates the impact of the decisions it makes
- My organisation's decision-making approach is transparent
- My organisation's decision-making is consistent
- My organisation is open to using better alternatives in its decision-making
- My organisation re-examines its decision-making as new information becomes available

- My organisation's decision-making is influenced by external stakeholder's demands

Individual Related Items (22-items):

- My procrastination has resulted in a negative outcome
- I have experienced "paralysis by analysis" caused by my slow decision-making
- Emotion is part of my decision-making
- I have experienced a negative outcome by a decision not being made
- In my decision-making, I make the same mistakes as made in the past
- Recent or dramatic events greatly impact my decision-making
- My decision-making could be improved by assigning weights
- I underestimate problems which adversely impact my decision-making
- I continue with projects which should be terminated at an earlier stage
- I feel that I could make better quality decisions
- I quantify the probability of success in my decision-making
- I qualify the probability of success in my decision-making
- I understand the context of the decision I am being asked to make
- I consider uncertainty and unknowns in my decision-making approach
- I present contingencies or achievable options as part of my decision-making
- My decision-making is consistent
- My decision-making approach is transparent
- I use a structured approach in my decision-making
- My decision-making is knowledge based
- I understand the importance of the decisions I make
- My professional experience is important when having to make challenging decisions
- I generate a SWOT (strengths, weaknesses, opportunities, threats) analysis in my decision-making.

Expert Team Review of The Themes that Emerged from The Qualitative Study

It is appreciated that factor analysis is a complex procedure, which is exacerbated by the lack of inferential statistics and the imperfections of "real world" data and can be

prone to subjective biases such as during the "eyeballing" stage. To address this a panel of expert can be used to review and make judgement concerning the deletion and retention of specific items (Denzin and Lincoln, 2005). The research team reviewed the initial emergent source themes on Organisational (21) and Individual (22) related decision-making behaviour. It was decided to retain some of the removed items which were very highly prevalent in the qualitative study. The additions below were proposed by the team based on their own personal and expert professional perspective and also with cognisance of the output from the key-opinion leaders interviews discussed in Chapter 3. These additions were:

Organisational related item additions:

- My organisation considers uncertainties in relation to decision-making
- My organisation provides training in the science of decision-making

Individual related item additions:

- I receive training in the science of decision-making
- I use intuition or "gut-feeling" in my decision-making

The outcome of the final factor analysis and the thorough review performed by the research team was the delivery of the 47-item QoDOS (Version 3) instrument. The instrument comprised of two domains; one for organisational level decision-making consisting of 23 items and individual level approaches consisting of 24 items. Subsequently each component was grouped into two separate domains representing the approach, culture, competence and decision-making style.

Overall, the factor analysis performed allowed for the organisation and individual influence items contained within the final instrument to be allocated to one of four categories, two relating to the organisation and two relating to the individual:

- *Organisational level influences - decision-making approach*
- *Organisational level influences - decision-making culture*
- *Individual level influences - decision-making competence*
- *Individual level influences - decision-making style*

The complete set of organisational related items and individual related items have been incorporated into the QoDOS instrument (Version 3) presented in Appendix V. This was tested for final validation which will be reported in Chapter 6.

DISCUSSION

There were two distinct but linked component stages in the factor analysis performed on the 76-item QoDOS (Version 2). The first stage involved the instrument being sent using Survey Monkey to over 600 potential research participants. A total of 120 evaluable individuals participated in this stage of the research and completed the developmental QoDOS questionnaire as requested. The research participants comprised of individuals from international regulatory agencies, international pharmaceutical companies and CROs (and two from Academia).

The timeframe for completion of the questionnaire was a defined four months over the summer period and this may have had an influence on the low response rate of 20%. Several measures reported in the literature (and introduced in Chapter 2) to boost response rates were employed including follow-up requests to complete, phone contacts and some personal one-to-one interactions (Diem, 2002b; Boynton, 2004; Survey Monkey, 2013). Factors other than the summer test period that might have influenced the low response rate could have included: the length of the questionnaire (76 items and perceived time-sacrifice burden), corporate position not allowing for surveys to be completed (as reported by several persons), potential participant apathy to the survey and to the research area and other contributory factors which are not easy to qualify or to quantify. However, the resultant data from the 120 person research sample provided a rich and valuable platform for developing insights into the decision-making practices of the individuals and the organisations who participated in the research. A wealth of resultant information was generated and this allowed several comparative reviews of perspective from that of the individual and the organisation.

The Survey Monkey and the SPSS statistical functionality allowed for a large amount of quantitative findings to be generated. Quantitative feedback results were generated for each of the three main organisations (Regulatory Agencies,

Pharmaceutical Companies and CROs) active in the research. The data provided insight into the variance in distribution of results to the 76-item question obtained from the three organisations. The results provided preliminary insight of differing construct dimensions of the decision-making perspective of the organisations compared with that of the individual. For Organisations, the *Modus Operandi*, the working environment and the shared beliefs and values of that organisation appeared to be important influences. For the Individual, the subjective elements of: professional experience, ability, empowerment or autonomy and preference appeared to be latent decision-making dimensions.

From the perspectives of the individual it was evident that people felt that they could make better decisions and that an investment in training and education in decision-making would benefit them and their decision-making. There was a lack or routine usage of decision-making tools such as SWOTs and limited experience of modelling and simulation. Other perspectives that emerged were that the individual felt that they were more accountable for their decisions than the organisation was at the organisational level. People firmly believed that professional experience was a key component that influenced decision-making. The results also showed the importance of clearly understanding the context of the decision. In total, the individual's perspective was obtained in response to 41 specific questions on their decision-making style, approach and factors that impact them.

Similarly, insights were gained from the 120 person sample on the decision-making perspective of the organisation. Thirty-five specific questions on organisational decision-making were responded to and yielded insights into the factors including: the culture of the organisation, the lack of training in decision-making being provided within organisations, the internal and external competitor influences, performing an impact analysis of decisions made, re-evaluating a decision on the basis of new data becoming available and transparency within the decision-making process. A variance in the distribution of the response profiles to the individual and organisational focused questions was evident across the three organisations involved in the research. The 'Box and Whisker' plot results give an interpretable visualisation of this variance and also indicated that the pharmaceutical cohort had a wider range of "outliers". This may be linked to the decision-making competence or style

approach of some individuals employed in this cohort on items such as use of "gut feeling /intuition" and the more competitive environment in which many decisions need to be made. These decision-making drivers will be further explored through the development of the developmental instrument. The research was enriching in several ways in that it not only successfully investigated the research aim, but it also allowed for an enabling, enriching and synergistic networking within the medicinal product development community.

The second distinct component stage of this chapter was that relating to the factor analysis performed on the original 76-item developmental instrument. Factor analysis was attempted on the 76-item QoDOS (Version 2) containing the combined organisational and individual item variables. Although the Cronbach's alpha result obtained (0.861) inferred good reliability (Pallant, 2005), the KMO measure of the adequacy value of 0.553 obtained inferred that the sample size was "mediocre" in nature. The "mediocre" KMO did not improve much as part of further reiterations attempts. This mediocre KMO results were reflective of the challenge of the sample size versus the number of items in the developmental instrument. The issue with the low KMO results and with failure to achieve successful extractions and item reductions, factor analysis and robust statistical analysis on the QoDOS (Version 2) appeared to be related to the research sample size data available for the analysis (n=120) versus the number of items (76) in the instrument. The 120 sample size was apparently too small for the 76 target items and a sample size in the magnitude of n=760 (in line with the 10:1 ratio detailed earlier) or potentially n=380 (on a 5:1 ratio) might have been sufficient to allow successful item extraction (Tabachnick and Fidell, 2001). However, the implications of aiming for an n=760 sample size would have required, in theory, making contact with 1,500 - 3,800 individuals on the premise of a 20% participation rate. This ideal sample size requirement was recognised as being prohibitive and the approach to split the 76-item into two separate blocks of 35 (Organisational related items) and 41 (Individual related items) seemed a plausible solution. The two blocks were given the coding nomenclature related to Organisational level issues Individual level issues. This resulted in the two blocks of Organisational and Individual related issues being mapped, analysed and presented. This approach of splitting the 76 items into the two component blocks was deemed pragmatic and valid.

The outcome of the factor-analysis and review was the extraction and reduction of items in both groups. Organisational items were reduced from 35 to 23 and the reduction of individual items from 41 to 24. The organisational and the Individual related domains (n=24) were categorised into two sub-category dimensions. For the Organisational items:“Decision-making approach” and “Decision-making culture” and “Decision-making competence” and “Decision-making style” for the individual items. These subcategory headings appeared to be the influences and behaviours that emerged from the questionnaire results and endorsed by the qualitative interviews conducted with the Key Opinion Leaders and reported previously. These four construct dimensions are deemed acceptable in terms of generalisability and applicability to a wider population outside the sample pool directly involved in this research.

The resultant outcome of the factor-analysis was the delivery of the final version of the QoDOS instrument (Version 3) capturing organisational and individual decision-making items grouped into two separate construct variable domains representing the approach, culture, competence and decision-making style. The factor-analysis was discriminatory in that different factor loadings were observed for the latent variables which also provided supportive evidence of construct validity. The reassurance on the validity of the four construct domains identified was also supported from the complimentary results of the KOL interviews conducted. In essence, the goal of conducting the KOL interviews was to identify the key aspects (or attributes) of the construct domain (MacKenzie et al., 2011). Greater discussion on the construct validation investigation will be presented in the discussion section of Chapter 6.

The 47-item QoDOS instrument has been developed using a step-wise and systematic scientific approach. Statistical validity and integrity were paramount in the instrument development. The research approach comprised qualitative and quantitative components which have been described in detail and which resulted in the duly validated instrument that is now available for final stage psychometric evaluation.

SUMMARY

- The post content validation evaluation QoDOS (Version 2) containing 76 decision-making items was used in this stage of the research. The QoDOS (Version 2) contained questions relating to the decision-making approach employed by "Organisations" (Regulatory Agencies and Pharmaceutical Industry) and that used by the "Individual" in the organisations
- One hundred and twenty experienced decision-makers from regulatory agencies, pharmaceutical companies, CROs and Academia (n=2) completed the QoDOS (Version 2) decision-making electronic questionnaire
- The Survey Monkey package was used in the issuance of the surveys, collection and management of the results which provided comparative insights into decision-making at an Individual and an Organisational level
- The statistical analyses results inferred the presence of differing construct dimensions between the decision-making approaches used by Organisations versus that used by Individuals
- Comparative insights were obtained on the decision-making approaches and influenced of organisations.
- Comparative insights were obtained on the variance of decision-making within the Regulatory Agency, Pharmaceutical Companies and CROs
- Insights were gained into the decision-making approaches and influences of individuals
- Potential gaps in the education and training and development needs of individuals and organisations were identified
- A detailed quantitative response analysis was generated for each of the 76-item questions contained within the developmental questionnaire
- Factor analysis investigation was performed on the 76-item QoDOS (Version 2) developmental instrument
- Successful factor analysis and item reduction was performed on the 35 organisational items leading to a reduced set of 23 variables
- Successful factor analysis and item reduction was performed on the 41 individual items leading to a reduced data set of 24 variables
- Four additional items (two organisational and two individual) from the original 76-items were re-instated to post-factor analysis items listings

- Two behavioural domain constructs were identified for the Organisational items and these related to decision-making approach and culture
- Two behavioural domain constructs were identified for the Individual items and these related to decision-making style and competence
- The 47-item QoDOS instrument was established.

CHAPTER 6

Reliability and Construct Validation of QoDOS and Hallmarks of Good Decision-Making Practice

INTRODUCTION

The factor analysis performed on the QoDOS developmental instrument was predicated on the belief that a battery of decision-making item tests could be described in terms of a smaller number of underlying factors. The underlying decision-making constructs caused a number of observable manifestations, which are captured within the QoDOS items. The construct domain dimensions revealed by the factor analysis were not directly observable from the data but rather were inferred from the patterns within the results that emerged. As a result, the 47-item QoDOS instrument yielded 4 construct domains, two relating to the organisation (Approach and Culture) and two to the individual (Competence and Style).

The next stage, after factor analysis was the testing, assessment and establishment of the reliability and construct validation of the 47-item QoDOS instrument using statistical analyses. The reliability and construct validity testing was done using 78 individuals from regulatory agencies and the pharmaceutical healthcare arena. Statistical analyses formed the basis of the construct validation and assessed the correlations between the QoDOS construct domains (latent variables). The data provided extra quantitative insights into the decision-making approaches from the perspective of the individual and the organisations in the cohort and was complimentary to the additional research sample results detailed in Chapter 5.

Following the conduct of the assessment of construct validity and reliability, research was conducted into the identification and qualification of the Hallmarks of good decision-making practice.

METHODS

The final 47-item version of the QoDOS instrument contained 23 organisational and 24 individual items and was tested for reliability and construct validity. The QoDOS instrument was sent to the study participants using the Survey Monkey online questionnaire survey tool as described previously in Chapter 2. Each prospective participant was provided with background information on the research project and given assurance on the confidentiality on all research related matters.

The 78 respondents provided their answers to each of the 47-item questions using a Likert 5-response option scale. Both the Survey Monkey functionality and Excel were used in the quantitative analysis of this component of the research. An Excel database was employed to capture the data returns from each of the research participants. The functionality of the Excel database facilitated the data management and interpretation of the results. The combined Survey Monkey and Excel functionality also allowed the generation of information in various result formats. The data were also analysed using the SPSS version 20 to examine the reliability and construct validity of the QoDOS. The reliability and construct validity were tested using standard statistical techniques including the Principal Component Analysis (PCA), Cronbach's alpha, Split-Half, Parallel and Gutmann testing for reliability accompanied by ICC coefficient and Spearman's 2-tailed correlation statistics. KMO and Bartlett's Sphericity testing and correlation statistics were also performed. A Multi-Trait Multi-Method (MTMM) table was generated capturing comparative statistical methodologies and results obtained in this reliability and validity examination stage. Excel was used to compute some of the quantitative output and generation of graphical outputs.

An extra research arm exercise was conducted to identify the "Hallmarks of good decision-making practice". This involved ranking a set of ten decision-making items in order of perceived preference. The hallmarks questionnaire was presented as an addendum to the QoDOS instrument questionnaire and was completed by a research sample of 78 senior decision-makers from regulatory agencies and the pharmaceutical and healthcare area.

RESULTS

The results obtained from the research sample provided comparative quantitative information on the decision-making approaches and influences from the perspective of the organisation and the individual. The results presented evidence to support the successful construct validation of the instrument and the underlying dimensions. The construct validation results are presented for the composite 23-item organisational and the 24-item individual decision-making scales followed by the results for each of the two latent sub-components contained within each scale. The results are presented

in two sections that relate to the Construct validation (n=78 representing a 100% response rate) and to the hallmarks of good decision-making practices (n=78 representing a 100% response rate).

Organisational Level Influences: The 23 organisational items, which comprised the two organisational level decision-making influence dimensions namely Approach and Culture were tested for construct validity (Table 6.1). The statistical results for the Cronbach's alpha, KMO and Bartlett's test for the 23-item organisational level influences in the two constructs were determined. The Cronbach's alpha level, indicative of reliability calculated for the 23 item instrument constructs was 0.746 which was acceptable/good. The KMO value of 0.794 was also acceptable. The Bartlett's test of Sphericity was 231 and the ICC was 0.746 (good). These results demonstrated adequate sample size for the analysis and good reliability from the Cronbach's alpha and ICC results obtained.

Table 6.1: Organisational level influences

Organisational Decision-Making Approach Dimension (12 items)	Organisational Decision-Making Culture Dimension (11 items)
1. My organisation evaluates the impact of the decisions it makes	1 My organisation's decision-making is influenced by company politics
2. My organisation's decision-making approach is transparent	2 My organisation has suffered a negative outcome due to slow decision-making
3. My organisation's decision-making is consistent	3 My organisation's culture has resulted in its inability to make a decision.
4. My company uses a structured approach in its decision-making	4 In my organisation's decision-making, it makes the same mistakes as made in the past
5. My organisation's decision-making is influenced by external stakeholder's demands	5 My organisation's decision-making is influenced by the vested interest of individuals
6. My organisation qualifies the probability of success in its decision-making	6 My organisation underestimates problems which adversely impacts its own decision-making
7. My organisation quantifies the probability of success in its decision-making	7 My organisation continues with projects which should be terminated at an earlier stage
8. My organisation is open to using better alternatives in its decision-making	8 My organisation's decision-making is influenced by competitors
9. My organisation encourages innovative decision-making	9 My organisation's decision-making is influenced by incentives or penalty payments
10. My organisation considers uncertainties in relation to its decision-making	10 My organisation effectively communicates the decisions it makes
11. My organisation provides training in the science of decision-making	11 My organisation provides clear and unambiguous instructions for decision-making
12. My organisation re-examines its decision-making as new information becomes available	

Organisational Level Influence Items: Decision-Making Approach Construct

Descriptive statistics, reliability testing and correlation testing on the 12 items in the organisational decision-making construct were performed. A tabular summary of the reliability and correlation testing on the 12 items is presented in Table 6.2.

The Cronbach's alpha level indicative of reliability, calculated for the 12 item construct was 0.731 (0.749 based on standardised items) which was "good". The KMO value of 0.726 was also acceptable / "strong" result. The Bartlett's test result was 55. The average ICC was 0.790. These results demonstrated adequate sample size for the analysis and good reliability from Cronbach's alpha, the other reliability tests and ICC results obtained.

Table 6.2: Summary results for the statistical testing performed on the 12 organisational approach items

Reliability Assessment (r)	**Intraclass Correlation Coefficient (ICC)**	**KMO (Sampling Adequacy)**	**Spearman's 2-tailed correlation**
Cronbach's α: 0.821 (0.786 std)	0.790 (avg. measure 95% CI p=.0001)	0.754	YES
Split-half: 0.734 / 0.51	0.790 (avg. measure 95% CI p=.0001)		
Parallel: 0.790 (0.794 unbiased)	0.790 (avg. measure 95% CI p=.0001)		
Guttman Split-Half Coefficient 0.773	0.790		

The nonparametric Spearman's correlation matrix generated for the 12 organisational approach variables is presented in Table 6.3. The data demonstrated the inter-correlation relationship of each of the items (positive and negative as testing was performed using a 2-tailed test). The results showed the statistical associations between any two of the variables. The V1-V12 items are as numbered in Table 6.1.

