



**ROBERT GORDON
UNIVERSITY•ABERDEEN**

OpenAIR@RGU

The Open Access Institutional Repository at Robert Gordon University

<http://openair.rgu.ac.uk>

Citation Details

Citation for the version of the work held in 'OpenAIR@RGU':

BONANNO, P. V., 2003. The managed entry of new drugs into a National Health Service: a case study for Malta. Available from *OpenAIR@RGU*. [online]. Available from: <http://openair.rgu.ac.uk>

Copyright

Items in 'OpenAIR@RGU', Robert Gordon University Open Access Institutional Repository, are protected by copyright and intellectual property law. If you believe that any material held in 'OpenAIR@RGU' infringes copyright, please contact openair-help@rgu.ac.uk with details. The item will be removed from the repository while the claim is investigated.

**The Managed Entry of New Drugs
into a National Health Service:
a Case Study for Malta**

PATRICIA VELLA BONANNO

A thesis submitted in partial fulfilment of the requirements of

The Robert Gordon University

for the degree of

DOCTOR OF PHILOSOPHY

Centre for Partnerships in Medicines for Health

June 2003

Faculty of Health and Social Care

The Robert Gordon University

Aberdeen

Scotland

“The reasonable man adapts himself to the world:
the unreasonable one persists on trying to adapt the world to himself.
Therefore, all progress depends on the unreasonable man.”

George Bernard Shaw

To David and Samwel for making life special

ABSTRACT

The research question was to determine if it is possible to develop a systematic approach to the managed entry of new drugs into a National Health Service (NHS), using Malta as a case study.

In early 1999, Malta had major problems with the managed entry of new drugs into the NHS. Some essential processes such as medicines registration did not exist, and the processes that existed were not systematic. The policy for the introduction of new drugs resulted in a large number of non-formulary requests for individual patients, with such applications rising to 14,129 by 1998. There were no set criteria for assessing these applications and this together with internal and external influences led to inequity of access to drugs within the NHS.

A case study was conducted. A descriptive evaluation was undertaken and a logic model was used to represent the case as in June 1999 (baseline). Areas for change were planned and prioritised. An action evaluation was undertaken and action research was implemented as an intervention for change. A second descriptive model was developed to represent the processes at the end of the action evaluation (December 2001). An outcome evaluation described the changes that took place during the action evaluation.

A number of improvements supporting a more systematic approach were achieved. Several policies were revised and new policies developed where appropriate. The outcome was that new drugs were to be approved on the formulary for groups of patients (rather than individuals) that met specific criteria. Due to limited NHS resources inequity remains. However, the approach is now systematic which has made the processes more transparent. Recommendations for further development of the systematic approach were made with the aim of further reducing inequity.

ACKNOWLEDGEMENTS

Throughout this thesis I was supervised by Professor Clare A. Mackie. I am deeply grateful for her strong support and for fervently sharing her expertise, enthusiasm, friendship and generous discipline, to which I owe the finalisation of this thesis to the end. I greatly appreciate the wholehearted and expert contribution of Dr Andrew Lamb and Dr Ross Taylor who were advisors on the supervisory team. I thank Ms Marthe Everard, now working at the World Health Organisation Office in Geneva, for her advice during the initial planning stage.

I appreciate the contribution of all my colleagues within the Department of Health in Malta, who supported the approval and implementation of the research since it started in 1998. I particularly thank Professor Carmel Mallia, Chairman of the Drug and Therapeutics Committee (DTC) who was my external advisor, Dr Ray Busuttil, Director General at the Health Division who was a major driver for the achievement of changes beyond what was originally considered feasible and Mrs Lilian Wismayer, Director at the Medicines Regulatory Unit. I sincerely thank Mrs Alexandra Lucas, my colleague within the secretariat of the DTC for her help and loyalty throughout, particularly during the time when I was in Aberdeen. I apologise to my colleagues, if they still feel any of the pains generated during the process of change.

The funding received from the Association of Commonwealth Universities of the Commonwealth Scholarship Commission in the United Kingdom and through the British Chevening Scholarship awarded by the British High Commission in Malta (for the first year of the research) made it financially possible for me to study in the United Kingdom, and for this I am very grateful. I would like to thank the British Council in Manchester for their support and understanding throughout.

My thanks also go to Mr A Wilson and Professor A Buhagiar for their advice on statistics. I appreciate all those who supported me during my stay in Aberdeen including Ms B Howitt, Ms F Sturgeon and Ms M Mannall.

A special thanks goes to my husband David, my parents and in-laws, our families and friends. A deep appreciation goes to Auntie Mary.

CONTENTS

Abstract	
Acknowledgements	
List of Contents	
List of Tables	
List of Figures	
List of Appendices	
Abbreviations	

CHAPTER 1: General Introduction	1-54
1.1 Introduction	1
1.1.1 The supply of drugs within the national health services in Malta - a general overview	1
1.1.2 Previous research on the entry of new drugs into the NHS in Malta	7
1.1.3 The managed entry of new drugs into the NHS in Malta in February 1999 - a cause for concern and an opportunity for change	9
1.2 Literature review	11
1.2.1 An overview of the changes that have influenced current practice in Europe	11
1.2.2 The impact of medicines registration on the access and supply of medicines through national health services in Europe	15
1.2.3 Pharmaceuticals as part of healthcare within national health services in European countries	19
1.2.4 Policies to control spending on drugs and to improve the efficiency of drug use within national health services in Europe	24
1.2.5 Reimbursement decisions and health technology assessment	30
1.2.6 Theories and knowledge from the field of change management applicable to the implementation of change in health care systems	35
1.2.7 Bringing about change in practice	43
1.2.8 Interventions for improvement in practice	49
1.3 Research question and aims	53

CHAPTER 2: General Methodology	55-91
2.1 The case study	55
2.1.1 The case study as a research method	55
2.1.2 The generalisability of case study findings	57
2.2 Design of the evaluation	58
2.2.1 Evaluation for action	58
2.2.2 Evaluation of health interventions	59
2.2.3 The application of the developmental category of evaluation	61
2.2.4 Types and design of evaluations within the developmental framework	63
2.2.5 Design of the evaluation used in this research	66
2.3 The logic model as a tool for the evaluation	67
2.3.1 Logic models	67
2.3.2 Building a logic model	70
2.3.3 The use of logic models in healthcare	72
2.4 Action research as an intervention for change	72
2.4.1 Comparison between action research and traditional research	73
2.4.2 The validity of action research	74
2.4.3 Characteristics of action research	75
2.5 The use of different methods for case study research, as relevant to this case study	77
2.5.1 Gathering and analysis of data for case study research	78
2.5.2 Methods used to collect data for this case study	80
2.6 Statistical handling during the research	86
2.7 Ethical and practical issues related to the research	89
2.7.1 Approval of the research by the participants within the practice	89
2.7.2 Ethical approval by the Research and Ethics Committee	90
2.8 Summary of the methodology used in the case study research	90

CHAPTER 3: Descriptive Evaluation	92-148
3.1 Introduction	92
3.2 Aim and objectives	93
3.3 Methods	94
3.3.1 Development of a 'General logic model'	94
3.3.2 Gathering information about the processes for the managed entry of new drugs into the NHS in Malta	95
3.3.2.1 Participant observation	95
3.3.2.2 Document and record research from 1991 to June 1999	96
3.3.2.3 Activity of the DTC from 1991 to 1998 in relation to 'new drug' applications	97
3.3.2.4 Consultant questionnaires	98
3.3.2.5 Patient interviews	99
3.3.2.6 Focus group discussions	100
3.3.2.7 Interviews with medical representatives	101
3.3.3 Development of 'Descriptive model 1' to represent the processes for the managed entry of new drugs into the NHS in Malta as in June 1999	102
3.4 Results	102
3.4.1 Development of a 'General logic model'	102
3.4.2 Gathering information about the processes for the managed entry of new drugs into the NHS in Malta	106
3.4.2.1 Participant observation and document and record research	106
3.4.2.2 Activity of the DTC from 1991 to 1998 in relation to 'new drug' applications	111
3.4.2.3 Consultant questionnaires	115
3.4.2.4 Patient interviews	120
3.4.2.5 Results of focus group discussions	122
3.4.2.6 Interviews with medical representatives	124
3.4.3 Development of 'Descriptive model 1' to represent the processes for the managed entry of new drugs into the NHS in Malta as in June 1999	127
3.5 Discussion	132
3.6 Summary	147

CHAPTER 4: Planning and Prioritisation for Change	149-167
4.1 Introduction	149
4.2 Aim and objectives	151
4.3 Methodology	151
4.4 Results	153
4.4.1 Organisation	153
4.4.2 Policy	156
4.4.3 Process	161
4.5 Discussion	163
4.6 Summary	167
CHAPTER 5: Action Evaluation	168-229
5.1 Introduction	168
5.2 Aim and objectives	171
5.3 Methodology	172
5.3.1 Gathering information to support the change process	172
5.3.1.1 Document and record research from July 1999 to December 2001	172
5.3.1.2 Activity of the DTC from January 1999 to December 2001 in relation to 'new drug' applications	172
5.3.1.3 Prospective follow-up of requests discussed by the DTC from July 1999 to December 2001	173
5.3.1.4 Case studies to illustrate key issues relevant to the managed entry of new drugs	174
5.3.2 The change process	175
5.3.3 Description of the processes for the managed entry of new drugs into the NHS in Malta as in December 2001	176
5.4 Results	177
5.4.1 Information gathered to support the change process	177

5.4.1.1	Document and record research from July 1999 to December 2001	177
5.4.1.2	New drug applications considered by the DTC from January 1999 to December 2001	180
5.4.1.3	Prospective follow-up of requests discussed by the DTC from July 1999 to December 2001	186
5.4.1.4	Case studies to illustrate key issues relevant to the managed entry of new drugs	190
5.4.2	The change process	200
5.4.2.1	Organisational change	200
5.4.2.2	Policy change	204
5.4.2.3	Change in the processes for the selection of new drugs into the NHS	208
5.4.3	Description of the processes for the managed entry of new drugs into the NHS in Malta as in December 2001	214
5.5	Discussion	220
5.6	Summary	229

CHAPTER 6:	Outcome Evaluation	230-248
6.1	Introduction	230
6.2	Aim and objectives	231
6.3	Methodology	231
6.4	Results	232
6.4.1	Organisation	232
6.4.2	Policy	234
6.4.3	Processes	236
6.5	Discussion	238
6.6	Summary	247

CHAPTER 7: General Discussion	249-283
7.1 The case study of Malta	251
7.2 Factors from the case study of Malta that inform case study research and developmental evaluation in healthcare	254
7.3 The use of action research as an intervention for change	258
7.4 The use of the case study for Malta to inform the systematic approach to the managed entry of new drugs into NHS	264
7.5 The implications of accession into the EU	267
7.6 General aspects of the main processes of the managed entry of new drugs into NHS	271
7.7 Summary and recommendations	278
7.8 Conclusions	283
References	284-305

LIST OF TABLES

1.1	Total expenditure on NHS drugs for the period 1991-1998	4
1.2	A framework for the continual improvement of healthcare	44
2.1	Categories most often used to evaluate different types of interventions for different items for evaluation	61
2.2	Elements of the logic model	69
2.3	Overview of timescale and methods relative to individual chapters	90
2.4	Detailed research methods and the developments in the logic model relative to individual chapters	91
3.1	The 'General logic model' representing the managed entry of new drugs into national health services in EU countries	103
3.2	Activity of the Drug and Therapeutics Committee in relation to 'new drug' applications from 1991-1998	112
3.3	Approval of drugs for individual patients from NHS hospitals (1995-1998)	113
3.4	A descriptive model of the managed entry of new drugs into NHS in Malta as in June 1999 'Descriptive model 1'	128
5.1	Medicinal products licensed for importation in Malta as at December 2000	177
5.2	Estimated cost for the supply of drugs through the NHS for in-patient and out-patient use	179
5.3	Activity of the Drug and Therapeutics Committee in relation to 'new drug' applications from 1995-2001	181
5.4	Approval of drugs for individual patients from NHS hospitals (1995-2001)	182
5.5	Summary details of 'new drug' and formulary update applications considered by the DTC during the action evaluation (July 1999-December 2001)	187
5.6	'Descriptive model 2' of the managed entry of new drugs into the NHS in Malta as in December 2001	215

LIST OF FIGURES

1.1	A model for improvement from Langley, Nolan and Nolan (1992)	47
1.2	Interactions between audit and research	51
2.1	The focus of different types of evaluation with respect to the timing of the intervention	64
2.2	Logic chart for a programme	71
3.1	Individual chart for percentage of requests approved (1991-1998)	114
3.2	Individual chart for percentage of requests decided without delay (1991-1998)	114
5.1	Individual chart for percentage of requests approved (1991-2001)	183
5.2	Individual chart for the percentage of requests decided without delay (1991-2001)	183
5.3	CUSUM Chart for the percentage of requests approved (1991-2001) V masked at 2001	184
5.4	CUSUM Chart for the percentage of requests decided without delay V masked at 2001	185
5.5	Drug and Therapeutics Committee (DTC) and Director General (DG) decisions for 'new drugs' during action evaluation period (July 1999-December 2001)	189
5.6	Drug and Therapeutics Committee (DTC) and Director General (DG) decisions for 'new drugs' during action evaluation period (July 1999-December 2001)	189

APPENDICES

Appendix I	Research Ethics Committee Approval
Appendix II	Questionnaire to Consultants (Questionnaire of 1999)
Appendix III	The Prioritisation Questionnaire to Consultants
Appendix IV	Form for Patient Interviews
Appendix V	Discussion Guide for Interviews with Medical Representatives
Appendix VI	Detailed Responses to the 1994 and the 1999 Questionnaires to Consultants
Appendix VII	Detailed Responses to the Prioritisation Questionnaire Sent to Consultants in 1999
Appendix VIII	Detailed Responses Collected during the Interviews with Patients
Appendix IX	Details of Case Studies to Illustrate Key Issues Associated with the Managed Entry of New Drugs into the NHS in Malta

ABBREVIATIONS

ADR	Adverse Drug Reaction
BNF	British National Formulary (United Kingdom)
CGMO	Chief Government Medical Officer (replaced by DG, Department of Health, Malta)
CPMP	Committee for Proprietary Medicinal Products (EMEA)
CPP	Certificate of Pharmaceutical Product (WHO)
DDD	Defined Daily Dose (WHO)
DG	Director General (Health Division, Malta)
DTC	Drug and Therapeutics Committee (Department of Health, Malta)
EMEA	European Medicines Evaluation Agency (European Union)
EPAR	European Public Assessment Report
EU	European Union
GP	General Practitioner
GPS	Government Pharmaceutical Services (Department of Health, Malta)
MA	Marketing Authorisation
MCA	Medicines Control Agency (United Kingdom)
MRAU	Medicines Regulatory Affairs Unit (replaced by MRU, GPS, Malta)
MRU	Medicines Regulatory Unit (Health Division, Malta)
NDP	National Drug Policy
NFM	National Formulary Management Section (GPS, Malta)
NHS	National Health Service
NICE	National Institute for Clinical Excellence (England and Wales)
NMPAU	National Medicines Policy and Audit Unit (Health Division, Malta)
SIGN	Scottish Intercollegiate Guidelines Network (Scotland)
SMC	Scottish Medicines Consortium (Scotland)
UK	United Kingdom
WHO	World Health Organisation

CHAPTER 1:

GENERAL INTRODUCTION

1.1 INTRODUCTION

1.1.1 The supply of drugs within the national health services in Malta - a general overview

The Maltese archipelago is made up of three main islands: Malta (the mainland), Gozo and Comino. It is in the south of Europe in the middle of the Mediterranean Sea. In 1997 the total population of the islands was reported as 376,513 (European observatory on health care systems, 1999). Within this thesis, Malta was considered to represent the archipelago, unless otherwise specified.

In the 1990s Malta went through a period of political and financial unrest. The nationalist government applied for European Union (EU) membership in 1990. When the labour party was elected in 1996 it froze the application for EU accession. Following an early election in September 1998, the nationalist party was returned to government and reactivated the EU application. During this period Malta was facing an economical imbalance in its public finances and external payments.

The ministry of health was responsible for the provision and financing of health care for all of the population. The state healthcare system was financed by general taxes collected at national level. Since 1991 absolute total health expenditure generally

increased from year to year. In 1994 the share of the Gross Domestic Product (GDP) spent on health care reached a maximum of 6.4%. This was lower than the Western European average of 8.2% for the same period (European observatory on health care systems, 1999).

Since 1987 all Maltese have been entitled to free treatment for chronic diseases that were listed on Schedule V of the Social Security Act (Laws of Malta, 1987) provided that the individual drugs were available within the National Health Services (NHS) in Malta. Only medical consultants could authorise drugs to treat chronic conditions covered by Schedule V. Since 1987 certain patients also had additional entitlement to free medicines through Schedule II of the Social Security Act, also known as the 'Pink card' system (Laws of Malta, 1987). The issue of 'Pink cards' was administered by the Department of Social Services following a means test and drugs were restricted to those available within the NHS.

Patients who required a drug to which they were not entitled (through the Schedule V or the Schedule II 'Pink card' system) or that was not available within the NHS, had to pay the full price. No co-payment system was in place; people either received the drug free from the NHS or had to pay privately. All hospital in-patient treatment was free. General practitioner (GP) authorisation was limited to 'Pink card' holders for a small number of drugs within the NHS. Overall, hospital-based consultants were responsible for authorising the majority of NHS drug treatment.

Following the 1998 election, a decentralisation exercise was taking place within the NHS and the Health Division was being restructured to take up a regulatory role. The

post of the Director General (DG) replaced that of the Chief Government Medical Officer (CGMO). The first DG was newly appointed to the post in February 1999. The DG was the head of the Health Division and also the Superintendent of Public Health. The DG took decisions on resource allocations based upon advice from various government Boards and Committees including the Drug and Therapeutics Committee (DTC). Consumers were not represented on decision-making bodies in health care. The health service in Malta was essentially hospital-based with a weak supporting primary care structure.

The process for the introduction of new drugs into the NHS in Malta was centralised. There was one DTC within the NHS. Consultants could request new drugs to be approved for a number of patients according to a specific protocol for use of the drug or else request that the drug be approved for a specific patient. Requests were considered by the DTC, which made recommendations to the DG, who considered these and made the final decision. If the drug was approved, the DTC was responsible for the implementation of the decision.

Once a drug was approved into the NHS according to a specific protocol, it became available through public hospitals and public outpatient dispensaries according to the criteria for which it was approved. These criteria were uniform throughout the NHS. In contrast once a drug was approved for a specific patient it was not automatically available for other patients with similar or identical conditions. A new application was required for each individual patient.

Medicines supplied through the NHS were procured by a centralised procurement system that was run by the Government Pharmaceutical Services (GPS). Drugs were procured generically unless specifically approved by trade name. Outpatients could only get medicines from the dispensaries of the NHS according to their entitlement. In addition to the four hospital dispensaries (three on mainland and one in Gozo) there were eight NHS outpatient dispensaries in Malta (seven on mainland and one in Gozo).

Expenditure on pharmaceuticals formed a substantial part of the public health care budget comprising 22% in 1997 (European observatory on health care systems, 1999). There was an annual increasing growth in public expenditure on pharmaceuticals and the lack of budget allocation for new drugs led to a situation whereby the budget ran out and there had to be authorisation of excess funding to prevent collapse of the system. The total expenditure on NHS drugs from 1991 to 1998 is provided in Table 1.1 (Accounts Payable Office of the Government Pharmaceutical Services, 1999). Total expenditure during any year includes payment for arrears from previous years and late payments. The sharp increase in expenditure on pharmaceuticals between 1996 and 1997 was partly due to payment of arrears to suppliers (European observatory on health care systems, 1999). However, having paid these arrears the figure for 1998 remained high reflecting growth in this area.

Table 1.1 Total expenditure on NHS drugs for the period 1991 – 1998

Year	1991	1992	1993	1994	1995	1996	1997	1998
Payments million (LM)*	2.5	3.1	2.9	3.2	4.0	3.7	7.1	6.9

One Maltese Lira (LM) is equivalent to approximately 1.55 Pounds Sterling (£)

The annual average inflation rate for the Central Bank of Malta for the period was approximately 2.9%. Although inflation may have contributed to some rise in expenditure, the increase in expenditure on drugs for this period was still much higher.

It was becoming increasingly difficult for the NHS in Malta to be able to provide all the new and expensive pharmaceuticals that became available for the treatment of Schedule V chronic conditions and priority setting in this field was urgently required. There were no formal mechanisms to deal with prioritisation and implicit ad hoc rationing by the DG informed by recommendations from the DTC was used to prioritise patients and treatments.

A number of political decisions were taken that affected the system of entitlement to free medicines. The labour government implemented a number of measures to control drug costs. In 1997-1998 certain expensive treatments such as multiple retroviral therapy, treatment for hepatitis C and cholesterol lowering agents were not supplied through the NHS because these were not covered by the entitlement criteria of Schedule V. In particular, lipid lowering drugs were not approved because the Schedule V list specified treatment of chronic diseases and not prophylaxis. In early 1998 a 50c prescription charge was introduced for prescriptions supplied through the NHS.

The election of September 1998 led to a revision of Schedule V and the 50c prescription charge to be stopped. Pressure was exerted on politicians to include certain diseases such as multiple sclerosis on the Schedule V list. This was supported by intensive lobbying by patient groups such as the Multiple Sclerosis Society (Dunn,

1998). In July 1998 ischaemic heart disease, HIV, multiple sclerosis and motor neurone disease were added to the Schedule V list of chronic conditions (Department of Health (Malta), 1998). The 50c prescription charge was scrapped when the nationalist government was elected in September 1998 “as it was considered to be regressive and of little revenue” (European observatory on health care systems, 1999).

Other measures for controlling the drug budget were mainly targeted at the system for approval and supply of expensive medicines. The classification of the drugs available within the NHS in February 1999 was complex. Drugs were classified as formulary or non-formulary. Formulary drugs were listed on ‘The Formulary of the Government Pharmaceutical Services’. The last publication of the formulary was in 1986 (Department of Health (Malta), 1986). In the meantime some drugs were still being approved as formulary but the updated list was not published.

Non-formulary drugs were classified as either ‘special’ or as ‘non-stock’. ‘Special’ drugs were approved either for specific clinical departments or for specific indications. Most of the ‘special’ drugs were approved with a protocol that specified the criteria (mainly the indications) for which the drug could be used. The ‘non-stock’ drugs were approved for specific patients.

Whenever a non-formulary drug was required a ‘Request for non-formulary drugs’ needed to be completed for each individual patient and sent to the respective hospital pharmacy. Requests for drugs that were approved as ‘special’ were vetted and approved by the hospital pharmacists. Requests for ‘non-stock’ drugs were recommended by the DTC (by the chairman or at a DTC meeting) and were

individually approved by the DG. Before treatment with a non-formulary drug ('special' or 'non-stock') could be started on an out-patient basis, the drug had to be procured and subsequently a letter of approval (usually valid for one year) was sent to the patient's home.

1.1.2 Previous research on the entry of new drugs into the NHS in Malta

The project entitled 'Introducing new drugs – current hospital practice' described and evaluated the practice for introducing new drugs into the NHS in Malta up to 1994 (Vella, 1995).

In 1994 the secretariat of the DTC was located at St Luke's Hospital (the main general hospital in Malta) and all operations for the introduction of new drugs and for implementation of the related policies including the formulary were centralised at this hospital. Although the project addressed 'hospital practice' it covered all drugs supplied by the NHS in Malta, both on an in-patient as well as an out-patient basis.

A policy for the introduction of new drugs into the NHS in Malta was set by the CGMO in 1993. This policy specified that for all new drugs requested for introduction into the NHS a protocol for the use of the drug had to be submitted as part of the request prior to consideration for approval. The 'expensive' drugs already available within the NHS in 1993 were targeted by the CGMO. Sub-committees were set up and protocols were prepared for the targeted drugs. Vella (1995) studied the impact of this policy on the drugs targeted by the CGMO. The opinions of consultants who worked

within the NHS in Malta, about various aspects of the local practice for introducing new drugs and about this policy for introducing new drugs were obtained.

The results showed that from 1991 to 1994 new drugs were increasingly restricted to the non-formulary category. The new policy initiated in 1993 significantly decreased the percentage of requests approved by the DTC but not the rate of increase in consumption and expenditure of the new drugs targeted by the policy. The protocols that were set for the 'expensive' drugs that were available in 1993 and for the new drugs that were introduced since then were not subsequently updated or monitored. All drugs with a protocol were classified as non-formulary and a 'Request for non-formulary drugs' had to be completed for each patient and approved by DTC prior to starting treatment.

At that time 64% of consultants were not satisfied with the practice for the introduction of new drugs in NHS hospitals. The majority of consultants (70%) did not feel involved and therefore lacked ownership of this policy. Consultants ranked 'medical opinion leaders' and medical representatives as providing the greatest influence on their prescribing of new drugs.

Pharmacists were too submerged in the administrative work generated by the vetting of non-formulary requests and sending approval letters to patients. This excessive administrative load prevented them from professional participation in the practice, such as through clinical pharmacy activities (Vella, 1995).

1.1.3 The managed entry of new drugs into the NHS in Malta in February 1999 – a cause for concern and an opportunity for change

Since 1995 the policy for the introduction of new drugs continued to be implemented coercively. No monitoring or evaluation of the policy was undertaken. Administrative problems due to the policy continued to increase leading to an unsustainable situation. By February 1999 there had therefore been little improvement in the processes for the introduction of new drugs into the NHS in Malta from what was previously presented by (Vella, 1995).

The most significant problem was that the number of approvals for drugs on a ‘non-stock’ basis kept increasing. There were no criteria for the submission of requests for ‘non-stock’ drugs by consultants, for subsequent recommendation by the DTC and for approval by the CGMO. Thus the system of approval of requests for ‘non-stock’ drugs was open to external influence leading to increased inequity in access to drugs through the NHS. Such external influence included lobbying by / or on behalf of individual patients and special interest groups such as the pharmaceutical industry or direct intervention by politicians.

The number of requests for non-formulary drugs increased from 4,596 in 1995 to 14,129 in 1998. This was due to a tendency towards increased approval of drugs as non-formulary (‘special’ and ‘non-stock’) rather than as formulary and was exacerbated by resistance to revision of the formulary. The volume of requests for non-formulary drugs increased the administrative burden. Although the authorities insisted that the information submitted by consultants on the requests was to be

audited with the patients' notes, the volume of work involved and the lack of prioritisation rendered such audit impossible.

The logistics of the process became more difficult when in February 1998 the secretariat of the DTC was transferred from the pharmacy at St Luke's Hospital to the national formulary management section of the government pharmaceutical services (GPS). The secretariat lost direct contact with consultants and the technical support of the clinical pharmacists at the hospital. The duties of the DTC secretariat now included the procurement of medicines and this put the secretariat in the conflicting roles of both regulator (the DTC) and purchaser (procurement).

The entry of new drugs into the NHS was managed by a number of isolated processes. The DTC and the secretariat had little control over these processes. The CGMO controlled the processes by ensuring that the policy for the introduction of new drugs was strictly followed. The DTC had an advisory role only, with all approval obtained directly from the CGMO. There was no possibility for the DTC to control the inputs and outputs of the various processes. For example the system for entitlement to free medicines was controlled politically and was beyond the remit of the DTC. The main legislation covering pharmaceuticals and pharmaceutical activities in Malta, the Medical and Kindred Professions Ordinance was set in 1901 (Laws of Malta, 1901). In spite of updates, the legislation was out of date and did not provide comprehensive coverage of the area. There was no system for the registration of medicines. The updating of the legislation was beyond the scope of the DTC. The licensing status of drugs and the licensing of indications were not considered by the DTC during the process of selection of new drugs. There were no standard criteria for the

recommendation of requests except for those set by the policy for the introduction of new drugs. The system of setting and implementing protocols was followed in spite of the fact that its value was limited.

A number of changes started happening following the election of September 1998. The reactivation of Malta's application for EU accession meant that Malta had to adopt EU legislation. A system for medicines registration would be required to be introduced. A system for the entry of new drugs into the NHS would need to be in line with the Transparency Directive (Council Directive 89/105/EEC). These factors together with the appointment of a new DG in February 1999 presented an opportunity for major reform in the policy for the introduction of new drugs into the NHS. The change needed to be specific to Malta whilst meeting the EU requirements. The literature was reviewed to learn lessons from the practice adopted by EU countries for the managed entry of new drugs within their NHS.

1.2 LITERATURE REVIEW

1.2.1 An overview of the changes that have influenced current practice in Europe

Within the twentieth century there were major advances in drug discovery. After the Second World War the "drug explosion" was well under way. The rapid introduction of thousands of different products for therapeutic use coincided with an increasing demand for health services. The latter was the result of developments in the economy and in living standards, linked to the creation of social security systems, national health services and schemes for reimbursement of the costs of drugs. The expansion in

the availability of drugs was highly influenced by the pressures exerted by drug manufacturers who sought to ensure a constant expansion of their market (Laporte *et al.*, 1993).