Table 6.3: Spearman's correlation inter-item correlation matrix for 12 organisational approach items

	V1	V2	V3	V4	V5	V6	V7	V8	V9	V10	V11	V12
V1 My organisation evaluates the impact of the decisions it makes	**1.00**											
V2.My organisation's decision-making approach is transparent	0.209*	**1.00**										
V3 My organisation's decision-making is consistent	0.125	0.13	**1.00**									
V4 My company uses a structured approach in its decision-making	0.057	0.11	-.117	**1.00**								
V5 My organisation's decision-making is influenced by external stakeholder's demands	0.188	.137	.042	0.45	**1.00**							
V6 My organisation qualifies the probability of success in its decision- making	0.134	0.155	0.131	0.162	0.185	**1.00**						
V7 My organisation quantifies the probability of success in its decision-making	0.175	0.134	0.177	.058	0.153	0.644	**1.00**					
V8 My organisation is open to using better alternatives in its decision-making	0.254**	0.450**	0.006	.02**	.252**	0.106	.139	**1.00**				
V9 My organisation encourages innovative decision-making	0.211**	0.351**	-.052	-.026	.120**	-.163	0.046*	0.336	**1.00**			
V10 My organisation considers uncertainties in relation to its decision-making	0.219*	0.290**	-.044	-.002	.194**	0.335	0.281*	0.216**	0.311	**1.00**		
V11 My organisation provides training in the science of decision-making	0.211*	0.061*	0.54	-.092	0.205	0.275	0.331*	0.184	0.062	0.392	**1.00**	
V12 My organisation re-examines its decision-making as new information becomes available	0.223*	0.255**	-.157	.098	.157**	0.181	0.061*	0.322**	0.322**	0.310	0.157	**1.00**

* Correlation is significant at the 0.01 level ** Correlation is significant at the 0.05 level

Organisational Level Influence Item: Decision-Making Culture Construct Results

Descriptive statistics, reliability testing and correlation testing were performed on the 11 items in the organisational decision-making approach construct. A tabular summary of the reliability and correlation testing and results on the 11 items are presented in Table 6.4.

The Cronbach's alpha level indicative of reliability was calculated for the 11 organisational culture construct was 0.741 (and 0.719 based on standardised items) which was "good". The KMO value of 0.846 was also acceptable / "very strong" result. The Bartlett's test result was 55 and the average ICC 0.743. These results demonstrated adequate sample size for the analysis and good reliability from Cronbach's alpha, the other reliability tests and ICC results obtained.

Table 6.4: Summary results for the statistical testing performed on the 11 "culture" items

Reliability Assessment (r)	**Intraclass Correlation Coefficient (ICC)**	**KMO (Sampling Adequacy)**	**Spearman's 2-tailed correlation**
Cronbach's α: 0.743 (0.719 std)	0.743 (avg. measure 95% CI p=.0001)	0.846	YES
Split-half: 0.802 / 0.06	0.743 (avg. measure 95% CI p=.0001)		
Parallel: 0.743 (0.748 unbiased)	0.731 (avg. measure 95% CI p=.0001)		
Guttman Split Half Coefficient 0.469			

The nonparametric Spearman's correlation matrix generated for the 11 organisational construct variables is presented in Table 6.5. The data demonstrated the inter-correlation relationship of each of the items (positive and negative as testing was performed using a 2 tailed test). The results showed the statistical associations between any two of the variables. The V1-V11 items are as numbered in Table 6.1.

Table 6.5: Spearman's correlation inter-item correlation matrix for 11 organisational culture items

	V1	V2	V3	V4	V5	V6	V7	V8	V9	V10	V11
V1 : My organisation's decision-making is influenced by company politics	**1**										
V2: My organisation has suffered a negative outcome due to slow decision-making	.537	**1**									
V3: My organisation's culture has resulted in its inability to make a decision.	.296**	.446	**1**								
V4: In my organisation's decision-making, it makes the same mistakes as made in the past	.266*	.279**	.271	**1**							
V5 My organisation's decision-making is influenced by vested interest of individuals	.291**	.197**	.293**	.653**	**1**						
V6 My organisation underestimates problems which adversely impacts its own decision-making	.395**	.320*	.287	.321	.202*	**1**					
V7 My organisation continues with projects which should be terminated at an earlier stage	.307	.281**	.202	.379	.286**	.566**	**1**				
V8 My organisation's decision-making is influenced by competitors	.324**	.422**	.207	.324**	.277**	.413*	.507**	**1**			
V9 My organisation's decision-making is influenced by incentives or penalty payments	.309**	.330**	.202	.312**	.196**	.520*	.449**	.513**	**1**		
V10 My organisation effectively communicates the decisions it makes	-.24**	-.41**	-.211	.288**	.005**	-.197*	.073**	.161**	-.118	**1**	
V11:My organisation provides clear and unambiguous instructions for decision-making	.378	.154	.202	.392	.482	.353*	.284	.309	.301	.232	**1**

* Correlation is significant at the 0.01 level ** Correlation is significant at the 0.05 level

Individual Level Influences Results

The two individual level decision-making influence dimensions which were reported post factor-analysis were tested for construct validity (Table 6.6).

The statistical results for Cronbach's alpha, KMO and Bartlett's test for the 24 item individual level influences in the two constructs were determined: the Cronbach's alpha calculated for the 24 item instrument constructs was 0.785 which was "good". The KMO value of 0.751 was also acceptable. The Bartlett's test was 276. The average measure ICC was 0.785. These results demonstrated adequate sample size for the analysis and good reliability from the Cronbach's alpha and ICC results obtained.

Table 6.6: Individual level influences

Individual Decision-Making Competence Dimension (14 items)	**Individual Decision-Making Style Dimension (10 items)**
1. I quantify the probability of success in my decision-making 2. I qualify the probability of success in my decision-making 3. I understand the context of the decision I am being asked to make 4. I consider uncertainty and unknowns in my decision-making approach 5. I present contingencies or achievable options as part of my decision-making 6. My decision-making is consistent 7. My decision-making approach is transparent 8. I use a structured approach in my decision-making 9. My decision-making is knowledge based 10. I understand the importance of the decisions I make 11. My professional experience is important when having to make challenging decisions. 12. I generate a SWOT (strengths, weaknesses, opportunities, threats) analysis in my decision-making 13. I receive training in the science of decision-making 14. I use intuition or "gut-feeling" in my decision-making	1. My procrastination has resulted in a negative outcome 2. I have experienced "paralysis by analysis" caused by my slow decision-making 3. Emotion is part of my decision-making 4. I have experienced a negative outcome by a decision not being made 5. In my decision-making, I make the same mistakes as made in the past 6. Recent or dramatic events greatly impact my decision-making 7. My decision-making could be improved by assigning weights 8. I underestimate problems which adversely impact my decision-making 9. I continue with projects which should be terminated at an earlier stage 10. I feel that I could make better quality decisions

Individual Level Influence Item: Decision-Making Competence Construct

Descriptive statistics, reliability testing and correlation testing on the 14 items in the individual decision-making competence construct were performed. A tabular summary of the reliability and correlation testing performed on the 14 items is presented in Table 6.7.

The Cronbach's alpha level, for the 14 item construct was 0.731 (and 0.749 based on standardised items) which was "good". The KMO value of 0.726 was also an acceptable/good result. The Bartlett's test result was 55. The average ICC was 0.743 (good). These results demonstrated adequate sample size for the analysis and good reliability from Cronbach's alpha, the other reliability tests and ICC results obtained.

Table 6.7: Summary results for the statistical testing performed on the 14 "competence" items

Reliability Assessment (r)	Intraclass Correlation Coefficient (ICC)	KMO (Sampling Adequacy)	Spearman's 2-tailed correlation
Cronbach's α: 0.731 (0.749 std)	0.731 (avg. measure 95% CI p=.0001)	0.726	YES
Split-half: 0.517 / 0.739	0.731 (avg. measure 95% CI p=.0001)		
Parallel: 0.731 (unbiased .736)	0.731 (avg. measure 95% CI p=.0001)		

The nonparametric Spearman's correlation matrix generated for the 14 individual decision-making influence variables is presented in Table 6.8. The data demonstrated the inter-correlation relationship for each of the items (positive and negative as testing was performed using a 2-tailed test). The results showed the statistical associations between any two of the variables. The V1-V14 items are as numbered in Table 6.8.

Table 6.8: Spearman's correlation inter-item correlation matrix for 14 individual competence items

	V1	V2	V3	V4	V5	V6	V7	V8	V9	V10	V11	V12	V13	V14
V1: I quantify the probability of success in my decision-making	**1**													
V2: I qualify the probability of success in my decision-making	.209*	**1**												
V3 I understand the context of the decision I am being asked to make	-.125	.13	**1**											
V4 I consider uncertainty and unknowns in my decision-making approach	.057	.11	.117	**1**										
V5: I present contingencies or achievable options as part of my decision-making	.188*	.137	,042	.045*	**1**									
V6 My decision-making is consistent	.134	.155	.131	.162	.185	**1**								
V7: My decision-making approach is transparent	.175	.134	.177	.058	.153	.644	**1**							
V8: I use a structured approach in my decision-making	.254**	-.450**	.006	,020**	.252**	.106	.139**	**1**						
V9: My decision-making is knowledge based	.211*	-.351**	-0.52	-.026*	.120**	-.163	.046*	.336**	**1**					
V10 I understand the importance of the decisions I make	.219*	.290**	-.044	-.020*	.194**	-.335	.281*	.216**	.311	**1**				
V11 My professional experience is important when having to make challenging decisions.	.211*	.061	.054	.092*	.205	.275	.331*	.184	.062	.392*	**1**			
V12 I generate a SWOT (strengths, weaknesses, opportunities, threats) analysis in my decision-making	.223*	.255**	-.157	.098*	.157**	.181	.061*	.322**	-.323	.310*	.157	**1**		
V13 I receive training in the science of decision-making	.154	.280*	.262*	-.222	.118*	.114	.81	.371*	.350	.382	.103*	.225	1	
V14: I use intuition or "gut-feeling" in my decision-making	.323*	.258	-.085	.005*	.144	.158	.107*	.334	.196	.303*	.187	.384	.257*	1

* Correlation is significant at the 0.01 level ** Correlation is significant at the 0.05 level

Individual Level Influence Item: Decision-Making Style Construct Results

The Cronbach's alpha calculated for the ten item construct was 0.731 (and 0.749 based on standardised items) which was "good". The KMO value of 0.726 was also an acceptable/good result. The Bartlett's test result was 55. The average ICC was 0.743 (good). These results demonstrated adequate sample size for the analysis and good reliability and from Cronbach's alpha, the other reliability tests and ICC results obtained.

Table 6.9: Summary results for the statistical testing performed on the 10 items

Reliability Assessment (r)	Intraclass Correlation Coefficient (ICC)	KMO (Sampling Adequacy)	Spearman's 2-tailed correlation
Cronbach's α: 0.822 (0.825 std)	0.822 (avg. measure 95% CI p=.0001)	0.832	YES
Split-half: 0.758 / 0.693	0.822 (avg. measure 95% CI p=.0001)		
Parallel: 0.822 (unbiased .825)	0.822 (avg. measure 95% CI p=.0001)		

The nonparametric Spearman's correlation matrix generated for the 10 individual style variables is presented in Table 6.9. The data demonstrated the inter-correlation relationship for each of the items (positive and negative as testing was performed using a 2-tailed test). The results showed the statistical associations between any two of the variables. The V1-V10 items are as numbered in Table 6.10.

Table 6.10: Spearman's correlation inter-item correlation matrix for the individual style items

	V1	V2	V3	V4	V5	V6	V7	V8	V9	V10
V1: My procrastination has resulted in a negative outcome	**1**									
V2 I have experienced "paralysis by analysis" caused by my slow decision-making	.177	**1**								
V3 Emotion is part of my decision-making	.351**	.363**	**1**							
V4 I have experienced a negative outcome by a decision not being made	.350**	.357**	.680**	**1**						
V5 In my decision-making, I make the same mistakes as made in the past	.226*	.366**	.477**	.517*	**1**					
V6 Recent or dramatic events greatly impact my decision-making	.178	.155	.311**	.291*	.235	**1**				
V7 My decision-making could be improved by assigning weights	.126	.334**	.382**	,364*	.296**	.335**	**1**			
V8: I underestimate problems which adversely impact my decision-making	.254**	.128	.380**	.437**	.290	.233**	.346**	**1**		
V9: I continue with projects which should be terminated at an earlier stage	.274**	.141	.275**	.212**	.309	.471**	.226**	.227	**1**	
V10: I feel that I could make better quality decisions	.332**	.311**	.383**	.424**	.410**	.312**	.305**	.314**	.416**	**1**

* Correlation is significant at the 0.01 level ** Correlation is significant at the 0.05 level

The MTMM matrix is an established technique for looking at convergent and discriminant validation simultaneously (Streiner and Norman, 2008; Trochim, 2006). The matrix facilitates the interpretation of construct results and presents the pattern of observation results across the constructs tested using the different statistical methodologies employed. The MTMM matrix generated from the different statistical test methods used in the QoDOS construct validation is presented in Table 6.11. The matrix pattern demonstrates the convergent nature of construct results obtained with high values for Cronbach's alpha and ICC reliability of the individual measures across all four constructs using the "homotrait–hetromethod" correlations. The matrix graphically demonstrates that the internal consistency measured by Cronbach's α was > 0.73 for all the four construct scales. The ICC was also >0.73 for all four constructs. In addition, the discriminatory nature of the testing is evident from the low correlation results across the inter-item correlations throughout the four different constructs.

Table 6.11: Multi-Trait Multi-Method for QoDOS construct validity

	ODMA	ODMC	IDMC	IDMS
Cronbach's α	0.786			
ICC	0.790	0.743		
Parallel reliability	0.793	0.743	0.731	
Inter-item Covariances (mean)	0.284	0.743	0.731	0.822
Inter-item correlations (mean)	0.250	0.253	0.731	0.832
Spearman-Brown Coefficient (Split-half)	0.65 (equal) 0.79 (unequal)	0.189	0.132	0.822
		0.62 (equal) 0.62 (unequal)	0.176	0.279
			0.58 (equal) 0.58(equal)	0.320
				0.76 (equal) 0.76 (unequal)

ODMA = Organisational decision-making approach, ODMC = Organisational decision- making culture
IDMC = Individual decision-making competence IDMS = Individual decision-making style

Additional evidence of validity was demonstrated graphically from of Box-and-Whisker profiles generated as part of the quantitative analyses.

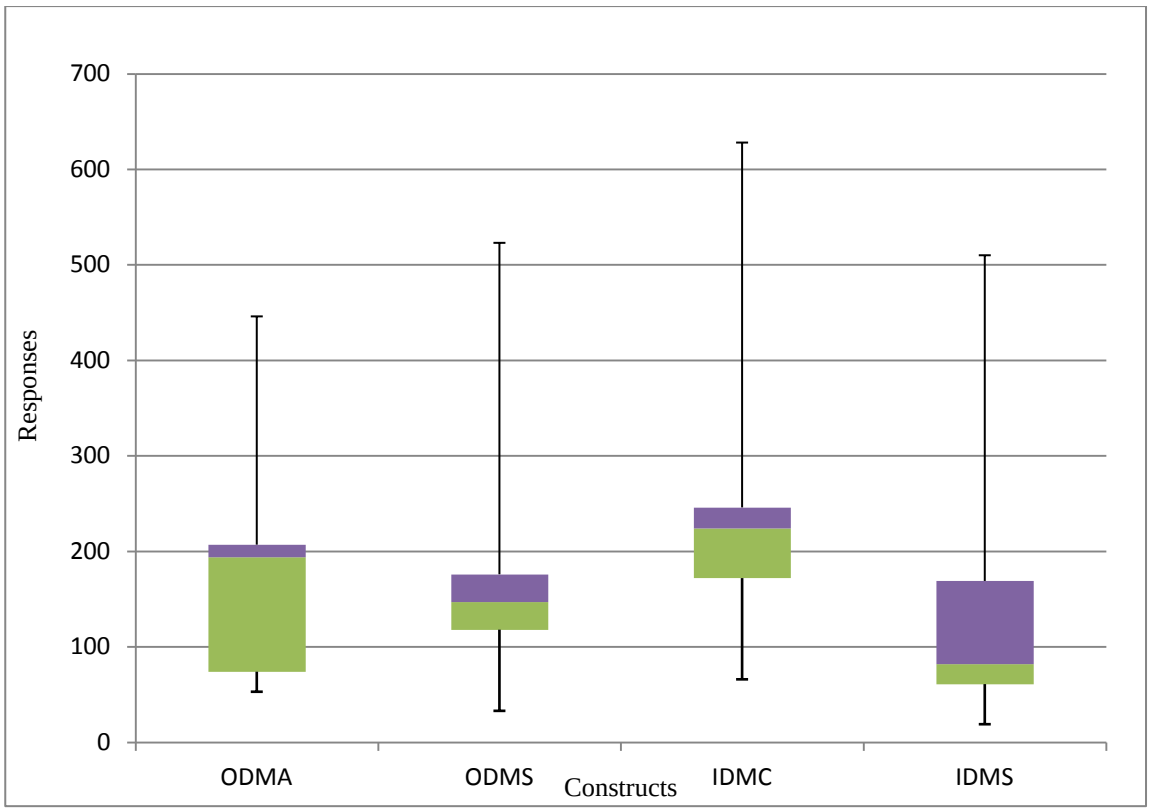
Quantitative Results: Organisation and Individual Related Item Responses

The data from the 78-person research sample provided quantitative insights into the decision-making approaches from the perspective of the individual and the organisations and was complimentary to the 120 person research sample results detailed in Chapter 5. The results allowed a quantification of the Likert scale ratings for each questionnaire item. In addition, it was possible to separate the composite results into two distinct categories: those responses which were answered from the Organisational perspective and those which were responded to from the perspective of the Individual.

The results provided insight of differing construct dimensions between decision-making influences and behaviours for Organisations and that of Individuals. The results also showed the discriminatory nature of the organisational and individual findings. Using a 'Box-and-Whisker' plot technique, a graphical comparison of the results for each of the four constructs was generated. The plot graphically describes the shape and characteristics of the distribution of the data from the QoDOS component construct analyses. The length of the box corresponds to the interquartile range (IQR) which is the difference (measure of dispersion) between the 75% and 25% percentile. The plot shows the range in distribution of responses for each construct. The median line (green/purple interface) describes the central tendency of the scores. The differing distribution of the results for each of the four constructs is shown in the Box-and-Whisker plot presented in Figure 6.1. The plot also allows for the organisational decision-making approach (ODMA) to be compared with the organisation decision-making-culture (ODMC) and for the Individual decision-making competence (IDMC) to be compared with Individual decision-making style (IDMS). In the plot of the QoDOS constructs, the length of the box tells us the spread or variability of the results for each of the four constructs. The range of results is shown by the length of the whiskers. The results show that the ODMS presents a symmetrical distribution within the IQR. For the ODMA, IDMC and IDMS results, there is a non-symmetrical distribution and the medians are not in the centre of

the IQR boxes. These indicate the 'skewness' of the results. The IDMS results with a median that is closer to the bottom of the box than the top, demonstrates 'positively skewed' data. For The ODMA and the IDMC, the median is closer to the top and shows "negatively skewed" data.

Figure 6.1: Box-and-Whisker plot of QoDOS construct result loadings' distribution



The Box-and-Whisker comparisons of the four plots indicate the range and spread and discriminatory patterns of results for each of the constructs.

The construct investigation results of the 78-person research sample provided further insight into the decision-making approach, behaviours and influences from the perspective of the individual and their organisation. In addition, to the analyses performed on the composite sample, each component item of the questionnaire for 23 organisational items and the 24 individual items was analysed. A selection of four of the organisational item response results and four individual related item response results are presented in Figures 6.2 - 6.9 respectively.

The results obtained infer that a structured approach to decision-making is not used routinely in 37 % (not at all /sometimes) of decision-making exercises (Figure 6.2). This 37% level and especially the 12% 'not at all' is surprising and infers that there is the potential for improvement in the organisational decision-making and promotion of a systematic or framework approach for quality decision-making.

Figure: 6.2: My organisation uses a structured approach in its decision-making

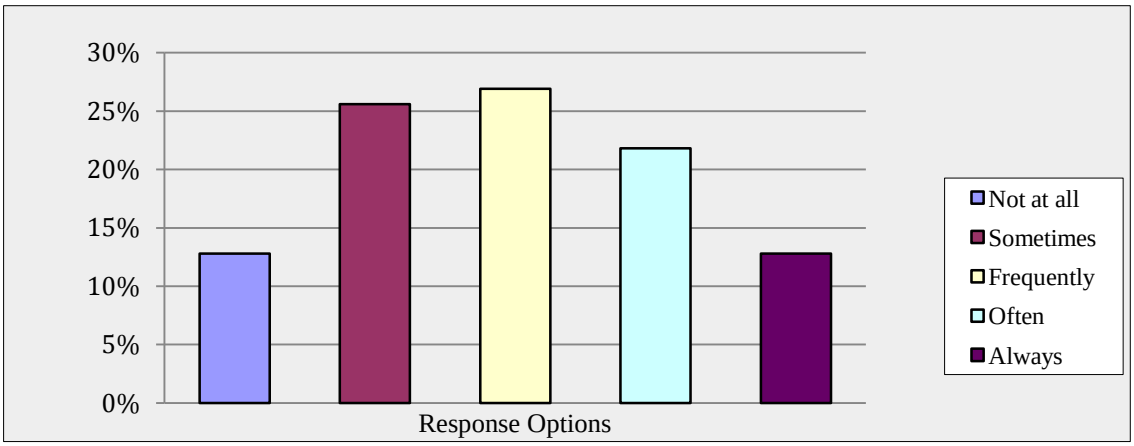
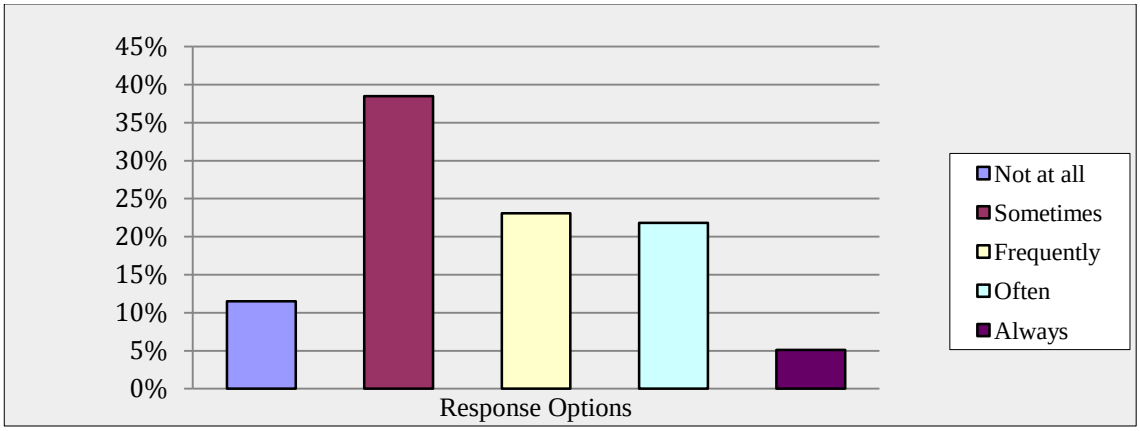


Figure 6.3: My organisation quantifies the probability of success in its decision-making

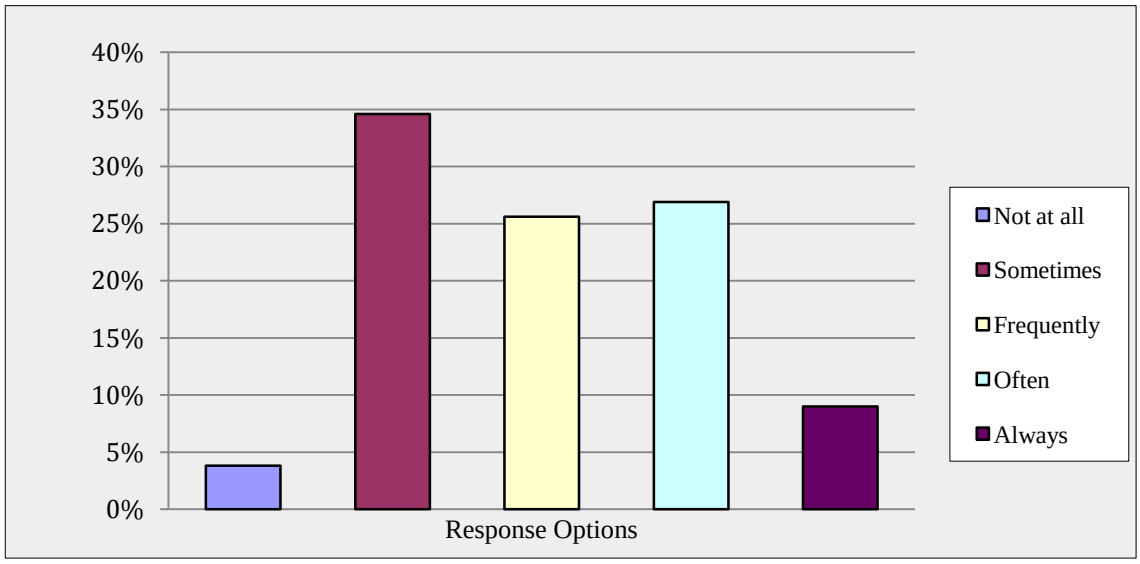


The strategy of trying to quantify the probability of success (Figure 6.3) appears to be the routine approach in only about 5% of situations and is performed in around 45% of other situations on a " frequently/often" basis and 'not at all' in 11% of cases. This result is something of an enigma as it infers that decision-makers are not trying to

quantify either the probability of success or by inference the probability of failure and associated risk factors. The results could be interpreted as indicating a naivety of both good business and decision-making. If the 12% cohort is not taking success probability into account then it is unlikely that they are considering additional factors both internal and external that could influence or impact the decision. The use of a systematic approach in this 11% cohort is questionable.

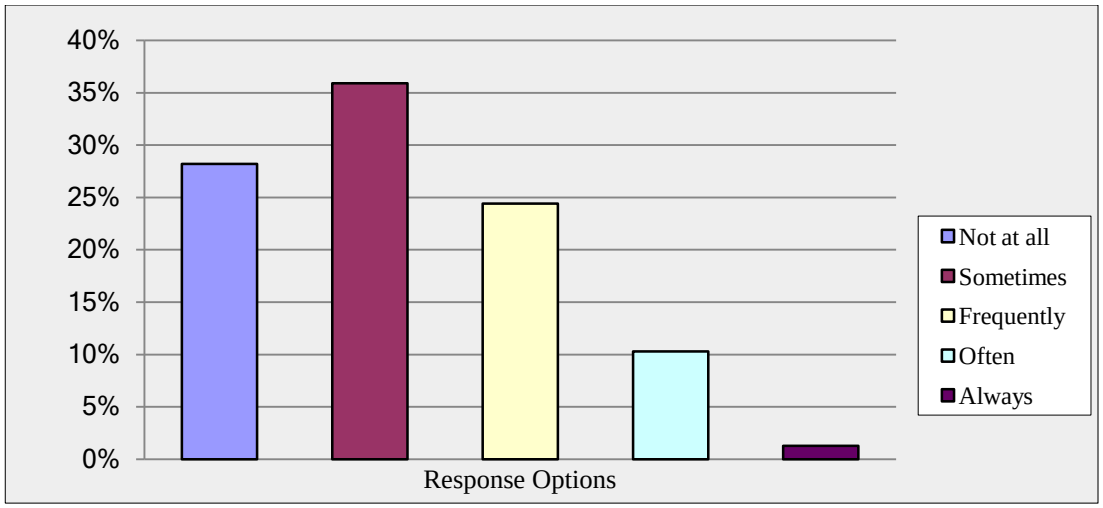
It would appear that re-examination of decision-making as new information is received (Figure 6.4) only on occurs a "sometimes" basis around 38% and may not occur in some rare exceptions (<5%). The results could infer that re-evaluation is occurring on a routine basis (often/always) in at least 35% of cases but also means there is room for an improved approach.

Figure 6.4: My organisation re-examines its decision-making as new information becomes available



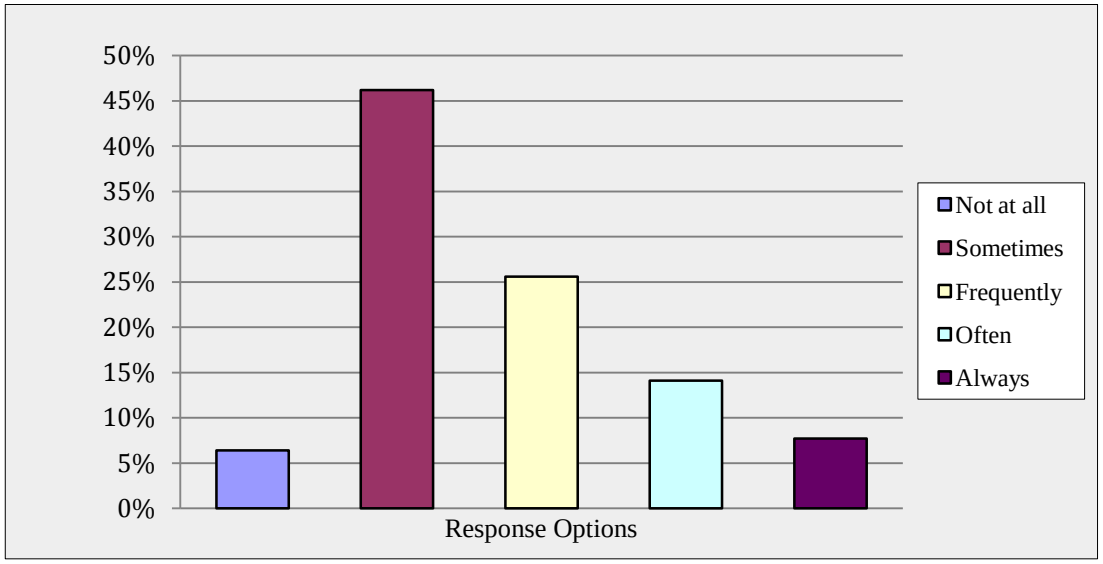
The culture of the organisation was seen to be an influencing factor in decision-making with only 27% of responses indicating that the culture did not impact at all in its ability to make a decision (Figure 6.5). These results imply that the culture of the organisation is a key decision-driver.

Figure 6.5: My organisation's culture has resulted in its inability to make a decision



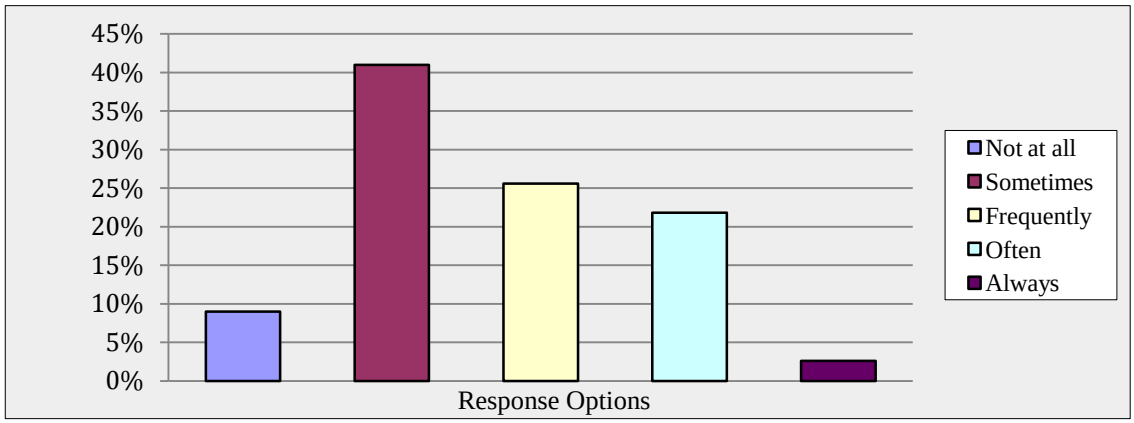
In regard to the potential to make better quality decision, almost 95% of the response indicated that individuals felt that their decision-making could be improved (Figure 6.6).

Figure 6.6: I feel that I could make better quality decisions



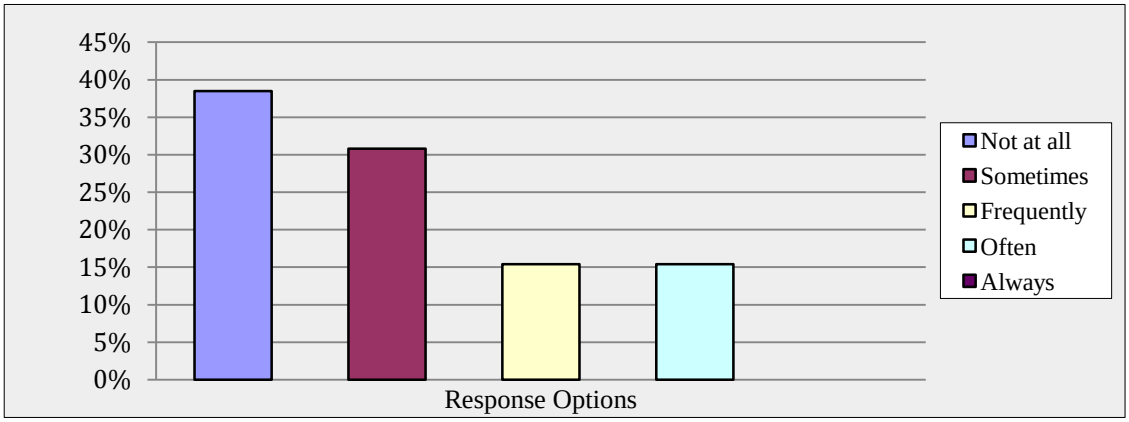
The results on the use of intuition or "gut-feeling" showed that its usage is quite common and that less than 10% of individuals would appear not to use it in their decision-making approach (Figure 6.7). This is an interesting result when one considers again the evidence-driven environment of medicines development, although it could be argued that intuition is taking evidence based outcomes into account implicitly.

Figure 6.7: I use intuition or "gut-feeling" in my decision-making



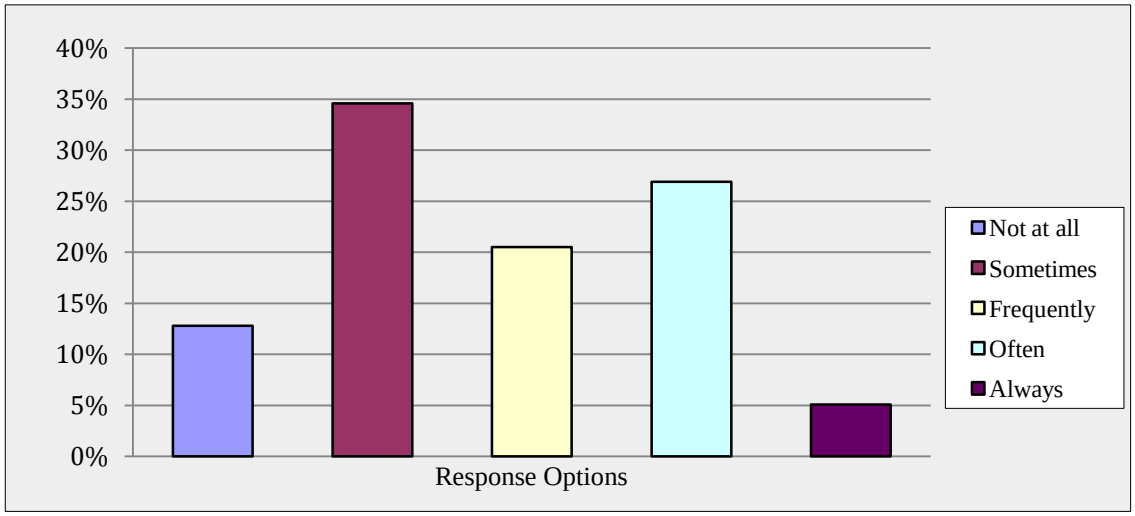
More than 35% of study participants indicated that they had not received any training in the science of decision-making (Figure 6.8). Only 15% of persons advise that they received training on an "often" (regular) basis (Figure 6.8). This is an interesting and disappointing finding when one considers the increased industry and agency support for a more structured approach to decision-making and the availability and usage of qualitative and quantitative decision-making tools.

Figure 6.8: I receive training in the science of decision-making



The well established technique of using a SWOT analysis in decision-making appears to be never considered by 12% of individuals. Another 35% only use the SWOT on a "sometimes" basis. This could infer that the individuals surveyed are not familiar with the SWOT tool and this might link to the results relating to the training offered and received (Figure 6.9).

Figure 6.9: I generate a SWOT analysis in my decision-making

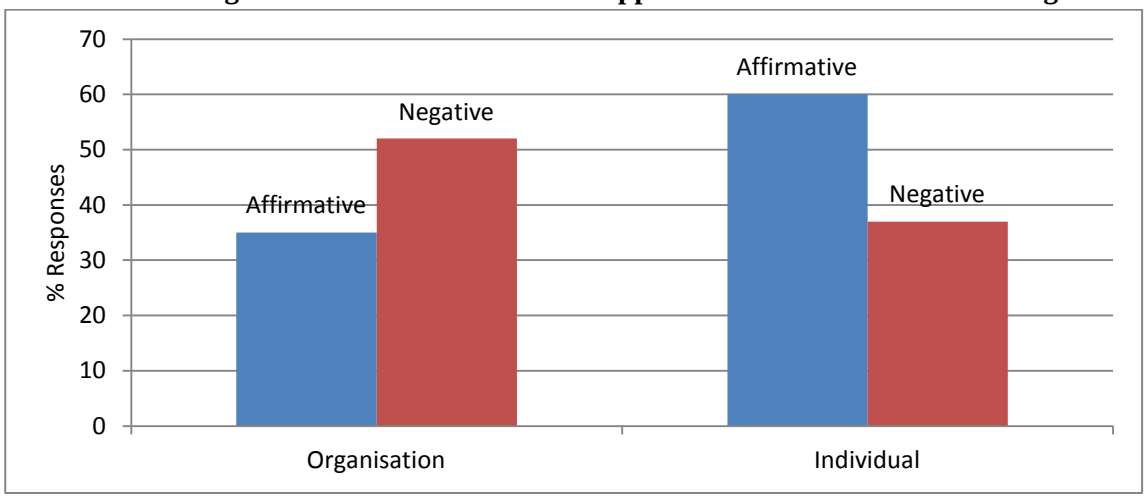


Organisation Versus Individual Analysis

A comparative analysis of the decision-making approach of the Organisation versus that of the Individual was performed. The results were paired on the basis of positive/affirmative and negative responses received for each of the QoDOS questions. The results provided insights into the differing importance and approach of both groups. A sample of four comparisons is presented in Figures 6.10 – 6.13.