Advances in drug regulation seemed to be initiated by misfortune. As society progressively became aware of the need for rigorous methodology in clinical trials, legislators moved to introduce reasonable proof of efficacy as a basic element in drug regulation. The most pivotal event in pharmacovigilance occurred in 1961 when an Australian obstetrician, William McBride reported a 20% increase in fetal malformation and the appearance of an otherwise rare malformation, phocomelia in association with the use of thalidomide in pregnancy. The thalidomide disaster stimulated the development of pharmacovigilance such as the UK's "yellow card" spontaneous reporting system (1964) followed by legislation to regulate medicines in the UK through the Medicines Act of 1968 and Europe (Council Directive 65/65/EEC). The World Health Organisation (WHO) international programme for drug monitoring was set up in 1964. Before the Medicines Act in the UK came into force in 1971, the Dunlop Committee, the forerunner of the UK Committee on the Safety of Medicines, provided independent advice on the safety of medicines (Routledge, 1998).

The mounting concern of national health systems about the level of drug expenditure was a major incentive in the development of statistics on drug usage, particularly of national figures independent of those produced by drug companies for marketing purposes. These were soon followed by investigations into prescribing habits of physicians and drug utilisation research. The WHO's Drug Utilisation Research Group

(DURG) was established in 1969. This led to the development and acceptance of a common drug classification and a common unit for measuring drug consumption – the defined daily dose (DDD), both of which rendered valid international consumption possible (Laporte *et al.*, 1993).

In 1976 the WHO prepared the first model list of essential drugs. The concept of essential drugs was rooted in an attempt to solve the supply problems of developing countries and as such was not aimed at restriction, but at expansion. The use of essential drugs focused attention on the fact that only a limited number of the many drugs on the world market were strictly necessary to provide rational therapy to treat the majority of conditions and to serve the needs of the population. This view strengthened the role of therapeutic formularies and provided them with a rational basis for drug selection aimed at high quality of care. It stimulated the medical community to take a positive action in the interest of good practice while also tackling the inflation of costs and the duplication of products (Tognoni and Lunde, 1993).

The medical community took various views on the development of formularies. Some were negative and felt the need to defend 'clinical freedom' (Hampton, 1983) whilst others were more positive and considered that formularies were educational, supported effective treatment, led to more predictable patterns of prescribing and purchasing (in hospitals) and reduced drug costs. In addition certain hospital doctors wished to have regular information about their individual prescribing patterns and the relative costs of drugs that they used (Petrie and Scott, 1987).

In the early 1990s there was a move towards the setting of formularies and formulary management systems in the UK. Hospitals and primary care trusts were encouraged to take a selection of drugs from the British National Formulary (BNF) (a compilation of all available medicines in the UK) and set local formularies and prescribing policies. They were also encouraged to develop a formulary management system which provided the infrastructure to initiate, monitor, manage and audit local formularies and prescribing policies (Lannigan, 1993).

The influx of evidence and the advocacy towards rational prescribing and appropriate and effective health care in daily practice led to the development of clinical guidelines and medicines management. These received international attention and several terms (clinical guidelines, treatment guidelines, treatment protocols, and prescribing policies) were used to indicate systematically developed statements to help practitioners make decisions about appropriate treatments for specific clinical conditions. The Scottish Intercollegiate Guidelines Network (SIGN) was established in 1993 to sponsor and support the development of evidence-based clinical guidelines for the NHS in Scotland. It was intended that these national guidelines were critically reviewed and tailored at a local level to produce local guidelines for implementation (Scottish Intercollegiate Guidelines Network, 1999). Several organisations were set up to enhance medicines management in the UK. Some were mainly managerial, for example the NHS Executive Prescribing Branch, and some mainly professional / academic such as the NHS Centre for Reviews and Dissemination, UK Cochrane Centre (Walley, 1998). With computer-based prescribing gaining popularity during the 1990's, the British National Formulary (BNF) became available electronically in 1995 (Wyatt and Walton, 1995).

In the absence of a structured system to limit overall spending on healthcare, which includes technological advances (including medicines), within available resources, a new specialty to assist health policy makers has emerged under the title of health technology assessment. The main focus of health technology assessment is synthesising scientific evidence including clinical and cost-effectiveness data together with an analysis of the social, ethical and economic implications of the dissemination and use of health technology (Jonsson and Banta, 1999).

1.2.2 The impact of medicines registration on the access and supply of medicines through national health services in Europe

The European Commission has made significant effort to push the EU towards a single market in medicines. It created the European Medicines Evaluation Agency (EMA) in 1995. The EMA was established in order to allow free movement of medicinal products, to provide the means to undertake scientific evaluations, to establish effective harmonisation of administrative decisions and to ensure that there is a mechanism in place for resolving disagreements between member states. The EMA is also responsible for coordinating the activities of member states in pharmacovigilance. The competent authorities of the member states, under the community legislation, have to establish national systems of pharmacovigilance and all information collected by these authorities should be brought to the attention of the EMA. The Committee for Proprietary Medicinal Products (CPMP) is exclusively responsible for preparing the Commission's opinion on medicinal products for human use (European Medicines Evaluation Agency, 1996).

Since 1 January 1998 parallel national applications for drug approvals in EU member states ceased. While it is still possible to use the national procedure to register a product in one state, it is only possible to market a new drug in more than one member state via European procedures. The EU's 'mutual recognition procedure', also known as the decentralised procedure, enables manufacturers to seek simultaneous marketing authorisation in two or more member states 'concerned member states', provided that they have an existing marketing authorisation for the drug in at least one member state, referred to as the 'reference member state'. If the 'concerned member states' fail to mutually recognise the marketing authorisation of the 'reference member state'; the matter is referred to the CPMP for arbitration. If the CPMP's advice is accepted by the Commission, then it is binding. The other procedure is the 'centralised procedure'. This is mandatory for biotechnology products, but is also optional for highly innovative new chemical entities. The 'centralised procedure' provides an EU-wide licensing recommendation and is managed by the EMEA. The EMEA chooses which member state acts as the 'rapporteur' for the centralised procedure. The 'rapporteur' prepares the evaluation of the medicine and receives fees for this work. The decisions for marketing authorisation through the 'centralised procedure' are binding in all EU Member States (Abraham and Lewis, 1999).

The European Commission has achieved agreement on directives on product classification, advertising and sales promotion, good manufacturing practice, wholesale distribution and provisions relating to labeling and package inserts (Kanavos and Mossialos, 1999).

A number of factors that could compromise the effectiveness of the EU regulatory system were voiced during interviews held with industrial scientists and regulators from the UK, Germany, Sweden, the EMEA and the Commission (Abraham and Lewis, 1999). Regulators were particularly concerned that the short time scales imposed to accommodate industry's desire for more rapid approval times could reduce safety standards. Competition for regulatory work between regulatory agencies, particularly for 'reference member state' status within the 'mutual recognition procedure' was another factor of concern. Regulatory work generated fees for regulatory agencies. Because of competition for 'regulatory business' national regulatory agencies were under considerable pressure to conform to these short timescales, as companies look for fast approval rates as one of the key criteria when choosing a 'reference member state'. The vast majority of respondents from the pharmaceutical industry did not think that this intra-agency competition posed a threat to public health. Regulators were evenly split in their response to this question. Many regulators and the respondents from the industry rebuffed the suggestion that the EU system of drug regulation resulted in regulatory authorities becoming so close to industry that they are in a danger of being influenced by industrial interests at the expense of protecting public health (Abraham and Lewis, 1999).

The EU system for medicines registration by 'mutual recognition' could lead to differences in access to medicines between EU countries as the industry could choose in which countries the product was registered. Companies may choose not to register a product in a specific country. This problem is however bypassed by the 'centralised procedure'. One study (Wu *et al.*, 1998) evaluated the 'drug lag' (the chronological difference of the time taken to approve a drug in a study country and the

corresponding time for approval of the same drug in the first approval country) for new drugs introduced in nine developed countries between 1970 – 1983. This study included four EU countries, however it covered the period before EMEA started to operate. The results showed that less stringent safety/efficacy control, greater price control and larger market size were associated with shorter ‘drug lag’ (Wu *et al.*, 1998).

The introduction of EU legislation by the EU accession countries (including Malta) could have some negative implications for the countries concerned. The EU Commission may challenge the current measures utilised by countries to protect the viability of their health care systems. The Commission communication on the single market in pharmaceuticals (European Community COM (1998) 588) stated “an industrial policy concern that some mechanisms by which the financial viability of health care systems is assured may unnecessarily distort the operation of the market leading to a reduction in the competitiveness of this sector in a global context”. A second concern was that if fees were introduced to counteract the fixed cost incurred in running a system for registration there could be reduced access to medicines in the accession countries as the pharmaceutical industry may not consider it to be worthwhile to pay the registration fee for a small market. The WHO noted that there were high fixed costs associated with many aspects of pharmaceutical regulation, and warned that small countries will always find these difficult to bear (Bennett *et al.*, 1997).

The literature was short of reports that described the practical difficulties faced by specific countries newly adopting EU legislation. A good insight was given through a

retrospective case study upon Norway (Norris, 1998). Although not a member of the EU, in 1992 Norway signed the European economic area (EEA) agreement and therefore formed part of the European internal market. This obliged Norway to make major changes in its domestic legislation. The Norwegian case study showed that European harmonisation represented an attempt to impose a set of policies based on a different world-view on a complex set of existing arrangements. The changes that were implemented in Norway were the result of the ongoing process of conflict and accommodation between the two different models. The most significant change with respect to reimbursement was the level of transparency for decision making required by EU legislation. Norris concluded that whilst the European Commission recognised the importance of safeguarding public health, in practice EU legislation primarily addressed medicines as commodities or items of trade. The author concluded that the role of medicines in public health and their recognition as an integral part of the social insurance schemes in member states was secondary to trade (Norris, 1998).

1.2.3 Pharmaceuticals as part of healthcare within national health services in European countries

The only directive specifically about pricing and reimbursement, the Transparency Directive (Council Directive 89/105/EEC), does not alter the rights of governments to manage pricing and reimbursement of pharmaceuticals. This Directive stipulated that the system must not discriminate against imports. Pricing and reimbursement decisions should be based on objective criteria and should be taken within specified time limits. In addition, a reason must be given for any refusal of a price or price

increase and a right of appeal should be provided in cases of national dispute (Council Directive, 1988).

Whilst considerable progress has been achieved towards the creation of a single market, the European market still remains fragmented, comprising 15 national markets, with varying attitudes and policies towards the industry and different policies regarding pricing and reimbursement of medicines (Kanavos and Mossialos, 1999).

Cross-border issues in the provision of services are a cause of concern throughout Europe. The potential to receive care in a different country raised concerns related to national differences in reimbursement packages, the implicit or explicit exclusion of services or products from reimbursement and the priorities set within different member states. Two cases were heard before the European Court concerning the treatment of citizens of one member state in another. The European Court of Justice ruling, from the case of *Nicholas Decker vs Caisse de Maladie des Employes, Luxembourg*, was that any regulation by a social security organisation in a member state that refused treatment in another member state on the basis that such treatment must be authorised before it actually takes place was against the Treaty. The ruling, from European Court of Justice on the case of *Raymond Kohll vs. Union des Caisses de Maladie, Luxembourg*, was that issues of an economic nature could not justify a barrier to the fundamental principle to provide services (Kanavos and Mossialos, 1999).

In the Scrip report on *Pharmaceutical Pricing and Reimbursement in Europe*, Wallerstein (1997) gave an overview of healthcare systems and detailed the methods

adopted for pricing and reimbursement in many individual European countries. European healthcare systems were founded on the principle of social solidarity. Contributions were usually income-related. Access was determined on the basis of medical need rather than the ability to pay. In most cases, treatment was provided free at the point of delivery. In all European countries the state paid for a large proportion of healthcare expenditure, but there were elements which were either not covered or required some contribution from patients. Exemptions on social and economic grounds were widespread (Wallerstein, 1997).

Health care spending has been under considerable and continuous pressure since the early 1990's, as national governments and other purchasers attempted to deliver improvements to patient care, enhance efficiency within their systems and contain costs. The increasing demand for healthcare was accentuated by demographic changes in European populations (the elderly forming a higher and growing proportion of the population), higher patient expectations, technological advances in healthcare, the changing epidemiology of some diseases as a result of longer life expectancy and improved survival rates for many diseases and conditions (Wallerstein, 1997).

It is impossible for any country to provide for all the health care needs of its population. The WHO considered a concept of a 'new universalism' in providing access to health care. Governments must ensure that good health care is accessible to everyone, but they should not attempt to provide all possible treatments. Priorities should be set on the basis of the resources available to each government and the cost of 'top priority interventions' (Brown, 1999).

Maynard (1996) explained that rationing was inherent in all healthcare systems. Rationing of care by rules that were not standardised, were incoherent and implicit lead to inefficiency and inequity. One of the major issues on rationing by the NHS in the UK was that of difference in decisions on rationing by different health authorities (Maynard, 1996; Walley *et al.*, 1997). Also much implicit rationing occurred as doctors decided what to allocate to individual patients particularly when there were capped budgets (Sabin, 1998).

There emerged fierce debate on rationing in the literature. The controversy was fed by specific cases which usually received high media coverage such as the case of child B, the girl with leukaemia whose father refused to accept the advice of doctors who counselled against further treatment and took the Health Authority to court for refusing to fund chemotherapy (Entwhistle *et al.*, 1996) and the availability of Viagra through the NHS in the UK (Chisholm, 1999). Possible explicit techniques for prioritisation included using factors such as age, capacity to benefit and by 'social utility'. Consideration of evidence, health gain and cost were also suggested (Malek and Langsdale, 1994). Priority setting was regarded as a complex interaction of multiple decisions at various levels that could not be reduced to a purely technical exercise (Leese, 1996; Klein, 1998).

Debates on priority setting brought the case for public participation into focus, particularly in difficult healthcare choices. Several factors were thought to impact on the opinions formed by the public. In addition to personal and attitudinal characteristics such as age, educational achievement and political ideology, other influences included the media, national, cultural and political contexts (Mossialos and

King, 1999). A number of qualitative studies (patient panels, focus groups and postal questionnaires) have been conducted to obtain the views of stakeholders on rationing (Dicker and Armstrong, 1995; Ryyanen *et al.*, 1999). The data showed that there were differences in the way that different stakeholders approached the issue of what should be included in a basic package of priorities. Healthcare professionals seemed to be most aware of maintaining equal access for everyone in need of healthcare (Stronks *et al.*, 1997).

Mossialos and King analysed data taken from the 1998 Eurobarometer Survey (International Research Associates (Europe), 1998) with questions pertaining to rationing and priority setting asked to the public in six countries of the EU (Britain, France, Germany, Italy, the Netherlands, and Sweden). The main results were that extra funding should come from lower national spending on other things. Respondents most frequently chose doctors as the preferred agents for setting priorities where limits needed to be set. Support for age-based priority setting was highest in Britain and Sweden, whereas in the other countries only about 10% of respondents agreed with age-based priority setting. When asked to choose the criteria they felt to be most important in setting priorities, a large number of respondents spontaneously expressed preferences for each case to be treated individually (Mossialos and King, 1999).

Wallerstein explained that the gross demographic changes in the European population resulted in a growing volume of demand for healthcare and especially for pharmaceuticals increasing faster than the growth of the population. Hence even if prices remained constant, expenditure would increase. The author argued that although the prices of drugs post launch had not generally increased, the unit price of medicines

at launch was increasing in real terms and the product mix was changing towards newer and more expensive products (Wallerstein, 1997).

1.2.4 Policies to control spending on drugs and to improve the efficiency of drug use within national health services in Europe

Wallerstein concluded that national legislation reflected the underlying national attitudes towards the provision and financing of healthcare and therefore it was difficult and slow to change. The main approaches to change and specific measures adopted were the result of traditional attitudes of governments and their ad hoc responses to medical, financial and political crises. Few governments had scrutinised the mechanisms available to devise new systems that achieved their long-term objectives. Implementing change was burdened and hindered by political difficulties. It was observed that pharmaceuticals were considered a soft target and were frequently the first commodity to be controlled when short-term financial savings were required (Wallerstein, 1997).

European countries have used a mixture of approaches to control pharmaceutical expenditure. Some countries put the emphasis on the supply side. Supply side controls were aimed at limiting the cost to the NHS. The most common methods were price (individual pricing, average pricing, reference pricing) and profit regulation control of licensing and reimbursement (positive and negative lists) and constraints on supply of drugs (wholesalers and pharmacists) (Wallerstein, 1997).

European countries differ in the ways in which they control reimbursement prices.

Direct price control leads to differences in prices between countries. This creates incentives for the import and resale of drugs between countries. Britain was unique in allowing freedom of pricing and controlled prices indirectly by setting target profits. In reference price systems, a reimbursement price is set for a therapeutic category of drugs and patients may pay any difference between the cost of the product prescribed and the reference price. New and innovative (breakthrough) drugs were usually not covered by reference price systems. In Sweden the introduction of a reference price scheme resulted in manufacturers cutting the price of their drugs that were priced above the reference price. In the Netherlands following the introduction of reference pricing there was an increase in the overall spending, although the Government claimed that the scheme contained costs. Germany's reference pricing system lowered prices for products where there were alternatives without patent protection (Bloor *et al.*, 1996). In some countries, including Greece, Ireland, the Netherlands and Portugal, the maximum retail price of a product was determined in relation to the price of the same product in a 'basket of countries', using a published formula (Wallerstein, 1997)

An overview of supply side controls by Bloor *et al.* (1996) concluded that price and profit controls contained few incentives for improving cost-effective use of drugs, and focused on cost containment and profitability of the domestic pharmaceutical industry. There were limited attempts to encourage cost-effectiveness by regulating prices. Price negotiations in France and the use of reference price systems could increase cost-effectiveness by allowing a premium price only if there was evidence of important additional therapeutic benefit. However without the use of carefully monitored economic evaluation, price regulation remained a crude method for containing costs and could result in poorer treatment of patients or increased overall costs to the

healthcare system if expensive but cost-effective drugs were discouraged (Bloor *et al.*, 1996).

Some countries emphasised controls on the demand side (the prescriber, the patient and the pharmacist). Measures included patient co-payment, guidelines for doctors, budgets for doctors, incentives to prescribe and dispense generic equivalents or parallel imports within the EU, or the transfer of products from prescription only to over the counter (OTC) status (Wallerstein, 1997).

In 1996 all countries in Europe operated restrictive lists. Governments restricted publicly reimbursed drugs by positive lists (France, Italy) or negative lists (Germany, Ireland, the Netherlands, Spain, UK) (Bloor *et al.*, 1996). The mechanisms by which drugs were evaluated for reimbursement status (placed on the positive list) and the criteria by which they were excluded from reimbursement (placed on the negative list) varied between countries. Usually therapeutic benefit was the most important consideration, although cost-effectiveness relative to products already reimbursed was growing in popularity. Some countries with positive lists were thought to delay the approval process for reimbursement of new drugs as a means of containment of pharmaceutical costs (Wallerstein, 1997).

Some countries introduced incentives for doctors to follow prescribing guidelines as a measure to reduce costs. In France a national contract introduced national medical guidelines for doctors with respect to diagnosis and treatments. As an incentive for following these guidelines, doctors were awarded a 5% increase in their fees. Those who failed dramatically to comply with the guidelines faced fines. In Germany

guidelines were introduced in 1995 to define the average prescription volume for each medical specialty according to the therapeutic use and category of drug. The guidelines were formulated so that the total volume of prescriptions did not exceed the regional budget and were therefore used as a means of budgetary control (Bloor and Freemantle, 1996).

Several countries had information feedback systems for physicians similar to the Prescribing Analysis and Cost (PACT) scheme used in England and the Scottish Prescribing Analysis (SPA) scheme. These schemes were advisory and provided information on the volume of prescribing and overall drug costs. These schemes did not give information on the cost-effectiveness of prescribing and so could potentially penalise the use of expensive drugs that had benefits worth the extra cost (Bloor and Freemantle, 1996).

Budgetary restrictions on doctors have been used to control costs in some countries such as Germany. Individual general practice budgets were introduced in Britain. In 1996 it was difficult to assess how financial incentives influenced prescribing as most studies of fund holding have been descriptive and none have been adequately controlled (Bloor and Freemantle, 1996). The Cochrane Effective Practice and Organisation of Care Group carried out an evaluation on the effects of capitation, salary, fee-for-service and mixed systems of payments on the behaviour of primary care physicians. Very few studies met the inclusion criteria. There was some evidence that the method of payment of primary care physicians affected their behaviour, but the generalisability of the findings was unknown (Gosden *et al.*, 2000).

The pharmaceutical industry plays an important role in disseminating information to prescribers, not all of which may be considered educational. The EU directives set standards for advertising of medicines. However, health authorities do not usually regulate the activity of medical representatives. The WHO have issued 'ethical criteria for medicinal drug promotion' (World Health Organisation, 1988). Pharmaceutical companies often conduct aggressive campaigns to change prescribers' habits and to distinguish their products from competing ones, even when the products are very similar. Kessler *et al.* (1994) gave a good insight into the tactics used by the industry. The authors pointed out that these "therapeutic-class wars" cost drug companies substantial amounts of money. Companies could sometimes charge more for a new drug, even in an already crowded class. 'Me too' drugs were promoted in a number of ways including 'seeding' trials, unsubstantiated claims of superiority over competing products and 'switch' campaigns. 'Seeding' trials are company-sponsored trials of approved drugs that serve little or no scientific purpose. Usually such trials incorporate study designs which do not support the stated research goals, target frequent prescribers of competing drugs as investigators and give disproportionately high payments to investigators. False and misleading claims usually rely on pharmacokinetic distinctions that have unknown clinical relevance. 'Switch' campaigns involve switching patients to another dosage form of the same product or to another product within the same therapeutic class (Kessler *et al.*, 1994).

National authorities often regulate the distribution margins for wholesale dealing and dispensing. In some countries both the wholesale and retail margins are specified, in others the overall distribution margin is set. Regressive margins have been introduced in a number of countries, especially for pharmacists to reduce the disincentive to

dispense cheaper medicines. Healthcare authorities often determine what pharmacists may dispense when presented with a prescription and how pharmacists' remuneration is set (Wallerstein, 1997).

Various interventions are used to depress the demand for drugs by limiting reimbursement of products and providing an incentive for patients to reduce their consumption of drugs. Co-payments require patients to pay a proportion of the cost of a prescribed product or a fixed charge. Patient caps limit the number of reimbursable prescriptions per patient. Freemantle and Bloor noted that the withdrawal of reimbursement of a drug could also be used in an attempt to reduce prescribing. Several countries were found to have co-payment systems. In Britain, co-payment takes the form of a flat rate prescription charge. In countries with a 'reference price' scheme, where a 'reference price' is allocated to a group of drugs, co-payments have commonly included a fixed charge plus any difference between the actual price and the 'reference price'. In France co-payments have been based on the drug reimbursement rate, which is assessed by the transparency commission (Freemantle and Bloor, 1996).

A review of the evidence in this field focused on the effect of co-payment schemes and of removing products from reimbursement (Freemantle and Bloor, 1996). Co-payments were shown to reduce use of drugs in a large non-equivalent group study with pre-post measures in the US. At moderate user charges, the use of drugs defined as essential were also reduced substantially. In a series of quasi-experimental studies 'patient caps' were shown to reduce the number of prescriptions filled compared with a prior co-payment system. These studies also revealed an increase in related

healthcare costs such as acute psychiatric services, institutionalisation in nursing homes for elderly people or a substantial reduction in the use of essential drugs. Restoring a co-payment system returned prescriptions to the level found before the 'patient caps' scheme. The review showed that removal of a product from reimbursement could also lead to unexpected and unwanted outcomes. Withdrawing payment for drugs that did not meet criteria for efficacy and safety did not necessarily result in improved drug use overall. A rigorous study in the United States showed that the withdrawal of 12 categories of drugs with questionable efficacy in a random Medicaid sample resulted in an increase in prescriptions overall, due to substitutions many of which were not desirable (Freemantle and Bloor, 1996).

1.2.5 Reimbursement decisions and health technology assessment

Because of the pressure that new healthcare interventions (technologies) are generating on health services worldwide, NHSs are under pressure to establish systems for evaluating new technologies and for dissemination of knowledge and implementation. Health technology assessment constructs the findings from clinical research and includes analysis of costs, cost-effectiveness and broader social aspects of health technology. In 1990, Banta and Andreasen noted that technology assessment was developing predominantly as a technical and professional activity. The authors emphasised that technology assessment must also relate to political decisions such as resource allocation. Since policies are determined by factors such as power and influence, technology assessment should be part of a political process (Banta and Buch Andreasen, 1990).

Health technology assessment is organised and implemented in a different way in each country. One of the main determinants of such differences is the nature of the health systems in the country. For example in Canada, France, Spain and Sweden, governmental agencies assess health technology. In addition many research institutions are concerned with health technology assessment (Jonsson and Banta, 1999). In the UK, the National Institute for Clinical Excellence (NICE) was inaugurated in April 1999. NICE was set up to identify best practice and advise practitioners on which treatments worked best for patients and were cost-effective. It was intended that NICE should appraise 30 to 50 technologies per year. NICE recommendations were to be taken up by Health Authorities so as to reduce 'postcode prescribing', whereby the various Health Authorities across the UK took different rationing decisions. The case of interferon beta for multiple sclerosis was an example of such 'postcode prescribing' throughout the UK and demonstrated the influence of pressure groups in such decisions (Richards, 1996; Rous *et al.*, 1996; Burnfield, 1997). In November 1999 NICE initiated an audit and guideline project (National Institute for Clinical Excellence, 1999). A Commission for Health Improvement with powers of inspection and enforcement was also legislated (Warden, 1999).

The factors considered in decisions for the reimbursement of drugs within the NHS and the role of technology assessment in these decisions varies between countries. An increasing number of countries include economic factors when deciding whether to reimburse a product. Australia and the province of Ontario in Canada were the first to include cost-effectiveness data in decisions about reimbursement (Langley, 1993; Langley, 1996; Glennie *et al.*, 1999). In Australia since 1993, drug companies have been required to include an economic evaluation in applications for reimbursement

through the pharmaceutical benefit scheme. New drugs with no demonstrable advantage over existing products are offered at the same price. Where clinical trials show superiority, incremental cost-effectiveness is assessed to determine whether a product represents value for money at the price sought (Langley, 1996). Britain, France and the United States have also implemented policies to encourage the provision of economic data. The objective of these policies is to increase the cost-effective use of drugs, but the approach between countries has varied (Maynard and Bloor, 1997).

Much literature has been generated on the methods and use of pharmacoeconomic analysis. Various aspects were addressed such as the need for methodological standardisation (Rovira and Antonanzas, 1995), the application of economic evaluation to different healthcare systems (Gorham, 1995; Nuijten *et al.*, 1998), the potential of bias in industry sponsored pharmacoeconomic analysis (Drummond, 1998) and evaluations of individual drugs or classes of drugs (O'Brien *et al.*, 1995). Methods such as modeling have been used to predict the use of health technologies and drugs in order to inform managerial decisions on costs (Scalon *et al.*, 1998).

Medicines registration considers quality, safety and efficacy of a drug but takes no account of comparative efficacy or cost-effectiveness. Maynard and Bloor (1997) suggested that a "fourth hurdle" of comparative cost-effectiveness should be adopted by the NHS (in Britain) before it agrees to pay for new drugs. This proposal has generated heated debate. The Australian Pharmaceutical Manufacturers' Association reiterated that the experience of Australia was ambiguous and was yet to be empirically tested for efficiency. In their experience there were adverse effects for the

community, doctors and pharmaceutical research, such as delayed access to new medicines, restricted prescribing choice and reduced funds for industry-sponsored research (as a consequence of reduced returns). In Australia, the industry had to pay substantial amounts for the cost-effectiveness evaluations (Clear and Grobler, 1998). The Association of the British Pharmaceutical Industry pointed out that the proposal that the NHS should pay only for medicines that have cleared a “fourth hurdle” of cost-effectiveness assumed that cost-effectiveness data could be derived at the time of licensing (Read, 1998). From the economics perspective, the proposal was also considered to be “a radical central rationing scheme that may well lead to higher (not lower) pharmaceutical pricing for the NHS in Britain” (Towse, 1998).

Concerns have been voiced that current licensing hurdles are not enough to earn a drug a place in an evidence-based healthcare system. The published evidence available for funding decisions is frequently inadequate. The licensing process cannot define uncommon adverse effects. Relative efficacy plays no part in licensing decisions and most early studies of new medicines are performed against placebo rather than established active agents, making it difficult to be sure of a new drug’s true utility. It was suggested that newly licensed drugs should be on probation until their value is demonstrated (Ferner, 1996).

Two examples by Dent and Hawke (1997) demonstrate the concerns about the extent of information available at the time of taking funding decisions. Donepezil, which was licensed for Alzheimer’s disease, was supported by only one randomised controlled trial in full, with follow-up of just 12 weeks. This was long enough to show a treatment effect but hardly useful for routine clinical practice where the issue is one of

longer-term efficacy and safety. Even practical aspects of its short-term use, such as how best to monitor clinical effect or define treatment failure, had not been adequately addressed. In the case of riluzole, which was licensed for amyotrophic lateral sclerosis, the evidence of benefit from the drug seemed weak. Riluzole clearly had some efficacy but because this was at best modest and the drug had no effect on muscle function, its role in treatment was uncertain. The authors pointed out that the unpublished data seen by the licensing authorities will not be scrutinised by the wider scientific community and may be of limited suitability for use in funding and prescribing decisions (Dent and Hawke, 1997).