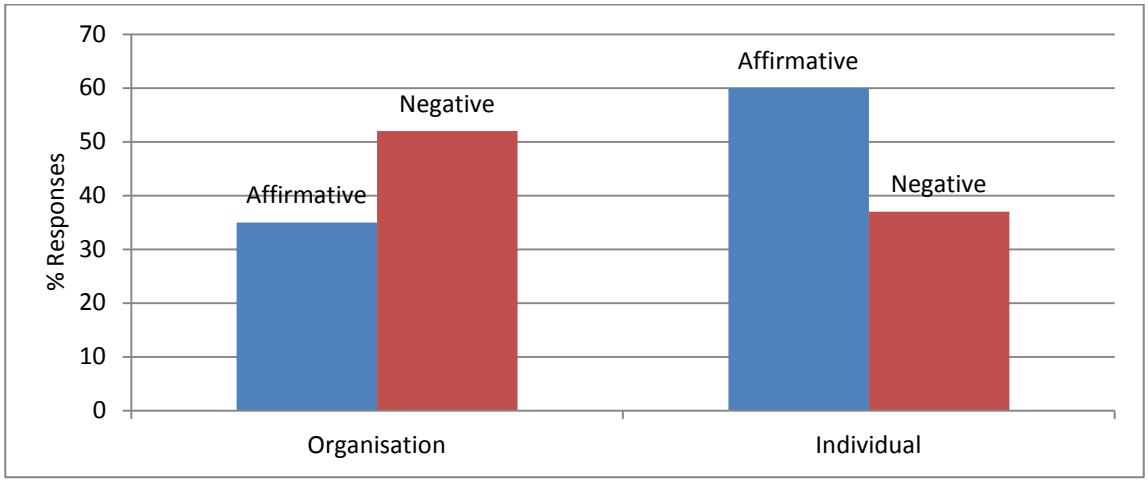
The results indicate that a structured approach is employed more at an individual level (60%) than at the organisational level (35%) (Figure 6.10).

Figure 6.10: Use of a structured approach is used in decision-making



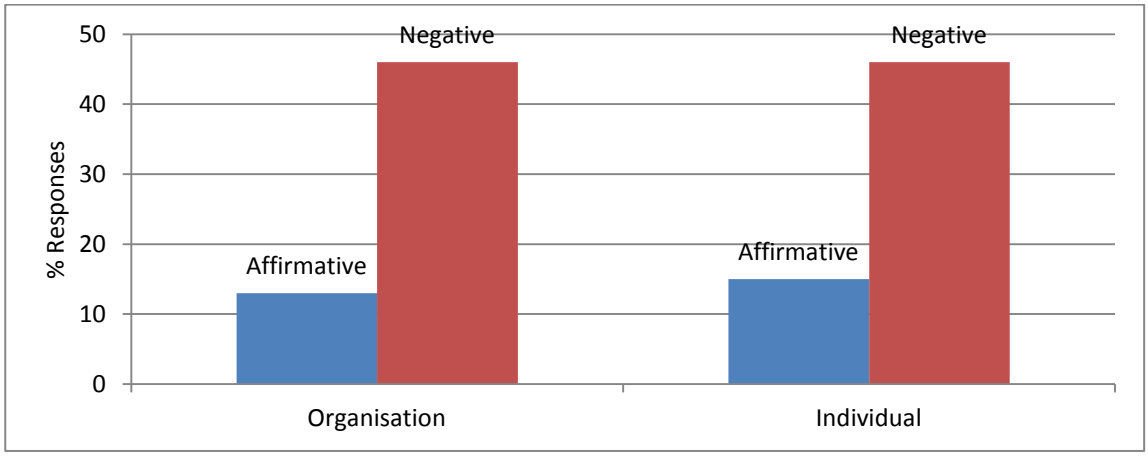
In regard to quantifying the probability of success in decision-making, the results inferred that less quantification was performed by organisations as compared to the approach by persons at an individual level (Figure 6.11). This could relate to factors such as a person being more accountable at a micro-level for the decisions they make as compared to the organisation on a macro-level, or indeed, their perception of the situation.

Figure 6:11: Quantification of the probability of success in decision-making by the organisation and the individual



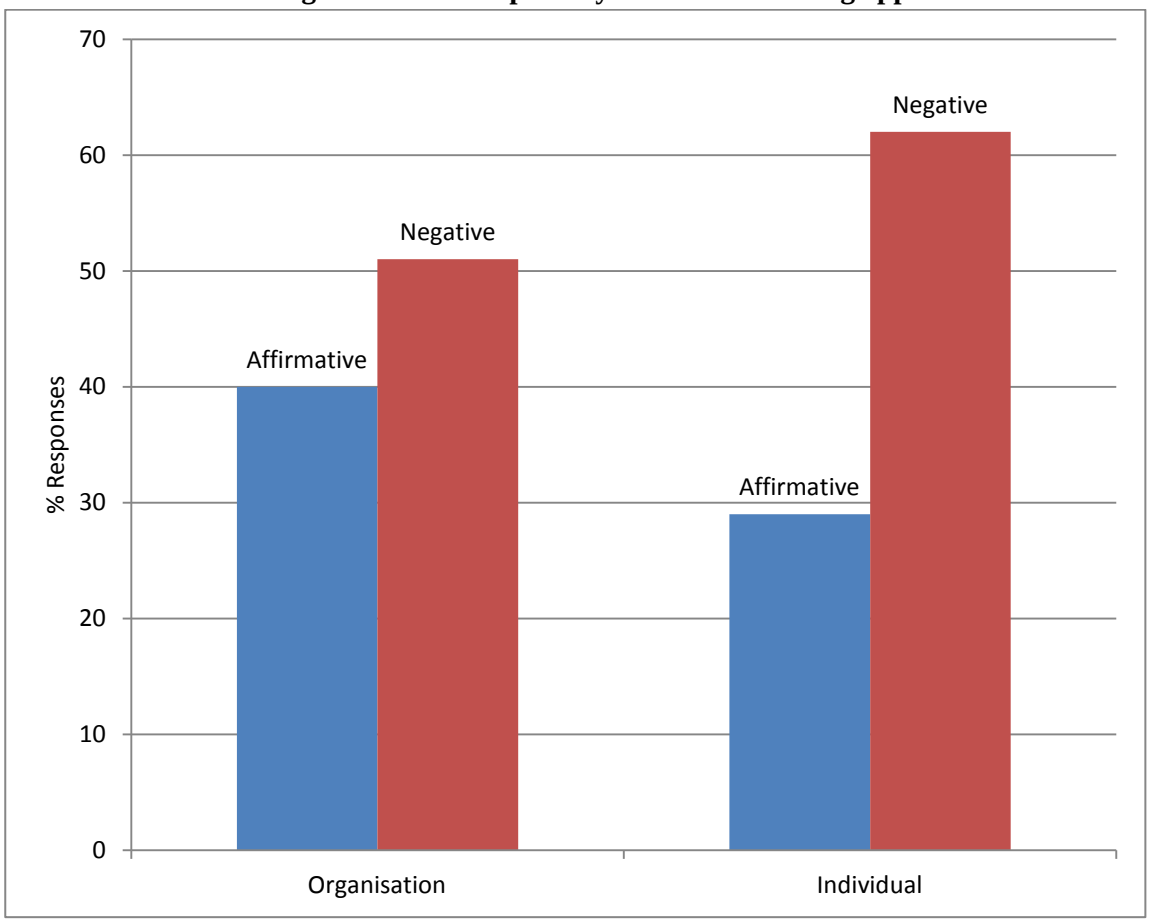
The research into training in the science of decision-making showed that only 15% of individuals within the research sample had received training in 'decision-making' which was similar to the percentage of organisations that had provided training in decision-making (Figure 6.12).

Figure 6.12: Training in the science of decision-making



Transparency in decision-making showed that there was more transparency in the approach of the organisation compared with that of the individual (Figure 6.13). This could be as a result of the widespread usage of defined work practices and quality management systems, Standard Operating Procedures (SOPs), templates, decision-analysis tools within many organisations. The results also infer that a high level of subjective non-structured approaches may be in use at the level of the individual.

Figure 6.13: Transparency in decision-making approach



The comparative analyses revealed that QoDOS was able to differentiate the decision-making behaviours of organisations from that of the individual. It also provided additional insights into the weighting or relative importance of decision-making factors from the perspective of both groups.

Hallmarks of Good Decision-Making Practice

The qualitative research into decision-making approaches of the individual and the organisation resulted in the identification of 19 main decision-making themes:

1. Quality and validity of data
2. Time considerations
3. Organisational, hierarchical and cultural influences
4. Analytical and logical approach
5. Qualification and experience in previous decision-making
6. Subjective and personal considerations
7. Political, financial, competitor and reward influences
8. Precedents for similar previous decisions
9. Perpetuating previous decision-making mistakes
10. Plunging in or procrastination with decision-making
11. Clear understanding or lack of understanding of the decision in question
12. Overconfidence in own judgement
13. Group successes and group failures
14. SWOT and alternate outcome planning in decision-making
15. Impact analyses of decisions
16. Decision-making audit trail
17. Education and awareness of evolving decision-making techniques
18. Individual versus Corporate decision-making
19. Quantitative frameworks.

It was hypothesised that the 19 emergent decision-making themes could also provide insight into the ‘Hallmarks of good decision-making’, so these 19 themes were reviewed and distilled into 10 good decision-making criteria. These were then mapped against the 47-items in the final version of the QoDOS (Table 6.12).

Table 6.12: Mapping of the QoDOS items to the hallmarks of good decision-making practice.

Good decision-making practice hallmark	QoDOS item number mapped to each hallmark
1. Employ scientific rigour and understand the decision context	30,31
2. Apply knowledge and experience	6,9,11,24,27,33,35,37,47
3. Examine the integrity of information for validation and confidence in the decision	18
4. Use an objective approach and maintain awareness of your biases and preferences	36,38,39,43,45,46
5. Consider uncertainty and examine alternative solutions	8,10,26,28
6. Assign values and relative importance to decision criteria	7,34,44
7. Re-evaluate as new information becomes available	12
8. Evaluate both internal and external influences	5,13,14,15, 17, 19, 20, 21,40,42
9. Apply a structured approach to aid transparency and record trail	2,3,4,16, 25,29,32,41
10. Perform impact analysis and effectively communicate the basis of the decision	1,22,23

Validation of The Hallmarks

In order to provide further validity to the list of ten hallmarks, the research sample of 78 international senior industry and regulatory agency decision-makers were asked to rank the "relative importance" of the hallmarks. They ranked the ten hallmarks in order of what they perceived were the most important hallmarks to the least important hallmarks on a scale of 1 to 10 (1 being the most important and 10 being the least important). They were provided with appropriate notice and background on the research aim of ranking the hallmarks and with assurance of confidentiality.

Ranking of The 10 Hallmarks of Good Decision-Making Practice

The composite ranking order of the ten hallmarks was:

1st *Employ scientific rigour and understand the decision context*

2nd *Apply knowledge and experience*

3rd *Examine the integrity of information for validation and confidence in the decision*

4th *Apply a structured approach to aid transparency and record trail*

5th *Use an objective approach and maintain awareness of your biases and preferences*

6th *Re-evaluate as new information becomes available*

7th *Evaluate both internal and external influences*

8th *Assign values and relative importance to decision criteria*

9th *Perform impact analysis and effectively communicate the basis of the decision*

10th *Consider uncertainty and examine alternative solutions.*

The quantified results of the research were analysed and graphical presentations of the 10 hallmarks rating placements generated. The two top-rated items represented the opinion of the majority of the research sample with regard to the need to employ scientific rigour and to understand the decision context (24%) with the need to apply one's knowledge and experience (22%) in decision-making approach (Figures 6.14-6.15). The results of the ranking exercise did not demonstrate any one wholly outstanding decision-making hallmark.

Figure 6.14: Employ scientific rigour and understand the decision context (Top rating)

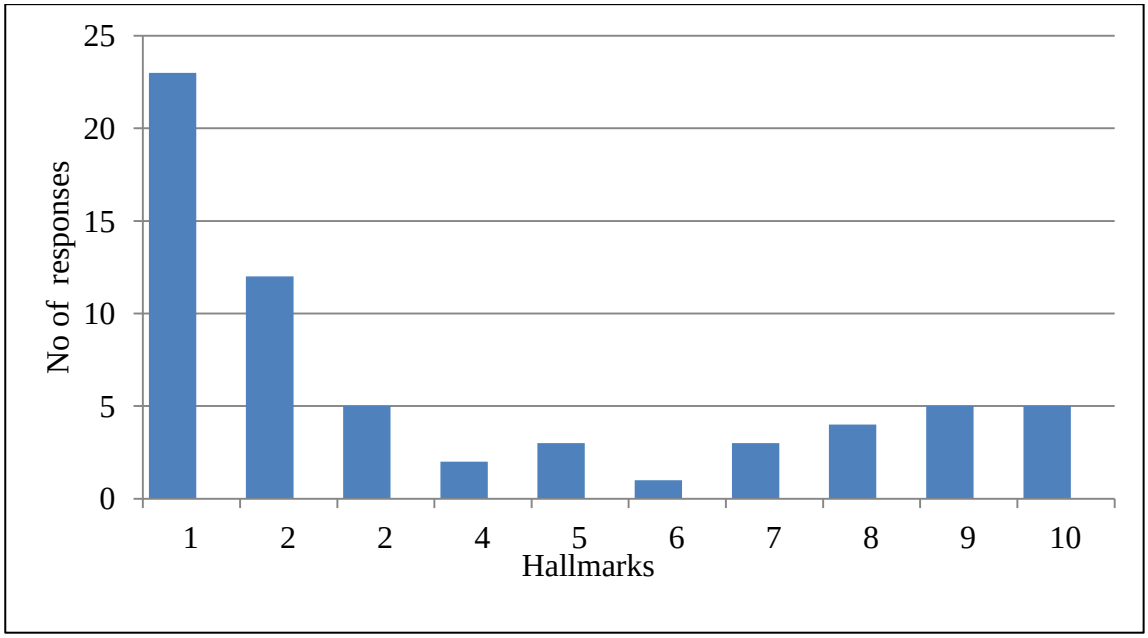
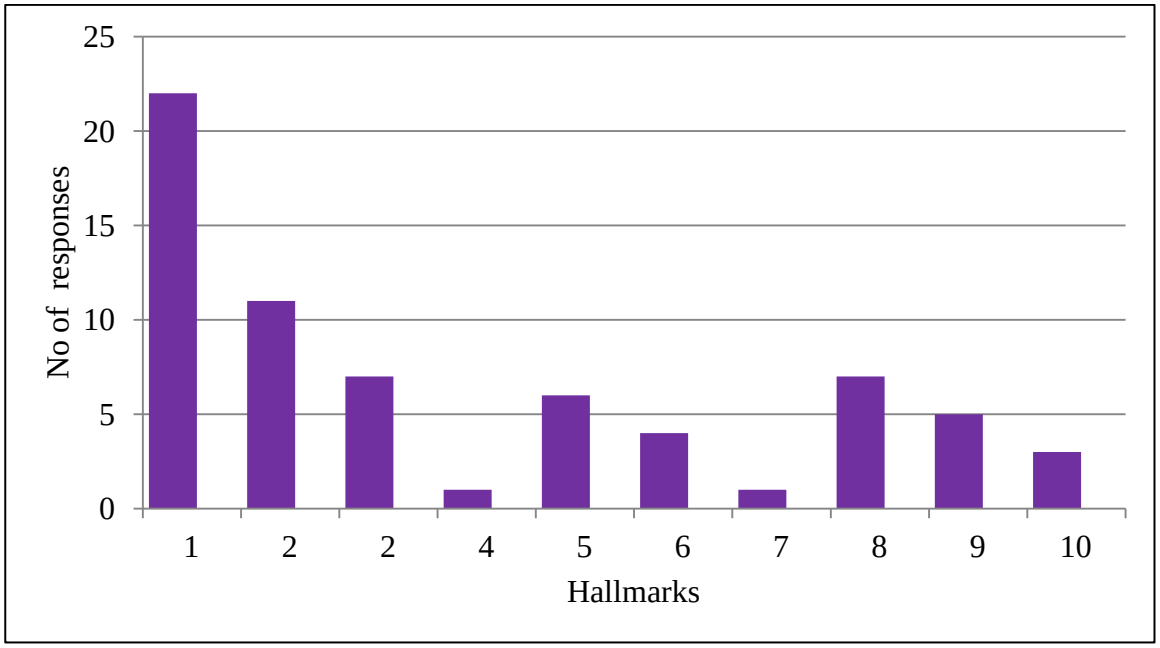


Figure 6.15: Apply knowledge and experience (2nd highest rating)



Application of QoDOS: An immediate application of QoDOS and the emergent hallmarks of good decision-making is the ability to generate a profile of an individual's decision-making approach. The 47 items in QoDOS have been mapped against the 10

hallmarks as presented in Table 6.12. An algorithm has been generated to apply weightings to each hallmark of good decision-making practice. Each hallmark component sub-theme has an associated weighting score range of 1-4 (1= sometimes, 2=frequently, 3=often and 4=always). For each hallmark, a theoretical value for best practice approach on the basis that a good hallmark's approach should be pursued all of the time.