Stevens and colleagues noted that in practice in the United Kingdom the handling of important (expensive) new technologies often included several well-defined stages. The primary data presented at licensing was used to report on the advantages and disadvantages of the health technology, who might prescribe and the need for further research. A rapid systematic review and cost-effectiveness modelling were then completed. These were followed by longer-term technology assessment, Cochrane review or other systematic review. Pragmatic randomised controlled trials to update the systematic reviews were set. The authors gave an example of this process by describing how the NHS Health Technology Assessment Programme in the UK tackled the problem presented at the launch of donepezil. When donepezil was launched in 1997 with only one published randomised control trial, the NHS Health Technology Assessment Programme considered the commissioning of research in this area. An editorial was published in the British Medical Journal a week after the launch and a “quick and clean” review was considered by the NHS’s development and evaluation system within three months of the drug’s launch. A conventional systematic

review was published in the Cochrane Library, and the NHS Executive funded a large pragmatic trial on new drugs in dementia (Stevens *et al.*, 1999). Freemantle and Mason criticised the review process that was used for regionally funded Development and Evaluation Committee (DEC) reports in the UK and which was also proposed to be adopted by NICE (Freemantle and Mason, 1999a; Freemantle and Mason 1999b).

Activities such as health technology assessment, evidence-based medicine and clinical practice guidelines were developed to identify, implement and monitor the available evidence in healthcare. Evidence is synthesised either as an evidence base or in the form of recommendations for supporting decision making in health care. The different activities are related to each other in three domains: input, dissemination / implementation and monitoring / outcome. These then provide evidence on the potential effects of healthcare interventions and policies, on ways to implement them and on ways to monitor their actual outcome (Haines and Donald, 1998). Despite the developments in health technology assessment, in evidence-based medicine and in clinical practice guidelines these activities still have little impact in the political world within healthcare organisations. The diffusion of these activities is determined by a complexity of forces such as clinician enthusiasm, media campaigns, public opinion, manufacturers' inducements, hospital developments and government regulations (Ronsen and Gabbay, 1999).

1.2.6 Theories and knowledge from the field of change management applicable to the implementation of change in health care systems

All improvement requires change and improving quality in health care involves

changing the way that things are done, changes in processes and in the behaviour of people and teams of people. Whether a quality improvement programme encompasses the whole organisation in 'macro' change or whether a team of people is reorganising a single clinic on a 'micro' scale, the same principles of change management apply. The health sector is able to learn a great deal from other industries and sectors and from the general literature on the management of change and organisational development (Garside, 1998).

Changing an organisation is a complex task. The more complex the organisation, the more complex the change process. Organisations have to be viewed as systems, with interrelated parts in which an apparently logical change in one part of the process may have unforeseen consequences if the system is not viewed as a whole. Changing organisations involves a series of cycles; this makes long range planning difficult and demands a continuous reassessment of changes and intermediate results. The goal for any organisation in a complex environment is to become a learning organisation, able to adapt to the changing demand of the environment (Koeck, 1998).

Organisational change is typically modelled as a three-part process that takes a flawed organisation, moves it through an arduous transition stage and deposits it at the end in the enriched desired state. As described by Garside (1998), Lewin's force field analysis remains a popular change management tool. It conceptualises organisational change as a process shaped by interaction of driving forces for change with restraining forces impeding change. Lewin argues that the best strategies for implementing change rest on reducing the restraining forces. A unilateral increase in the driving forces will meet with an opposite increase in resisting forces (Garside, 1998).

In his article on improvement of systems, Berwick provided a number of principles on improvement and change derived from what he authoritatively called 'the central law of improvement'. This stated that every system was perfectly designed to achieve the results it achieved. Berwick stressed on the 'indissoluble bond between improvement and change' and explained that 'not all change is improvement, but all improvement is change'. The central law of improvement reframed performance from a matter of effort to a matter of design. Better or worse performance could not be obtained from a system of work (any set of activities with a common aim) merely on demand. Although effort alone could achieve some improvement, this improvement was not fundamental and did not often represent a new level of capability. Performance was a property inherent in the system and improved results could only be expected through the creation of new systems. Berwick stressed the need to change a system, rather than bringing about change within a system. Stressing the current system (relying on more of the same) hits without much effect on the historical walls of performance while introducing a truly new system leaps over these walls. Improvement begins as an intent but can only be achieved through a method for systematic change (Berwick, 1996).

Another area covered by organisational and management literature was that of change in organisational culture. Davies *et al.* (2000) conceived organisational culture as an emergent property of the organisation's constituent parts. Characteristics of that culture could be described and assessed in terms of their functionality in relation to the organisation's goals. Organisational culture emerges from that which is shared between colleagues in an organisation, including shared beliefs, attitudes, values and norms of behaviour. Thus, organisational culture is reflected by a common way of

making sense of the organisation that allows people to see situations and events in a similar and distinctive way. It is “the way things are done here”, as well as the way things are understood, judged and valued (Davies *et al.*, 2000).

Within an organisation there may be cultural diversity, for example within different occupational or professional groups. Such sub-cultures may be associated with different levels of power and influence within the organisation, whose dynamics may alter over time. Different sub-cultures may be more or less malleable or may be highly resistant to change. Organisations receive many cultural influences from outside the organisation, for example the prevailing culture of professions nationally and internationally, and these influences may be at odds with the internal culture. Culture is dynamic and there may be rapid swings in organisational norms. Newcomers to an organisation may bring with them prior expectations, but culture is also transmitted to new arrivals by established staff (Davies *et al.*, 2000).

Any strategy for cultural change should be selective, aiming for a balance between continuity and renewal, identifying those cultural aspects to keep and reinforce, and those that need to be reworked. Cultural change cannot be easily undertaken from the top down. Successful strategies need to take into account the needs, fears, and motivations of staff of all levels. The organisational culture cannot be tackled in isolation from the organisational structure, financial arrangements and human resource management initiatives. The influence of outside professional bodies, specialist professional societies, patient interest groups and the media may cut across and sometimes work against efforts of internal reform. Identifying areas of consensus and

consistency in the values espoused by these organisations and attempting limited cultural shifts in these areas may therefore be advantageous (Davies *et al.*, 2000).

Policies are an integral part of any health care system. The term policy is inevitably closely associated with politics and politicians although it is also used in other ways such as managerial policy and clinical policy. In these broader definitions a policy may be defined as “a course of action that an authority states should be followed”. Political decisions are based upon values and beliefs as well as evidence (Muir Gray, 1998).

A wide variety of policies to improve the health of populations are made by governments and these may be divided into two types: health policies (designed to promote and protect health) and health care policies (these govern the funding and organisation of health services). Health care policies can be evidence-driven or resource driven. When resources get tight and new options have to be considered, then evidence is assembled to inform cost and benefit of different policy options. This level of policy option appraisal was developed mainly by economists and terms such as cost-benefit analysis, cost-effectiveness analysis and decision analysis are increasingly used in policy making (Muir Gray, 1998).

Policy reform is a political process because it seeks to change who gets valued goods in society. Politics effects the origins, the formulation and the implementation of public policy, especially when significant changes are involved. Reich (1995) proposed five reasons to explain the political dimensions of policy reform. Reform presents a selection of values that express a particular view of the society. Reform has distinct distributional consequences across different social groups in the allocation of

both benefit and harm. Reform promotes competition among groups that seek to influence the distributional consequences such as interest groups, bureaucratic agencies and political parties (Reich, 1995).

Reich used three case studies of national pharmaceutical policy reform to identify common conditions that made these reforms politically feasible. The author suggested that health care reform was feasible at certain definable and perhaps predictable political moments, especially in the early periods of new regimes. The most important and manipulated political factors were political timing (which provided opportunities for policy entrepreneurs to introduce their ideas into public debate) and political management of group competition (which allowed leaders to control the political effects of distributional consequences and protect the regime's stability). The author argued that for reform to succeed, policy makers must develop methods to understand, analyse and then manipulate the political conditions in favor of policy reform (Reich, 1995).

National drug policies (NDP) are a good example of the development of systematic national policy in the field of pharmaceuticals. A NDP is a guide for action and provides a framework to coordinate activities in the pharmaceutical sector. Since the 1970s, the WHO has been active in developing and promoting the idea of a NDP. The experience of developments in NDPs in 12 developing countries showed that radical changes were more likely to happen when there were political windows of opportunities and changes in the global political/economic environment. When such opportunities presented themselves, it was possible to implement quick, radical and

widespread changes. When such opportunities were not available it could be better to use low profile, step by step strategies (World Health Organisation, 1997a).

In the developed world, many countries do not have written NDPs, yet are successful in pursuing pharmaceutical sector goals. However even in these countries, some experts advocate having a document that clearly outlines the objectives of a NDP (Quick *et al.*, 1997). Australia published its national medicines policy in 1999 (Commonwealth of Australia, 1999a) and evaluated the 'quality use of medicines' component within its national medicines policy (Commonwealth of Australia, 1999b).

Different types of intervention can be used to promote behavioural change among healthcare professionals and to support the implementation of research findings in clinical practice. GroI gave an overview of theories underlying different approaches to implementing guidelines and changing practice. The approaches discussed included educational, epidemiological, marketing, behavioural, organisational, social interaction and coercive approaches (pressure and control as a method for change) (GroI, 1997).

Bero *et al.* (1998) noted that when interpreting the results of different trials of behavioural change during systematic reviews it was difficult to disentangle the effects of the intervention from the influence of contextual factors. Following a systematic review of 102 trials of interventions to improve professional practice Oxman and colleagues concluded that there were no 'magic bullets' for improving the quality of healthcare. There were however a range of interventions available that, if used appropriately, could lead to substantial improvements in clinical care derived from the

best available evidence (Oxman *et al.*, 1995). These conclusions were also supported by other systematic evaluations and studies on implementing guidelines, research findings and changes in clinical practice (Wensing and Grol, 1994; Grol, 1997; Grol *et al.*, 1998).

The Cochrane Effective Practice and Organisation of Care Group is undertaking a series of evaluations on factors that effect change in behaviour of consultants. In 1998 Bero and colleagues published results of a systematic review from 1966 up to June 1995. Most of the reviews identified modest improvements in performance after intervention. It was found that the passive dissemination of information and didactic educational meetings were generally ineffective in altering practice no matter how important the issue. Audit and feedback, the use of local opinion leaders, local consensus processes and patient-mediated interventions were found to be of variable effectiveness. The use of computerised decision support systems led to improvements in the performance of doctors in terms of decisions on drug dosage and the clinical management of patients. Educational outreach visits resulted in improvement in prescribing decisions in North America. Multifaceted interventions (a combination of methods that included two or more interventions) seemed to be more effective than a single intervention (Bero *et al.*, 1998).

Systematic reviews of the evidence suggested that clinical practice guidelines were most likely to be adopted in practice when dissemination and implementation strategies incorporated several features including involvement of end user clinicians in guideline development, implementation strategies which include a participatory educational intervention, and integration of guidelines into the process of care. The

most crucial point from systematic reviews was that a multifaceted dissemination and implementation strategy is much more likely to increase the probability of uptake in practice than reliance upon a single intervention (Grimshaw *et al.*, 1995; Feder *et al.*, 1999; Moulding *et al.*, 1999).

1.2.7 Bringing about change in practice

Most of the initiatives for improvement in healthcare have focused on clinical and service quality. WHO divides quality into four aspects: professional quality, resource use, risk management and patient satisfaction with the service provided. The new quality programme for the NHS in Britain has clinical governance as its core component. Clinical governance was defined as “a system through which the NHS organisations are accountable for continuously improving the quality of their services and safeguarding high standards of care by creating an environment in which excellence in clinical care will flourish” (Sally and Donaldson, 1998).

Central to the continual improvement of healthcare is the application of professional and improvement knowledge to daily work. Transforming a health care organisation so that it is capable of continual improvement requires a framework for the continual improvement of healthcare. One such framework has been developed by Batalden and Stoltz (1993) and is reproduced in Table 1.2.

Table 1.2 A framework for the continual improvement of healthcare

Underlying knowledge	Policy for leadership	Tools and methods	Daily work and applications
Professional knowledge: <ul style="list-style-type: none"> • subject • discipline • values 	Mission, vision, and quality definition	Process, system Group process and collaborative work	Models for testing change and making improvement
Improvement knowledge: <ul style="list-style-type: none"> • system • variation • psychology • theory of knowledge 	Guiding principles Integration with values	Statistical methods Planning and analysis	Review of improvement

(Batalden and Stoltz, 1993)

The framework in Table 1.2 consists of development of new knowledge, creation of leadership policy that fosters a shared sense of purpose and promotes organisational learning, mastery of tools and methods that accelerate improvement of work and application of systematic strategies for building and using knowledge to the process of daily work.

Continual improvement becomes possible when professional knowledge is linked with improvement knowledge. Improvement knowledge incorporates knowledge of the system, of variation, of psychology and theory of knowledge (Batalden and Stoltz, 1993). Guiding an organisation effectively toward continual improvement depends on the organisation's leaders developing, basing their leadership on, and communicating to everyone knowledge of the organisation as a system of production, that is, a group of interdependent people, items, processes, and products and services that have a common purpose or aim (Nolan and Provost, 1990).

Variation is always present in processes, products and people. Batalden and Stoltz explained how understanding variation over time was key to recognising and using differences observed for the purpose of continual improvement (Batalden and Stoltz, 1993). Deming (1993) described two types of causes of variation: 'common causes' (or causes found regularly within every occurrence of the process) and 'special causes' (a specific cause or set of circumstances not regularly present in the system which influence variation). Distinguishing the type of variation present in a process was critical for improvement because each type of variation requires a different type of action (Deming, 1993).

The third dimension of improvement knowledge (Table 1.2) was knowledge of psychology, which included the psychology of work and the psychology of change. Deming pointed out that in the vast majority of cases the variation in outputs could be attributed to the effect of multiple causes in a system of common-cause variation, not to individual workers. Improving the performance of such a system required fundamental change in the system, not further work on the behaviour of the below-average worker (Deming, 1993).

Batalden and Stoltz (1993) explained that the linking of theory and action led to the potential for learning and building knowledge and that prediction and measurement helped to link theory and action. The authors discussed how clinicians use the model for building knowledge and learning in the routine management of patients. A preliminary diagnosis is established (theory), a trial of therapy is instituted (action), a particular response is anticipated within a certain time frame (prediction) and at the appropriate time the response is evaluated (measurement). If the predicted effect of the

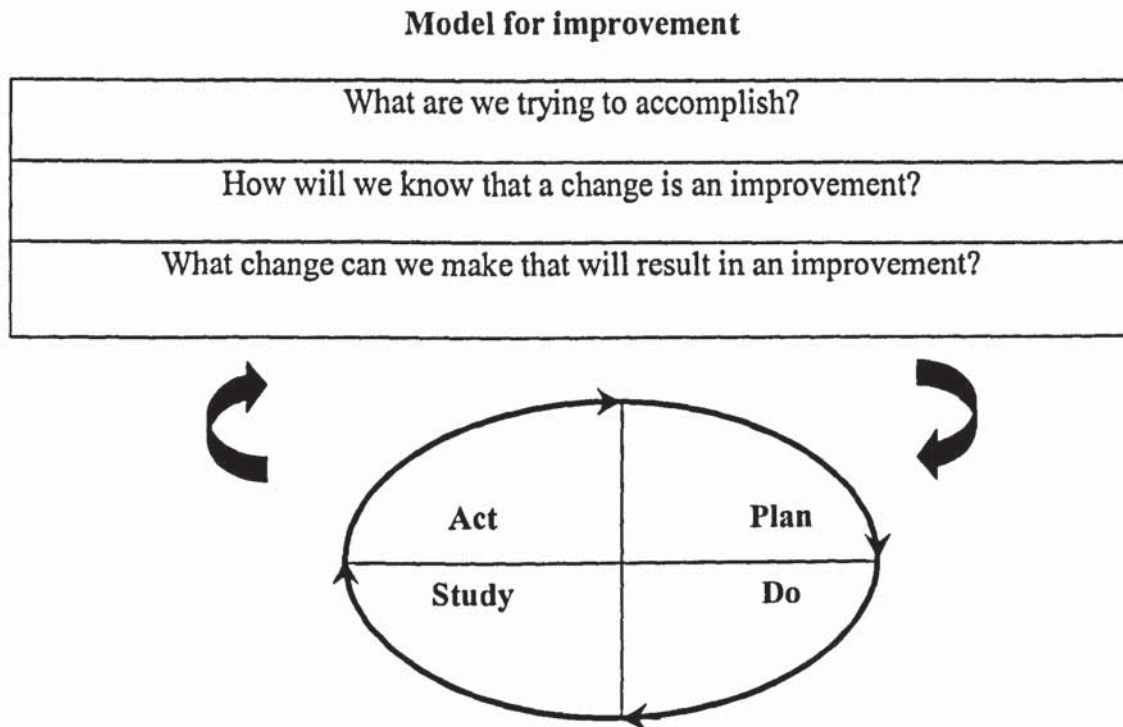
trial and the actual response are close, the clinician has useful confirmatory knowledge, the diagnosis is probably right and the treatment probably effective. The clinician has new knowledge for managing the patient from this point on. The clinician has linked theory and action with prediction and measurement to create new knowledge that can be used to guide the next step (Batalden and Stoltz, 1993).

Tools and methods are available that can accelerate building and using knowledge and communicating that understanding to others. A simple method for conducting knowledge building experiments in practice, consistent with a theory of knowledge, is the Plan-Do-Study-Act (PDSA) cycle. Repeated PDSA cycles allow improvement as each action is informed by learning from the action before (Deming, 1993). The purpose of process and system tools is to make visible the steps and their relationships in the conduct of work. Many models have been developed for testing change and making improvement (Batalden and Stoltz, 1993). One such model is the model for improvement from Langley, Nolan and Nolan (1992).

A model for testing change and making improvement

Langley Nolan and Nolan (1992) devised a simple model for achieving changes that were improvement. Berwick (1996) described this model and demonstrated its applicability in practice. Figure 1.1 illustrates the model which comprised three basic questions and a fourth element that described a cycle for testing innovations (Deming's PDSA cycle) (Berwick, 1996).

Figure 1.1 A model for improvement from Langley, Nolan and Nolan (1992)



Adopted from Berwick (1996)

Berwick (1996) explained that the first question: ‘What are we trying to accomplish?’ was built on the theory that improvement must be intended and that specific aims were crucial. The more specific the aim the more likely the improvement. Leaders bore the obligation to clarify aims. People in health care organisations often rebelled against the idea of pulling together around a small set of shared purposes. Berwick suggested that ‘aims should be ambitious’.

The second question ‘How will we know that a change is an improvement?’ stressed the need for ‘measuring’ for the purpose of learning (such as from experiment/research, from others, or from history). Berwick explained that ‘measuring’ helped to inform whether a particular innovation should be kept, changed or rejected, could help understanding of causes and help clarification of aims (leading

to redefinition of the answer to the model's first question). The author clarified that when trying to improve a system there was no need for perfect inference about a pre-existing hypotheses. Just enough information was required to take the next step in learning (Berwick, 1996).

The third question: 'What change can we make that will result in improvement?' directly addresses the central law of improvement. Since new aims require changes of systems, it is important to be able to identify promising changes and to avoid useless ones (Berwick, 1996).

The plan-do-study-act (PDSA) cycle described in essence, inductive learning – the growth of knowledge through making changes and then reflecting on the consequences of those changes – testing changes in real work settings. Such inductive learning was familiar to scientists but such formal cycles of action and reflection were unusual in daily work. The science within the PDSA cycle was in the act of reflection and learning from what one did (Berwick, 1996).

Berwick recommended that leaders should model reflection on action in their personal behaviour. The model intended that the enterprise of testing change in informative cycles should be part of normal daily activity throughout an organisation. Berwick was confident that the application of the model promoted a new view to the nature of work itself and if made part of work it could convert a system from at best a merely stable one to one capable of continuous learning, embracing change and stimulating improvement (Berwick, 1996)

1.2.8 Interventions for improvement in practice

Audit and quality improvement

The changes within the NHS associated with quality improvement processes have a developmental history including medical audit, clinical audit and the re-engineering of systems and processes in departments and specialties. Total quality management and continuous quality improvement have been pursued variably and with inconsistent success (Garside, 1998).

Black explained that audit used 'evaluative research' as a basis for defining what was good quality care. Audit consisted of reviewing and monitoring current practice and evaluation (comparison of performance) against agreed predefined standards. Audit involved the definition of standards, the measurement of the achievement of these standards and the mechanisms employed to improve performance (Black, 1992).

Bowling explained that audit was directed at the maintenance and achievement of quality in health care. In theory, it should lead to change in clinical practice by encouraging a reflective culture of reviewing current practice, and by inducing changes that lead to better outcomes (Bowling, 1997).

Action research

The style of research known as action research is particularly suited to identify problems in clinical practice and helping to develop potential solutions in order to improve practice. For this reason action research has enjoyed increasing popularity

across a wide range of disciplines (Holter and Schwartz-Barcott, 1993). In the healthcare field it is mainly used by the nursing profession and is common in nursing literature (Hart, 1995).

Action research was developed in the 1940's as a specific response to bridge the gap between theory, research and practice (the 'theory-practice' gap). It incorporates both humanistic and naturalistic scientific methods (Nolan and Grant, 1993). The emphasis of action research today has shifted to a method of community or organisational development by awareness raising, empowerment and collaborative investigation (Bowling, 1997). Waterman (1996) adopted the following definition of action research: "a type of self-reflective enquiry undertaken by participants in social situations in order to improve the rationality and justice of their own practices, their understandings of these practices and the situations in which these practices are carried out" (Waterman, 1996).

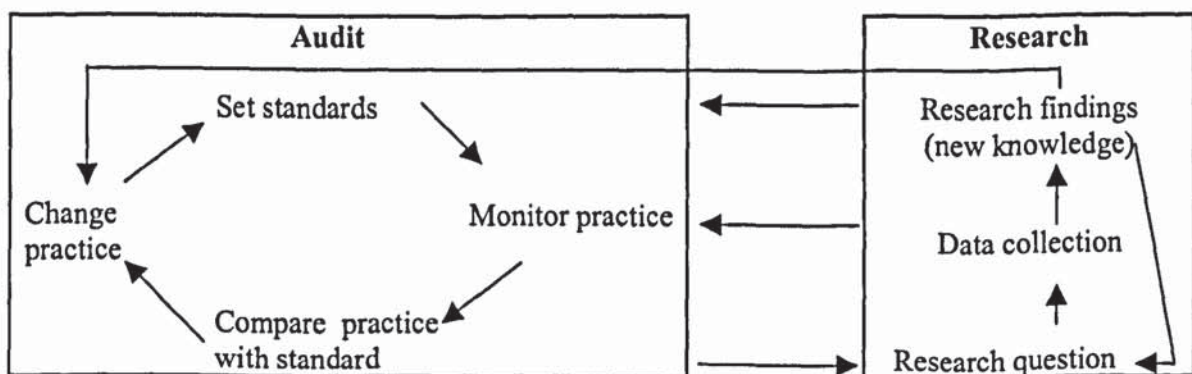
Holter and Schwartz-Barcott (1993) described how in action research the problem was defined in relation to a specific situation and setting. Various methods have been used for data collection in action research programmes. The change process was based on the intervention created by the researcher and the practitioners. The actual change that occurred depended on the nature of the problem identified. In addition to changing practice, action research also aimed to develop theory. New theory was developed or existing theory was expanded or enhanced. Four characteristics of action research were identified: collaboration between researcher and practitioner, solution of practical problems, change in practice and development of theory (Holter and Schwartz-Barcott, 1993).

Hart and Bond (1995) showed how some key characteristics distinguished action research from other methodologies and determined the range of approaches to action research. They presented a typology of action research identifying four basic types: experimental, organisational, professionalising and empowering. The criteria used for the typology were educative base, the role of individuals in the group, problem focus, change intervention, improvement and involvement, cyclic process and research relationship. The authors suggested that each type embodied a different theoretical perspective on society (Hart and Bond, 1995). Whilst the typology was useful in understanding the wide range of action research, its multi-dimensional nature meant that it was not particularly easy to classify individual studies. Hart and Bond (1996) used three action research projects to demonstrate how they could be dominated by one type in the beginning and may shift to a different type in the course of time.

A comparison between audit and action research

Closs and Cheater (1996) compared audit and research. The main points from their comparison are outlined in Figure 1.2.

Figure 1.2 Interactions between audit and research



(Closs and Cheater, 1996)

The authors concluded that the main distinction between audit and research lay not in the activities themselves, but rather in their purposes and use of theory. Audit, unlike research, did not necessarily extend the knowledge base for health-care practice. Audit was heavily dependent on published research and where research was lacking consensus guidelines or local experts provide agreed acceptable standards. Research was often concerned with generating new knowledge that will have general application (Closs and Cheater, 1996).

Waterman (1996) discussed the comparison between audit and action research. Superficially action research and audit had much in common, however a closer examination revealed fundamental differences. Action research and quality assurance systems both aimed to improve quality and employed methods that were cyclical in nature. Changing clinical practice for the better was also an attribute common to both approaches. In contrast, while the emphasis in quality assurance schemes was to ensure that healthcare organisations satisfy customer requirements, action research emphasised professional, personal and group development through democratic processes and was frequently used to generate new theories (Waterman, 1996).

1.3 RESEARCH QUESTION AND AIMS

The overall research question is to determine if it is possible to develop a systematic approach to the managed entry of new drugs into a National Health Service (NHS), using Malta as a case study.

In order to answer this research question a number of aims were set as follows:

1. To describe the processes for the managed entry of new drugs into the NHS in Malta in June 1999.
2. To identify and prioritise potential changes in the processes involved in the managed entry of new drugs into the NHS.
3. To promote the development of a more systematic approach for the managed entry of new drugs into the NHS using an action research methodology.
4. To identify and evaluate changes in the processes for the managed entry of new drugs from June 1999 (baseline) to December 2001.
5. To reflect on the case study methodology and identify elements of the systematic approach to the managed entry of new drugs which are generalisable to EU countries.

Critical appraisal of experimental literature related to the managed entry of new drugs was not possible as the only case study from the literature (Norris, 1998) was a retrospective study which did not enable an intervention phase to be implemented. Instead the literature on change management was used to inform the development of methodology, which is further discussed in chapter 2.

CHAPTER 2:

GENERAL METHODOLOGY

2.1 THE CASE STUDY

As presented in Chapter 1, in February 1999 Malta had significant problems with the processes that existed for the managed entry of new drugs into the National Health Service (NHS). At that time in Malta a number of political developments were happening, which were considered to be conducive to major changes and reform. The overall research question is to determine if it is possible to develop a systematic approach to the managed entry of new drugs into a NHS, using Malta as a case study.

2.1.1 The case study as a research method

Many critics of case study methods simply saw a case study as a loosely constructed story which lacked rigor, was selected at random, or worse because the researcher was connected to the case in some manner (Yin, 1994; Fitzgerald, 1999). This undervalued the approach and underestimated the current stage of development of the case study research. Over the past fifteen years the importance of non-experimental case study research has increased in line with the major growth in ecological psychology, the study of humans in interaction with their environments (Fitzgerald, 1999).

A 'case' was defined by Gillham (2000) as "a unit of human activity embedded in the real world, which can only be studied or understood in context, which exists in the

here and now, that merges in with a context so the precise boundaries are difficult to draw". He further defined a case study as "a study which investigates the case to answer specific research questions (that may be fairly loose to begin with) and which seeks a range of different kinds of evidence, evidence which is there in the case setting, and which is to be abstracted and collated to get the best possible answers to the research questions" (Gillham, 2000).

Gillham (2000) explained that experimental natural scientific type approaches were ill suited to the complexity, embedded character and specificity of real-life phenomena. In human behaviour generalisation is often suspect, the degree of specificity is unknown and the likely facts are unique. The author supported this conclusion by a comparison between natural and social science research. The major distinction between them is the greater concern of social science case study research with subjectivity, the phenomenological meaning. Social science research seeks mainly the qualitative element. Concern with process can be key to understanding what needs to be done to change things. The social science researcher is not a detached scientist but a participant observer who acknowledges, and looks out for, his role in what he discovers (Gillham, 2000).

Gillham (2000) described and highlighted the differences in the processes for conducting natural science research and social science research. Natural science research was aimed at generalisable findings. In natural science style the literature was studied to work out if existing findings and theories were adequate. If something was missing or needed testing, experimental procedures were set to yield new data, the deductive model.

In social science research the data and theories in the literature may have little bearing upon the case under investigation. The researcher needs to know what others have done but cannot be sure they are relevant. The first stage is to review the context from which the research questions, the means of investigating them and the likely explanations will emerge. An emergent design is characteristic of this style along with inductive theorising, making sense of what is found at that time. The researcher works inductively from what there is in the research setting and develops grounded theory, theory that is grounded in the evidence that is turned up (Gillham, 2000).