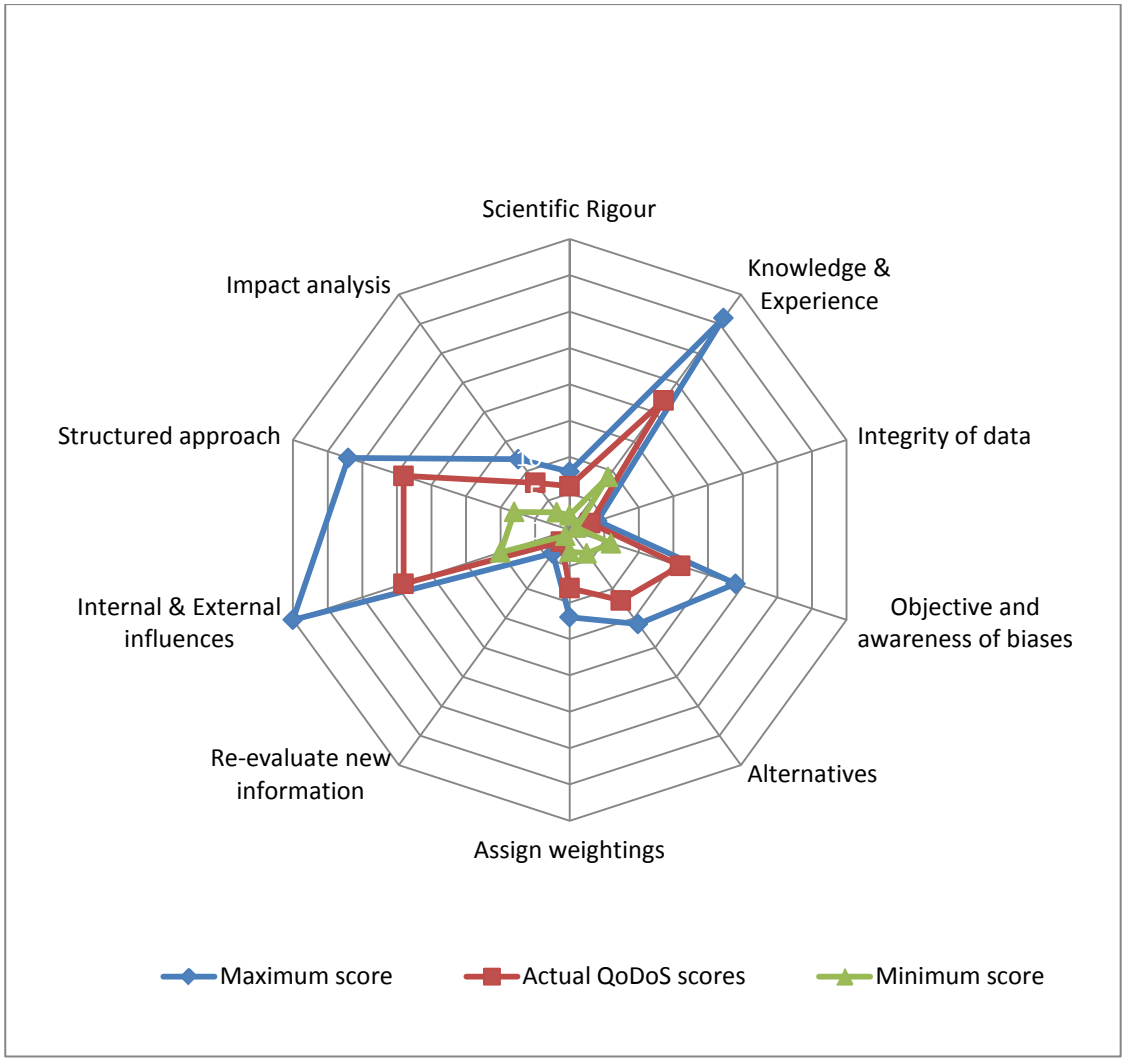
For any individual, their responses to the 47 items in the QoDOS instrument can be mapped to the hallmarks to present a profile of that person's decision-making approach using the algorithm above. This approach allows for a person's profile (for the day on which it was completed) to be generated from their actual response scores on a comparative scale. Their response score can be presented on an assessment scale showing theoretical optimum (maximum) and poor (minimum) profile results. This profiling allows for an individual to identify their normal approach to decision-making, their areas of strength in good decision-making practice and importantly, their areas warranting further attention and development. This profiling which is performed as a point in time assessment should allow an individual to monitor the changes in their decision-making approaches over time. An example of an actual profile for one of the participants in the research is presented in the spider plot in Figure 6.16.

The algorithmic approach to profiling an individual's decision-making technique using the QoDOS instrument is an easy to apply technique and should be generalisable outside of the research sample in which it has been developed. A simple spider-plot charting technique can be used to generate a profile of the decision-making responses, developmental areas and to provide a time-course record of the decision-making approach for a given individual. This graphical representation provides a focus for identification of gaps and issues to address in a person's decision-making approach (Figure 6.16).

The visualisation of an individual's decision-making profile may also enable better communication of the profile and of its interpretation. Such visualisation techniques of

decision-making outcomes are actively being progressed and their importance is increasingly being recognised (IMI-EFPIA, 2013a; Walker, 2011).

Figure 6.16: Decision-making profile of an individual



DISCUSSION

The QoDOS instrument underwent factor-analysis which yielded four main construct domains, two relating to organisation level influences i.e. organisational decision-making approach (ODMA), organisational decision-making culture (ODMC); and two to individual level influences i.e. individual decision-making competence (IDMC) and individual level decision-making style (IDMS). The 47-instrument items were grouped

into one of the four domains and assessed for appropriate reliability and construct validity.

Reliability and construct validity testing was performed on the QoDOS instrument and the four component constructs using statistical methodologies complimented by additional semi-quantitative techniques. For each of the four construct dimensions, reliability was tested and demonstrated using several reliability methods including Cronbach's alpha and ICC testing. In all four construct investigations, reliability was shown to be above a Cronbach's alpha of 0.73 and ICC of > 0.73 in a battery of tests. The consistency and reproducibility of the reliability finding across time as well as the different items and measurement methodologies used supported the assertion that appropriate reliability was observed. The reliability, the internal consistency and the ICC of the measures observed were also indicative of the homogeneity of the component items that tapped into each of the four constructs.

Construct validity testing is concerned with how well the results obtained from the use of a measure fit the theoretical foundations from which it is designed. Construct validation contains two validity sub-categories (convergent and discriminant validity). Convergent validity is the degree to which the concepts that should be related theoretically are interrelated in reality. Discriminant validity is the degree to which concepts should *not* be related theoretically and are in fact *not* interrelated in reality. It is recognised that the area of construct validation is in itself somewhat theoretical by its very nature as it involves a latent theoretical aspect of a measure. There are several challenges associated with construct validation of a new instrument. These include items such as: the somewhat ethereal definition of what "construct validation" relates to and how it is suitably demonstrated (Nunnally and Bernstein, 1994; MacKenzie et al., 2011). There is also the challenge that constructs may have more than one conceptually distinguishable aspect or sub-dimension which can in itself be confounding. If a construct is multidimensional, which was the case with the four QoDOS constructs, then it is important to ensure that the sub-component characteristics are distinctive from each other (apart from their common theme). There are three major aspects of construct

validation: (1) specifying the correct domain of observables related to the construct; (2) determining the extent to which observables tend to measure the same thing from empirical research and statistical analyses; (3) performing subsequent individual difference studies and / or experiments to determine the extent to which supposed measures of the construct are consistent "best guesses" about the construct (Nunnally and Bernstein, 1994; Holstein, 2001). Overall, the multi-dimensional approach adopted in the construct validity evaluation and the triangulation of the complimentary and supportive validation techniques provided robust evidence of good construct validity of the QoDOS instrument.

The development of QoDOS also facilitated the investigation into the hallmarks of good decision-making practice. It enabled the identification and rating of the hallmarks to be performed which in itself provided additional insights into the establishment of quality decision-making practice. The resultant top-three messages on best practice were: to use scientific rigour and ensure one understands the decision context; to apply one's knowledge and experience; and to check the integrity of the information provided on which to make a decision. However, it is also interesting that some items were considered to be markedly less important in the ranking order. The hallmarks which received the lowest rank ordering related to: performing an impact analysis; clear and effective communication of the decision; considerations of uncertainty, unknowns and examination of alternative solutions or options.

The hallmarks investigation included 78 senior decision-makers from regulatory agencies and pharmaceutical companies and provided additional insight into their approach and considerations in decision-making. These insights could be deemed to warrant further research in this area and to involve a much larger sample to provide additional validity and generalisability to the hallmark rating results. The ten hallmarks and their rank-order provide a useful reference to good decision-making practice and could also be beneficial to a wider audience outside that of the regulatory agencies and pharmaceutical industry.

Overall, the main outcome was that of evaluating the reliability and construct validity of the QoDOS instrument. Robust and appropriate assessments were performed demonstrating the successful reliability and construct validity of the QoDOS decision-making instrument. Additional and complimentary insights were gained on the decision-making approaches and influences of individuals in the regulatory agencies and pharmaceutical healthcare arena along with recommendations on good decision-making practice. The potential of QoDOS to enable better decision-making has been established. For organisations, the working environment and the shared beliefs and values of the organisation appeared again to be important dimensions in decision-making. For the individual, the subjective elements of: professional experience, competence, personal style and autonomy appeared to influence decision-making.

SUMMARY

- The QoDOS instrument that had undergone factor analysis and yielded four constructs domains was evaluated for reliability and construct validity
- Seventy eight experienced decision-makers from regulatory agencies and pharmaceutical healthcare companies were involved in this analysis
- SPSS statistical methodologies and Excel were used in the analyses of the research sample findings. The reliability of each construct domain was above 0.73 and the ICC of each construct domain was above 0.73
- Convergent and discriminatory validity testing was performed and demonstrated. Quantitative analyses also supported the construct validity testing performed using the SPSS methodologies
- The quantitative results provided additional insights into the decision-making influences and approaches of individuals and organisations
- Comparative results were obtained for each of the four constructs. This enabled a comparative review of both the Organisational Versus the Individual influences, the intra-organisational influences (Approach and Culture) and the intra-individual influences (Competence and Style)

- Ten hallmarks of good decision-making practice from the investigation into decision-making approaches of individuals and organisations were identified and mapped against QoDOS
- The ten hallmarks were ranked in order of perceived importance by a group of 78 senior decision-makers. The top-three ranking items were: (1) Employ scientific rigour and understand the decision context, (2) Apply knowledge and experience and (3) Examine the integrity of information for validation and confidence in the decision
- Profiling and visualisation of an individual's decision-making approach has been enabled by the QoDOS instrument.

CHAPTER 7

General Discussion

The complexity of today's pharmaceutical development and regulatory decisions has created a drive for optimisation of the processes involved. To this end, decision-making and its quality have become the central focus for the major stakeholders and policy makers. It is this notion that has fuelled the initiative behind this research.

The qualitative research involved the conduct of interviews with a variety of key opinion leaders from the European Medicines Agency, national European regulatory agencies, the international pharmaceutical industry and clinical research organisations. These interviews generated valuable insights into the decision-making approaches both from the perspective of the individual and their organisations. The interviews were conducted until saturation level was achieved at which point no new decision-making themes emerged. The semi-structured interviews were conducted in an informal environment and the key opinion leaders were both engaged and supportive. The confidential and open conversation resulted in valuable insights into their decision-making. In addition, they identified factors that influenced their decisions and their organisations in which they were employed. It was appreciated that the panel of interviewees were all experienced key opinion leaders from the regulatory agencies and industry. For the first time a number of overarching decision-making factors were identified which have a prominent impact on the quality of decision-making from the perspective of the individual and the organisation.

For example, the quality and the validity of the data is a fundamental prerequisite to making a quality decision. This would ensure that the information that is being used to make a decision is valid, is as complete as possible and of optimum quality. Decisions in drug development are made on the basis of information, its analysis and interpretation and one should question, where did this evidence come from? How do you know the evidence is reliable? Is it factually correct? Has it been analysed and interpreted objectively and is it biased?

Another key factor is that of experience and expertise which is directly related to the competence and confidence in decision-making. Hindsight into previous decision-

making and the success and failure of such decisions and their subsequent impact also have a significant influence. These experiences provide a baseline for potential outcomes from such decisions and also an appreciation of possible alternative solutions that may be incorporated into future decision-making tasks. Furthermore, such experiences give the decision maker confidence in their own ability to make such decisions. Professional experience and exposure to different challenges are seen as a valuable asset and part of the development of a quality decision-maker.

The culture of an organisation and its hierarchy is also a driving factor in regard to decision-making within the organisation. In large pharmaceutical organisations, there appears to be a defined chain-of-command in how decisions are made. This approach impacts on the level of autonomy of the decision-makers and results in a formal escalation of requirements and added bureaucracy in reaching a decision. It could also be interpreted as stifling an individual's creativity, diluting accountability in the decision-making stages leading to the final decision. This means that more time could be required for a decision to be made and by inference suppresses the possibility for quick decisions and limits the level of empowerment of people within the organisation. The difference between regulatory agencies and the pharmaceutical industry is that agencies' use of committees may result in the decision being made whereas in the industry they are used to facilitate rather than make the final decision.

Intuition or "gut feeling" is seen as a positive attribute within drug development and the regulatory review. The use of intuition by an experienced professional appears to expedite the decision-making process and avoids procrastination. It appears to be a non-quantifiable skill which is a useful and valuable tool in decision-making. However, it is not a systematic or structured approach and therefore is not infallible. It may be prone to prejudices and biases, but if these are taken into account it can be a valuable asset. Drug development and the regulatory review normally operates in a structured and standardised manner and therefore it is interesting to appreciate the prominence that has been given to intuition in decision-making.

Finally, while training in the science of decision-making was considered important, there is a limited amount of training investment by both the regulatory agencies and the industry. All of the interviewees advised that both they and their organisation would benefit from training in decision-making. Such training was recommended to be almost mandatory for decision-makers at a managerial or executive level and ideally should be incorporated into personal and organisational development plans. Training in best practice decision-making techniques, awareness of the tools to assist with routine best practices and frameworks would help in different functions of the organisation. In addition, training was perceived as developing the competence, capability and confidence in decision-making.

At the level of the individual, the main confirmatory finding of the qualitative investigation was the presence of a strong subjective element or style in decision-making. The other factors included competence based on professional experience, education and training, the ability to focus on the decision to be made and awareness of personal biases. The presence of additional extrinsic organisational factors such as the size of the organisation, the level of empowerment, autonomy and accountability given to the person also are factors to be considered.

In terms of factors influencing organisational decision-making one should consider the size, the time/cost, the culture, decision-making hierarchy, internal and external political aspects, vested interests of individuals, competitor status and territorial tendencies. Additional factors include, the organisation's approach to marketing, whether current projects requiring a decision originated from within or outside the organisation and its willingness to embrace new technologies.

It was observed that in smaller organisations and within the regulatory agencies, there was some evidence that decisions are made more rapidly than in larger ones. This appears to be related to the increased responsibility and demand on individuals to make decisions sooner rather than later. There appears to be less time/cost tolerance for smaller pharmaceutical organisations and within regulatory agencies compared to larger

organisations. Another insight was that different decision-making approaches occur within the functional groups of the same organisation.

The qualitative investigation resulted in the identification and consolidation of decision-making themes into a developmental generic instrument to be used for assessing the quality of decision-making. The prototype instrument was subjected to a structured and systematic development followed by content validity evaluation by an expert panel. The consensus of the panel was that the generic development tool was fit-for-purpose and appropriate to progress to further psychometric testing.

The quantitative study recruited participants from several EU countries, the United States and China. Ninety-four decision-making themes emerged from the qualitative phase of the research and these formed the basis for the development of the QoDOS instrument. The combination of the qualitative components supported and complimented by the quantitative methodologies, provided confidence in the robustness and fit-for-purpose evolution of the developmental instrument. The instrument items went through several stages of refinement resulting in a final 47-item version of the instrument. The instrument demonstrated good reliability and validity and these favourable psychometric properties were further underpinned by the previous robust and rigorous qualitative phase. This provided extra confidence in the intended utility of the tool. However, what is missing at present from these frameworks and from other decision-making approaches within drug development is a mechanism to enable and measure the subjective decision-making of the individual and that of their organisation. The QoDOS instrument aims to bridge this gap.

The main review of a marketing authorisation application or Health Technology Assessment are inherently linked to the quality of the dossier submission and the quality of the review (Salek et al., 2012). What is again missing at present is a tool to bridge the unknown subjective decision-making that is a component of the quality submission and the quality review and the QoDOS instrument provides this bridge. Furthermore, the QoDOS was applied to a cohort of decision-makers from the industry and the regulatory

agencies and it did demonstrate the difference in the comparative approach and behaviours of the individual versus that of the organisation. There were a number of differences between the organisation and the individual which included:

- Use of structured approaches to decision-making - the results showed that individuals within the organisation reported using a structured approach more frequently in their personal decision-making than did their organisation

- Quantification of probability of success – these results showed that individuals are more disciplined in quantifying such probability than their organisations

- Transparency in decision-making approach - individuals reported that their own decision-making approach was not as transparent as that of their organisation. This could be related to the quality management systems in place which aim to standardise certain decision-making tasks and this in turn facilitates transparency

- Training in decision-making - the comparative results showed that the amount of training in the science of decision-making that had been received by an individual and the level of support offered by their organisation was very limited.

What QoDOS is now offering is an addition to the decision-making armamentarium. It aims to address that void in the understanding of the quality of the decision-making being applied both within the benefit-risk assessment frameworks, drug development and beyond. One of the unique, attractive and beneficial features of QoDOS is that it allows the individual or their organisation to visualise their decision-making approach. This visualisation in turn presents and facilitates profiling and communication of decision-making. In addition it provides a time-curve record of changes or improvements in a person's (or an organisation's) decision-making approach. It presents a platform to add consistency, transparency and communication to the

subjective decision-making element. This will in turn allow greater predictability and auditability of the individual and their organisation.

QoDOS has also enabled the identification of the hallmarks of good decision-making practice and a recommended decision-making framework (Figure 7.1). The structure of this framework includes 10 items as outlined:

Figure 7.1: Quality of decision-making framework reflecting good decision-making practice

The rationale for each of the ten steps in the framework:

Step 1 – Employ Scientific Rigour and Understand The Decision Context

For any decision in drug development or the regulatory review it is important that firstly the decision-context is clearly understood as if this is not achieved then the decision process may be compromised.

Step 2 - Apply Knowledge and Experience

It has been demonstrated that decision-making knowledge and experience is critical.

Step 3 - Collect and Check Validity and Integrity of Information

The quality of any decision is directly related to the validity and integrity of the information underpinning the ultimate decision. One should ensure that the information collected is of the required quality in order to give the necessary confidence to the decision maker.

Step 4 - Use of Objective Approach and Awareness of Biases

This adds another dimension to the subjective individual judgement and yet again improved the robustness of the ultimate decision. Use an objective approach and be aware of your personal biases.

Step 5 - Consider Uncertainties and Develop Alternate Solutions

Uncertainties are a reality of any decision-making. However, not identifying such uncertainties could contribute to the risk of failure of the decision. Equally consideration of the alternate solutions will lead to a more balanced decision.

Step 6 - Assign Values and Importance to Decision Criteria

There is a general agreement that not all criteria used either by the individual or the organisation is of equal value and importance. It is therefore imperative to involve careful examination of the relative importance of such criteria for decision-making.

Step 7 - Re-evaluate any New Information

The dynamic nature of scientific information and the speed with which that travels globally in today's environment makes it absolutely imperative on an individual and organisation to revisit criteria used for any previous decision.

Step 8 - Evaluate any Internal or External Influences

Any organisation or individual must be constantly aware of any internal and external influences on their decision-making for example previous experience with medicines in a similar therapeutic class, an untoward spontaneous event or considerations such as company politics and competitors.

Step 9 - Use a Structured Approach To Aid Transparency and Audit Trail

This underlines the fact that using a structured approach will aid transparency as well as providing an audit trail to those wishing to understand the basis of the decision.