2.1.2 The generalisability of case study findings

One of the greatest criticisms of case study research is the generalisability of case study findings (Yin, 1994). Cormack (2000) grouped generalisation into broad categories. The author explained that empirical generalisation was used to select a random sample from a population to calculate the probability that the sample is representative. This was difficult in practice in the real world because it was hard to identify known and finite populations. Cormack explained that study of a sample from a population was further complicated by the fact that findings from this sort of research may only be generalisable to the sample population and may not be legitimately generalised for future events or situations to make predictions. The nature of these relationships could only be worked out and explained by researchers by using theories, models and concepts to produce explanations. Theoretical generalisation was a way in which researchers could generate a theory about phenomena that explained the relationship between them. The in-depth study of one case or a larger number of cases could achieve the generation of theory. The aim was to make a generalisation

based on the plausibility of the link between the characteristics of the phenomena being studied (Cormack, 2000).

The case study for Malta was to be used to generate knowledge that could be generalised to inform improvement towards the systematic approach to the managed entry of new drugs into the NHS and for bringing about change in healthcare in Malta and possibly also in other countries.

2.2 DESIGN OF THE EVALUATION

The aims of the case study for Malta were to describe the processes for the managed entry of new drugs into the NHS in June 1999; to plan and implement change to promote the development of a more systematic approach for the managed entry of new drugs using an action research methodology; to identify and evaluate the changes that occurred between July 1999 and December 2001 and to generalise the findings to countries of the European Union (EU). An evaluation design that met these aims was required. The item being evaluated 'the managed entry of new drugs into the NHS in Malta' was difficult to define and was to be changed during the evaluation.

2.2.1 Evaluation for action

The definition of evaluation by Ovretveit (1998) was considered to be the most applicable definition to this research. Ovretveit stated that "evaluation is attributing value to an intervention by gathering reliable and valid information about it in a systematic way, and by making comparisons, for the purposes of making more

informed decisions or understanding causal mechanisms or general principles”. The author emphasised his perspective by calling it ‘evaluation for action’ – an objective and systematic approach for making a comparative judgement of the value of an item against criteria, in order to decide how to act. The intervention was usually an action on, or attempt to change the ‘item’ that was being evaluated (Ovretveit, 1998).

Ovretveit (1998) explained that the aim of ‘evaluation for action’ was to enable practitioners, managers and others to do things differently and better as a result of the evaluation. The aim of ‘evaluation for action’, similar to the aim of a health intervention was to make a difference, even if the difference was only that people continued to do what they did before, but with more confidence that they were doing things right. The author explained that ‘evaluation for action’ was an umbrella term for a variety of different approaches that could be used for the purpose of practical improvement (Ovretveit, 1998). The aim of ‘evaluation for action’ was congruent with the aim of the case study for Malta, which was to bring about improvement in practice.

2.2.2 Evaluation of health interventions

The relevant theory was used to enable the choice and planning of the evaluation to achieve the objectives of this research. There are different types of health interventions and approaches to their evaluation vary. Even for an intervention of one type, many evaluation designs and methods are possible. The perspective, design and methods used in an evaluation should be suited to the purpose of the evaluation and to the type of intervention being evaluated and should be credible to the users and help them make more informed decisions.

Ovretveit described the approaches to the evaluation of health interventions within four broad categories of experimental, economic, developmental and managerial evaluations and gave the strengths and weaknesses of each category. Experimental evaluation was designed to test hypotheses and followed the model of a scientific experiment. Control of the intervention and of other possible influences was maximised. Economic evaluations aimed to discover how resources were consumed by using an intervention and usually also to quantify the consequences of an intervention, sometimes in monetary terms. Developmental evaluations were based on a different philosophy of science. They used systematic methods and theories within an evaluation framework to enable service providers to develop and improve their treatments, services, policies or organisational interventions. Developmental evaluations had an immediate practical focus and involved the evaluator working with providers or could be carried out by providers themselves. Managerial evaluations were made for managers and supervisory boards to monitor or improve the performance of services or policies or to check that agreed changes or projects were implemented as intended (Ovretveit, 1998).

The category of the evaluation chosen depended mainly on the purpose of the evaluation and on the nature of the item that was evaluated and its predicted effects. Table 2.1 summarises the categories of evaluation most often used to evaluate different interventions in healthcare.

Table 2.1 Categories most often used to evaluate different types of interventions for different items for evaluation

Item being evaluated	Category of the evaluation			
	Experimental	Economic	Developmental	Managerial
Treatment	often	often	rarely	rarely
Service	sometimes	often	often	often
Policy	rarely	sometimes	often	often
Intervention to organisation	sometimes	sometimes	often	often

Adapted from Ovretveit (1998)

2.2.3 The application of the developmental category of evaluation

The developmental category of evaluation was considered the most suited for this research. Ovretveit (1998) described that the developmental category of evaluation grew out of a critique of natural science methods applied to social phenomena. Experimental and economic evaluations were often not possible especially for services, policies, health reforms and many interventions to organisations. These 'items' often changed, were ill-defined, had multiple and contradictory objectives and had a variety of effects. Valid information often included an understanding of patients' and professionals' experiences and perceptions. This and other types of information could help users to judge the value of an intervention and could be more helpful to them for deciding how to act than information about outcomes and costs (Ovretveit, 1998).

There are different types of evaluation within the developmental category. They all share a pragmatic developmental aim, a flexible approach to choosing methods and a close and continual link between the emerging findings of the evaluation and practical action. Evaluations within the developmental category include descriptive evaluations, active evaluations and pragmatic experimental evaluations (Ovretveit, 1998).

Ovretveit (1998) explained that researchers often needed to evaluate a service or policy which was poorly defined, or where there were different views about what the service or policy was, or about its objectives. The author suggested that it could be premature to start developing evaluation criteria until the item was defined more clearly and thus a researcher could choose a developmental approach to an evaluation using a descriptive design. A researcher conducting a descriptive evaluation sought to evaluate the item by describing it and by trying to deepen understanding of what it was and how it worked. Many descriptive evaluations aimed to describe the inputs and processes of the item being evaluated, its boundaries, the context, and often also the outputs. They could be used as a study preliminary to an experimental or other type of evaluation to do an evaluability assessment. The quality and usefulness of evaluations of this type were dependent on the theory and models that they used to select what to describe. Ovretveit explained that some descriptive evaluations started off with a clear model or theoretical perspective that they then used to select what to describe and to guide data gathering. Some worked inductively, seeking to build models out of the data to describe key features of the item being evaluated (Ovretveit, 1998).

Action evaluations aim to change the item while evaluating it. Action orientation is an integral part of the approach in action evaluation. As described by Ovretveit (1998),

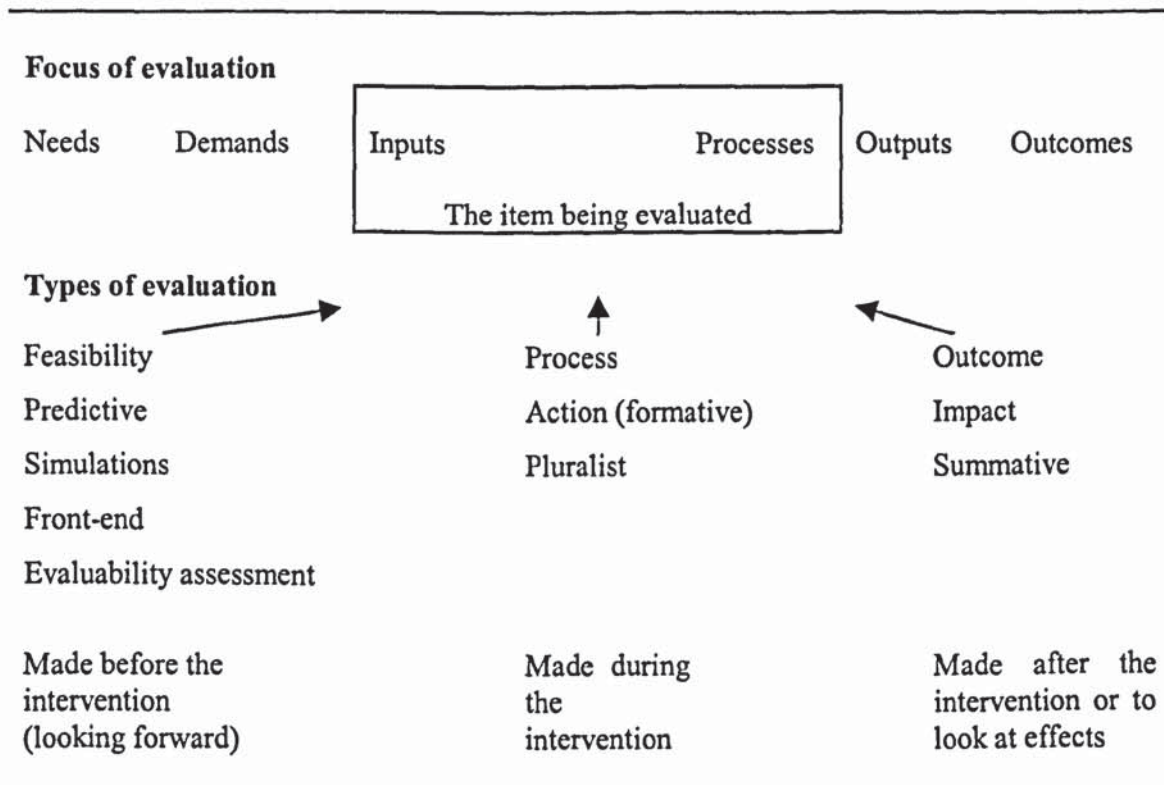
evaluation for action was politically aware, recognising the perspective of the different stakeholders who have an interest in the results of the evaluation and in the item being evaluated. Action evaluations were criterion-based and used criteria agreed by one or more stakeholders to decide which data to gather and how to judge the value of the item. Ovretveit explained that action evaluation was multidisciplinary and used the most relevant theory and methods from different disciplines for the purpose of the evaluation, to help decide evaluation criteria, to gather and analyse data, and to clarify the implications for judging value for carrying out action (Ovretveit, 1998).

2.2.4 Types and design of evaluations within the developmental framework

Ovretveit (1998) described that developmental evaluations could use quantitative methods and experimental principles. Within a developmental framework, evaluations used before-after designs, comparative designs, hypothesis testing and small scale experiments, even if these designs and data gathering methods might not meet the same rigorous standards as those used in a full experimental evaluation. Developmental evaluations also included a sub-group of evaluations which used experimental principles, but used qualitative methods, sought information about a number of types of outcome and accepted providers' and beneficiaries' accounts (subjective data) as valid insight into and data for valuing the item being evaluated. There was a fine dividing line between quasi-experimental evaluations and some developmental evaluations, as some of the latter attempted to get evidence about outcome, but did so without the rigorous controls or techniques to reduce bias of the full experimental evaluation or of the single case experimental design (Ovretveit, 1998).

Ovretveit (1998) demonstrated that different types of evaluation were suited to the timing of the evaluation with respect to the intervention, whether the evaluation was made before, during or after an intervention, as described in Figure 2.1.

Figure 2.1 The focus of different types of evaluation with respect to the timing of the intervention



Adopted from Ovretveit (1998)

Ovretveit (1998) explained that an evaluability assessment was an assessment that was carried out to decide whether or not to make a full evaluation. Such an assessment clarified the item to be evaluated, its boundaries and its principal components and the main evaluation question. It reported the different possible ways in which the item could be evaluated. Of the evaluations made during an intervention, action (formative) evaluation was one type of developmental evaluation. Its purpose was to give information and assistance to people who were able to make changes to an

intervention so that they could make improvements. Action evaluations also gave a description of the evolution of the intervention. Because the evaluator has usually had some influence on the evolution of the intervention, this description could be of limited value to other services. Action evaluations were best suited to services in an early developmental stage, in a crisis or in transition (Ovretveit, 1998). Formative evaluations are one type of action research (Hart and Bond, 1995). Process evaluation only looked at processes whereas formative evaluation also looked at outcomes.

Some outcome or impact evaluations have been criticised for adopting one view of what is a valued outcome, often the view of those in power. Pluralistic evaluation investigates the views of different interest groups about what was success and their views of the extent to which an intervention was a success. Outcome or impact evaluations concentrate on discovering the outcomes or wider impact of a treatment, service or policy. An outcome evaluation might be part of an action evaluation but will not be a part of a process evaluation (Ovretveit, 1998).

Ovretveit (1998) explained that the purpose of the primary user of the evaluation should decide the design and perspective of the evaluation. Most evaluations used one of six types of design: descriptive, audit, outcome, comparative, randomised-controlled experiment and intervention to a service. Ovretveit gave an overview of evaluation perspectives and explained that evaluations were designed to answer the questions of one or more perspectives or interest groups or users. Perspective both 'sees' and 'focuses' on certain aspects of an evaluation and on its consequences. Some things were not seen because the perspective was selective. Perspective carried assumptions about what was valid knowledge, about the aspects of the evaluated that

were selected and about how to create this knowledge, the methodology. These assumptions framed how the researcher conceptualised the intervention and shaped the evaluation design and the data gathering and analysis methods. It was important to consider what questions the evaluation aimed to answer and which decisions and actions should be better informed as a result. The author noted that one must consider how much resources and time were available (Ovretveit, 1998).

2.2.5 Design of the evaluation used in this research

The evaluation for this research was planned in line with the aims set. The design of this research involved an intervention to a system, whereby action research was applied as an intervention for change within the processes for the managed entry of new drugs into the NHS in Malta.

Before the intervention a descriptive evaluation was carried out to describe at baseline the 'managed entry of new drugs into the NHS in Malta' and to set its boundaries and describe the processes within it. An evaluability assessment was undertaken using the model of the managed entry of new drugs into NHS in European countries. This model was used to guide data gathering for the managed entry of new drugs into the NHS in Malta. An action evaluation was conducted during the implementation of the intervention and the managed entry of new drugs into the NHS in Malta was evaluated while it was being changed. At the end of the action evaluation, an outcome evaluation was made to look at the changes that occurred. Because of the time limits set for this research the descriptive evaluation was planned for June 1999, the action evaluation

was to be conducted over the period July 1999 to December 2001 and the outcome evaluation was undertaken throughout 2002.

The primary user of this research was the researcher as a practitioner within the Health Division in the NHS in Malta. This was the perspective adopted throughout the research.

2.3 THE LOGIC MODEL AS A TOOL FOR THE EVALUATION

In February 1999, the 'managed entry of new drugs into the NHS in Malta' was a complex real-life set of processes that were difficult to define. In order to be able to conduct the evaluation the processes needed to be well defined and clearly described. Ovretveit emphasised on the need to define what was being evaluated. This was not always straightforward, particularly when it involved social systems such as services and health policy. The key features of the evaluated which were thought to be significant needed to be described, usually because they might cause or influence the effect (Ovretveit, 1998). The first step in the research was the carrying out of a descriptive evaluation. As explained above, the descriptive evaluation started off with a model of the managed entry of new drugs into European countries, that was used to select what to describe and to guide data gathering during the descriptive evaluation.

2.3.1 Logic models

Cropper and Forte (1997) described models as representations of real processes, events and structure that provided a discipline in understanding the nature of the

problem and in exploring options for future policy and action. To be of help in decision making, models must capture those characteristics of a decision situation believed to give rise to critical outcomes or potential points for management intervention. Models could be used to assess the results of particular assumptions and to undertake appraisal of different options for intervention (Cropper and Forte, 1997).

Dwyer and Makin (1997) described logic models as word or pictorial depictions of real life events/processes that depicted graphically the underlying assumptions or bases upon which the undertaking of one activity was expected to lead to the occurrence of another event. Logic models showed causal relationships as they related to one another (Dwyer and Makin, 1997). Variations of the logic model are called by different names. For example chains of reasoning is a combination of text and a graphic image which presents the activities of the programme, the goals to be attained, additional assumptions and links between them (Torvatn, 1999). The Logic Model and its variations are all related to programme theory. In this research logic models were used to represent the managed entry of new drugs into the NHS.

McLaughlin and Jordan (1999) gave a comprehensive general description of the elements of the logic model, as depicted in Table 2.2. This description was adopted for the logic models used in this research. The logic model described the logical linkages among programme resources, activities, outputs, customers reached and outcomes. A critical feature of the performance story was the identification and description of key contextual factors external to the programme and not under its control that could influence its success either positively or negatively.

Table 2.2 Elements of the logic model

Outcomes – changes or benefits resulting from activities and outputs					
Resources	Activities	Outputs	Customer reached	Short term	Long term
Human and financial resources	All the action steps necessary to produce programme outputs	The products, goods and services provided to the programme outputs	Customers served and the people who work with the partners who work with the program to enable actions to lead to results	Those changes or benefits that are most closely associated with or caused by the program outputs.	Program impacts – follow from the benefits accrued through the intermediate outcomes
Inputs required to support the programme		direct customers			

External influences: factors external to the programme and not under its control that could influence its success either positively or negatively

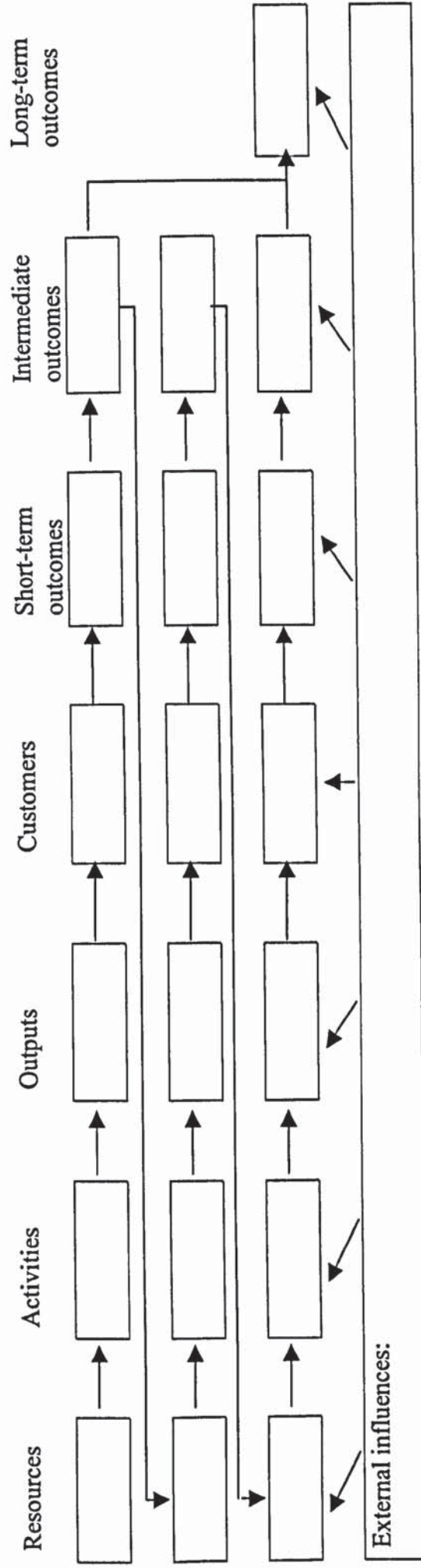
Adapted from McLaughlin and Jordan (1999)

2.3.2 Building a logic model

McLaughlin and Jordan (1999) gave detailed guidance of five steps for building a logic model and explained how the logic model process helped to answer useful questions. Their instructions were accompanied by practical recommendations.

Stage 1 involved collecting the relevant information from multiple sources. Conducting a literature review gave an insight into what others did to solve similar problems. Stage 2 required clearly defining the problem and its context. A programme should be grounded in an understanding of the problem that drives the need for the programme. The authors explained that one of the greatest challenges faced in developing logic models was describing where this programme ended and other programmes started and advised that for the process of building a specific programme's logic model, the programme's performance ended with the problem it was designed to solve. Stage 3 involved defining the elements of the logic model. The authors recommended starting building the logic model by categorising the information collected into columns in a table with headings similar to those in Table 2.2. All the key elements needed to be identified and there was to be a flow from left to right. Stage 4 required the drawing of the logic model to capture the logical flow and linkages that existed in the performance story. The model was usually set as a diagram with columns and rows with the abbreviated text put in a box and linkages shown with one way arrows as depicted in Figure 2.2. Stage 5 consisted of verification of the logic model with stakeholders (McLaughlin and Jordan, 1999).

Figure 2.2. Logic chart for a programme



Adapted from a logic chart for a research and technology development and deployment programme from McLaughlin and Jordan (1999)

2.3.3 The use of logic models in healthcare

The logic model and its variations have been used to support evaluation in healthcare. Julian and colleagues described two case management projects (Julian *et al.*, 1995). The authors performed a qualitative evaluation of the first case study 'The Family Development Case Study' and used the lessons from it to guide the second study. Problems identified from the first study included lack of cohesiveness, structure and leadership related to project oversight and lack of clear statement of the goals and expectations of the programme. In the second case the logic model and open systems evaluation were used to facilitate the development of an evaluation plan for the 'Perinatal addiction program'. The exercise provided an opportunity to develop consensus around project goals, programming and success criteria (Julian *et al.*, 1995).

In this research, the logic model was used to give a general framework of the managed entry of new drugs into the NHS in European countries and to describe the managed entry of new drugs into the NHS in Malta.

2.4 ACTION RESEARCH AS AN INTERVENTION FOR CHANGE

As specified in the aims of this research, action research was employed as an intervention to bring about change in the processes that existed for the managed entry of new drugs into the NHS in Malta. Action research is concerned with intervening to change and improve practice and engages participants in the struggle for improvement (Meyer, 2000). The definitions and context of action research were described in Chapter 1. The attributes and process of action research have been further explained in

this chapter.

2.4.1 Comparison between action research and traditional research

Waterman (1995) outlined the characteristics of action research that distinguished it from more traditional methods. The author went on to discuss issues of validity in action research (Waterman, 1998). These works formed the basis for the comparison between action research and traditional research that were presented by Cormack (2000). Within the positivist traditional research approach theory was determined scientifically and applied to practice. In action research theory and practice were intertwined and dynamic and interacted with each other. The conceptual framework reflected a spiral of theory-practice development. Action research used a cyclical approach where feedback from action taken in a previous stage determined the action in a subsequent stage. It was a flexible, unpredictable process, unlike the more traditional methods that were planned, articulated and conducted in an inflexible framework. In action research the plan changed as the research progressed (Cormack, 2000).

Action research and traditional research also differed in the method of data collection and in the role of the researcher. In traditional research there was a strong emphasis on quantitative data that was statistically proved and generalisable. Many action research projects by their very nature generated qualitative data, although some have also utilised quantitative methods effectively. Whilst in the traditional approach every care was taken to ensure that the researcher was neutral, without bias, objective and outside

of the research situation, in action research the researcher was part of the research process and was inside the research situation (Cormack, 2000).

Ethical issues are important in all kinds of research. Meyer (1993) identified that action research was often written as case studies and this presented a potential problem in protecting the anonymity and confidentiality of participants.

2.4.2 The validity of action research

Since its inception, action research has received much criticism regarding its scientific basis and in some instances has been considered not worth the label of research. Much of this criticism centred around the debate as to its validity and reliability (Cormack, 2000). Titchen (1995) emphasised that appropriate standards of rigour against which the success of change could be assessed were to be utilised within an overall research framework that remained faithful to the needs of practice. Valid knowledge, in the form of principles for action or theorised accounts of change could be generated through action research, the final test of validity being the degree to which the research was useful in guiding practice for other practitioners. Validation processes were part of the collaborative nature of action research, and were built in because data had to be reflected upon and evaluated. Valid action research was an ethical enterprise which rested with the researcher's honesty, trustworthiness and integrity (Titchen, 1995).

Waterman (1998) explained that validity in action research could be determined by analysing its three major qualities: dilectual validity, critical validity and reflexive validity. The author stressed that the fact that by its very nature action research

addressed the tensions and difficulties that arose in practice, was a strength of action research that demonstrated validity. The dialectical property of action research which involved theory, research and practice as a dynamic, intertwined process concerned in bringing about change in the real world, was a positive indicator of the validity of action research. The author suggested that there was an emancipating element in action research that tried to make things better. This attempt to bring about improvement rather than the degree to which it actually affected change was crucial in assessing validity (Waterman, 1998).

2.4.3 Characteristics of action research

Action research involves research in the field and close involvement with the key players in order to identify problems and implement reforms. Hart and Bond (1995) explained how action research could be carried out by providers themselves as part of their everyday work or as a special project. Throughout the action research, the study findings were fed back to the participants for validation and to inform decisions about the next step of the study. This formative style of research was thus responsive to events as they naturally occurred in the field and frequently entailed collaborative spirals of planning, acting, observing, reflecting and replanning. These action-reflection spirals were characteristic of any action study. Meyer described McNiff's visual depiction of action research as a three dimensional tree of spirals, allowing for smaller 'spin-off spirals' to branch out from larger spiral activity. Practitioners engaging in action research could address many different problems at one time without losing sight of the main issues. It also captured the frequently seemingly chaotic nature of change in organisations and practice settings (Meyer, 2000).

Meyer (1993) used a case study to demonstrate the 'trials and tribulations' of action research. One issue raised was the potentially threatening nature of a collaborative relationship between researcher and participants. The author remarked that while collaborative approaches assumed that research was done with and for people rather than on people, this was not possible in reality. Meyer (1993) also warned that action research was difficult and it required a lot of energy to collect data and facilitate change. Meyer (2000) observed that democratic practice was not always a feature of healthcare settings and care needed to be taken in undertaking democratic action research. Excellent interpersonal skills in addition to research ability were of paramount importance (Meyer, 2000).

Action research projects are frequently written up as case studies. Percy and Draper used a case study of a ward to demonstrate the use of action research as an approach to facilitate research utilisation (Percy and Draper, 1996). Bellman used the enhancement approach to action research to change practice through reflection using a published model (Bellman, 1996).

Meyer (2000) pointed out that in considering the contribution of action research to knowledge, it was important to note that generalisations made from action research differed from those made from more conventional forms of research. To some extent reports of action research studies relied on the reader to underwrite the account of the research by drawing on their own knowledge of human situations. It was therefore important when reporting action research to describe the work in its rich contextual detail. The onus was on the researcher to make personal values and beliefs explicit in the account of the research so that any biases were evident. The quality of the account

enabled readers to assess its relevance to themselves in their own practice situations. Interpreting the relevance of findings to any practice situation ultimately rested with the reader. The strength of action research lay in its ability to influence practice positively in the course of the study, whilst systematically gathering data to share with a wider audience. The involvement of practitioners in this process ensured not only more likelihood of discovering successful solutions to problems, but also of obtaining a more relevant and meaningful body of knowledge for practitioners. The authors noted that change was problematic and whilst action research was useful to the discovery of solutions, its success was not to be judged solely in terms of the size of the change achieved. Instead success could often be viewed in relation to what was learnt from the experience of undertaking the research (Meyer, 2000).

In the case study for Malta, action research was employed as an intervention to bring about change in aspects of the managed entry of new drugs into the NHS in Malta. The main characteristic of action research was its use of the cyclical approach of planning and action. The 'model from improvement' from Langley, Nolan and Nolan (1992) adopted from Berwick (1996), described in Chapter 1, was used to plan and prioritise change in the beginning of and throughout the action research.

2.5 THE USE OF DIFFERENT METHODS FOR CASE STUDY RESEARCH, AS RELEVANT TO THIS CASE STUDY

The case study was the main method deployed in this thesis. Case studies use multiple sources of evidence, each with inherent strengths and weaknesses. Within the case study in this thesis other research methods, including action research, were used.

2.5.1 Gathering and analysis of data for case study research

Keen and Packwood (2000) explained that case studies could use both historical and real-time data. It was frequently important to understand and map the historical developments of an issue. Case studies allowed tracking processes through time. The authors explained that case studies could employ various forms and sources of data. The case could be built up using descriptive and inferential statistics and facts drawn from current sources. These facts could be supplemented with new data produced by interviewing or surveying a range of people who had knowledge to bring to bear on the theme under investigation. Cases could also employ observational data (Keen and Packwood, 2000).

Gillham (2000) insisted that regular and systematic reviewing and summarising was essential to the discipline of case study research. This enabled plotting of the progression of thinking. The author warned that case study research could easily lose shape because of the complexity of the material. The researcher was to maintain a research log that was kept on their person all the time. The researcher was to record evidence as well as personal notes, with entries best made immediately. Gillham noted that writing things down had a focusing effect on the mind. The information in the logbook was to be used to make up notes. The researcher was to regularly review their notes and prepare a summary of the different types of evidence uncovered, the immediate priorities for action, any reworking of the research aims and theorising about how the data could be explained (Gillham, 2000).

Once data were collected they needed to be analysed and used to develop explanatory

and descriptive themes which were robust. Gillham explained that there were various established methods of data analysis using interactive processes of content analysis to produce analytical themes. The evidence could be specific to the case in question and analysis needed to be appropriate so as not to deform the findings (Gillham, 2000).

Different opinions were expressed on the use of data from different methods within case study research. Gillham (2000) explained that data accumulated by different methods but bearing on the same issue were part of the multi-media approach. Different methods had different strengths and weaknesses. If they converged there was confidence that a true picture was being built. If they did not agree one had to explain this or question the adequacy of the methods. This approach from different methodological standpoints is known as triangulation. Gillham noted that there was a common discrepancy between what people believed, said, and what they did (Gillham, 2000). Keen and Packwood (2000) expressed reservations about the use of information from different methods in qualitative research. The authors considered that different methods and sources of data tended to provide different sorts of insights rather than contribute to a single, accumulating picture (Keen and Packwood, 2000).

Gillham (2000) explained that evidence was primary, but theory was not. The author described that good researchers tested their assumptions positively looking out for evidence that challenged their understanding. New knowledge was mainly interpreted in terms of what was known, until it proved so inadequate that the knowledge frame underwent a radical reorganisation, a paradigm shift. The author explained that interpretation of data was more than a matter of good intention, it required discipline and concentration to present a true picture and not to compromise the validity of the

research. One of the most significant aspects of analysis was to be able to document the foundational data and exemplification of this data (Gillham, 2000). In the end all the evidence needed to be woven into a narrative account presenting what Yin (1994), called a 'chain of evidence', that is each key element in the account is supported by or related to evidence of different kinds.

2.5.2 Methods used to collect data for this case study

In this thesis a descriptive evaluation was conducted up to June 1999. An action evaluation was then undertaken between July 1999 and December 2001 using action research as an intervention for change. An outcome evaluation was then presented. During the research different research methods were used to inform the case study.

A literature review was conducted at the beginning of the research. The information from this literature review was used during the descriptive evaluation to build a model of the managed entry of new drugs into the NHS in European countries. The literature review was continued throughout the research and proceeded to support the planning of the action research. Gillham (2000) insisted that the notion that one did an extensive literature review from which a hypothesis to test was derived was a 'nonsense' in real-world research. It represented an adherence to an inappropriate paradigm. However in the literature there will always be elements that sharpen the insight of the researcher. The author recommended that the two processes of getting to know the literature and getting to know the case should proceed simultaneously so that the reading and what is turning up in the case interact and feed into each other. Gillham explained that the researcher would not know what was required from the

literature until the real context was reached. What was found in the literature sensitised the perceptions of the researcher. This progressive influence was one dimension of the emergent character of the case study. Gillham recommended that at some point a literature review was attempted as a means to clarify things and improve thinking (Gillham, 2000).

Document and media research was carried out throughout the case study. Published or publicly available documents and records help to appraise the wider context of the case. Institutions have their own literature which is usually neither published nor in public domain. In the case study these are a kind of evidence. Gillham distinguished between documents, policy statements, minutes of meetings and reports of one kind or another, and records (often computer stored). The author noted that getting into records could present some problems. Due to ethical problems, permission and approval for access and use was required. The data may not be easily accessible to the researcher because of technical reasons or because of the format. Although these sources were usually very useful for case study research, they were not designed for this purpose (Gillham, 2000).

Measurement methods were used throughout the case study. Gillham explained that although qualitative methods and data were predominant in case study research, quantitative data extended the range of evidence on the topics under investigation and qualified what was learnt from other sources. This kind of cross-referencing was part of the internal validity of a case study (Gillham, 2000).

Gillham described the types of quantitative data most frequently encountered in case study research. Quantitative data often came in categories or could be put into them, usually to make comparisons between the different groups for example by age and/or gender. Data could also come as weekly, monthly or annual statistics showing rates and possibly trends over time. Abstracting data from statistical records over time was a good way of evaluating trends and drawing inferences. Pattern matching and time series analysis referred to a predictive approach to interventions. They involved a series of data for different intervals, usually annual, over a period of time and with enough data pre-intervention to make claims for changes to be credible. Time series analysis could be used with successive observations of the structured kind, usually where some changes were going to be introduced after a period of baseline observations. The technique could also be used simply to display “normal” variations over time. The author emphasised that it was important that the baseline data was collected over a significant length of time because if there was just one pre-intervention reading, no comparison of trends could be made (Gillham, 2000).

For case study research operating in the real world, quantitative data analysis had to be subjected to the scrutiny of what it might mean – whether or not it was statistically significant. Even if the numbers involved did not yield a statistically significant difference, there could be important differences in reality and in more subtle human terms. Statistics were of two kinds: descriptive and inferential. Descriptive statistics included things like averages that described data in summary fashion. Inferential statistics were those which enabled the researcher to draw potentially meaningful conclusions on the extent of correlation, for example the significance of differences between groups or the significance of changes following an intervention. Both have a

place in the case study. Gillham explained that statistics did not speak for themselves and had to be explained or interpreted. One of the most significant sources of error in time series analysis was a change in criteria for inclusion of the data when an intervention was applied. It was important that one compared 'like with like' (Gillham, 2000).

The researcher was a participant observer throughout the case study. During the descriptive evaluation the participant observation was mainly passive. During the action evaluation the participant was an active part of the action research. Gillham stressed on the need for the participant observer to identify himself and to tell the purpose of the research. The author explained that this did not bias the members of the group. Bias was only created if the researcher explained what answers he expected to find. The researcher was to work on developing a relationship with the individuals concerned but was to be wary about forming, or appearing to form, relationships with particular members of the group (Gillham, 2000).

In the descriptive evaluation different methods were used to study the opinions of stakeholders. Structured questionnaires were used to study the opinion of consultants working within the NHS. Structured interviews were used to get the views of patients and unstructured interviews to get information from medical representatives. Focus group discussions were held with representatives of the public.

Questionnaires can be structured or semi-structured. A structured questionnaire was used to study the opinion of consultants working within the NHS. Structured questionnaires involve the use of fixed questions, batteries of questions, and/ or scales

that are presented to respondents in the same way, with no variation in questionnaire wording, and with many pre-coded response choices. The strength of the structured questionnaire is the ability to collect unambiguous and easy to count answers, leading to quantitative data for analysis. It is relatively economical and large samples of people can be included. The weaknesses of the structured questionnaire include that the pre-coded response choices may not be sufficiently comprehensive and not all the answers may be easily accommodated. The questions must be worded and ordered in a way that will be understood by all respondents. Questionnaires rely on unstated general knowledge about the respondent group, particularly concerning the perceptual and interpretative processes in the interviewer and the participants. The method is best suited for obtaining factual data but can be subject to error in relation to the collection of information about attitudes and behaviour. The self-administered questionnaire is useful in minimising interviewer bias and for sensitive topics, as there can be anonymity. The questions must be straightforward and the population must be literate and speak a common language. The self-administered questionnaire is less suitable for complex issues and is inappropriate if spontaneous replies are required. The data obtained is usually less reliable than with face to face interviews as interviewers are not present to clarify questions or to probe (Bowling, 1997).

Interviews involve the collection of data through talking to respondents and recording their response. Face to face interview methods vary from in-depth, unstructured or semi-structured. For example they may include structured questions without response codes to highly structured pre-coded response interviewing forms. They can involve a combination of these. Structured and semi-structured interviewing forms, if carefully designed, can yield highly accurate data. During the research structured interviews

were conducted with patients. Semi-structured interviews were used for studying the opinions of medical representatives.

Semi-structured interview schedules include mainly fixed questions but with no or few response codes and are used flexibly to allow the interviewer to probe and to enable respondents to raise other relevant issues not covered by the interview schedule. Some semi-structured schedules permit the interviewer to ask questions out of order at appropriate opportunities during the interview. Open-ended questions could be included in the interviewing form to enable respondents to give their opinions in full on more complex topics. Open-ended questions are used for topics that are largely unknown or complex (Bowling, 1997). Details of how to conduct interviews and analysis of interview data were given by Gillham (2000).

Bowling (1997) described that the advantages of interviews were that interviewers could probe fully for response and clarify any ambiguities, more detailed and complicated questions could be asked, more information of greater depth could be obtained, inconsistencies and misinterpretations could be checked and there were no literacy requirements for respondents. The overwhelming strength of the face-to-face interview was the richness of the communication that was possible. The author warned that interviews were time consuming and there was a potential for interviewer bias. The time cost is a major factor in deciding what place interviewing should have in a study. This was not just the time to conduct the interview but also the time involved in transcription and analysis where a factor of ten at least is involved (Bowling, 1997).

Focus group discussions were conducted with a group representing the public. Focus group discussions are unstructured interviews with small groups of people who interact with each other and the group leader. They are particularly useful to get an early orientation on the research topic. Issues of conflict or disagreement may alert the researcher to hidden complexities. They utilise group dynamics to stimulate discussion to generate ideas to pursue a topic in depth. It is a useful technique to explore cultural values. Attention to group composition is important. Group dynamics can be a powerful distorting force. The group dynamic's potential for conflict is one of its strengths in that it may bring out tensions and reveal groupings not apparent in an individual interview (Bowling, 1997; Gillham, 2000).

During the action evaluation in addition to action research, which was the main method, other methods were used to inform the evaluation. The document and media research and the measurement methods were continued from the descriptive evaluation. Multiple case studies were used.

2.6 STATISTICAL HANDLING DURING THE RESEARCH

The main use of statistics in this research was for the quasi-experimental design which compared the results of the consultant questionnaires in 1994 (Vella, 1995) with the response to the same questionnaire in 1999 and for the measurement data representing the process for the managed entry of new drugs into the NHS in Malta.

The consultant questionnaires in 1994 and in 1999 were sent to all clinical consultants working within the NHS in Malta at the respective points in time. The population of

consultants in the two instances was different; in 1999 some consultants had left the service while new consultants were employed. The two samples were therefore considered to be independent. The questionnaire contained mainly questions requiring YES/NO answers and ranking questions. The Mann Whitney test was used for comparing results of ranking questions for 2 independent samples.

Data from the consultant questionnaires and the patient interviews were entered into Microsoft Excel Version 7 and statistics calculated using Biomedical Data Package (BMDP) software Version 1990.

The data for the activity of the Drug and Therapeutics Committee in relation to 'new drug' applications was analysed using process statistical methods. The principles of process control, as applied in industry, were applied. The principles of process control are based on the fact that in any production process, some variation in quality is unavoidable. This variation can be either random variation, the natural inherent variation of a production process, or variation due to special or assignable causes, those causes that are not part of the system all the time and arise due to special circumstances (Deming, 1993).

The text by Wetherill and Brown (1991) was used as the main reference for the statistical analysis of the process time series analysis. In this research the results of the values measured were in the form of percentage figures for consecutive years and thus Individual Charts (I Charts), a type of Shewhart Charts, were used. I Charts were used with a simple decision rule (the action and warning lines) to see when the process was out of control. The action lines were placed at the lower control limit (LCL) and the

upper control limit (UCL) at 3 sigma (3 standard deviations from the mean) whilst the warning limits were set at 2 sigma from the mean (Wetherill and Brown, 1991).

The CuSum chart was a different way of deciding when a process was or was not in control. CuSum charting has been used a great deal in industry. CuSum plotting was a useful technique to highlight changes in the process average level. The principle was to subtract the overall mean from the data, and then cumulate the difference. Changes of mean were shown up in CuSum charts by changes of inclination of the chart and this gave CuSum charts greater visual impact. A horizontal trace implied that the overall mean holds. A change in the slope of the CuSum plot represented a change in the mean. Any deviations from the mean were shown by a change of the slope from the horizontal. By using the CuSum plot it was often possible to detect clearly when change in the process average occurred. This was of particular value because an indication of when changes occurred assisted in diagnosing the causes of the changes. While the I Charts were used with a simple decision rule, the action and warning lines, to see when the process was out of control, CuSum plots could also be used with decision rules to decide when a shift in process average occurred (Wetherill and Brown, 1991).

The simplest CuSum decision rule used a truncated V-mask. The V mask point was placed on the latest CuSum value and an out of control signal was given when the previous trace crossed the arms of the mask. The shift in mean could have occurred some time before it was signaled and estimation of the point of change and of its magnitude could be made from the CuSum chart simply by looking to see when the chart changed its slope. The advantages of the CuSum chart over the I Chart included

that a change in the mean could be detected visually by a change in slope and the point of change can be detected easily. One disadvantage of CuSum charts was that they are more complex to use (Wetherill and Brown, 1991).

MINITAB for Windows 98 Statistical Software was used to analyse the data and to present the plots in this thesis.

2.7 ETHICAL AND PRACTICAL ISSUES RELATED TO THE RESEARCH

2.7.1 Approval of the research by the participants within the practice

Before initiating the project the research proposal was discussed with the main participants, the Director General (DG), the Chairman of the Drug and Therapeutics committee (DTC) and the director of the Government Pharmaceutical Services (GPS). All participants approved the proposal. The Department of Health supported conduct of the research within the practice.

The research proposal was presented at the 99th meeting of the DTC (1999) and was discussed. Two members of the DTC expressed concern on whether the research will influence the progress of issues being processed by the DTC and the flow of requests to the DTC. They were particularly worried that issues would be postponed to the time when the action evaluation was being conducted. It was confirmed that the project would not effect the proceedings of the DTC in any way and that members were to proceed with their interventions in the normal way. The members of the DTC promised full support for the research.

2.7.2 Ethical approval by the Research and Ethics Committee

The hospitals of the NHS in Malta are 'teaching hospitals' of the Medical School of the University of Malta. Approval was obtained from the Research and Ethics Committee of the Medical School of the University of Malta. The research proposal was approved. A copy of the approval of the Research and Ethics Committee is provided in Appendix I.

2.8 SUMMARY OF THE METHODOLOGY USED IN THE CASE STUDY RESEARCH

The overall research question is to determine if it is possible to develop a systematic approach to the managed entry of new drugs into a NHS, using Malta as a case study.

The research was conducted from January 1999 to December 2002 as outlined in Table 2.3.

Table 2.3 Overview of timescale and methods relative to individual chapters

Time line	Up to June 1999	July to Sept. 1999	July 99 to Dec. 2001	January to December 2002	
Method/	Case study research				
Objective	Evaluations of the developmental category				Generalisation of the case study
	Descriptive evaluation	Planning and prioritisation	Action evaluation	Outcome evaluation	
Chapter	3	4	5	6	7

The detailed research methods and the developments in the logic model relative to individual chapters are summarised in Table 2.4.

Table 2.4 Detailed research methods and the developments in the logic model relative to individual chapters

Research method	Brief description	Chapters
Document and media search	Used to collect data about the various aspects (mainly qualitative)	3 and 5
Measurement methods	Used to collect data on the activity of the DTC in relation to 'new drug' applications (quantitative)	3 and 5
Questionnaires	Structured questionnaire to consultants	3
Interviews	Structured interview with patients	3
	Unstructured interviews with medical representatives	3
Focus group	Focus group discussions with representatives of the public	3
Action research	Action research method applied to bring about change	5
Case studies (multiple)	Used to illustrate specific aspects	5
The logic model as an evaluation tool	'General logic model' The 'General logic model' was constructed from the information in the literature	3
The logic model as an evaluation tool	'Descriptive model 1' 'Descriptive model 1' represented the managed entry of new drugs into the NHS in Malta as in June 1999	3
The logic model as an evaluation tool	'Descriptive model 2' 'Descriptive model 2' represented the managed entry of new drugs into the NHS in Malta as in December 2001	5

CHAPTER 3:

DESCRIPTIVE EVALUATION

3.1 INTRODUCTION

A descriptive evaluation of the managed entry of new drugs into the National Health Service (NHS) in Malta was conducted.

The item for assessment ‘the managed entry of new drugs into NHS’ was a complex system. An evaluability assessment was carried out to ensure that the managed entry of new drugs into the NHS could be evaluated and presented in a comprehensive way, and to define its boundaries. As Malta was adopting European Union (EU) legislation in preparation for accession into the EU, the evaluability assessment was done using information from the literature about the managed entry of new drugs into the NHS in EU countries. The logic model was found to be a good tool to represent the different processes and components and the links between the different processes within this complex system. A ‘General logic model’ was developed from the information from the literature about the entry of new drugs into European countries, which was presented in Chapter 1.

This ‘General logic model’ was used to guide what information needed to be gathered for the descriptive evaluation of the managed entry of new drugs into the NHS in Malta and to decide on the choice of methods to obtain the required information.

Definition of 'new drug'

A 'new drug' was defined as a drug that had not previously been procured by the Government Pharmaceutical Services (GPS) for a particular indication.

Within this definition a number of drugs were excluded:

- branded products of which a generic alternative is already available within the GPS
- combination products where the different components are available separately or as part of another combination product
- different doses/strengths of drugs which are already available within the GPS
- different dosage forms of drugs which are already available within the GPS

This definition was previously used by Vella (1995) and allowed for consistency in the collection of data. The term 'drugs' and not 'medicines' was generally used because in Malta there was no system for the registration of medicines as in the EU and therefore the definition of 'medicines' as in Council Directive 65/65/EEC did not apply in Malta. In this research no distinction was made between 'drugs' and 'medicines'.

3.2 AIM AND OBJECTIVES

The aim of this descriptive evaluation was to describe the processes for the managed entry of new drugs into the NHS in Malta in June 1999.

This was achieved by addressing a number of objectives:

1. to develop a 'General logic model' of the managed entry of new drugs into the NHS in European Union (EU) countries
2. to obtain information to describe the processes for the managed entry of new drugs
3. to obtain the opinion of stakeholders about the practice and about related issues
4. to identify problems that existed with processes for the managed entry of new drugs
5. to present the information gathered from the different methods to populate a descriptive model to provide an overview of the processes for the managed entry of new drugs

3.3 METHODS

3.3.1 Development of a 'General logic model'

The information about the managed entry of new drugs into the NHS in EU countries that was obtained from the literature review presented in Chapter 1 was analysed to identify the components and key processes involved.

The literature was used to study different tools that could be used to represent this

information and to support the aims of this research. The logic model (McLaughlin and Jordan, 1999) presented in Chapter 2 was considered to be the best tool to represent the information and to guide the implementation of the planned intervention for change. The 'General logic model' was used to represent the different components, the processes and the links (relationships) between them. The main areas of the model were also identified.

3.3.2 Gathering information about the processes for the managed entry of new drugs into the NHS in Malta

The researcher was a pharmacist who worked in various positions within the NHS in Malta since 1991. Since 1998 the researcher held the post of secretary of the Drug and Therapeutics Committee (DTC) and was in charge of the National Formulary Management (NFM) section, which was responsible for the procurement of drugs within the GPS.

The researcher took an active role in each of the following methods used to gather information.

3.3.2.1 Participant observation

The researcher had a central role in the processes for the managed entry of new drugs by nature of position within the NHS. This allowed the researcher to directly observe a number of processes first hand and enabled additional information to be gathered over and above that which was formally documented. A diary was kept in which brief daily

notes were entered. At the end of each day the notes were studied and compared to the 'General logic model' to identify what further information was required. Activities were planned to find the required information. The information collected was analysed and accumulated in the same way and in the same table as for the document and record research described below.

3.3.2.2 Document and record research from 1991 to June 1999

The information contained in the introductory section of the project by Vella (1995) was analysed. This covered the introduction of new drugs in Malta up to the end of 1994, up to the 80th DTC meeting. The document and record research was followed-up for the period January 1995 to the end of June 1999. The main documents searched were the minutes of the DTC from the beginning of 1995 to end June 1999, from the 81st to the 99th DTC meetings, and the correspondence of the DTC during the same period. Other sources of data analysed included correspondence, reports and circulars of the Department of Health and of the GPS.

The data was grouped under the areas identified through the 'General logic model' and was further divided into the components using subject headings. The information was entered in chronological order. The source of the information was referenced for each entry. A table format was used to collate the information.

3.3.2.3 Activity of the DTC from 1991 to 1998 in relation to 'new drug' applications

The information from the measurement methods used to analyse the process for selection of new drugs that was presented by Vella (1995) was followed up from 1995 to 1998. The results were updated accordingly. The measurement methods consisted of simple annual statistics and of measurements of outcomes of the process for the selection of new drugs, which were presented as percentages.

The measurements of the outcomes of the process for the selection of new drugs were analysed using the process statistical methods described in Chapter 2. The Individual Charts (I Charts) were drawn for the information on two indicators used to monitor the process for approval: the percentage of requests approved and the percentage of requests decided without delay. Where 'without delay' was defined as a decision being made at the first meeting of the DTC at which the drug was considered. The action lines (at 3 sigma) were drawn for each set of data. The warning limits for the I Charts (the values at 2 sigma) were also calculated.

MINITAB for Windows 98 statistical software package was used to perform the calculations and to draw the figures. A statistician and a standard reference text (Wetherill and Brown, 1991) were used for reference.

3.3.2.4 Consultant questionnaires

Questionnaires were conducted with clinical consultants who worked within the NHS. The aims of these questionnaires were to obtain the opinion of clinical consultants on different aspects related to the managed entry of new drugs as in 1999 and to study the opinion of consultants on prioritisation and allocation of resources.

The same questionnaire that was administered to clinical consultants working within the NHS in Malta in 1994 (Vella, 1995) was repeated. This questionnaire had already been validated for face and content validity in 1994. Minor additions to the ranking lists in some questions were made, however these were considered insignificant and it was not felt necessary to revalidate the questionnaire.

A second questionnaire, on prioritisation, was included in 1999. The prioritisation questionnaire was piloted for face and content validity, prior to sending.

The two questionnaires were left anonymous and were sent out together with an introductory letter explaining the purpose of the study. A stamped addressed envelope was included. Questionnaires were sent to all the clinical consultants working within the NHS. The updated list of consultants was obtained from the personnel section of the NHS.

One reminder was sent to all consultants to improve the response rate.

The results of the questionnaires of 1994 and of 1999 were analysed and compared using Biomedical Data Package (BMDP) Version 1990. In the prioritisation questionnaire to consultants, the ranking for the results of question 2 was calculated by mean rank. The factors in question 4 were sorted by the mean score of evidence and were prioritised starting with 1 for the highest priority.

A copy of the questionnaire to consultants is provided in Appendix II. A copy of the prioritisation questionnaire of 1999 is included in Appendix III.

3.3.2.5 Patient interviews

Patient interviews were conducted to obtain the opinion and expectations of patients regarding aspects related to the practice for the introduction of new drugs, the national system for reimbursement and prioritisation and allocation of resources.

As part of the Patient Charter Initiatives of the Ministry of Health in Malta for 1999, the GPS was assigned to study the opinion of patients about the services offered by the out-patient dispensary at St Luke's Hospital. Following a piloting exercise, structured interviews were chosen as the method to obtain information from patients. Questions to cover the above aims were included as part of a more extensive interview. The interviewing form and its translation in Maltese were validated for face and content validity.

Following the pilot study, interviewing was limited to patients who had at least one non-formulary drug prescribed. Relatives and carers of patients were excluded from

the interviews. The last person who was in the waiting room at the out-patient dispensary at St Luke's Hospital waiting to be served and who satisfied the inclusion criteria, was invited for the interview. Interviews were conducted in Maltese by one pharmacist. The pharmacist filled the information in the interviewing form. The relevant questions from the interviewing form are included in Appendix IV.

Data from the interviews was entered into a database using Microsoft Excel Version 7. Statistical correlation was studied using the Biomedical Data Package (BMDP) Version 1990.

3.3.2.6 Focus group discussions

In December 1999 the researcher conducted two discussion sessions with the theme 'availability of medicines and allocation of resources for pharmaceuticals through the NHS in Malta' with a specific focus group. This focus group was set up by the Foundation for Medical Services in preparation for the conference entitled 'A National Agenda for Sustainable Healthcare'. This consensus conference on the future of health care in Malta was organised by the Foundation for Medical Services and the Forum of Healthcare Professions and was held between 18 - 20th February 2000.

The focus group consisted of a general practitioner as chairman, two Jesuit priests from the Centre of Faith and Justice, a student from the student council of the University of Malta, a student from a higher secondary school, a news editor of a major local newspaper, 2 trade union representatives (one retired) representing the two main trade unions, the administrative secretary of the Foundation for Medical Services

and the Chairman of the Foundation for Medical Services who was formerly a clinical consultant within the NHS. The researcher took field notes during the discussion that were later analysed and a summary of key points prepared. Two meetings were held with the focus group, each lasting about two hours. At each meeting the researcher did a short presentation and this was followed by discussion.

3.3.2.7 Interviews with medical representatives

In Malta there are no major drug companies, but local agents represent drug companies. Medical representatives are employed directly by drug companies or by local agents. Interviews were conducted with medical representatives to obtain their opinion of aspects related to the managed entry of new drugs into the NHS in Malta and to identify the areas that medical representatives considered to be problematic.

A discussion guide with open questions was prepared in order to guide the interviews and to enable easier compilation of replies. A copy of the discussion guide used for the interviews with medical representatives is provided in Appendix V. The data was coded by open coding and later analysed. A summary of key points was prepared.

The interviews were conducted by the researcher during the exhibition of the Medical School Conference, which was held in February 1999. Permission was obtained to conduct the interviews from the organisers of the conference. During the session when the medical representatives were not busy, the researcher visited the different stands and explained the process and the purpose of the interview. It was emphasised that the interviews were being conducted for research purposes. Medical representatives were

invited to participate in the interviews.

The interviews were guided in order to ensure that all the relevant areas were covered. The interviewing form was used. During some of the interviews, the medical representatives asked direct questions in relation to the procurement of specific drugs. These questions were not answered. Brief notes were taken during the interview – mainly key words and statements and these were expanded immediately after each interview.

3.3.3 Development of ‘Descriptive model 1’ to represent the processes for the managed entry of new drugs into the NHS in Malta as in June 1999

A logic model representing the managed entry of new drugs into the NHS in Malta as in June 1999 ‘Descriptive model 1’ was built using the areas and the framework identified from the ‘General logic model’ from the method employed in 3.3.1. The information from the methods in 3.3.2 above was used to populate ‘Descriptive model 1’.

3.4 RESULTS

3.4.1 Development of a ‘General logic model’

The ‘General logic model’ is presented in Table 3.1. This model represented the managed entry of new drugs into the NHS in EU countries and incorporated the elements of the logic model (McLaughlin and Jordan, 1999), as detailed in Chapter 2.

Table 3.1 The 'General logic model' representing the managed entry of new drugs into national health services in EU countries

Resources	Activities	Outputs	Customers reached	Short term outcomes	Medium/long-term outcomes
Structural and human industry					
Inputs to support					
Pharmaceutical industry	EU/ national legislation for manufacturing, clinical trials	Research and development	Regulatory authorities - national and the European Medicines Evaluation Agency (EMA)	medicines to treat a wider range of disease, increased efficacy and safety	Financial gain by the industry leading to more research and development
	Code of ethics for the pharmaceutical industry	Manufacture of new drugs			Financial profit
		Application for registration			
Regulatory authorities					
	EU legislation	Registration of drugs in line with legislation	Industry	Quality, safety, efficacy	Health-related outcome measures
	National legislation	Pharmacovigilance	National drug markets	Rational drug use	
	Policy for issue of marketing authorisation based on national policy for pricing and reimbursement	Updated information on licensed use of the drug			
		Ensure quality, safety and efficacy of drug			

Table 3.1 Continued

Structural and human resources	Inputs to support	Activities	Outputs	Customers reached	Short term outcomes	Medium/long-term outcomes
Industry/ National drug market	Code of ethics for drug promotion & use of samples	Local supply Importation, distribution, promotion	Sale of the drug Consideration for reimbursement and for pricing	National health authority Reimbursement committee	Access, drug financing	Health-related outcome measures Satisfaction with health care
National bodies for reimbursement and pricing	EU legislation National /local policies for reimbursement, pricing of medicines	Reimbursement pricing decisions setting of priorities	Update of reimbursement list, recommendations for use, agreed price	Health care providers, patients	Access, affordability, equity, effective use of health-care resources, rational drug use	Health-related outcome measures Satisfaction with health care
Organisations responsible for assessment of new drugs such as NICE	Equity and prioritisation					
DTC committee & Health care providers in 1° & 2° care	National and local service provider guidelines such as hospital formularies	Update of formulary, prescribing guidelines Stock the drug according to need	Drug on the formulary/ prescribing list Drug available in hospital, in pharmacies	Procurement / supply Prescribers	Access to treatment, equity	Impact on the budget, allocation of resources Possibility of wastage
Procurement/ supply						
Prescribers	Diagnosis of patient's disease, prescription of drug, advise on use		Prescription	Health care worker, Patient	Rational use	Cost-effective use of resources Health-related outcome measures

Table 3.1 Continued

Resources	Activities	Outputs	Customers reached	Short term outcomes	Medium/long-term outcomes
Structural and human Patient/ health care worker	Takes prescription for drug to pharmacy	Pharmacist review of appropriateness	Pharmacy	Proceed to dispense according to availability	Audit process
Pharmacy	Dispensing of drug according to reimbursement criteria	Drug available for patient	Patient/health care worker	Availability of the drug	Satisfaction with health care
Patient/ health care worker	Administration of medicine	Patient took the medicine as recommended by the prescriber	Patient	Improved symptoms, rational use	Health-related patient outcome measures Satisfaction with health care

External influences :

Pressures by different stake holders including the industry, medical representatives, prescribers, patients, public

National 'criteria' for prioritisation and allocation of resources

International and national legislation and policy for example the National Drug Policy

International and national politics

Audit and quality improvement may be an integral part of activities in different sectors

The first column 'resources' was divided into two: the 'structural and human resources' mainly described the components of the organisation while the 'inputs to support' described components of policy. The rows within the logic model described the components (organisation and policy), the activities, the outputs, the customers reached and the outcomes. The external influences to the programme were listed in the box at the bottom of the logic model.