Step 10 - Perform Impact Analysis and Effectively Communicate The Decision

It is important in any decision-making to examine the impact the decision has on stakeholders. Having a structured systematic framework would enable decisions that are made to be effectively communicated, for example from pharmaceutical company to regulatory agency, regulatory agency to physician and physician to patient.

LIMITATIONS OF THE STUDY

As with any research there are a number of limitations including the following:

- The participants in the qualitative phase of the study were all senior decision-makers or Key Opinion Leaders. Whilst this cohort provided rich insights into their decision-making approaches and style, these were not truly representative of personnel involved in medicines research and review. However, if less experienced people had participated then some decision-making themes may have not have emerged

- Whereas the sample size achieved in the qualitative phase was satisfactory, this was not the case in the quantitative phase. It was disappointing that only a 20% response rate was achieved in the quantitative phase and this was despite using recognised techniques of follow-up including repeat emails and phone calls. The number of participants in the final sample should ideally have been between 350–760. This would have involved recruiting up to 3,500 people and this target was not achievable

- Whilst the QoDOS research was international in nature and did include participants from several EU countries, United States and China, it did not include South America, Japan, Southeast Asia and the Middle East and decision-making in these regions may differ because of experience and culture

- The lack of a validated "gold-standard" instrument could be perceived as a limiting factor as it precluded the opportunity for a head-to-head comparison, which in turn would have reduced the sample size requirement and would have provided a different construct validation approach.

RECOMMENDATIONS

As a result of this research there are a number of recommendations that can be made:

- QoDOS should be applied as a strategic planning tool at the different stage-gates in drug development within the pharmaceutical industry. This would include decision points during the nonclinical and clinical development phases and would hopefully improve the robustness of decision-making and improve attrition rates and delayed/premature terminations in drug development

- QoDOS can provide the opportunity to bridge the gap between the submission of a quality dossier and a quality review leading to a seamless and comprehensive platform for more predictable outcomes and increased public confidence

- QoDOS should be used as a training tool for decision-making which would promote a better understanding of the science of decision-making and improve the overall quality

- The routine application of QoDOS has the potential to change the organisational culture and their approach to decision-making with an increased awareness of its quality.

FUTURE WORK

- It would be of value to initiate a study to assess the quality of decision-making within the various functions of the pharmaceutical industry which would include: discovery pre-clinical, clinical, regulatory and pharmacovigilance. This would allow a comparison of the quality of decision-making between the various departments and identify differences between individuals and their departments.

- It would be advantageous to compare the decision-making of big Pharma with Small and Medium Enterprises (SMEs) and small biotech companies. It is hoped that this would identify whether culture and organisational hierarchy impact on the quality of decision-making and whether in small companies there is a greater demand for accountability of the decisions made.

- Clearly there are differences between the larger mature established regulatory authorities and those in the emerging markets. Therefore, it would be of interest to design a study to examine whether there is a difference in the quality of the decision-making between these two groups. Of specific importance, would be to examine the differences between the seven Gulf States in the Middle East as they differ in expertise and resources.

- QoDOS has identified the importance of examining not only the impact of the decision made but also the importance of re-examining the decision when new information becomes available. Therefore, it would be important to examine the quality of decision-making in the pre-licensing and post-licensing divisions within a number of regulatory authorities.

- The regulatory authorities in the emerging markets often have a different approach to the evaluation of new medicines depending on where they have been approved for marketing. This includes a full review, abridged review and a verification review. It would be of value to determine whether the quality of decision-making differs according to the type of review.

- Patients are challenged in that the approval of a new medicine for marketing does not necessarily mean that the product will be available for reimbursement. Therefore a study to examine the quality of decision-making within different Health Technology Assessment Agencies may explain why some of these differences occur and this will greatly influence patients' access to new medicines.

- It would be of importance to initiate a survey as an urgent piece of future work to determine acceptability of the quality of decision-making framework by the pharmaceutical industry, regulatory authorities and health technology assessment agencies in both the mature and the emerging markets.

The QoDOS has been developed as an instrument for assessing the quality of decision-making within regulatory agencies and pharmaceutical companies and has identified a framework for quality decision-making. This has the potential to not only revolutionise the way in which the whole regulatory submission and review is viewed but also to fill the missing piece of the entire process which is building quality into the lifecycle of medicines.

REFERENCES

Ansoff, H.I. 1979. Strategic Management, London. Macmillan

Attridge-Stirling 2001. Thematic networks: an analytic tool for qualitative research. *Qualitative research,* 1**,** pp. 385-405.

Barbour, V., Chinnock, P., Peiperl, L., Veitch, E. & Yamey, G. 2008. From theory to practice: translating research into health outcomes. *PLoS Med,* 5**,** e15.

Basit, T. N. 2003. Manual or Electronic? The role of Coding in Qualitative Data Analysis. *Educational Researcher,* 45**,** pp. 143-154.

Basu, R. 2004. Implementing quality: A practical guide to tools and techniques., *Thomson Learning*.

Bazeley, P. 2007. Qualitative data analysis with NVivo, London, *Sage Publications.*

Bhatti, Z. U., Salek, S. & Finlay, A. Y. 2013a. Concept of major life-changing decisions in life course research. *Curr Probl Dermatol,* 44**,** pp. 52-66.

Bhatti, Z. U., Salek, S. S., Bolton, C. E., George, L., Halcox, J. P., Jones, S. M., Ketchell, I. R., Moore, R. H., Sabit, R., Piguet, V. & Finlay, A. Y. 2013b. The development and validation of the major life changing decision profile (MLCDP). *Health Qual Life Outcomes,* 11**,** 78.

Bougie, S. A. 2010. *Research methods for business: a skill building approach*

Boynton, P. M. 2004. Administering, analysing, and reporting your questionnaire. *BMJ,* 328**,** pp. 1372-5.

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

Breckenridge, A., Feldschreiber, P., Gregor, S., Raine, J. & Mulchay, L. A. 2011. Evolution of regulatory frameworks. *Nat Rev Drug Discov,* 10**,** pp. 3-4.

Breckenridge, A. & Walley, T. 2008. Early access to new medicines. *Clin Pharmacol Ther,* 84**,** pp. 23-5.

Breckenridge, A. & Woods, K. 2005. Medicines regulation and the pharmaceutical industry. *BMJ,* 331**,** pp. 834-6.

Breckenridge, A., Woods, K. & Wallely, T. 2010. Medicines regulation and health technology assessment. *Clin Pharmacol Ther,* 87**,** pp. 152-4.

Campbell, D. T. & Fiske, D. W. 1959. Convergent and discriminant validation by the multitrait-multimethod matrix. *Psychol Bull,* 56**,** pp. 81-105.

Casey, M., McNamera, M., Fealy, G. & Geragherty, R. 2011. Nurses' and midwives' clinical leadership development needs: a mixed methods study. *J Adv Nurs,* 67**,** pp. 1502-13.

Cattell, R. B. 1978. The Scientific Use of Factor Analysis, New York, *Plenum Press*.

UIC (Chicago). 2013. *Department of Infomation and Decision Sciences, Chicago,* http://business.uic.edu/home-uic-business/faculty-departments-research/department-of-ids.

Chung-Stein, K. E. A. 2011. A Quantitative Approach for Making Go/No-Go Decisions in Drug Development. *DIA Information Journal,* 14**,** pp. 187-202.

CIRS, 2012. Buiding the benefit-risk toolbox: Are there enough common elements across the different methodologies to enable a concensus on a scientifically acceptable framework for making benefit-risk decisions? Workshop synopsis, June 20-21.

Collis, J. H., R 2009. Businees research: A practical guide for undergraduate and postgraduate students. *Palgrave MacMillan*

Colwrick, I., Hedner, T., Wolf, R., Olausson, M. & Klofsten, M. 2011. Decision-making in the pharmaceutical industry: analysis of entrepreneurial risk and attitude using uncertain information. *R&D Management,* 41**,** pp. 331-336.

Coplan, P. M., Noel, R. A., Levitan, B. S., Ferguson, J. & Mussen, F. 2011. Development of a framework for enhancing the transparency, reproducibility and communication of the benefit-risk balance of medicines. *Clin Pharmacol Ther,* 89**,** pp. 312-5.

Coyne Karin S., M. M. K., Murphy Jeanne., Spies James. 2012. Validation of the UFS-QOL-Hysterectomy Questionnaire: Modifying an existing measure for the comparative effectiveness research *Value in Health* 15**,** pp. 674-679.

Crabtree & Miller, A. 1999. Doing quantitative research, *Sage Publications*

Creswell, J. W. 2003. Research design: qualitative; quantative and mixed methods *Sage Publications*.

Dash, M. & Jones, D. 2010. Good Review Practices at the MHRA. *Regulatory Rapporteur,* 7. *TOPRA*

Davidshofer, K. & Murphy, C. 2005. *Psychological testing: principles and applications,* Upper Saddle River, NJ, *Pearson/Prentice Hall.*

Davis, J. 1989. Measurement, construct validity and pattern matching: Construct validity in measurement: A pattern matching approach, *Evaluation and Program Planning, Vol 12, pp. 31-36,* USA. *Pergamon Press*

Denzin, N. & Lincoln, Y. 2005. *The handbook of qualitative research,* Thousand Oaks, CA, USA, Sage Publications.

Dhamu, M. K. 2003. Psychological models of professional decision-making. *Psychol Sci,* 14**,** pp. 175-80.

Dicicco--Bloom, B., & CRABTREE, B.F 2006. The qualitative research interview *Med. Educ* 40**,** pp. 314-21.

Diem, K. G. 2002b. A Step-by-step guide to developing effective questionnaires and survey procedures for program evaluation and research New Jersey. *Rutgers*

Dodgson, J. S. 2009. Multi-criteria analysis: a manual. Communities and Local Government Publications: London

Doyle, L., Brady, A-M., & Byrne, G. 2012 An overview of mixed methods research. *American Journal of evaluation* 33**,** pp. 221-239.

ECORYS, 2009. Competitveness of the EU Market and Industry for Pharmaceuticals. Report for the European Commission, Directorate General Enterprise & Industry. Rotterdam.

Eichler, H. G., Oye, K., Baird, L. G., Abadie, E., Brown, J., Drum, C. L., Ferguson, J., Garner, S., Honig, P., Hukkelhoven, M., Lim, J. C., Lim, R., Lumpkin, M. M., Neil, G., O'Rourke, B., Pezalla, E., Shoda, D., Seyfert-Margolis, V., Sigal, E. V., Sobotka, J., Tan, D., Undger, T. F. & Hirsch, G. 2012. Adaptive licensing: taking the next step in the evolution of drug approval. *Clin Pharmacol Ther,* 91**,** pp. 426-37.

Eichler, H. G., Pignatti, F., Flamion, B., Leufkens, H. & Breckenridge, A. 2008. Balancing early market access to new drugs with the need for benefit/risk data: a mounting dilemma. *Nat Rev Drug Discov,* 7**,** pp. 818-26.

Eisinga, R., Grotenhuis, M. T. & Pelzer, B. 2013. The reliability of a two-item scale: Pearson, Cronbach, or Spearman-Brown? *Int J Public Health,* 58**,** pp. 637-42.

European Medicines Agency (EMA) 2010. Description of the benefit-risk assessment models already being used in the European Union's regulatory network: Work Package 1 Report. London. EMA www.ema.europa.**eu**/docs/en_GB/document.../WC500109478.pdf

European Medicines Agency (EMA) 2011. Benefit-risk methodology project: Work package 3 report: Field tests. London. EMA www.ema.europa.eu/docs/en_GB/.../Report/.../WC500112088.pdf

European Medicines Agency (EMA) 2011b. Road Map to 2015: The Agency's contribution to science, medicines, health. London. EMA. http://www.ema.europa.eu/docs/en_GB/document_library/Report/2011/01/WC500101373.pdf

European Medicines Agency (EMA). 2013b. *EUnetHTA*, London, EMA [Online]. Available: http://www.eunethta.eu/ema.

European Medicines Agency (EMA). 2013c. *PRAC: Pharmacovigilance Risk Advisory Committee* [Online]. London, EMA. Available: http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_000537.jsp&mid=WC0b01ac058058cb18.

European Medicines Agency (EMA). 2010. European Medicines Agency Benefit–Risk Methodology Project, London, EMA.

ESPRINT Group, E. S., Investigators, Valero, A., Alonso, J., Antepara, I., Baro, E., Colas, C., Del Cuvillo, A., Ferrer, M., Herdman, M., Marti-Guadano, E., Monclus, L., Mullol, J., Navarro-Pulido, A. M., Navas, C., Sastre, J., Baltasar, M., Bartra, J., Serrano, C., Cardona, V., Castillo, J. A., Cerda, M. T., Cistero, A., Conejero, A., Davila, I., Escudero, C., Hernandez, E., Vereda, A., Fernandez, B., Mencia, J., Fernandez, J., Florido, J., Quiralte, J., Guardia, P., Malek, T., Montoro, J., Orta, J. C., Oehling, A., Pascual, M. J., De La Parte, B., Raga, E., Rubira, N., Ranea, S., Rivas, P., Serra, J. & Tabar, A. 2007. Development and validation of a new Spanish instrument to measure health-related quality of life in patients with allergic rhinitis: the ESPRINT questionnaire. *Value Health,* 10 (6)**,** pp. 466-77.

Fayers, P. M. & Hand, D. J. 1997. Factor analysis, causal indicators and quality of life. *Qual of Life Research,* 6 (2)**,** pp. 139-50.

Field 2005. Discovering statistics using SPSS. 2nd edition, London, Sage Publications.

Field 2009. Discovering statistics with SPSS. 3rd edition, London, Sage Publications.

Floyd, F. J., & Widaman, K.F 1995. factor analysis in the development and refinement of clinical assessment instruments *Psychological Assessment***,** 286-299.

Food and Drug Administration (FDA) 2005. Guidance for review staff and industry, good review management principles and practices for PDUFA products. FDA, USA.

Food and Drug Administration (FDA) 2006. Good review practices. Manual of policies and procedures, FDA, USA.[Accessed: 14th October 2012].

Food and Drug Administration (FDA) 2009. Manual of Policies and Procedures (CDER). FDA, USA [Accessed: 14th October 2012].

Food and Drug Administration (FDA) 2010. A United States regulators perspective on benefit-risk considerations. FDA, USA. [Accessed: 14th October 2012].
http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/UCM210155.pdf

Fredheim, O. M., Borchgrevink, P. C., Saltnes, T. & Kaasa, S. 2007. Validation and comparison of the health-related quality-of-life instruments EORTC QLQ-C30 and SF-36 in assessment of patients with chronic nonmalignant pain. *J Pain Symptom Manage*, 34**,** pp. 657-65.

Frey, P. 2012. Benefit-risk considerations in CDER: Development of a Qualitative Framework. (DIA meeting). Silver Spring, MD: Food and Drug Administration, Centre for Drug Evaluation and Research. http://www.fda.gov/downloads/AboutFDA/CentresOffices/OfficerofMedicalProductsand Tobacco/CDER/UCM317788.pdf.

Genesis. 2013. *Genesis strategic decision process* [Online]. Available: http://www.genesismc.co.uk/blog/effective-decision-making/.

Government (US Small Business Administration). 2013. *Decision-making* [Online]. Available: US Government, US http://www.sba.gov/content/making-decisions.

Graneheim, U. H. & Lundman, B. 2004. Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness. *Nurse Educ Today,* 24**,** pp. 105-12.

Guo, J. J., Pandey, S., Doyle, J., Bian, B., Lis, Y. & Raksch, D. W. 2010b. A Review of Quantitative Risk–Benefit Methodologies for Assessing Drug Safety and Efficacy—Report of the ISPOR Risk–Benefit Management Working Group. *Value in Health,* 13**,** pp. 657-666.

Guyatt, G. F., D 1993. Measuring health related quality of life *Annals of Internal Medicine,* 118 (8)**,** pp. 622-629.

Halcomb, E. J. & Davidson, P. M. 2006. Is verbatim transcription of interview data always necessary? *Appl Nurs Res,* 19**,** 38-42.

Hammond, K., Raiffa 2002. *Smart choices*: A Practical Guide to Making Better Decisions, *Crown Business*

Hammond, S., Keeney, R. & Raiffa, H. 2011. *Making Smart Decisions,* Boston, *Harvard Business Review*.

Hanson, W., Creswell.J.W, Plano Clark, V., Petska, K. & Creswell, J. D. 2005. Mixed Methods Research Designs in Counseling Psychology. *Journal of Counseling Psychology,* 52**,** pp. 224-235.

Harris, R. 2012. *Introduction to decision-making* [Online]. Available: http://www.virtualsalt.com/crebook5.htm.

Haynes, S., Richard, D. & Kubany, E. 1995. Content validity in psychological assessment: A functional approach to concepts and methods *Psychological Assessment*. 7(3), pp. 238-247.

Hazard, M. B. 2011. Statistical methods for health care research *Lippincott Williams and Wilkins*.

Higginson, I., J., & Carr, A. J. 2001. Measuring quality of life using a qualit of life measures in the clinical setting. *British Medical Journal***,** pp. 297-1300.

Heads of Medicines Agency (HMA), 2013. Benchmarking of European Medicines Agencies (BEMA). London, EMA. http://www.hma.eu/300.html

Holstein, G. 2001. Handbook of interview research: concepts, procedures and measures to achieve trustworthiness *Sage Publications*.

IBM. 2011. *SPSS Statistics 20 Brief Guide* [Online]. Available: http://www-01.ibm.com/support/docview.wss?uid=swg21509012.

IMI-EFPIA 2013a. IMI-PROTECT Benefit-Risk Group Recommendations Report Recommendations for the methodology and visualisation techniques to be used in the assessment of benefit and risk of medicines. *In:* IMI-EFPIA (ed.).

IMI-EFPIA. 2013b. *IMI Protect Project* [Online]. Available: http://www.imi-protect.eu/.

Ivanova, E. & Gibcus, P. 2003. The decision-making entrepreneur. Literature review. Literature Review, SCALES-paper N200219, EIM Business & Policy Research, Holland.

Jackson, K. & Trochim, W. M. 2002. Concept Mapping as an Alternative Approach for the Analysis of Open-Ended Survey Responses,*Organizational Research Methods,* 5**,** pp. 307-336.

Jefferys, D. 2000. The development of quality assurance within the Medicines Control Agency. *International Journal of Pharmaceutical Medicine* 14**,** pp. 29-32.

John, O. & Benet-Martinez, V. 2000a. Handbook or research methods in social and personality psychology, *Cambridge University Press*.

Kahneman, D. 2003. A perspective on judgment and choice: mapping bounded rationality. *Am Psychol,* 58**,** pp. 697-720.

Kahenman, D. 2012. *Thinking Fast and Slow*, London, Penguin Books.

Kahneman, D., Lovallo, D. & Sibony, O. 2011. Before you make that big decision. *Harv Bus Rev*, 89**,** 50-60, pp. 137.

Kahneman, D. & Tversky, A. 1982. Variants of uncertainty. *Cognition,* 11**,** pp. 143-57.