The activities within the 'General logic model' were then grouped into six key processes as follows:

- Availability of medicines
- Medicines registration
- Access to medicines through the NHS
- Selection of drugs for the NHS
- Procurement, distribution and supply
- Rational use and monitoring

3.4.2 Gathering information about the processes for the managed entry of new drugs into the NHS in Malta

3.4.2.1 Participant observation and document and record research

The results from the participant observation and from the document and record research were descriptive and mainly qualitative. As described in section 3.3.2, the information from these two methods was entered under the processes identified from

the 'General logic model'. Data collection for these two methods for the purpose of the descriptive evaluation was stopped at the end of June 1999.

A summary of the key findings is presented below. The sources of the information are noted as follows: (DR) – document and record research and (PO) – participant observation. The information obtained from the minutes of the DTC was referenced as follows: (DTC number of the DTC meeting, year) for example (DTC 92, 1997).

1. Availability of medicines

Only generic pharmaceutical products were produced in Malta (PO). The WHO Certification Scheme on the Quality of Pharmaceutical Products moving in International Commerce which used Certificates of Pharmaceutical Products (CPPs) (World Health Organisation, 1997b) was applied for the licensing of importation of pharmaceutical products. Since 1998, products could only be imported by the specific agent or wholesale dealer that submitted the CPP for them. This resulted in local agents getting exclusivity of the market even for GPS tenders (PO). When no local supplier was found, the GPS acted as an importer (PO).

2. Medicines registration

In 1997, in Malta it was not considered feasible to set a regulatory system in line with that of the European Union (EU) because of limited resources. It was planned that the Maltese authorities recognised the registration status granted by the EU (DTC 94, 1997). In June 1999 there was still no system for registration of medicines. The

Medicines Regulatory Affairs Unit (MRAU) within the GPS was responsible for pharmacovigilance issues, however there is no functional system for pharmacovigilance (PO). In 1999 the MRAU started the process of adoption of EU legislation related to pharmaceuticals in line with the government policy for EU accession (PO).

3. Access to medicines through the NHS

A National Drug Policy (NDP) was drafted in May 1998 but it did not get published (PO). There was no policy for the pricing of medicines in Malta (PO).

The Ministry of Finance allocated the annual drug budget, but did not allocate additional budget for new drugs (DTC 92, 1997). The update of the Schedule V list was political and did not consider the recommendations of the DTC (DTC 99, 1999). Ad hoc measures for the control of the rising drug budget were implemented by the Chief Government Medical Officer (CGMO) (DTC 93, 1997). The DTC recommended that a long-term comprehensive approach to rationing be adopted and that prioritisation decisions be taken on a national level and not be left to individual physicians or groups of physicians. The DTC emphasised that while clinicians should fulfil their collective social responsibilities their role should always be that of patient advocates (DTC 93, 1997).

The policies for the supply and use of samples and for the conduct of clinical trials within the NHS were leading to patients being started on drugs that were not available

within the NHS and then expecting the NHS to continue providing the treatment (DTC correspondence, 1998; PO).

4. Selection of drugs for the NHS

The DTC was mainly composed of consultants (DTC correspondence, 1999). The terms of reference of the DTC included: update of the formulary; recommendation of requests for non-formulary drugs for specific patients when formulary drugs were not effective; formulation and monitoring of protocols and control and monitoring of the use of drugs and of the system for procurement (DTC correspondence, 1996). The DTC had a number of sub-committees whose remit was to set protocols, revise the formulary and to audit the use of drugs for the relevant therapeutic area.

A policy for the introduction of new drugs was set in 1993 with the intention of curbing drug costs. This policy stated that when presenting a request for a new drug the head of department concerned was to submit a protocol for the use of the drug including a realistic estimate of consumption (DTC correspondence, 1993). The DTC considered it to be unacceptable that patients who were prescribed non-formulary medicines had to buy their drugs until stock arrived (DTC correspondence, 1996).

The formulary was last published in 1986. The number of drugs that were being approved as non-formulary was increasing dramatically (DTC 87, 1996). A lot of time was wasted in correspondence related to follow-up of requests for non-formulary drugs (PO). From 1996 to 1998 various attempts to update the formulary were made but these were all blocked, mainly due to concern from the authorities that the revision

will increase costs (DTC correspondence, 1996 to 1998). Protocols were set for the high-cost drugs targeted by the CGMO to control expenditure (DTC 74, 1993) and for the new drugs that were approved subsequently.

The process for the selection of new drugs into the NHS consisted of 4 steps. Requests for new drugs were submitted to the DTC by consultants working within the NHS. Requests could be for a drug for a particular indication or for a named-patient. A case was compiled on the agenda for the DTC meeting by the DTC secretariat. The cases on the agenda generally reproduced the information that was given on the consultants' requests. The DTC discussed the cases during DTC meetings. In between meetings, the Chairman of the DTC dealt with urgent requests and some requests for named-patients. The outcome of the DTC meetings was presented in the minutes. The CGMO/ Director General (DG) considered the request and the recommendations of the DTC and approved, deferred or rejected the request (PO).

5. Procurement, distribution and supply

All medicines used within the NHS, within hospitals as well as for out-patients, were procured by the GPS through a centralised procurement system that was based on public tendering (PO). The GPS had problems with ensuring the availability of stock of non-formulary drugs and thus patients could only be started when stock was available (DTC 84, 1995; PO).

Products could be imported in Malta and agents and wholesale dealers could tender for GPS offers as long as they had a CPP. There were problems with the bioequivalence

of some generic products but no solution was found to prevent this problem (DTC 95, 1997; DTC 98, 1998).

6. Rational use and monitoring

There was no support for implementation and monitoring of prescribing. The information submitted by consultant requests for non-formulary drugs was vetted against the protocol or prescribing criteria. Dispensaries had no records of drugs dispensed (PO).

3.4.2.2 Activity of the DTC from 1991 to 1998 in relation to 'new drug' applications

The measurement data from the study by Vella (1995) focused on the process of selection of new drugs within the NHS. Table 3.2 provides a summary of the measurement data for the process of selection of new drugs into the NHS in Malta as conducted during DTC meetings for the period 1991 to 1998.

The total cost of drugs approved following DTC meetings between 1991 and 1998 surged during 1996 and 1998. These figures represent what was approved by DTC and not what was actually spent on the approved drugs by GPS.

Table 3.2 Activity of the Drug and Therapeutics Committee in relation to 'new drug' applications from 1991 – 1998

Year		1991	1992	1993	1994	1995	1996	1997	1998
Number of meetings		4	4	4	4	5	6	5	2
Total number of requests ¹		25	35	44	35	18	68	31	23
Outcome of the requests considered during that year	No. (%) of requests approved	23 (92)	33 (94)	41 (93)	26 (74)	16 (89)	59 (87)	20 (65)	20 (87)
	No. of requests not approved	2	2	2	5	0	8	9	2
	No. (%) of requests pending ²	0	0	1 (2)	4 (11)	2 (11)	1 (2)	2 (6)	1 (4)
Number and (%) of requests which were decided without delay ³		23 (92)	31 (89)	36 (82)	24 (65)	15 (83)	61 (90)	19 (61)	22 (96)
Approved category	'non-stock'	6	5	3	13	2	24	14	6
	'special' formulary	13	17	33	12	14	34	6	11
	trials/studies	4	7	5			1		3
			4		1				
Total Cost (Lm) (x 1,000)		19	81	69	97	77	157	85	124

¹ total number of requests for different drugs discussed during the year. Each 'new drug' has only been counted once within each year

² requests remaining pending a decision at the end of the respective year

³ without delay means that a decision was made at the first consideration by the DTC

SOURCE: Minutes of meetings of the DTC

Table 3.3 provides details of the number of different drugs approved on an individual basis and the number of individual patient requests (new cases together with renewals) approved from NHS hospitals every year. In line with the policy for the introduction of

new drugs of 1993, during this period all non-formulary ('non-stock' and 'special') drugs were approved on a named-patient basis. Approvals were generally valid for one year and therefore the figures were cumulative.

Table 3.3 Approval of drugs for individual patients from NHS hospitals (1995-1998)

Year	1995	1996	1997	1998
Number of different drugs approved for individual patients	272	281	321	328
Total number of approvals for individual patients	4,596	7,034	11,226	14,129

The number of approvals of non-formulary drugs for individual patients increased from 4,596 in 1995 to 14,129 in 1998, leading to a situation that was not sustainable.

The trends in the percentage of requests approved and in the percentage of requests that were decided without delay from Table 3.2 were represented in individual charts (I Charts), Figure 3.1 and Figure 3.2 respectively. The lower control limit (LCL) and the upper control limit (UCL) at 3 sigma (3 standard deviations from the mean) were drawn for each set of data. In both cases all the values were within the 3-sigma confidence limits. The warning limit for the individual chart would be at 2 sigma. The 2-sigma limits for Figure 3.1 were at 85.1 ± 21.0 thus the upper and lower warning limits were 106.1 and 64.1 respectively. The 2-sigma limits for Figure 3.2 were at 82.3 ± 29.4 and were 111.7 and 52.9. Thus for both these figures the results were within both the action limits as well as within the warning limits, indicating that the variation in the data for 1991 to 1998 was random.

Figure 3.1 Individual chart for percentage of requests approved (1991-1998)

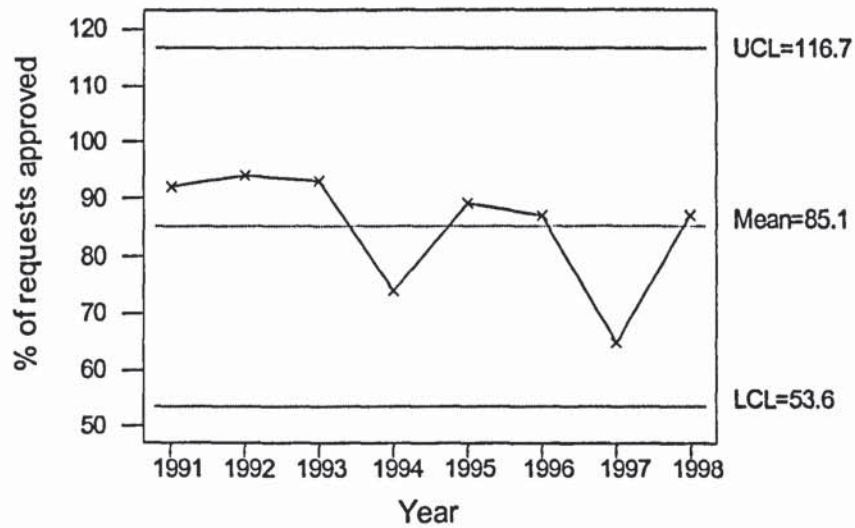
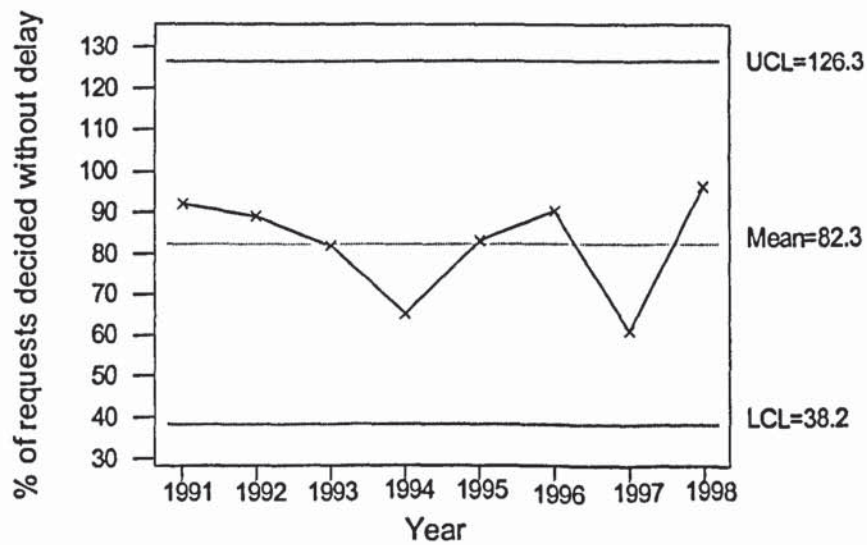


Figure 3.2 Individual chart for percentage of requests decided without delay (1991-1998)



3.4.2.3 Consultant questionnaires

The results of the questionnaires of 1994 and 1999

There were 47 responses (75%) in 1994 and 46 responses (66%) in 1999. 63% of consultants who answered the questionnaire in 1999 had also participated in 1994. The main results from the consultant questionnaires of 1994 and 1999 are given below.

In 1999, only 52% of consultants had a copy of the formulary, compared to 87% in 1994. This decrease was statistically significant ($p < 0.001$). In 1999 only 15% of consultants considered that the formulary was significantly updated and 43% were involved in decisions regarding additions and deletions to the formulary. In 1999, only 33% of consultants felt that they were adequately informed of alterations to the formulary and this was a significant decrease from the 51% result of 1994 ($p < 0.03$).

In 1999 consultants got to know of new drugs through (first 5 in rank order starting with the highest rank): medical journals, medical representatives, conferences abroad, colleagues and conferences in Malta.

In 1999 consultants considered that the most influential pressures to prescribe new drugs were (in rank order): medical opinion leaders, advertising, controls and regulations by health authorities, limitations of the hospital formulary, demands from patients, demands from pressure groups and the media and the press.

In 1999 33% of consultants admitted that the pharmaceutical industry had offered them financial or material benefits to influence the prescription of new drugs. These were mainly in the form of sponsorship to participate in domestic and international symposia. Consultants considered that symposia and scientific meetings organised by local drug firms in order to introduce new drugs were of good standard (82%), educational (76%) and scientific (74%). Only 34% considered that these symposia were too promotional.

In 1999 consultants ranked the factors that they considered prior to prescribing new drugs in the following order: reports of clinical trials, safety, literature and information about the drug, comparison with other drugs available, cost-effectiveness, advantages in administration, licensed indications, costs and unlicensed use. In 1999 cost-effectiveness was ranked significantly higher ($p < 0.0001$) and costs significantly lower ($p < 0.03$) than in 1994.

In 1999 consultants reported that they obtained information on new drugs from the following sources (in rank order): medical journals, conferences abroad, information supplied directly by drug companies, Internet, conferences in Malta, information supplied by the drug information unit and information supplied by the DTC.

In 1999 the majority of consultants felt that they were not well-informed of the decisions of the DTC (85%), were not represented on the DTC (67%), did not have the opportunity to contribute in the setting up of DTC policies (65%), were not involved in the setting of protocols for new drugs that were set up by the DTC (64%) and were not even aware of the protocols for new drug (59%). There was a statistically

significant decrease in the % of consultants who felt that they were well informed about the decisions of the DTC in 1999 compared to 1994 ($p < 0.01$).

In 1999, 22% of consultants had participated in clinical trials of drugs prior to licensing on the market, 33% had participated in trials post-licensing and 31% had used a new drug for unlicensed indications. 72% were of the opinion that authorities should be informed of clinical trials. Consultants agreed that post-marketing scientific studies were used as a disguised form of promotion (54%), that samples of new drugs should not be used on patients within the NHS without permission (52%) and that if a patient was started on a new drug using samples, the DTC was not bound to approve the drug (78%).

93% of consultants were of the opinion that in Malta there should be a national adverse drug reaction reporting system. Moreover it was suggested that because Malta is small, information from other countries should also be considered.

The roles of the hospital pharmacist that were most accepted by consultants were: supply of information about new drugs on request by consultants (100%), participation as members of the DTC (98%), participation as members of the sub-committees involved in the setting up of protocols for new drugs (96%), organisation and participation in audit and drug-use evaluation studies (89%), participation in clinical trials (87%), supply of information about new drugs as soon as they are introduced (85%) and evaluation of whether requests for new drugs were according to criteria set in the established protocols (82%). Consultants were not so supportive of the option

that hospital pharmacists evaluated new drugs as soon as they were introduced on the market (58%).

In 1999, 93% of consultants considered that the system for introducing new drugs in hospital was not efficient. This was a significant increase from the (64%) response in 1994 ($p < 0.01$). The most problematic areas in 1999 included: the time-lag until the drug was approved (96%), the availability of stock of the drug (86%), the paper work involved (79%), the importance given to the cost of the drug (70%), subsequent renewal of approval (58%) and the number of requests that were not approved (54%). The majority of consultants did not consider that the following factors were a problem: the involvement of pharmacists in the processing of requests (88%), the availability of adequate information prior to requesting new drugs (79%) and having requests for new drugs submitted through the head of department (63%). There was a statistically significant decrease in the % of consultants that considered that the involvement of pharmacists in the processing of requests for new drugs was a problem ($p < 0.04$).

More detailed results from the 1994 and the 1999 consultant questionnaires are presented in Appendix VI.

The results of the prioritisation questionnaire sent to consultants in 1999

There were 43 (65%) responses to this questionnaire.

67% of consultants felt that the system for allocation of resources within the NHS was not adequate. 70% considered that the present system for entitlement to free medicines

was not fair and reasonable. 70% agreed that there should be some form of rationing in the practice for introducing new drugs into the NHS. Only 28% considered that physicians within the government health services should be allowed to treat their patients with whatever they felt that was best for the individual patient without having to consider the costs. 58% considered that rationing was ethical, 28% that it was not ethical and 14% did not know.

Consultants ranked a set of given options of how new drugs should be introduced into the NHS in Malta in the following order (starting from the highest rank): study of cost-effectiveness as compared to existing drugs, development of new ways of using existing resources more effectively, setting of prioritisation within a limited budget, assessment of the significance and impact of disease for the population and all requests for new drugs should be approved without restriction.

Consultants ranked who should be involved in the setting of priorities for the introduction of new drugs into the NHS in the following ranking order: DTC, clinical consultants, policy makers, consultants in public health and representatives of patients.

Out of a list of 31 factors, consultants ranked the following as the most important 10 factors to be considered when deciding whether to introduce a new drug into the NHS:

1. evidence from clinical trials that the drug has proven efficacy
2. evidence that the drug is effective in clinical practice
3. evidence about safety
4. drug improves quality of life
5. whether it is ethical to use the drug

6. the cost-effectiveness of the drug
7. prognosis of the disease condition without the drug
8. if no other treatment is available for the disease condition
9. whether the indication for use of the drug is licensed or not
10. how much an individual patient would possibly benefit

Appendix VII contains further detail of the results of the prioritisation questionnaire to consultants.

3.4.2.4 Patient interviews

166 persons were approached to be interviewed. 63 were excluded: 44 were not collecting medicines for themselves and 19 patients were not taking any non-formulary drugs. 2 patients refused to be interviewed. One old lady with hearing problems could not be interviewed. 100 patients were interviewed.

As predicted from the pilot, patients were very eager to discuss their personal problems with the service and the pharmacist discussed personal issues after the interview. Some patients did not like answering short direct questions and the interviewer conducted the interview in the form of a conversation to answer the questions.

The key results from the interviews are presented below.

88% of patients encountered inconveniences until they received approval for their entitlement to free medication, mainly due to delay in receiving the Schedule V approval. 94% of patients were pleased with the policies entitling patients to free treatment, however 76% still believed that the system could be improved.

Patients waited for a median of 2 to 4 weeks before they received their approval for non-formulary drugs. In the meantime the majority of patients (68%) bought the medicines themselves.

Patients gave the following responses to questions about prioritisation of health care resources: only 22 patients considered that the financial resources allocated to the healthcare system were properly utilised. 74 patients were of the opinion that doctors employed within the NHS should take the price of the medicines that they prescribe into consideration. 87 patients agreed that if two medicines achieved the same desired therapeutic effect, doctors should prescribe the cheapest one. 84 patients said that the NHS needed systems to monitor the expenditure of new drugs. Only 40 patients considered that requests for new drugs made by doctors should be approved immediately without being discussed. 88 patients considered that the NHS should look into new ways of how the available budget could be used more efficiently.

Patients ranked 'who should make decisions on which medicines should be introduced into the NHS' as follows: individual consultant physicians, a group of consultants, general practitioners, the DTC and patient groups. When asked to choose between two options for decision making when considering the introduction of new drugs into NHS, 71 patients considered that the interests of an individual patient should be

weighed against the interests of other patients while 29 patients considered that any potentially useful medicine should be procured.

The following are some of the themes arising from patient responses when they were asked an open question regarding the factors that should be considered when introducing new drugs: high safety, low side-effects, proven therapeutic effects, cost-effectiveness, consideration of alternative treatments and quality of medicines.

Further detail of the patient interviews is provided in Appendix VIII.

3.4.2.5 Results of focus group discussions

Two sessions of the focus group were held. The members asked questions which related to their direct personal experience of the NHS. Patients also had questions or clarifications related to information or complaints that they encountered through the media or through their work or people they knew. Once these questions were answered, the focus group was guided to adopt the perspective of society. The discussion often ended in the formulation of further questions. Points from the discussions were noted below.

One of the main concerns, particularly of the priests from the Centre for Faith and Justice who were strong representatives of the 'poor', was whether the system for entitlement of patients to free medicines was equitable, particularly to this group within society. This led to a discussion on who the 'poor' of the society were. The system of means testing used by the Department of Social Security was not efficient.

The fact that Schedule V covered all the Maltese population and even the very rich were entitled to drugs on Schedule V totally free of charge was considered to be too benevolent and it was recommended that these resources could be utilised better. It was pointed out that in Malta there is a big 'middle-class', which up to a certain extent was the most disadvantaged of the three categories (poor, middle-class and rich). This 'middle-class' still had to pay full cost for medicines that were not entitled on Schedule V or that were not available within the NHS.

It was agreed that because drugs were given totally free, patients were not appreciative of what they got and this could lead to wastage. There was a tendency that patients hoarded medicines in case the GPS was out of stock. One of the priests mentioned that when a patient passed away, he was handed a whole garbage bag full of unused medicines. Most of the medicines were expired and he ended up with a problem how to dispose of them.

It was noted that any changes in the system for reimbursement required a cabinet decision and had political implications. Usually the list was revised before general elections. The percentage of funds from the budget being allotted to health and to the procurement of drugs was considered to be low. There was no tax rebate for people having private insurance so there was no incentive for people to get private insurance. The population took the view that because they paid taxes and social security contributions, the state was to provide all their needs.

The group considered that consultants were the main advocates of the patient and protected him from the interests of the Department of Health. The group was of the

opinion that the perspective of the NHS was that its main priority was to save the budget and not the interest of patients. The ethics behind prioritisation and rationing was questioned. While it was understood that the NHS needed to ensure best utilisation of its resources, there was a strong feeling that the NHS should be supplied with all the resources that were required. Charging of fees at the point of service was considered to be unfair and inefficient. It was recommended that the NHS continued to be financed from government taxes.

3.4.2.6 Interviews with medical representatives

All medical representatives invited accepted to participate. The interviews were conducted in an informal atmosphere on an individual basis and took between 45 minutes to one hour each. A total of 28 medical representatives were interviewed. 24 of the medical representatives were pharmacists, 2 were B.Sc. graduates and 2 were administrators/ sales managers.

The information from the interviews was arranged under the processes that were derived from the 'General logic model'. The main points from the interviews are presented below.

Representatives were pressurised by their employers to deliver. Companies set targets for the representatives in the form of success in getting new drugs on the market particularly within the NHS and trends in sales. Representatives felt that there was a lack of communication and support from the NHS and that this caused them problems. Some representatives felt that they needed to get the product manager from the mother

company to Malta to support them, particularly when they wanted to introduce a new drug into the NHS. Some mother companies grouped Malta with Europe but the majority of drug companies grouped Malta under their office in the Middle East. This categorisation effected the timing when new drugs were introduced in Malta.

Most representatives were pharmacists. Representatives claimed that there could be conflict between the role of the medical representative and good professional practice. Literature was supplied through parent companies from abroad. Updates of information and clinical trial material were received regularly. Updated papers were particularly useful for specialist consultants. Material summarising the papers, for example leaflets was considered important as most doctors did not have time to read full papers. Representatives considered that one of their major roles was to clear doctors' misconceptions and to make sure that doctors 'did not take up misconceptions'. When promoting new 'prescription only' products, especially specialised products medical representatives targeted the 'influential doctors' who were usually the consultants working in hospitals of the NHS as these influenced other doctors. Representatives claimed that they only promoted the licensed indications of drugs, as the drug companies only supported the licensed indications.

Representatives strongly complained about the fact that first they did a lot of work to get a product introduced within the NHS and then when tenders were issued the tender was awarded to a parallel importer. Representatives stressed that they only supported the NHS with information about the product and with information on pharmacovigilance if the product was procured through their local agent.

Representatives complained that the NHS did not accept samples that were offered and the samples given were not utilised and were left to expire. Companies were ready to support the NHS by supplying drugs free of charge for some time and through the supply of samples. Companies could also supply protocols for the use of their drugs.

Representatives were rather 'happy' about the fact that there was no system for registration of drugs and that they just needed a CPP to import a product. Representatives considered that from the point of view of marketing, the fact that there was no registration is to their advantage. Some representatives commented that the registration systems in other countries were a means of 'making money' for the regulators.

Representatives complained that there was lack of communication between representatives and the DTC. It was pointed out that the DTC had too many sub-committees but these did not meet regularly. Representatives recommended that the DTC made use of the resources of drug companies and asked companies to help with information. Representatives recommended that there should be an official contact person from the DTC whom to inform of new drugs and whom to contact. Representatives also complained that they had a problem in contacting doctors because if doctors got involved in clinical trials or were sent abroad for a conference, the NHS considered that the doctors were being bribed. Consultants asked to be sent to conferences and for educational support.

Representatives complained that the process for introducing new drugs was lengthy, very slow and bureaucratic. However in some cases the delay helped to avoid the use

of drugs which were withdrawn from the market. There was no planning of DTC meetings and no long-term agenda. It was recommended that DTC should give feedback to representatives to keep them updated with the progress of the requests. It was pointed out that some specialties for example haematology were not established within the NHS in Malta and therefore there were no new drugs requested in these areas.

3.4.3 Development of 'Descriptive model 1' to represent the processes for the managed entry of new drugs into the NHS in Malta as in June 1999

The above information was used to construct a logic model to represent the managed entry of new drugs into the NHS in Malta as in June 1999. This model was named 'Descriptive model 1' and is presented in Table 3.4. The same conditions for the interpretation of 'Descriptive model 1' as was explained for the 'General logic model' in section 3.4.1 apply.

Table 3.4 A descriptive model of the managed entry of new drugs into NHS in Malta as in June 1999 'Descriptive model 1'

Resources		Activities	Outputs	Customers reached	Outcomes
Structural & human	Inputs to support				
Local agents	Policy for clinical trials did not exist.	Promote new drug to consultants.	Consultants are informed of new drugs. Consultants encouraged to prescribe new drugs.	Consultants	Consultant prescribes the drug for patients within the NHS.
MRAU	Keep database of CPPs. No ADR reporting system. Entitlement to free medicines implemented through the Schedule V list and Schedule II, 'Pink Card'. Prioritisation through ad hoc decisions by DG.	Submit a CPP to MRAU. Issue license for agent to enable importation. Minimal pharmacovigilance. Political update of entitlement criteria Enforcement	MRAU give receipt for CPP. Agent gets license.	MRAU Local agents	Agent can import the drug Agent gets license to import drug.
Government / Minister for Social Security in discussion with Minister for Health			Medicines (formulary and non-formulary) are potentially free, limited to diseases listed on the Schedule V list. Medicines (formulary and non-formulary) are potentially free, based on personal entitlement (Schedule II, 'Pink card') irrespective of disease.	Consultants DTC Pharmacies Patients	NHS provide free formulary drugs to both groups. Non-formulary drugs ('special' and 'non-stock') are considered on a named-patient basis.

NHS= national health services; CPP= certificate of pharmaceutical product; MRAU= medicines regulatory affairs unit; ADR= adverse drug reaction; DG= Director General; DTC= Drug and Therapeutics Committee

Table 3.4 Continued

Resources		Activities	Outputs	Customers reached	Outcomes
Structural & human	Inputs to support				
Consultants within the NHS	Policy for introduction of new drugs set in 1993.	Prescribe new drug to patients and submit a request for reimbursement of drug to DTC secretariat.	Patient takes prescription to private pharmacy or patient awaits non-formulary approval.	Patient	Drug is purchased privately or patient remains without drug.
			No formal confirmation of request given to consultant.	DTC secretariat	DTC secretariat discusses case with Chairman.
		Make requests for new drug to be introduced in NHS.	The request is sent to DTC secretariat.	DTC secretariat	DTC secretariat presents the information to the DTC as submitted.
DTC		Minutes of DTC meetings are sent to CGMO/DG.	CGMO/DG ratifies or rejects DTC's recommendation, or requests further information.	CGMO/DG	Decision made by DTC. Drug is approved, rejected or decision left pending.
CGMO/DG (since February 1999)	Drug budget allocation. Formulary/ Non-formulary drug list (not documented)	Reimbursement within NHS occasionally linked to a protocol.	Drug is categorised as formulary or non-formulary ('special' or 'non-stock'). Non-formulary drugs are approved and supplied on a named-patient basis.	DTC	
DTC		DTC notifies GPS of approval.	GPS start procurement.	GPS	GPS source the product through a tendering process

DTC= Drug and Therapeutics Committee; CGMO= Chief Government Medical Officer; DG= Director General; GPS= government pharmaceutical services.