Korteweg, M. 2002. Benchmarking of good regulatory practices – Quality management systems in the framework of PERF. *Regulatory Affairs Journal Pharma.* February 2002, pp. 109-113.

Korvivk, J. 2008. Current and future approaches to benefit-risk assessment for Regulatory agencies. In: Cone, M. and Lisinski, T. (Eds.) Measuring benefit and balancing risk: strategies for the benefit-risk assessment of new medicines in a risk-averse environment. CMR International Institute for Regulatory Science workshop report. Surrey: CMR International.

Kostopoulou, O. & Wildman, M. 2004. Sources of variability in uncertain medical decisions in the ICU: a process tracing study. *Qual Saf Health Care,* 13**,** 272-80.

Kriston, L., Scholl, I., Holzel, L., Simon, D., Loh, A. & Harter, M. 2010. The 9-item Shared Decision-making Questionnaire (SDM-Q-9). Development and psychometric properties in a primary care sample. *Patient Educ Couns,* 80**,** pp. 94-9.

Kumanyika, S., Brownson, R. C. & Cheadle, A. 2012. The L.E.A.D. framework: using tools from evidence-based public health to address evidence needs for obesity prevention. *Prev Chronic Dis,* 9**,** E125.

Langham, S., Maggi, M., Schulman, C., Quinton, R. & UHL-Hochgraeber, K. 2008. Health-related quality of life instruments in studies of adult men with testosterone deficiency syndrome: a critical assessment. *J Sex Med,* 5**,** pp. 2842-52.

Leong, J., McAuslane, N., Walker, S. & Salek, S. 2013. Is there a need for a universal benefit-risk assessment framework for medicines? Regulatory and industry perspectives. *Pharmacoepidemiol Drug Saf,* 22**,** pp. 1004-12.

Levitan, B. & Mussein, F. 2012. Evaluating benefit-risk during and beyond drug development: an industry view. Regulatory Rapporteur, 9. *TOPRA*

Liang, M. H. 2000. Longitudinal construct validity: establishment of clinical meaning in patient evaluate instruments. *Med Care***,** pp. 1184-90.

Lovallo, D. & Kahneman, D. 2003. Delusions of success. How optimism undermines executives' decisions. *Harv Bus Rev,* 81**,** 56-63, p. 117.

Lumkin, M. 2000. Assessing quality of the regulatory review function *DIA Annual Meeting 2000.*

Lynn, M. R. 1986. determination and quantification of content validity.*Nursing research,* 35 (6), pp. 382-385

MacKenzie, S., Podsakoff, P. & Podsakoff, N. 2011. Construct Measurement and Validation Procedures in MIS and Behavioural Research: Integrating New and Existing Techniques. *MIS Quarterly,* 35**,** pp. 293-334.

MacLeod, L. 2011. Avoiding "groupthink": a manager's challenge. *Nursing Management,* 42 (10)**,** pp. 44-8.

Marquart, J. 1989. A pattern matching approach to assess the construct validity of an evaluation instrument. *Concept mapping for evaluation and planning.* USA: *Pergamon Press.*

Mathers, N., Fox, N. & Hunn, A., 2002. Using interviews in a research project *Institute of General Practice, Sheffield, UK*

Mattes, W. B., Walker, E. G., Abadie, E., Sistare, F. D., Vonderscher, J., Woodcock, J. & Woosley, R. L. 2010. Research at the interface of industry, academia and regulatory science. *Nat Biotechnol,* 28**,** pp. 432-3.

Mc Cauley, C. 1998. Group Dynamics in Janis's Theory of Groupthink: Backward and Forward. *Organ Behav Hum Decis Process,* 73**,** pp. 142-62.

McDaniel, C. & Gates, R. 2002. Contemporary marketing research: the impact of the Internet. 5th ed. Cincinnati (OH): South-Western College Publishing;

McDermott, R. 2008. Medical decision-making: Lessons from psychology. *Urologic Oncology: Seminars and Original Investigations,* 26**,** pp. 665-668.

Medicines and Healthcare products Regulatory Agency (MHRA) 2009. The European Medicines Agency's Integrated Quality Management System. London.

Medicines and Healthcare products Regulatory Agency (MHRA) 2013. *Report of the Expert Group on innovation in the regulation of healthcare* [Online]. London. http://www.mhra.gov.uk/home/groups/pl-a/documents/websiteresources/con336728.pdf.

Meehhl, C. A. 1955. Construct Validity in Psychological Tests. *Psychological Bulletin,* 52.

Messicks, D. & Bazerman, M. 1996. Ethical leadership and the psychology of decision-making. *Sloan Management Review***,** pp. 9-22.

Meyrick, J. 2006. What is good qualitative research? A first step towards a comprehensive approach to judging rigour/quality. *J Health Psychol,* 11**,** pp. 799-808.

Milkman, K., Chugh, D. & Bazerman, M. 2008. How can decision-making be improved? USA, *Harvard Business Review*.

Mindtools. 2013. *Decision-making* [Online]. Available: http://www.mindtools.com/pages/main/newMN_TED.htm.

Mintzberg, H. & Westley, F. 2001. Decision-making: It's not what you think. *Sloan Management Review,* 42**,** pp. 89-93.

Molzon ,J., Giaquinto, A., Lindstrom, L., Tominaga, T., Ward, M., Doerr, P., Hunt, L., Rago, L, 2011. The Value and Benefits of the International Conference on Harmonisation to Drug Regulatory Authorities: Advancing Harmonization for Better Public Health. *Clinical Pharmacology & Therapeutics* 89, pp. 503-512.

Moule, P. & Goodman, R. 2009. *Nursing Research: An introduction*, London, Sage Publications.

Mussen, F., Salek, S. & Walker, S. R. 2009. Benefit-risk appraisal of medicines. A systematic approach to decision-making. *Wiley*

Neudert, C., Wasner, M. & Borasio, G. D. 2001. Patients' assessment of quality of life instruments: a randomised study of SIP, SF-36 and SEIQoL-DW in patients with amyotrophic lateral sclerosis. *J Neurol Sci,* 191**,** pp. 103-9.

NIH 2012. PROMIS® Instrument Development and Psychometric Evaluation Scientific Standards. USA, *National Institute of Health.*

Norusis, M. J. 1993. SPSS for windows: base systems user's guide, Chicago, *SPSS Inc.*

Nunnally, J. C. & Berstein, L. 1994. *Psychometric theory*, McGraw Hill.

Pallant, J. 2005. *SPSS Survival Manual:* A step by step guide to data analysis using SPSS, for Windows (Version 12). 2nd ed. Maidenhead: Open University Press.

Patrick, D. L., Burke, L. B., Gwaltney, C. J., Leidy, N. K., Martin, M. L., Molsen, E. & Ring, L. 2011a. Content Validity—Establishing and Reporting the Evidence in Newly Developed Patient-Reported Outcomes (PRO) Instruments for Medical Product Evaluation: ISPOR PRO Good Research Practices Task Force Report: Part 1—Eliciting Concepts for a New PRO Instrument. *Value in Health,* 14**,** pp. 967-977

Patrick, D. L., Burke, L. B., Gwaltney, C. J., Leidy, N. K., Martin, M. L., Molsen, E. & Ring, L. 2011b. Content Validity—Establishing and Reporting the Evidence in Newly Developed Patient-Reported Outcomes (PRO) Instruments for Medical Product Evaluation: ISPOR PRO Good Research Practices Task Force Report: Part 2—Assessing Respondent Understanding. *Value in Health,* 14**,** pp. 978-988.

Patrick, D. L. C., Y.P. 2000. Measurement of health outcomes in treatment effectiveness evaluations: conceptual and methodological challenges *Med Care***,** pp. 1114-25.

Patton, M. Q. 2002. Qualitative research & evaluations methods, Sage Publications.

Petter, E. A. 2007. Specifying formative constructs in IS research. *MIS Quarterly,* 31**,** pp. 623-656.

Pijls-Johannesma, M. C., Pijpe, A., Kempen, G. I., Lambin, P. & Dagnelie, P. C. 2005. Health related quality of life assessment instruments: a prospective study on preference and acceptability among cancer patients referred for radiotherapy. *Eur J Cancer,* 41**,** pp. 2250-6.

Polit, D. and Beck, C.T., 2006. The content validity index: Are you sure you know what's being reported? critque and recommendations. *Research in Nursing & Health 29 (5)* pp. 489-497.

Pritchard, J. F., Jurima-Romet, M., Reimer, M. L., Mortimer, E., Rolfe, B. & Cayen, M. N. 2003. Making better drugs: Decision gates in non-clinical drug development. *Nat Rev Drug Discov,* 2**,** pp. 542-53.

PWC 2012. From vision to decision. *In:* (ED), P. (ed.).

Quernk, N. L. 2009. Essentials of Myers-Briggs Type Indicator Assessment (Essentials of Psychological Assessment), *John Wiley & Sons.*

Rawlins, M. 2011. Therapeutics, evidence and decision-making, RSM Books, *CRC Press.*

Remenyi, D.,Williams, A., Swartz & Ethne 1998. Doing Research in Business and Management. An Introduction to Process and Method, London.

Richards, L. 2005. Handling qualitative data: A practical guide. *Sage Publications*.

Ritchie, J. Spencer, L. 1994. Qualitative data analysis for applied policy research. In Analyzing Qualitative Data. Edited by Bryman A, Burgess RG. London: Routledge

Rothman, M., Burke, L., Erickson, P., Leidy, N. K., Patrick, D. L. & Petrie, C. D. 2009. Use of existing patient-reported outcome (PRO) instruments and their modification: the ISPOR Good Research Practices for Evaluating and Documenting Content Validity for the Use of Existing Instruments and Their Modification PRO Task Force Report. *Value in Health,* 12**,** pp. 1075-83.

Rowe, A. J. & Bougarides, J. D. 1983. Decision styles - A perspective, . *Leadership and organizational development journal,* 4**,** pp. 3-9.

Ruiz, M. A., Pardo, A., Rejas, J., Soto, J., Villasante, F. & Aranguren, J. L. 2008. Development and validation of the "Treatment Satisfaction with Medicines Questionnaire" (SATMED-Q). *Value Health,* 11**,** pp. 913-26.

Ryan, C. A. C. 2007. Step-by-step guide to critiquing research. Part 2: quaiitative research. *Bristish Journal of Nursing,* 16.

Salek, M., Khan, G. & Finlay, A. 1996. Questionnaire techniques in assessing acne handicap: reliability and validity study. *Quality of life research,* 5**,** pp. 131-138.

Salek, S., Mallia-Milanes, A., McAuslane, N. & Walker, S. 2012. Development and Application of Scorecards to Assess the Quality of a Reulatory Submission and Its Review. *DIA Information Journal,* 46.

Salkind, N. 2006. *Exploring research,* New Jersey, Pearson education.

Samuelson, W. & Zeckhauser, R. 1988. Status quo bias in decision making. *Journal of risk and uncertainty,* 1**,** pp. 7-59.

Sarac, S. B., Rasmussen, C. H., Rasmussen, M. A., Hallgreen, C. E., Soeborg, T., Colding-Jorgensen, M., Christensen, P. K., Thirstrup, S. & Mosekilde, E. 2012. A comprehensive approach to benefit-risk assessment in drug development. *Basic Clin Pharmacol Toxicol,* 111**,** pp. 65-72.

Saunders, L., Thornhill 2009. *Research methods for business students*. England, *Pearson Education Limited.*

Schleyer & Titus, .K.L 2000. Methods for the design and administration of web-based surveys *Journal of American Medical Informatics Association* 7.

Sekaran, U. & Bougie, R. 2010. *Research Methods for Business,* Wiley.

Silverman 2000. *Handbook of quantitative research*. Thousand Oaks, CA: *Sage Publications*

Simon, D., Schorr, G., Wirtz, M., Vodermaier, A., Caspari, C., Neuner, B., Spies, C., Krontes, T., Keller, H., Edwards, A., Loh, A. & Harter, M. 2006. Development and first validation of the shared decision-making questionnaire (SDM-Q). *Patient Educ Couns,* 63**,** pp. 319-27.

Stanford University, 2013a. *Decision-making* [Online]. Stanford, USA. Available: http://search.gsb.stanford.edu/search?q=decision-making&site

Stellenbosch University, S. 2013b. *Information Science: Centre for knowledge dynamics and decision-making* [Online]. Available: http://www.informatics.sun.ac.za/.

Strauss, A. & Corbin, J. 1998. *Basics of qualitative research,* Thousand Oaks, Sage Publications.

Streiner, D. & Norman, G. 2008. Health Measurement Scales: a practical guide to their development and use, Oxford.Oxford University Press.

SurveyMonkey. 2013. *SurveyMonkey Official website* [Online]. Available: http://www.surveymonkey.com.

Tabachnick, B. & Fidell 2001. *Using multivariate statistics,* New York, *Harper Collins*.

Terwee, C. B., Bot, S. D., De Boer, M. R., Van Der Windt, D. A., Knol, D. L., Dekker, J., Bouter, L. M. & De Vet, H. C. 2007. Quality criteria were proposed for measurement properties of health status questionnaires. *Journal of Clinical Epidemiology,* 60 (1)**,** pp. 34-42.

TGA (Therapeutics Goods Agency), Canada, H. 2013. Therapeutic Products Directorate Good Review Practices Project. 21 June 2013.

Tony, M., Wagner, M., Khoury, H., Rindress, D., Papastavros, T., Oh, P. & Goetghebeur, M. M. 2011. Bridging health technology assessment (HTA) with multicriteria decision analyses (MCDA): field testing of the EVIDEM framework for coverage decisions by a public payer in Canada. *BMC Health Serv Res,* 11**,** p. 329.

Trochim, W. 2006. *Construct validity, research methods knowledge base*. http://www.socialresearchmethods.net/kb/constval.php

Trochim, W. M. 1989. An introduction to concept mapping for evaluation and planning, *Evaluation and Program Planning,* 12, pp. 1-16. *Pergamon Press.*

Van Assen, M., Van Den Berg, G. & Piestersma, P. 2009. *Key management models*, Great Britain, Prentice Hall.

Verma, D. 2009. *Decision-making style: Social and creative dimensions,* New Delhi, India, Global India Publications Pvt Ltd.

Von Bergen, C. W., JR. & Kirk, R. J. 1978. Groupthink: when too many heads spoil the decision. *Manage Rev,* 67**,** pp. 44-9.

Walker, S., Cone, M. & McAuslane, N. 2007. Quality decision-making: procedures and pracitices in drug development and the regulatory review. CMR International Institute Workshop. Surrey: CMR International.

Walker, S. L., Liberti, L., Connelly, P. 2011. Visualising benefit-risk of assessment of medicines: The key to develop a framework that informs stakeholder perspective and clarity of decision making. CIRS Workshop. Surrey. CIRS.

Web, H. B. R. 2012. *Decision-making* [Online]. Available: http://hbr.org/web/management-tip/tips-on-decision-making.

Wellard, S. & McKenna, L. 2001. Turning tapes into text: issues surrounding the transcription of interviews. *Contemp Nurse,* 11**,** pp. 180-6.

Westaby, J. D., Probst, T. M. & Lee, B. C. 2010. Leadership decision-making: A behavioral reasoning theory analysis. *The Leadership Quarterly,* 21**,** 481-495.

Westen, D. & Rosenthal, R. 2003. Quantifying construct validity: Two simple measures. *Journal of Personality and Social Psychology,* 84**,** pp. 608-618.

Wethey, D. 2013. *Decide,* London, Kogan Page.

Zuckerman, D. 2006. *Pharmaceutical Metrics: Measuring and improving R & D performance*, Gower Publishing Company. P.112.

APPENDIX I

Quality of Decision-Making: Research Outline

Background: The Centre for Innovation in Regulatory Science (CIRS), formerly known as "CMR International Institute for Regulatory Science", in collaboration with the Welsh School of Pharmacy, Cardiff University is currently performing research into the "quality of decision-making" within the pharmaceutical development arena and the associated regulatory review.

Research Objective: to explore the ways in which different companies/organisations manage decision-making. In turn, to help facilitate and promote quality within the decision-making processes within the pharmaceutical arena and regulatory authorities

Research Methodology: This research involves a two-stage investigation and involves participants from the pharmaceutical arena and the regulatory authorities.

Stage 1: Is an initial validation stage and consists of the conduct of semi-structured interviews on the subject of "Quality of decision-making", with interviewees from the pharmaceutical arena and regulatory authorities. The interviews comprise of six main questions covering an interviewee's views on:

- General understanding or perception of decision-making
- Decision-making within the drug development arena
- Decision-making within the regulatory review
- Decision-making within their organisation
- Awareness and use of decision-making techniques
- Impact and monitoring of decisions

The interviews are all treated with due confidentiality and this is detailed before the start of any interview. The interviews require around 30-45 minutes of an interviewee's time and will be conducted in October and November 2011.

The results of the Stage 1 interviews performed should facilitate and validate the generation of a quality instrument tool to support and promote quality within the decision-making process.

Stage 2, will comprise of an e-mail questionnaire survey (of the quality instrument tool) to a larger sample size of targeted persons working within the pharmaceutical arena and regulatory agencies. The questionnaire will comprise of a Likert type response format with the option for free text. It will comprise of questions enquiring on how respondents and their company/organisation manage the decision-making process. Again, the stage 2 research will be managed with due confidentiality and the findings of the investigation will be made available to all of the research participants.

APPENDIX II

Content Validation of a Tool to Assess the Quality of Decision-Making

Introduction

Many people find it hard to believe that there can be a "science of decision-making". However, there is such a science and it is based on a very coherent theory about how to make better decisions.

"Contrary to expectations a quality decision and decision-making process should not be tested by looking at the outcomes and consequences. In an uncertain world, it is perfectly possible to take a good decision that has poor consequences and, equally, to make a bad decision and come up with a good outcome. On balance, however, the long-running use of good systems for making decisions will generally give better outcomes."

Companies and regulatory agencies are working to develop frameworks for making decisions that are systematic, transparent and accountable. The question is how good are the approaches within companies and agencies for making decisions and what are the challenges and enablers to ensure good quality decisions? One way of testing this, is to look at how individuals and organisations make decisions based on custom and practices and map this to against best practice decision-making.

Background

The Centre for Innovation in Regulatory Science in collaboration with the Welsh School of Pharmacy, Cardiff University, has developed a tool consisting of a number of statements to evaluate the quality of decision-making for individuals and their organisations. This was as a result of conducing twenty nine semi-structured interviews with individuals from regulatory authorities (nine), pharmaceutical companies (ten) and CROs (ten) when the follow themes were explored:

Best practice perceptions of decision-making;

Decision-making within drug development;

Decision-making within the regulatory review;

Decision-making within their individual organisation;

Awareness and use of decision-making techniques;

The impact and monitoring of decisions

As an outcome of these interviews, a tool for measuring the quality of decision-making has been developed consisting of 94 items (statements) which cover many aspects of decision-making within an organisation.