Table 3.4 Continued

Structural & human Resources	Inputs to support	Activities	Outputs	Customers reached	Outcomes
GPS		Tenders arranged in order of price.	Lowest price with CPP accepted.	Local agent/ foreign wholesale dealer	Higher price may be paid due to need to have CPP. No tender approved due to lack of quotes and/or CPP.
Local agent/ wholesale dealer		Importation of drug.	Drug supplied to GPS.	GPS	GPS receives drug
GPS		GPS should inform DTC of availability of drug.	DTC may get to know that the drug is now available – ad hoc process.	DTC	Drug available within NHS.
DTC		Stock of the drug	Stock distribution	Government pharmacies	Availability of drug within specific locations of NHS.
		DTC notifies named patients that approved drug now available.	Letter of approval sent to patient.	Patient	Patient has letter of approval for prescription to be dispensed.
		DTC vets additional requests for the non-formulary drug.	DTC gets inundated with requests for many additional named-patients.	A large number of patients	Patients are notified of approval when stock is available.
Patient		Dispensing of drug from pharmacy.	Drug available for patient.	Government pharmacy	Patient commences therapy from NHS.
Patient/ carer		Administration of medicine.	Patient takes the medicine as recommended by the prescriber or patient does not comply.	Patient	Aim is improved symptoms, rational use, health-related outcomes.

GPS= government pharmaceutical services; CPP= certificate of pharmaceutical product; DTC= Drug and Therapeutics Committee

Table 3.4 Continued**External influences :**

1. **Political picture:** In September 1998 Malta had a change in government following an early election. The previous Labour Government (which had been in office since 1996) had frozen the application for Malta' accession into the European Union (EU).
2. **Government policy:** the Nationalist Government reactivated Malta's application for EU accession. Malta was to introduce a system for medicines registration in line with EU legislation.
3. **Policies of the Department of Health –** the NHS was planning a separation of the operational and regulatory structures and functions (in line with government policy and the proposal of the National Health Policy).
4. **The Director General** took up post in February 1999. His predecessor was a Chief Government Medical Officer.
5. **National health-related policies:** the National Drug Policy document was drafted but was shelved.
6. **Different stakeholders** including politicians, consultants, medical representatives, patients and the public exerted pressures.

3.5 DISCUSSION

The aim of this descriptive evaluation was to describe the processes for the managed entry of new drugs into the NHS in Malta in June 1999. The 'General logic model' identified six key processes: availability of medicines; medicines registration; access to medicines through the NHS; selection of drugs for the NHS; procurement, distribution and supply; and rational use and monitoring. The 'General logic model' was used to guide what information was needed to describe the processes for the managed entry of new drugs into the NHS in Malta. A number of methods were employed to gather information. The results from the different methods were useful in achieving the aims of the descriptive evaluation. The information from the methods was used to present 'Descriptive model 1'. The information was useful to identify problems with the managed entry of new drugs into the NHS in Malta as in June 1999 and to plan feasible change. The most relevant result was that in Malta in June 1999, there was a lack of a systematic approach to the managed entry of new drugs into the NHS.

This descriptive evaluation was intended to form a baseline before an intervention for change was implemented and to support the planning for change. Ovretveit (1998) explained two approaches to descriptive evaluations. In the first approach, descriptive evaluations work inductively, seeking to build models out of data to describe key features of the evaluated. In the second approach, descriptive evaluations start off with a clear model or theoretical perspective that they then use to select what to describe and to guide data gathering (Ovretveit, 1998). The research by Vella (1995), adopted the first approach and described the introduction of new drugs into the NHS in Malta

using an inductive approach. In the descriptive evaluation presented in this chapter, the second approach described by Ovretveit (1998) was adopted. As Malta was preparing for accession into the EU and as a major reform in the managed entry of new drugs into the NHS was planned, a model, the 'General logic model' was developed to guide the descriptive evaluation. The 'General logic model' was built to represent the general framework for the managed entry of new drugs into the NHS in European countries.

As described by Ovretveit (1998), the aim of descriptive evaluations is to describe the inputs and processes of the evaluated, its boundaries, the context and often also its outputs. Research methods were chosen to obtain as much of the required information as possible, to study the perspectives of the different stakeholders and to give an insight into the problems and to factors that effected the feasibility for change. Each of the methods had inherent strengths and limitations.

Although the participant observation was conducted during the descriptive evaluation, the researcher had worked within the NHS since 1991 and was secretary of the DTC since January 1998. This gave the researcher a good background of the case, which was useful. Gillham (2000) noted that case study research could easily loose shape because of the complexity of the material. Participant observation supported regular review and enabled progression of thinking. This method helped to focus on the information required with the support of the 'General logic model'. Participant observation allowed identification and clarification of areas that were not covered by the other research methods and helped to answer questions that emerged from the other methods. The insight from the participant observation was particularly useful to

determine the feasibility of change.

The main limitation of participant observation was that the insight obtained through this method could be subjective. It was not possible to remove the subjectivity of the researcher from participant observation. For example the observation that there was conflict in the centralised role of the GPS, because the GPS was responsible for operational as well as regulatory functions could be criticised as being subjective. The perspective of the director of the GPS was also considered to balance the element of subjectivity, however this introduced subjectivity from another perspective.

The main sources of information available were the documents and records of the DTC. As the researcher was the secretary of the DTC, the problems with accessibility of documents described by Gillham (2000) were not applicable in this research. The main strength of the document research was that it allowed longitudinal study and follow-up and provided a good overview. The document search showed how specific problems evolved. For example follow-up of the minutes of the DTC showed that a number of patients were started on treatment by NHS consultants using samples, and then there was pressure on the DTC to support continuation of treatment. This led to consideration of revision of the policy for the use of samples.

The main limitation of the minutes of the DTC was that they were not verbatim notes. They were edited by the secretariat and the chairman of the DTC and were finally approved by CGMO. The minutes up to June 1999 were usually quite brief and summarised the main points. They were devoid of details that were 'politically' sensitive and rarely reflected the opinions of the individuals and the dynamics within

the DTC committee, unless something was specifically stated to be minuted. For example the recording of the DTC's opinion about prioritisation in the minutes of the 93rd DTC meeting contrasted to the usual style of minutes. It was clear that the DTC wanted to send a message to the CGMO. From the retrospective study of the minutes it was not possible to study the factors that were considered during decision making and the follow-up could not address the quality of decisions and the extent of use of evidence. The correspondence of the DTC gave more insight into the 'politics' of situations and of conflicts between different stakeholders. For example the GPS's attempts to pass the responsibility of the problem of bioequivalence of generic products onto the DTC resulted in heated correspondence.

The document search showed that although some changes were known to be important, they were not brought about. In 1997 the problem that there was no system for medicines registration had been discussed by the DTC and at that time it was explained that it was difficult to set a system for registration because of limited resources. The document search also provided the opportunity for drawing up theory. Analysis of the attempts of the GPS to try to solve the problems with bioequivalence of products available through the NHS, showed that problems with bioequivalence of products were of great concern. This problem with bioequivalence confirmed that the lack of a system for medicines registration resulted in the availability of some products of questionable quality within the NHS in Malta.

Follow-up of the quantitative data on the activity of the DTC in relation to new drug applications from Vella (1995) produced a longitudinal trend from 1991 to 1998, which was a significant period of follow-up. The same definitions and raw data were

used to ensure comparability of the results for the whole period. Gillham's (2000) observation that quantitative data extended the range of evidence on the topics under study was applicable to this descriptive evaluation. For example the increasing annual number of patient requests for non-formulary drugs and particularly the fact that in 1998 there were 14,129 requests, supported the participant observation that the process was becoming impossible to manage. Moreover combination of the knowledge that approval on a named-patient basis was leading to inequity with the fact that there were 14,129 approvals of named-patient requests in 1998, prioritised inequity as a cause for concern.

The application of the principles of process control showed that there was no significant change in the process for selection of new drugs from 1991 to 1998, for the outcome measures selected. This implied that there was normal variation and supported the observation that no significant changes had been applied to improve the process. The main limitation of the quantitative data on the activity of the DTC in relation to new drug applications in this research was that the only outcome measures that could be selected were the percentage of approvals and the percentage of requests approved without delay. These measures did not comprehensively cover the activities of the DTC in relation to 'new drug' applications and gave no insight into the selection process. From the information that was available it was not possible to find other objective outcomes.

The historical data was supplemented with new data produced by research with stakeholders. The main aim of this research with stakeholders was to identify problems with the managed entry of new drugs into the NHS in Malta and to study the

opinion of stakeholders on prioritisation and allocation of resources. Consultants working within the NHS were considered to be the main stakeholders. As outlined in 'Descriptive model 1', consultants were responsible for the inputs (submission of requests for new drugs and application for patient entitlement to free drugs) as well as for the outputs (prescription of all treatment on Schedule V and of some treatment on the Schedule II, 'Pink card') of the process for the selection of new drugs within the NHS in Malta. This contrasted with the 'General logic model' where hospital consultants were mainly involved at the level of setting hospital formularies.

A study of the opinion of stakeholders on prioritisation and allocation of resources was included as part of the research, mainly because there was a growing literature on the involvement of stakeholders in priority setting (Stronks *et al.*, 1997; Mossialos and King, 1999). A standard questionnaire for the study of allocation of resources to allow comparison of responses between different stakeholders was set. The piloting of this questionnaire showed that whilst consultants had no difficulty with face and content validity of the set questionnaire, literate members of the public struggled and found the questions too technical. Interviews with a sample of patients proved that patients did not understand the concept of prioritisation, because to them the NHS provided them with healthcare according to their needs.

This lack of success in measuring patients' views of priority setting was consistent with the literature. Dicker and Armstrong (1995) tried to do an interview survey with patients but found that interviewees were not persuaded that they had a legitimate role to play in the prioritisation of services. Interviewees were reluctant to use their own personal needs as a basis to allocate resources and argued from what they perceived to

be the needs of others (Dicker and Armstrong, 1995). Stronks *et al.* (1997) utilised panel data to study the opinion of different stakeholders on priorities in healthcare. Such a detailed comparison was considered beyond the scope of this research. Moreover it was questionable how useful information on the opinion of stakeholders on the allocation of resources was in practice considering that these decisions were usually taken at a political level in Malta. This experience of the pilot exercise for prioritisation showed the importance of piloting and generated information that was used to find alternative methods for the study of prioritisation.

Different methods were chosen to obtain the opinion of stakeholders. A repeat of the questionnaire to consultants (Vella, 1995) enabled comparison of the opinion of consultants about different aspects related to the managed entry of new drugs after five years. This study allowed a quasi-experimental design and as the results of the questionnaires were mainly quantitative or semi-quantitative, the two sets of data could be analysed for statistical significance. This comparative nature of the longitudinal data is a strength of quantitative research methods.

63% of consultants who participated in 1999 had also filled the questionnaire of 1994. Twenty years ago many consultants left Malta following a doctors' dispute with the government. However, with a new government in 1987 matters resolved and some Maltese doctors returned, many taking up consultant posts. Hence, the populations of consultants for both the 1994 and the 1999 questionnaires were considered homogenous.

In the statistical comparison of the responses of 1994 and of 1999 the Mann Whitney

test was used to compare the responses of the ranking questions in the two questionnaires. The Mann Whitney test assumes independence between samples, but in this case the samples were not fully independent. The Wilcoxon matched pairs signed rank test would have been more appropriate for the paired data. As the responses were anonymous it was not possible to pair the data. Moreover not all the respondents had participated in both questionnaires. The Mann Whitney test was considered the most appropriate statistical test in these circumstances.

The longitudinal comparison showed that in the opinion of consultants had deteriorated on a number of components. The fact that the formulary was last published in 1986 justified the decrease in use of the formulary. It was surprising that 15% of consultants still considered that the formulary was updated. The level of communication between the DTC and consultants worsened and this was partly due to the fact that the secretariat of the DTC was moved to the GPS in 1998 and had no support, resulting in cessation of sending of regular circulars to consultants. The fact that the majority of consultants did not have the opportunity to contribute to policies for prescribing reflected that there was lack of feelings of ownership in the process. This result had important implications to change management because systematic reviews suggest that clinical practice guidelines were most likely to be adopted in practice when development, dissemination and implementation strategies incorporated the involvement of end user clinicians (Grimshaw *et al.*, 1995; Feder *et al.*, 1999).

As explained by Bowling (1997) the strength of the structured questionnaire is the ability to collect unambiguous data and easy to count answers leading to quantitative data for analysis. The self-administered questionnaire is suitable in minimising

interviewer bias and for sensitive topics (Bowling, 1997). In this research the quantitative data from the structured questionnaires of 1994 and 1999 enabled comparison of responses at two points in time. While in 1994 the researcher was a clinical pharmacist within St Luke's Hospital, in 1999 the researcher was secretary to the DTC. Although the research was clearly explained in the letter sent with the questionnaires, the new role of the researcher could have introduced some bias. The anonymous self-administered questionnaire was an appropriate method to reduce this researcher bias. Questionnaires rely on unstated general knowledge about the respondent group, particularly concerning the interpretative processes of the participants (Bowling, 1997). As the researcher worked with consultants within the NHS, this knowledge was incorporated within the questionnaires. The main limitation encountered with the use of the structured questionnaire was that it limited deep study of complex issues. It would have been useful to probe into certain aspects such as ways for improving the system for entitlement to free medicines and prioritisation.

Interviews were used to get information from patients and from medical representatives. Different types of interviews were used for the two groups. The patient interview was very structured, as the aim was to obtain specific information. It would have been preferred to use a structured questionnaire for patients (as had been used for consultants), as this would have allowed study using a greater number of patients. However the pilot study with patients showed that there was variability in the level of literacy of patients, and therefore structured interviews were more appropriate.

Bowling (1997) explained that one of the advantages of interviews was that the interviewer could probe fully for response and clarify ambiguities. As the level of

understanding of patients varied, it was possible for the interviewer to ensure that the patients understood the questions. One of the main sources of bias in these interviews was that the interviewer was a pharmacist who worked within the NHS. At times some patients went on the defensive if they felt that too much probing was being done by the interviewer. Although the purpose of the interviews was well explained at the beginning of each interview, some patients were suspicious that the interviewer was checking on them and they were afraid that their entitlement to free medicines would be stopped. Some of the patients interviewed took a very personal perspective and asked questions about the system as related to them. They considered the interview to be an opportunity to ask questions. The interviewer was not a direct service provider to the patients and therefore it was less likely that the patients would tell him things to please him. It was more likely that patients could exaggerate on the level of problems that they encountered.

In the interviews with medical representatives, open questions were used to obtain an insight into this area. Interviews were found to be a good method to collect information from representatives, who are usually competitors in business and may have a problem to discuss certain issues in front of each other within a focus group setting. If the questionnaires were sent out to medical representatives at their place of work, which was usually at the premises of local agents, the replies could have been vetted. Not all the medical representatives were members of the Malta Association of Medical Representatives and it was considered inappropriate for the researcher to link with the association, particularly due to the role as secretary to the DTC.

The role of the researcher as secretary to the DTC could have introduced bias in the

responses to the interviews with medical representatives, even though before each interview it was clarified that the exercise was held as part of research. The high participation rate for the interviews could have been effected by this position. As the representatives saw the DTC as a barrier to the introduction of new drugs, this could make them cautious or too critical during the interviews. On the other hand there were occasions where the representatives tried to be pleasant during the interview to achieve a level of confidence or a situation of bartering in exchange for their cooperation with the interviews that allowed them to ask questions that the interviewer considered to be confidential. In such cases the interviewer explained that the information could not be discussed. The interviewer was very careful not to divulge any such information.

Whilst in the open interviews an interviewing guide was used to enable collation of the themes, the focus group allowed a less structured approach. By allowing the focus group to take the lead for parts of the session, an in depth view of the opinion of the members of the focus group was obtained. Had specific structured questions been set, only the replies to those questions would have been answered. The members of the focus group were chosen so that they could be part of the team leading workshops during a conference. These members were well informed and literate and thus the focus group had a limitation that it did not really represent the general public in society. On the other hand having such an informed group achieved information on the perspectives of society rather than on personal interests as was the trend with some of the patients from the patient interviews. The fact that there were two doctors (including the chairman) on the focus group could have biased the opinion of the group in favour of doctors, although the members of the group were considered to be

assertive. Bowling (1997) and Gillham (2000) noted that the group dynamic's potential for conflict is one of its strengths in that it may bring out tensions. For example the one sided advocacy for the poor by two members of the group was balanced out by inclusion of consideration of other classes by the other members of the group.

The results from the methods needed to be understood and interpreted within the context and the culture of the NHS in Malta. For example the documentation did not refer to 'reimbursement'. As the process of selection of drugs into the NHS in Malta resulted in the approval of drugs as formulary or non-formulary, the process of selection of new drugs into the NHS was always referred to as management of the formulary.

The data from the different methods contributed to a description of the processes for the managed entry of new drugs into the NHS in Malta. Gillham (2000) explained the process of triangulation, whereby data bearing on the same issue was accumulated by different methods. If results from methods converge, there is confidence that a true picture is being built (Gillham, 2000). Keen and Packwood (2000) expressed reservations about the use of information from different methods in qualitative research, given that different methods and sources of data will tend to provide different sorts of insights rather than contribute to a single, accumulating picture. The descriptive evaluation in this research utilised both of these approaches, depending on what was being described and on the aim of the description.

The objective of studying the opinion of stakeholders on the system for entitlement to

free medicines, on the allocation of the resources of the NHS and on prioritisation was to obtain and compare the views of the different stakeholder groups and to enable the planning and prioritisation for change. It was not expected that the opinion of the stakeholders would be the same.

Although the opinions of the stakeholders on the system for entitlement to free treatment differed, there was general consensus that this system needed to be revised. The structured question set in the consultant questionnaire showed that the majority of consultants felt that the system for entitlement was not fair. The focus group with representatives of the public provided further support for this and the discussion of the focus group allowed deeper insight to the problems with the Schedule V system. The Schedule V system was considered to be too benevolent with patients who suffered from diseases listed on the Schedule V list, who received all their treatment free even though they could afford to contribute, and was considered to be of great burden for patients who had diseases which were not listed on the Schedule V list, who had to pay the full costs of treatment, even if they could not afford them. As could have been expected the majority (94%) of patients who were getting free treatment from the NHS, were pleased with the policies entitling patients to free treatment. However 76% of patients still believed that the policy for entitlement to free medicines could be improved. This result supported the need for the revision of the system for entitlement to free medicines in the NHS in Malta and this was to be considered when planning and prioritising activities for change. Although all stakeholders agreed that the system for allocation of resources within the NHS was not adequate, the allocation of the budget was within the remit of the Ministry of Finance and it was considered to be unfeasible to plan change in this area.

The greatest contrast in the opinion of stakeholders was on the issue of rationing and prioritisation. The fact that during the pilot study it was difficult to explain rationing and prioritisation to patients, as patients considered that the NHS supported their healthcare needs showed that prioritisation was a politically sensitive subject. The literature confirmed these differences in opinions found. Stronks *et al.* (1997) concluded that stakeholders differed in the way that they approached the issue of priorities. Healthcare professionals seemed to be most aware of maintaining equal access for everyone in need of care (Stronks *et al.*, 1997).

The opinion of the focus group that the NHS in Malta were more concerned with the management of resources than with the interests of patients and the fact the focus group strongly felt that consultants working within the NHS acted as advocates for patients within the NHS and protected patients against the interest of the NHS reflected the opinion of the expert public on the NHS. This opinion that consultants working within the NHS should be involved in the setting of priorities was also evident in the patient interviews. These findings concur with the analysis from the Eurobarometer survey that was reported by Mossialos and King (1999). The members of the public that participated in the Eurobarometer Survey of 1998 most frequently chose doctors as the preferred agents for setting priorities if limits had to be set (Mossialos and King, 1999).

The conflicts involved in prioritisation decisions and the role of clinicians as patient advocates were also reflected in the recommendations of the DTC, which was mainly composed of consultants. The DTC recommended that there should be a long-term comprehensive approach to rationing and that prioritisation decisions should be taken

on a national level and should not be left to individual physicians or groups of physicians. The DTC had emphasised that while clinicians should fulfil their collective social responsibilities, their role should always be that of patient advocates (DTC 93, 1997). Up to June 1999, decisions on prioritisation as part of the process for the selection of new drugs into the NHS were being taken by the DG. Change in the system for the setting of priorities was considered to be difficult.

Whilst the study of entitlement to free medicines, allocation of resources and prioritisation involved mainly comparison of opinions, triangulation was useful to identify problems with the managed entry of new drugs into the NHS as in June 1999. The use of triangulation increased validity of the information and ensured that the information did not represent the interest of one particular stakeholder group. The fact that there were delays in starting patients with treatment for non-formulary drugs was highlighted in the patient questionnaires and was also confirmed through participant observation, through the consultant questionnaires and the document research.

Although data may be triangulated from different methods, stakeholders could still vary in their perspectives of interpreting the same data. The fact that patients were started on samples of drugs that were not available within the NHS was confirmed through different methods. However the stakeholders interpreted this information differently. The DTC considered that this practice of use of samples was undesirable as the DTC was being pressurised to approve such drugs for individual patients once the stock of samples was exhausted. 54% of consultants agreed that post-marketing scientific studies could be used as a disguised form of promotion. Medical representatives claimed that the industry supplied samples to support the NHS.

Gillham (2000) explained that a common problem encountered in triangulation was that there was discrepancy between what people believe (say) and what they do. The responses from the consultant questionnaires prioritised the increased use of evidence and the consideration of cost-effectiveness rather than costs as the factors that they considered when requesting new drugs. This response was in line with the development in the trends for reimbursement decisions in the literature (Maynard and Bloor, 1997). It is recommended to study whether the practice of consultants was in line with the replies obtained from this questionnaire.

3.6 SUMMARY

This chapter presented a descriptive evaluation of the managed entry of new drugs into the NHS in Malta as in June 1999. It also provided an insight into the problems and into factors that affected the feasibility for change.

A 'General logic model' was used to represent the managed entry of new drugs into the NHS in European countries. This 'General logic model' was used to identify the key processes and to select the methods to gather information about the managed entry of new drugs into the NHS in Malta.

A descriptive model of the managed entry of new drugs into the NHS in Malta as in June 1999, 'Descriptive model 1' was presented.

The descriptive evaluation covered the organisation and the policy components as well as the processes of the managed entry of new drugs into the NHS in Malta. There was

a main process, the process for the selection of new drugs and this had minimal links with any other processes. There were no systems for medicines registration and for pharmacovigilance. The policy for the introduction of new drugs of 1993 produced inequity and inefficiency, mainly because a lack of update of the formulary and due to approval of requests for non-formulary drugs. The number of requests for non-formulary drugs approved in 1998 had exceeded 14,000, leading to an unmanageable situation. The policies for prescribing were coercively implemented and there was no monitoring of prescribing. Consultants had a monopoly over the process for selection of new drugs. Consultants submitted the requests for new drugs, the recommendations of whether a drug was introduced into the NHS were based on the evidence submitted by consultants and most prescribing within the NHS was restricted to consultants.

The outputs of this descriptive evaluation included: the 'General logic model', the results from the individual methods including the insight gained into the problems and into factors that effected the feasibility for change, 'Descriptive model 1' and the knowledge gained in the interpretation and application of information from different methods. The information and knowledge gained from the descriptive evaluation were used in the exercise conducted to plan and prioritise for change, which is presented in Chapter 4.

CHAPTER 4:

PLANNING AND PRIORITISATION FOR CHANGE

4.1 INTRODUCTION

The developmental evaluation covering this research was conducted in three steps: a descriptive evaluation was carried out to obtain a baseline as in June 1999 to enable the planning of the intervention for change, an action evaluation described the implementation of change between July 1999 and December 2001 and consequently an outcome evaluation was undertaken to analyse the changes.

The descriptive evaluation was presented in Chapter 3. A logic model that represented the main components and processes that constituted the general framework for the managed entry of new drugs into National Health Services (NHS) in European countries, the 'General logic model', was produced. The 'General logic model' was used to select methods to obtain information about the managed entry of new drugs into the NHS in Malta. The results of the investigation gave an insight into the problems that existed and into factors that were considered to effect the feasibility of change. Information from the results was used to present a model that described the managed entry of new drugs into the NHS in Malta as in June 1999, 'Descriptive model 1'.

At the beginning of the action evaluation between July and September 1999, it was considered necessary to carry out an exercise to plan and prioritise areas for change. This exercise for planning and prioritisation of change is described in this chapter. The

feasibility of change was the main factor considered for prioritisation. This was mainly determined using the insight gained from the descriptive evaluation together with knowledge of the reforms that were going on in both the political environment and within the NHS in Malta. As explained in Chapter 1, the Nationalist government was elected in September 1998. Consequently Malta's application for European Union (EU) accession was reactivated and Malta started the process of adoption of EU legislation. Moreover the government supported the policy for separation of operations from regulatory functions, and the Health Division was to strengthen its role as a regulator. In February 1999, the post of Director General (DG) was created and an appointment made, this replacing the previous post of Chief Government Medical Officer (CGMO). Experience has shown that radical changes within national policy in a country were most likely to succeed at a time of political reform (World Health Organisation, 1997a). It was expected that the political developments that were happening in Malta would support the implementation of major change in the processes for the managed entry of new drugs.

The model for improvement from Langley, Nolan and Nolan (1992) that was described by Berwick (1996), previously discussed in Chapter 1, was used to plan change. Planning included the choice of the best actions to take and how to implement them. These decisions incorporated the evidence about the effectiveness of interventions for change and the knowledge about bringing about change from the literature.

4.2 AIM AND OBJECTIVES

The aim of this exercise was to identify, plan and prioritise potential changes in the processes involved in the managed entry of new drugs into the NHS in Malta.

This was achieved through the following objectives:

1. To identify potential areas for change
2. To review the feasibility of change and prioritise potential changes
3. To plan actions to implement potential changes

4.3 METHODOLOGY

'Descriptive model 1' was used to guide the exercise of planning for change. The exercise considered three main factors: organisation components, policy components and processes. The organisation and policy components were identified under the heading of 'resources'. The organisation components were in the first column 'structural and human' and the policy components within the second column 'inputs to support' of 'Descriptive model 1'. The processes were identified through the rows of 'Descriptive model 1'.

The questions in the model for improvement by Langley, Nolan and Nolan (1992) were applied to the components and the processes identified from 'Descriptive model 1'. The first two questions of the model for improvement: 'What are we trying to

accomplish?’ and ‘How will we know that a change is an improvement?’ were mainly answered through the comparison of ‘Descriptive model 1’ with the ‘General logic model’. The third question, ‘What changes can be made that will result in an improvement’ was answered considering the feasibility of change, the external factors affecting change, the use of information about the effectiveness of different actions from the literature and the application of theory for change. The DG, the chairman of the Drug and Therapeutics Committee (DTC) and the director of the Government Pharmaceutical Services (GPS), who were considered to be major participants, were consulted in the planning exercise. In this way an insight into different alternatives for change was obtained.

Information from the literature relating to the NHS in Malta (Chapter 1), ‘Descriptive model 1’ and the results of the methods used in the descriptive evaluation (Chapter 3) were used in this exercise. The sources of information from the methods used in the descriptive evaluation were referenced as follows: document and record research (DR), participant observation (PO), activity of the DTC in relation to ‘new drug’ applications (DTC), consultant questionnaires (QC), patient interviews (PI), focus group discussions (FG) and medical representatives interviews (RI).

The information was entered into a table. The results from the exercise were analysed and presented under the headings of organisation, policy and processes.

4.4 RESULTS

4.4.1 Organisation

The planning for organisational change considered problems with the organisation, factors that would effect the feasibility of change, the external factors affecting change and the knowledge on bringing about change from the literature. A series of plans for organisational change were set.

There was no system for medicines registration (DR) and as a result there were problems with the bioequivalence of products supplied through the NHS (DR). There was no functional system of pharmacovigilance (PO). A system for the registration of medicines in line with EU legislation was to be introduced in view of plans for Malta's accession into the EU. New legislation was being drafted to this effect. An independent authority for medicines regulation was to be established. The setting of a system for pharmacovigilance was a priority and Malta could join the World Health Organisation (WHO) international programme for drug monitoring.

As the GPS was responsible for all pharmaceutical operations, regulation and policy within the NHS there could be conflict of responsibilities and interests (PO). Although EU legislation required that the responsibility for medicines regulation was separate from the operational functions, the director of the GPS did not plan a complete and physical separation of the section responsible for the setting up of medicines regulation from the other sections of the GPS. All the GPS was to remain under one director. In spite of the fact that 'the central law of improvement' stressed the need to

change a system, rather than bringing about change within a system (Berwick, 1996), only minor organisational changes could be planned for the GPS. The national formulary management section of the GPS was to be reorganised, to separate the secretariat of the DTC from the functions of procurement and to release senior pharmacists from administrative duties in order to enable them to perform formulary management activities.