Objectives

This measurement tool now needs to be validated for its content and you are asked to rate each of the following statements for:

A. Language clarity: the sentence and wording should be clear, understandable, straight forward and simple. Phrases and wording should be unambiguous and jargon free

B. Completeness: The sentence should be complete, not broken and should end appropriately.

C. Relevance: Each item should be relevant to the subject area and target population.

D. Scaling: The scoring system uses a four point Likert scale. You should rate the Likert scaling system as to whether the response options fit the question or no

Outcome

It is envisaged that this tool will be sent to a number of regulatory authorities and pharmaceutical organisations inviting them to complete and assess each statement so that an organisation can compare its decision-making approach with the principles of good quality decision-making.

As part of the standardised approach for the development of tools of this nature, it is ideal for a panel discussion following completion of the ratings by all panel members.

Ronan Donelan, Sam Salek and Stuart Walker
16 May 2012

APPENDIX III

A COPY OF THE 94-ITEM CHECKLIST

(The first nine items in the checklist are included for reference example)

A copy of the 94-item Checklist

Validation of Questionnaire Feedback Form

Quality of Decision-making Orientation Scheme (QoDOS)

Name . . . . . Specialty . . . . . .

Thank you for agreeing to take part in the questionnaire feedback as part of the content validity.

Each item on the questionnaire needs to be assessed for language clarity, completeness, relevance and scaling. The following definitions are provided to ensure standardisation and so that each person has the same understanding of these criteria.

Please rate each of the following questionnaire items on the following:

A. Language clarity: the sentence and wording should be clear, understandable, straightforward and simple. Phrases and wording should be unambiguous and jargon free

B. Completeness: the sentences should be complete, not broken and should end appropriately.

C. Relevance: each item should be relevant to the subject area and target population.

D. Scaling: the scoring system uses a 4 point Likert scale. You should rate the Likert scaling system as to whether the response options fit the question, or not.

A copy of the 94-item Checklist

Item 1: I use a structured approach in my decision-making

	Strongly agree	Agree	Disagree	Strongly disagree	Any Comments:
Language Clarity	☐	☐	☐	☐	
Completeness	☐	☐	☐	☐	
Relevance	☐	☐	☐	☐	
Scaling	☐	☐	☐	☐	

Item 2: My company uses a structured approach in its decision-making

	Strongly agree	Agree	Disagree	Strongly disagree	Any Comments:
Language Clarity	☐	☐	☐	☐	
Completeness	☐	☐	☐	☐	
Relevance	☐	☐	☐	☐	
Scaling	☐	☐	☐	☐	

Item 3: I evaluate the impact of the decisions I make

	Strongly agree	Agree	Disagree	Strongly disagree	Any Comments:
Language Clarity	☐	☐	☐	☐	
Completeness	☐	☐	☐	☐	
Relevance	☐	☐	☐	☐	
Scaling	☐	☐	☐	☐	

Item 4: My organisation evaluates the impact of the decisions it makes

	Strongly agree	Agree	Disagree	Strongly disagree	Any Comments:
Language Clarity	☐	☐	☐	☐	
Completeness	☐	☐	☐	☐	
Relevance	☐	☐	☐	☐	
Scaling	☐	☐	☐	☐	

Item 5: I understand the importance of the decisions I make

	Strongly agree	Agree	Disagree	Strongly disagree	Any Comments:
Language Clarity	☐	☐	☐	☐	
Completeness	☐	☐	☐	☐	
Relevance	☐	☐	☐	☐	
Scaling	☐	☐	☐	☐	

Item 6: My organisation's decision-making is influenced by its strategy

	Strongly agree	Agree	Disagree	Strongly disagree	Any Comments:
Language Clarity	☐	☐	☐	☐	
Completeness	☐	☐	☐	☐	
Relevance	☐	☐	☐	☐	
Scaling	☐	☐	☐	☐	

Item 7: My organisation's decision-making is influenced by external stakeholder

demands

	Strongly agree	Agree	Disagree	Strongly disagree	Any Comments:
Language Clarity	☐	☐	☐	☐	
Completeness	☐	☐	☐	☐	
Relevance	☐	☐	☐	☐	
Scaling	☐	☐	☐	☐	

Item 8: My organisation's decision-making is influenced by competitors

	Strongly agree	Agree	Disagree	Strongly disagree	Any Comments:
Language Clarity	☐	☐	☐	☐	
Completeness	☐	☐	☐	☐	
Relevance	☐	☐	☐	☐	
Scaling	☐	☐	☐	☐	

Item 9: My organisation's decision-making is influenced by the vested interest of individuals

	Strongly agree	Agree	Disagree	Strongly disagree	Any Comments:
Language Clarity	☐	☐	☐	☐	
Completeness	☐	☐	☐	☐	
Relevance	☐	☐	☐	☐	
Scaling	☐	☐	☐	☐	

APPENDIX IV

QoDOS DEVELOPMENTAL INSTRUMENT (VERSION 2)

Quality of Decision-Making Orientation Scheme (QoDOS)

The statements in the questionnaire relate to your views on your personal and organisations decision-making processes. Please mark clearly one box for each statement. Please remember, this questionnaire is about **your/company's** views and not the views of others.

Quality of Decision-Making Orientation Scheme (QoDOS)

	Never	Rarely	Sometimes	Often	Always	Not Applicable
1. I use a structured approach in my decision-making	☐	☐	☐	☐	☐	☐
2. My company uses a structured approach in its decision-making	☐	☐	☐	☐	☐	☐
3. I evaluate the impact of the decisions I make	☐	☐	☐	☐	☐	☐
4. My organisation evaluates the impact of the decisions it makes	☐	☐	☐	☐	☐	☐
5. I understand the importance of the decisions I make	☐	☐	☐	☐	☐	☐
6. My organisation's decision-making is influenced by its strategy	☐	☐	☐	☐	☐	☐
7. My organisation's decision-making is influenced by external stakeholder demands	☐	☐	☐	☐	☐	☐
8. My organisation's decision-making is influenced by competitors	☐	☐	☐	☐	☐	☐

	Never	Rarely	Sometimes	Often	Always	Not Applicable
9. My organisation's decision-making is influenced by the vested interest of individuals	☐	☐	☐	☐	☐	☐
10. My organisation's decision-making is influenced by deadlines	☐	☐	☐	☐	☐	☐
11. My organisation's decision-making is influenced by Company politics	☐	☐	☐	☐	☐	☐
12. My organisation's decision-making is influenced by incentives or penalty payments	☐	☐	☐	☐	☐	☐
13. My decision-making is influenced by my previous experience	☐	☐	☐	☐	☐	☐
14. My organisation's decision-making is influenced by its previous experience	☐	☐	☐	☐	☐	☐
15. My decision-making is influenced by the experience of others	☐	☐	☐	☐	☐	☐
16. I use intuition or "gut-feeling" in my decision-making	☐	☐	☐	☐	☐	☐
17. In my organisation, people are held accountable for their decisions	☐	☐	☐	☐	☐	☐
18. I am accountable for my decisions	☐	☐	☐	☐	☐	☐
19. I have acquiesced to my line management on project decisions	☐	☐	☐	☐	☐	☐

	Never	Rarely	Sometimes	Often	Always	Not Applicable
20. My organisation has acquiesced to external experts on project decisions	☐	☐	☐	☐	☐	☐
21. I feel better qualified to make a decision compared to others who are empowered to make decisions	☐	☐	☐	☐	☐	☐
22. I feel that I could make better quality decisions	☐	☐	☐	☐	☐	☐
23. My organisation could make better quality decisions	☐	☐	☐	☐	☐	☐
24. I receive training in the science of decision-making	☐	☐	☐	☐	☐	☐
25. I use tools e.g. modelling or decision trees which facilitate my decision-making	☐	☐	☐	☐	☐	☐
26. My professional experience is important when having to make challenging decisions	☐	☐	☐	☐	☐	☐
27. I continue with projects which should be terminated at an earlier stage	☐	☐	☐	☐	☐	☐
28. My organisation continues with projects which should be terminated at an earlier stage	☐	☐	☐	☐	☐	☐
29. I have experienced “paralysis by analysis” caused by my slow decision-making	☐	☐	☐	☐	☐	☐
30. My procrastination has resulted in a negative outcome	☐	☐	☐	☐	☐	☐

	Never	Rarely	Sometimes	Often	Always	Not Applicable
31. My organisation has suffered a negative outcome due to slow decision-making	☐	☐	☐	☐	☐	☐
32. I have experienced a negative outcome by a decision <u>not</u> being made	☐	☐	☐	☐	☐	☐
33. My organisation's culture has resulted in its inability to make a decision	☐	☐	☐	☐	☐	☐
34. I qualify the probability of success in my decision-making	☐	☐	☐	☐	☐	☐
35. My organisation qualifies the probability of success in its decision-making	☐	☐	☐	☐	☐	☐
36. I quantify the probability of success in my decision-making	☐	☐	☐	☐	☐	☐
37. My organisation quantifies the probability of success in its decision-making	☐	☐	☐	☐	☐	☐
38. I understand the context of the decision I am being asked to make	☐	☐	☐	☐	☐	☐
39. My organisation provides clear and unambiguous instructions for decision-making	☐	☐	☐	☐	☐	☐
40. My decision-making approach is transparent	☐	☐	☐	☐	☐	☐

	Never	Rarely	Sometimes	Often	Always	Not Applicable
41. My organisation's decision-making approach is transparent	☐	☐	☐	☐	☐	☐
42. My decision-making could be improved by assigning weights	☐	☐	☐	☐	☐	☐
43. I present contingencies or achievable options as part of my decision-making	☐	☐	☐	☐	☐	☐
44. I generate a SWOT (strengths, weaknesses, opportunities, threats) analysis in my decision-making	☐	☐	☐	☐	☐	☐
45. I consider uncertainty and unknowns in my decision-making approach	☐	☐	☐	☐	☐	☐
46. I use negotiation in my decision-making	☐	☐	☐	☐	☐	☐
47. My decision-making is consistent	☐	☐	☐	☐	☐	☐
48. My organisations decision-making is consistent	☐	☐	☐	☐	☐	☐
49. My organisation re-examines its decision-making as new information becomes available	☐	☐	☐	☐	☐	☐
50. I am open to using better alternatives in my current decision-making	☐	☐	☐	☐	☐	☐

	Never	Rarely	Sometimes	Often	Always	Not

						Applicable
51. My organisation is open to using better alternatives in its decision-making	☐	☐	☐	☐	☐	☐
52. In my decision-making, I make the same mistakes as made in the past	☐	☐	☐	☐	☐	☐
53. In my organisations decision-making, it makes the same mistakes as made in the past	☐	☐	☐	☐	☐	☐
54. My organisation welcomes information supporting their existing biases and discounts opposing information	☐	☐	☐	☐	☐	☐
55. I underestimate problems which adversely impact my decision-making	☐	☐	☐	☐	☐	☐
56. My organisation underestimates problems which adversely impacts its decision-making	☐	☐	☐	☐	☐	☐
57. I am overcautious when estimating uncertainties related to my decisions	☐	☐	☐	☐	☐	☐
58. My organisation is overcautious when estimating uncertainties related to its decisions	☐	☐	☐	☐	☐	☐
59. Recent or dramatic events greatly impact my decision-making	☐	☐	☐	☐	☐	☐

	Never	**Rarely**	**Sometimes**	**Often**	**Always**	**Not**

						Applicable
60. Recent or dramatic events greatly impact my organisations decision-making	☐	☐	☐	☐	☐	☐
61. I weigh up the opinions of others in my decision-making	☐	☐	☐	☐	☐	☐
62. My decision-making is innovative	☐	☐	☐	☐	☐	☐
63. My organisation encourages innovative decision-making	☐	☐	☐	☐	☐	☐
64. I maintain an auditable record of my decisions	☐	☐	☐	☐	☐	☐
65. My organisation maintains an auditable record of its decisions	☐	☐	☐	☐	☐	☐
66. Emotion is part of my decision-making	☐	☐	☐	☐	☐	☐
67. My approach to decision-making is predictable	☐	☐	☐	☐	☐	☐
68. My organisation's approach to decision-making is predictable	☐	☐	☐	☐	☐	☐
69. My decision-making is knowledge based	☐	☐	☐	☐	☐	☐
70. My organisations decision-making is knowledge based	☐	☐	☐	☐	☐	☐
71. I use benchmarking in my decision-making	☐	☐	☐	☐	☐	☐

	Never	Rarely	Sometimes	Often	Always	Not

						Applicable
72. My organisation uses benchmarking in its decision-making	☐	☐	☐	☐	☐	☐
73. I effectively communicate the decisions I make	☐	☐	☐	☐	☐	☐
74. My organisation effectively communicates the decisions it makes	☐	☐	☐	☐	☐	☐
75. My organisation effectively communicates the decisions it makes	☐	☐	☐	☐	☐	☐
76. Decision-making in my organisation tends to be final and not open to reinterpretation or discussion	☐	☐	☐	☐	☐	☐

Please check that you have answered all 76 questions.

Thank you for your cooperation with this exercise
Please feel free to add comments, recommendations, suggestions or the like on the free text page overleaf.

Free Text Commentary

.....

.....

.....

.....

.....

.....

.....

.....

.....

Please answer the following questions:

Job Title:

How many years of professional experience have you to date?

Type of Organisation:

Regulatory Agency	Pharmaceutical Industry	Academia	CRO	Other
☐	☐	☐	☐	☐

Thank you for your participation.

APPENDIX V

THE 47-ITEM QoDOS INSTRUMENT (VERSION 3)

Quality of Decision-Making Orientation Scheme (QoDOS)©

The statements in the questionnaire relate to your views on your personal and organisations decision-making processes. Please mark clearly one box for each statement. Please remember, this questionnaire is about your/company's views and not of others.

Please answer the following questions:
Job title: _____
How many years of professional experience have you to date? _____

Type of Organisation:
Regulatory Agency ☐ Pharmaceutical Industry ☐ Academia ☐ CRO ☐ Other ☐

Part I: Organisational level influences

A. Decision-making approach

		Not at all	Sometimes	Frequently	Often	Always
1.	My organisation evaluates the impact of the decisions it makes	☐	☐	☐	☐	☐
2.	My organisation's decision-making is transparent	☐	☐	☐	☐	☐
3.	My organisation's decision-making is consistent	☐	☐	☐	☐	☐
4.	My organisation uses a structured approach in its decision-making	☐	☐	☐	☐	☐
5.	My organisation's decision-making is influenced by external stakeholder's demands	☐	☐	☐	☐	☐
6.	My organisation qualifies the probability of success in its decision-making	☐	☐	☐	☐	☐
7.	My organisation quantifies the probability of success in its decision-making	☐	☐	☐	☐	☐
8.	My organisation is open to using better alternatives in its decision-making	☐	☐	☐	☐	☐
9.	My organisation encourages innovative decision-making	☐	☐	☐	☐	☐
10.	My organisation considers uncertainties in relation to its decision-making	☐	☐	☐	☐	☐
11.	My organisation provides training in the science of decision-making	☐	☐	☐	☐	☐
12.	My organisation re-examines its decision-making as new information becomes available	☐	☐	☐	☐	☐

B. Decision-making culture

	Not at all	Sometimes	Frequently	Often	Always
13. My organisation has suffered a negative outcome due to slow decision-making	☐	☐	☐	☐	☐
14. My organisation's culture has resulted in its inability to make a decision	☐	☐	☐	☐	☐
15. My organisation's decision-making is influenced by company politics	☐	☐	☐	☐	☐
16. My organisation's decision-making, it makes the same mistakes as in the past.	☐	☐	☐	☐	☐
17. My organisation's decision-making its influenced by the vested interest of individuals	☐	☐	☐	☐	☐
18. My organisation underestimates problems which adversely impacts its own decisions	☐	☐	☐	☐	☐
19. My organisation continues with projects which should be terminated at an earlier stage	☐	☐	☐	☐	☐
20. My organisation decision-making its influenced by competitors	☐	☐	☐	☐	☐
21. My organisation's decision-making is influenced by incentives or penalty payments	☐	☐	☐	☐	☐
22. My organisation effectively communicates the decisions it makes	☐	☐	☐	☐	☐
23. My organisation provides clear and unambiguous instructions for decision-making	☐	☐	☐	☐	☐

PART II: Individual level influences

A. Decision-making competence

	Not at all	Sometimes	Frequently	Often	Always
24. My decision-making is knowledge based	☐	☐	☐	☐	☐
25. My decision-making is consistent	☐	☐	☐	☐	☐
26. I consider uncertainty and unknowns in my decision-making approach	☐	☐	☐	☐	☐
27. I generate a SWOT analysis in my decision-making	☐	☐	☐	☐	☐
28. I present contingencies or achievable options as part of my decision-making	☐	☐	☐	☐	☐
29. My decision-making is transparent	☐	☐	☐	☐	☐
30. I understand the context of the decision I am being asked to make	☐	☐	☐	☐	☐
31. I understand the importance of the decisions I make	☐	☐	☐	☐	☐
32. I use a structured approach in my decision-making	☐	☐	☐	☐	☐
33. I qualify the probability of success in my decision-making	☐	☐	☐	☐	☐
34. I quantify the probability of success in my decision-making	☐	☐	☐	☐	☐
35. I receive training in the science of decision-making	☐	☐	☐	☐	☐
36. I use intuition or “gut-feeling” in my decision-making	☐	☐	☐	☐	☐
37. My professional experience is important when having to make challenging decisions	☐	☐	☐	☐	☐

B: Decision-making style

	Not at all	Sometimes	Frequently	Often	Always
38. Emotion is part of my decision-making	☐	☐	☐	☐	☐
39. I have experienced "paralysis by analysis" caused by my slow decision-making	☐	☐	☐	☐	☐
40. I have experienced a negative outcome by a decision not being made	☐	☐	☐	☐	☐
41. In my decision-making, I make the same mistakes as in the past	☐	☐	☐	☐	☐
42. Recent or dramatic events greatly impact my decision-making	☐	☐	☐	☐	☐
43. My procrastination has resulted in a negative outcome	☐	☐	☐	☐	☐
44. My decision-making could be improved by assigning weights	☐	☐	☐	☐	☐
45. I underestimate problems which adversely impact my decision-making	☐	☐	☐	☐	☐
46. I continue with projects which should be terminated at an early stage	☐	☐	☐	☐	☐
47. I feel that I could make better quality decisions	☐	☐	☐	☐	☐

Please check that you have answered all 47 questions.
Thank you for your cooperation with this exercise
Please feel free to add comments, recommendations, suggestions or the like on the free text page overleaf.

Please feel free to add comments, recommendations or suggestions below:

Comments

Confidentiality

All information collected from individual agencies and companies will be kept strictly confidential. No data that will identify an individual agency or company will be reported, or detail made to a third party. External reports or presentation of the data will include only anonymous figures and any appropriate analytical interpretation. Agency or company data will only be provided to the relevant organisation concerned.

Centre for Socioeconomic Research, Cardiff University, Cardiff, United Kingdom
SalekS@CF.AC.UK