In Malta there was no major pharmaceutical industry and local agents represented the pharmaceutical companies (RI). The pharmaceutical industry exerted pressure for the introduction of new drugs (QC, RI). Following the insight from the descriptive evaluation (PO, QC, RI), implementation of strict regulations on the activities of medical representatives within the NHS was considered to be impractical and in certain ways not beneficial. Strengthening of the DTC secretariat and revision of the policy for the introduction of new drugs and of the policy for the use of samples within the NHS were considered to be better alternatives to counteract any negative impact from the activity of medical representatives.

Consultants submitted requests for the introduction of new drugs to the DTC (QC, DR). The main remit of the DTC was of setting recommendations for the introduction of new drugs into the NHS and of updating and implementing the formulary and other prescribing policies (DR). The DG took decisions about which drugs were introduced within the NHS (DR). In Malta the reimbursement decisions and decisions of formulary management were incorporated into the same process as one decision. Within the NHS in Malta there was no concept of 'reimbursement' and the remit of the DTC focused on a centralised national system of formulary management. As

shown by the 'General logic model', many European countries distinguish between reimbursement (at a national level) and formulary management (at the level of service providers).

In line with government policy for the separation of regulation and service provision and also in preparation of the adoption and implementation of the Transparency Directive (Council Directive 89/105/EEC), it was planned that the DTC should start developing its role as a reimbursement committee and focused its remit on the setting of policy. It was planned that once the new remit of the DTC was established and developed, the composition of the DTC would be revised to support the new functions. In the meantime the service providers were to start taking up their responsibilities for implementation and monitoring of policy and for supporting cost-effective and rational drug use.

The developmental evaluation as at June 1999 highlighted that the setting and implementation of policies for prescribing were done coercively and there were no structures to support and monitor cost-effective use of drugs supplied through the NHS (DR, QC, PO). The pharmacists at the hospital dispensaries vetted requests for non-formulary drugs in the name of the secretary of the DTC (PO). The CGMO/DG insisted on this approach, with the intention of controlling the drug bill. In particular the number of 'non-stock' requests increased so much that there was insufficient time and resources for development of more proactive functions such as clinical pharmacy. The level of involvement of consultants in the setting of policy for prescribing was minimal (QC).

The development of the necessary policy and formulary management functions and of the required structures within the NHS required organisational changes as well as changes in the organisational culture of all stakeholders including the DG, the DTC and the healthcare workers within the service provider units. A new DG had just been appointed and this was considered to increase the feasibility of change. The developmental evaluation showed that consultants working within the NHS were the key stakeholders. The responses to the consultant questionnaires showed that consultants were aware of the problems with the managed entry of new drugs and were knowledgeable of the evidence that supported good practice (QC). These results were no guarantee that this knowledge would be reflected in improved practice nor that consultants would support change. At the time of the planning exercise the DG was responsible for both policy and service provision within the NHS. It was planned that once the hospitals became autonomous service providers, they would set up an organisational framework to support their new responsibilities with regard to setting, implementation and monitoring of policies.

4.4.2 Policy

A new national legislation for medicines, 'The Medicines Act' was being drafted. This legislation was to incorporate most EU legislation concerned with medicines including medicines regulation, together with an update of current national legislation. The Department of Health decided to tender the drafting of the legislation to a private legal firm. In the event, the legal firm required extensive input from the Medicines Regulatory Affairs Unit (MRAU). Because of the political commitment towards EU

accession, a system for medicines registration in line with EU legislation was now a priority.

The entitlement to free medicines through the NHS was set by the legislation (Laws of Malta, 1987). All the stakeholders were of the opinion that the system for entitlement to free medicines through the NHS needed to be revised (QC, FG, PI). The changes in the system for entitlement to free medicines introduced in 1998 did not consider the recommendations of the DTC and were mainly decided politically (DR). As the 50c prescription charge was removed by the nationalist government soon after it came to office in 1998, it was unlikely that the same government would introduce a system of co-payment. As described by Reich (1995), healthcare reform was more likely at certain definable and perhaps predictable political moment, especially in the early periods of new regimes. It was considered that if any changes in the system for entitlement to free medicines were made, these would have to be in the beginning of the term of a new government. In Malta in 1999 the Health Division set a working group to explore the alternatives for the revision of the system for entitlement to free medicines.

There were no formal mechanisms to deal with prioritisation and implicit ad hoc rationing by the DG informed by recommendations from the DTC was used to prioritise patients and their treatments. The DTC did not consider that it was its remit to decide on prioritisation (DR). Unless there was a change in the remit and composition of the DTC, it was unlikely that the system for setting prioritisation for the selection of new drugs into the NHS was going to change. It was unlikely that the public or other stakeholders were going to be included as members of the DTC

because in Malta there was no history of consumer representation on decision-making bodies in healthcare (European observatory on health care systems, 1999).

Although the European Union Directives do not specify the system chosen for reimbursement, accession into the EU required that Malta adopted the Transparency Directive (Council Directive, 1988). This directive stipulates that pricing and reimbursement decisions should be taken on objective criteria and should be taken within specified time limits. Once this directive is implemented, all drugs that are registered would automatically need to be considered for reimbursement. Thus the practice whereby new drugs were requested to be introduced into the NHS through requests submitted by consultants (PO, DR) would have to be revised. It was also considered that adoption of the Transparency Directive would help to overcome the monopoly exerted by consultants on the system for requesting new drugs. The main problem envisaged with the adoption of the Transparency Directive was that Malta did not have a clear process for decision making and for setting priorities for the selection of new drugs to be introduced into the NHS. This problem had previously been faced by Norway when EU legislation was adopted in 1992 (Norris, 1998).

There was no national policy for pricing of medicines in Malta (PO). Drugs supplied through the NHS were procured centrally and the prices offered for reimbursed drugs were controlled through a centralised tendering procedure (PO). Most European countries adopted policies for the pricing of medicines on their market (Bloor *et al.*, 1996; Wallerstein, 1997). Setting policy for the pricing of medicines in Malta would control the prices of drugs available on the retail market. Control of prices was particularly important, as the reimbursement system in Malta did not cover all the

medicines used by the population. The setting of a pricing policy would require a political decision.

The policy for the introduction of new drugs of 1993 was leading to an increase in the number of drugs that were approved as non-formulary, reaching more than 14,000 non-formulary approvals in 1998 (DTC, PO). The greatest concern was that the approval of non-formulary drugs as 'non-stock' drugs for individual patients led to inequity. Moreover the system of approval of non-formulary drugs was inefficient (QC), resulted in delays before the patient was started on prescribed treatment within the NHS (QC, PI) and involved a lot of paper work (QC). Protocols were set for all new drugs introduced since 1993. The protocols specified the indications for which the drug could be used and protocols were used to vet each patient request that was submitted for protocol-regulated drugs. The formulary was last published in 1986 (Department of Health (Malta), 1986) and the authorities had resisted the revision of the formulary (DR, PO).

As part of this exercise for planning and prioritisation for change it was recommended that the policy for the introduction of new drugs should be changed. All drugs should ideally be approved on the NHS as formulary, although some drugs may still be approved with a protocol. It is recommended that the protocols should include guidance to ensure quality and cost-effective prescribing. Approval of non-formulary drugs should be restricted to exceptional circumstances. Ideally the approval of named-patient requests against specific protocols should be reduced to a few medicines. It is recommended that alternative methods be used to implement and monitor prescribing, protocols and therapeutic guidelines. Moreover once a drug is

approved to be included in the formulary, procurement should proceed according to demand and patients should be started on treatment as soon as possible, without having to wait for procurement of stock.

It was recommended that the formulary be revised in line with the above proposals and be published on the intranet, so that it could be kept up to date and be immediately accessible. Consultants should be more involved in the setting of guidelines and in the revision of the formulary, to ensure ownership by this influential group. The revision of the policy for the introduction of new drugs and the proposals for the revision of the formulary require approval from the DG. The fact that there was a new DG was considered to be inductive to change. The revision of the formulary required pharmacists to do the secretariat work involved.

As the use of samples of drugs (that were not available within the NHS) by consultants to treat NHS patients was leading to pressure on the DTC to continue to support these new drugs (DR, PO), it was important to ensure that any new policy removed the responsibility and liability of the NHS to continue treatment that was started through the use of samples.

While in the developed world many countries do not have written national drug policies (NDPs), some experts advocate having a document that clearly outlines the objectives of a NDP (Quick *et al.*, 1997) and some developed countries such as Australia have published a NDP (Commonwealth of Australia, 1999a). In Malta a NDP was drafted but the exercise was stopped in 1998, before it was adopted (DR, PO) because after the election of September 1998 all the resources of the GPS were

concentrated on the adoption of EU legislation for pharmaceuticals and on the introduction of a system for medicines registration. Although it was considered that Malta would benefit from a NDP it was unlikely that the work on the NDP would be prioritised at this time.

4.4.3 Process

The 'General logic model' represented the process for the selection of new drugs into the NHS with the main activities identified being reimbursement, pricing and priority setting. The other processes were represented as inputs (availability of medicines by the pharmaceutical industry and medicines registration) and outputs (procurement, distribution, supply, rational use and monitoring) for the process for the selection of new drugs into the NHS. 'Descriptive model 1' highlighted that in Malta the process for selection of new drugs into the NHS and the setting of the formulary and prescribing protocols were centralised as one process. This process started with the submission of requests for new drugs by consultants. There was no direct input from the pharmaceutical industry in terms of submission of requests for registration and for reimbursement and there was no consideration of registration status of medicines during the reimbursement decision. The main outputs from the process were approval or non-approval of the drug within the NHS and if the drug was approved, its formulary status and a protocol for the use of the drug. Thus in Malta the approach to the entry of new drugs included a number of isolated processes which were not systematic.

The main plans for change in the processes focused on development of a more systematic approach to the selection of new drugs into the NHS in Malta. This approach could be facilitated by changes that would need to be implemented in order to adopt EU legislation particularly medicines registration and Council Directive 89/105/EEC which required an increase in the transparency of the process. However in the meantime the selection of new drugs into the NHS in Malta was to consider the licensing status of the drug within the EU and would only approve drugs that had a marketing authorisation within the EU. The submission of requests for new drugs by consultants working within the NHS would need to be maintained at least until medicines registration was implemented.

As part of the exercise for planning and prioritisation for change it was planned that the secretariat of the DTC should prepare additional information such as the available evidence on the efficacy, safety and cost-effectiveness of the drug. The secretariat of the DTC should increase its participation during the discussions within the DTC. The minutes of the DTC were to include the main points of the discussion and the reasons for not recommending requests. It is planned to consider prioritisation during the decision process and to generate standards for decision-making to make decisions more robust. The protocols were to be improved to increase their role in supporting quality and cost-effective prescribing. The formulary was to be updated in the process. The secretariat of the DTC in cooperation with the chairman of the DTC and DG were to implement the required actions to improve the process for the selection of new drugs into the NHS in Malta.

4.5 DISCUSSION

The aim of this exercise was to identify, plan and prioritise potential changes in the processes involved in the managed entry of new drugs into the NHS in Malta. The aim was met and many potential changes were identified, which required prioritisation.

The information from the descriptive evaluation in Chapter 3 was used as a baseline for planning change. The questions in the model by Langley, Nolan and Nolan (1992) were applied to structure the exercise. Additional knowledge from theory and recommendations from the field of change were used. The external factors (particularly government policy to separate regulatory and operational functions and the preparations for EU accession) and their influence on the process of change were also considered. The links within 'Descriptive model 1' (Chapter 3) showed how the components and the processes effected each other and how change could influence different parts of the system.

The planning and prioritisation was presented as a narrative which showed how the different types of information were collated to inform the action that needed to be taken and how it was to be implemented. The prioritisation for change depended mainly on the severity of the problem being tackled and the feasibility to bring about change to solve the problems. The action was chosen as part of the planning. Moreover the action was to be implemented when deemed feasible and of most advantage.

The questions from the model of improvement from Langley, Nolan and Nolan (1992) which were described and discussed by Berwick (1996) were used to guide the planning of change. The first question from the model for improvement was 'What are we trying to accomplish?' Ideally the highest amount of improvement was to be accomplished. Within the general framework for European countries the system for medicines registration was well defined and standardised and therefore for the area of medicines registration there was a definite answer to the first question. In the other areas such as reimbursement and the selection of drugs into the NHS there was generally no defined standard to be met. Each country had to set its own systems. In the case study of Malta the required improvement was mainly determined using the information about the NHS in Malta.

The second question of the model for improvement was 'How will we know that a change is an improvement?' For a number of problems this question could be answered through the application of basic knowledge or through the utilisation of evidence on the effectiveness of specific actions, when this was available. The revision of the policy for the introduction of new drugs of 1993 to remove inequity was considered to be an improvement of a fundamental principle for any NHS. Maynard (1996) stated that rationing care by rules that differed, were incoherent and implicit led to inefficiency and inequity. Thus the implementation of an explicit policy made transparent the problem of inequity.

The third question of the model for improvement 'What change can we make that will result in an improvement?' is of major importance in complex real-life situations where feasibility is a major determinant of the choice of the intervention. Certain

interventions for change such as audit and quality assurance target predefined and agreed levels of care and/or service provision and place the emphasis on the need for healthcare organisations to satisfy customer requirements. While still aiming to produce improvement, the emphasis in action research is development through a democratic process (Waterman, 1996). The fact that the model for improvement allowed planning according to the needs and feasibility of the change was a major advantage for its applicability in the conduct of action research in practice.

The planning of any change will be specific to the case under study, the feasibility of the planned action and the subjectivity of the researcher and the participants who plan the change. The fact that the DG was newly appointed to post and had not been involved in the setting of the policy that was proposed for change, led to support for the proposals for change in policy.

There was a linkage between the different components and processes and this interdependence influenced the planning for change. The different policies such as the policy for the introduction of new drugs, the policy for setting of the formulary and the setting of protocols for new drugs were linked. If the policy for the introduction of new drugs was changed, it was necessary to change the related policies. Once it was proposed to revise the formulary, organisational changes had to be planned in order to release pharmacists to do this work.

Some changes that were supported by theory and by external factors were still considered of low feasibility, mainly due to opposition to change. For example when the organisational change for the GPS was being planned, the evidence from the

literature strongly suggested that there should be a major change of the system and not smaller changes within the system (Berwick, 1996). Moreover government policy and also the EU legislation prioritised the separation of the regulatory from operational functions. However it was considered that it was unlikely that the director of the GPS would accept total separation within the GPS and relinquish part of the authority. It was not considered possible to overcome this opposition to change as part of this research.

Some changes required a political decision. In such cases the Health Division submitted its proposal for consideration by the minister. The legislation for entitlement to free medicines was an example of this.

Some changes were mainly determined by external factors and could not be influenced by the research. However these changes may have direct and indirect influences on the application of the intervention for change. The impact of the introduction of EU legislation on the managed entry of new drugs into the NHS in Malta was studied from the literature. The main direct impact was due to implementation of the Transparency Directive (Council Directive, 1988). It was considered necessary to study the impact of the implementation of this directive within the NHS in Malta. The case study by Norris (1998) highlighted the difficulties faced in Norway in terms of bringing in transparency in decision making as required by this directive. The study and improvement of the process for selection of drugs into the NHS was prioritised for the action evaluation.

4.6 SUMMARY

This chapter involved planning for change. The areas that seemed most feasible for change were to be prioritised for implementation.

Some changes started being implemented due to external factors. These included the revision of the national legislation related to medicines, the establishment of medicines registration in line with EU legislation, plans for the setting of a system for pharmacovigilance and the setting of recommendations for the revision of the legislation on entitlement to free medicines.

The key areas for potential change identified included:

- reorganisation of the national formulary management section of the GPS
- strengthening of the resources of the DTC secretariat
- revision of the remit and composition of the DTC
- the taking up of responsibilities for implementation and monitoring of policy and for support of cost-effective and rational drug use by service providers
- the setting and implementation of a new policy for the introduction of new drugs
- revision of the formulary
- revision of the policy for the use of samples of drugs within the NHS
- revision of the process for the selection of drugs into the NHS in preparation of the adoption of EU legislation.

This planning formed the baseline on which to implement the intervention and the action evaluation, which is described in Chapter 5.

CHAPTER 5:

ACTION EVALUATION

5.1 INTRODUCTION

This Chapter describes the action evaluation that was conducted from July 1999 to December 2001.

A descriptive evaluation of the managed entry of new drugs into the NHS in Malta was conducted (Chapter 3). The results were used to present a logic model of the managed entry of new drugs into the NHS in Malta as in June 1999, 'Descriptive model 1'. The results also gave an insight into the problems and into factors that effected the feasibility of change. Between July and September 1999 an exercise on planning and prioritisation of potential changes was conducted, utilising information from the descriptive evaluation (Chapter 4). This exercise prioritised potential changes under organisation, policy and processes and was used to plan actions for change during the action evaluation.

The prioritised changes in organisation components included the introduction of a system for medicines registration and the setting of a system for pharmacovigilance. The actions for these changes were mainly co-ordinated by the director of the Government Pharmaceutical Services (GPS) and were not directly part of the action research, although they interacted with it. A reorganisation of the National Formulary Management (NFM) section of the GPS was planned, with the aim of increasing support for formulary management. The strengthening of the remit of the Drug and

Therapeutics Committee (DTC) as a regulatory committee, the development of its function in reimbursement and the handing over of operational functions of implementation and monitoring of policies to service providers were linked and dependent on each other and were to proceed gradually.

The main planned change in policy was the setting up of a new policy for the introduction of new drugs, to reduce the inequity caused by the policy of 1993. Consequently the categorisation of drugs within the NHS was to be reviewed and the formulary and prescribing protocols were to be revised. These changes required planning and approval from the Director General (DG) and implementation mainly by the secretariat of the DTC. The legislation related to medicines was being changed to implement the European Union (EU) directives. Changes in legislation were suggested for the policy of entitlement to free medicines, however these required political approval.

The processes for the selection of new drugs were to be made more systematic through the building of links with other related processes. Decision-making was to be made more transparent and standardised. The status of medicines registration within the EU was to be considered. Evidence on efficacy, safety, clinical and cost-effectiveness was to be included. Protocols were to be improved to support prescribing. Prioritisation was to be considered as part of the reimbursement decision, if and where appropriate.

As the action evaluation proceeded, further planning for change was required, in line with the changes that were taking place. The information from the descriptive

evaluation was utilised during the action evaluation, particularly to guide the planning for change that needed to be done throughout the action evaluation.

Action research was implemented throughout the action evaluation as an intervention to bring about change. Action research allowed the implementation of different types of actions. The cyclical process of planning and action initially adopted the recommendations set in the exercise presented in Chapter 4 and then proceeded in line with the requirements for change as they developed.

The environment was dynamic and the system was complex. 'Descriptive model 1' was used as a tool to guide the action evaluation and to keep track of the overall picture. This model was updated with the changes throughout the action evaluation and the updated version was used to guide further change.

The same definition of 'new drugs' as used in the descriptive evaluation in Chapter 3 was used for the document and record research and for the measurement methods in the action evaluation so as to ensure validity of the longitudinal data.

In the prospective follow-up of requests discussed by the DTC from July 1999 to December 2001, 'different doses/strengths of drugs that are already available within the GPS' and 'different dosage forms of drugs that are already available within the GPS' were also separately considered. This prospective follow-up intended to mirror the process for the selection of new drugs if EU legislation were adopted.

The role of the researcher

The participatory action research involved the practitioner acting as a researcher within the practice. The researcher was part of the action organisation and performed an 'insider' role. This role involved the combination of roles of change agent, to some extent clinical leader and the role of a researcher. The role of the practitioner within the practice was significant and complementary to the participatory action research. The practitioner was secretary to the DTC throughout the action evaluation.

5.2 AIM AND OBJECTIVES

The aim of this action evaluation was to promote the development of a more systematic approach for the managed entry of new drugs into the NHS in Malta using an action research methodology.

Specific objectives included:

1. To implement action research as an intervention for change
2. To bring about change within the processes for the managed entry of new drugs into the NHS in Malta
3. To describe the processes of change that occurred during the action evaluation
4. To use the 'descriptive model' to present a revised model of the managed entry of new drugs into the NHS in Malta as in December 2001

5.3 METHODOLOGY

5.3.1 Gathering information to support the change process

5.3.1.1 Document and record research from July 1999 to December 2001

The method for document and record research that was started during the descriptive evaluation in Chapter 3 was continued prospectively. The information was entered under the areas identified from the 'General logic model'. A summary of the key points was presented.

5.3.1.2 Activity of the DTC from January 1999 to December 2001 in relation to 'new drug' applications

The measurement of the outcomes of the process for the selection of new drugs that were started in Chapter 3 were continued to allow follow-up of the longitudinal data up to December 2001 and were analysed using the process statistical methods previously described (Chapter 2). The measured outcomes of the process for decision making, namely the percentage of new drugs which were approved and the percentage of requests which were decided without delay per annum, were followed up using Individual (Shewhart) Charts and CuSum charts to see if there was a statistically significant change in these outcomes. For the Individual Charts (I Charts), the mean and the upper and lower control and action limits were set at previous values (Chapter 3) as the aim was to monitor for change as from 1998. For the CuSum Chart the

inclination (slope) of the chart was followed and measured and a V mask point was placed on the CuSum value for each year.

5.3.1.3 Prospective follow-up of requests discussed by the DTC from July 1999 to December 2001

This prospective follow-up covered all requests for the introduction of new drugs and included requests to update the formulary as discussed by the DTC during the action evaluation.

The prospective follow-up was carried out during the action evaluation, from July 1999 to December 2001. Prior to each DTC meeting the agenda for the meeting was compiled. The requests for new drugs and for update of the formulary selected for discussion at that meeting were analysed and used together with additional information such as licensing status of the drug within the EU, evidence on efficacy, clinical effectiveness and cost-effectiveness. The researcher, who was the secretary of the DTC, attended the DTC meetings and participated during the discussions as a member of the committee. Minutes of each meeting were compiled by the secretariat of the DTC and reviewed by the chairman of the DTC. The draft minutes were sent to the DG for consideration and approval or otherwise of the DTC recommendations. Following response from the DG to each recommendation the draft minutes (with DG's written responses) were then circulated to all members and confirmed at the next DTC meeting.

Following endorsement, the minutes were analysed. The information about each drug was compiled. The process of approval was divided into a number of steps and information was entered under the relevant sections. Data about each drug was followed up from the time when the drug was first requested until a final decision was taken or up to December 2001, whichever came first.

The experience and the knowledge built through analysis of the minutes of each meeting were used to improve the presentation of information on the agenda and the intervention at subsequent meetings in line with the cyclical process of planning and action.

Eleven DTC meetings were held during this period, number 101 to 111. An overview of the information from the requests considered is presented in the results. The experience of bringing about change in the process of selection of new drugs is presented as a narrative as part of the results of the change process. Additional knowledge generated through this prospective follow-up was also presented.

5.3.1.4 Case studies to illustrate key issues relevant to the managed entry of new drugs

A convenient sample of cases was chosen retrospectively from minutes and correspondence of the DTC up to June 1999. Cases were chosen that highlighted specific issues relevant to the managed entry of new drugs. In addition some cases raising new issues originated during the action evaluation and these were followed-up prospectively. All cases were followed-up to December 2001.

The information from the case studies was grounded and was presented under the key areas from the logic model. During the action evaluation the information from the case studies was used to inform the change process as it progressed.

5.3.2 The change process

Action research was employed as an intervention for change. This developed as a serial of cycles of planning and action. The process of change was dynamic and had to respond to the changes that were going on within the case study. Actions were implemented when the timing was considered to be right. Opportunities for change were utilised. On the other hand, urgent decisions and actions had to be taken to support the change process when it was effected negatively by changes within the environment of the case or by external factors. The change process was presented as a narrative.

Information from a number of additional methods was utilised to inform the change process and to support the planning and action of the action research. The descriptive model was updated regularly with the changes that happened during the action evaluation. This served as a tool to identify priorities for change and to study the impact of change.

Participant observation was an integral part of day to day management of the process for change. The researcher kept a personal diary at all times and made notes. Matters to be discussed with the different participants were noted in the diary. An agenda was prepared before each meeting, either a formal agenda or less formally in the form of a

list of questions within the diary. Points were noted during meetings and full minutes prepared for formal meetings. Frequent communication through formal or informal meetings was maintained with the main participants. Main participants included the DG (all matters were discussed), the chairman of the DTC (regarding the functions, operations and policies of the DTC) and the director of the GPS (regarding the GPS and the developments of the regulatory functions). The participants knew about the academic needs of the research. In practice the plans and changes were mainly presented as an integral part of ongoing work within the Department of Health.

5.3.3 Description of the processes for the managed entry of new drugs into the NHS in Malta as in December 2001

The information from the methods above was used to populate a logic model as at the end of December 2001, 'Descriptive model 2'. This model was an updated version of 'Descriptive model 1' after all the changes implemented in the action evaluation were made. The major changes in 'Descriptive model 2' when compared to 'Descriptive model 1' were highlighted.

5.4 RESULTS

5.4.1 Information gathered to support the change process

5.4.1.1 Document and record research from July 1999 to December 2001

A summary of the key data from July 1999 to December 2001 are given below under the headings previously identified in the 'General logic model' (Chapter 3).

1. Availability of medicines

As shown in Table 5.1, 70% of medicines licensed for importation in Malta were registered in the EU.

Table 5.1 Medicinal products licensed for importation in Malta as at December 2000

Region where the product is registered	No of products	% of total
European Union	3794	69.5
European economic area (Norway and Iceland)	9	0.2
EU applicant countries	394	7.2
European (non EU) Switzerland and Turkey	388	7.1
Others (non-European)	871	16.0
Total	5456	100

Source: Medicines Regulatory Affairs Unit (MRAU), GPS, 2001

2. Medicines registration

Malta planned to introduce a system for medicines registration in line with EU legislation by 1st January 2003. During the Intergovernmental Conference on the accession of Malta to the EU on the 21st December 2000, Malta requested and obtained a transitional period of four years for the implementation of Council Directive 65/65/EEC and its amendments with regard to licensing and the implementation of pharmacovigilance of medicinal products for human use, for those products already on the market on 1st January 2003.

When in mid-2001 the GPS was split up into different departments, the Medicines Regulatory Affairs Unit (MRAU) of the GPS, which up to then was responsible for medicines regulation, was dismantled. A new department (independent of the GPS), the Medicines Regulatory Unit (MRU), was set up with new staff and location.

3. Access to medicines through the NHS

The figures of total expenditure on NHS drugs generally continued to increase. The expenditure was LM 6.8 m in 1999, LM 8.6 m in 2000 and LM 9.9 m in 2001. One Maltese Lira (LM) is equivalent to approximately 1.55 Pounds Sterling (£).

In July 1999 the Ministerial Management Committee revised the criteria for entitlement for Schedule II 'Pink card' holders. New requests on behalf of 'Pink card' holders were now only approved for formulary medicines that were not covered by a protocol (Department of Health (Malta), 1999).

4. Selection of drugs for the NHS

In 1999 a new policy for the introduction of new drugs was introduced, replacing the policy of 1993. Consultants wishing to have a drug included in the protocol-regulated list of the formulary were to make a submission to the DTC that was to include the relevant details including a detailed protocol and an estimate of the number of patients who were likely to fit the protocol. In addition the DG specified that in considering the inclusion of a drug on the formulary, the DTC was to consider the financial limitations that existed within the NHS. A cost-effectiveness analysis was to be made and in submitting its recommendations to the DG, the DTC was to consider priorities between submissions made by the various consultants. No submissions for named-patients were to be entertained even if the patient was already on the drug through the use of samples (DTC correspondence, 1999).

5. Procurement, distribution and supply

Table 5.2 shows that the estimated cost of the supply of drugs through the NHS is approximately similar in relation to in-patient and out-patient use.

Table 5.2 Estimated cost for the supply of drugs through the NIHS for in-patient and out-patient use

	1998 (LM)	1999 (LM)
In-patient supply in hospitals (all NHS hospitals)	4,666,993	4,230,386
Out-patient supply from health centres and hospitals	3,113,070	4,046,452
Total	7,780,063	8,276,838

Following the new policy for the introduction of new drugs of 1999, once a drug was approved on the formulary by the DG, the GPS started procurement. Once stock was received the formulary was updated and consultants were able to prescribe it after completing a protocol declaration (DTC correspondence, 1999).

6. Rational use and monitoring

Consultants recommended that when protocols were established, audit should be an integral part of system. It was recommended that such audit should be integrated as part of routine activity within clinical practice (DTC 102, 1999).

By the end of 2001 there were 14 therapeutic guidelines, 71 hospital protocols and 95 medicines protocols. The formulary chapter and the protocols for cardiology were the first to be published in the revised formulary. These were proposed by the senior consultant cardiologist and supported by the head of department of medicine (DTC 106, 2000).

5.4.1.2 New drug applications considered by the DTC from January 1999 to December 2001

Table 5.3 summarises the annual activity of the DTC in relation to 'new drug' applications from 1995 to 2001.

Table 5.3 Activity of the Drug and Therapeutics Committee in relation to 'new drug' applications from 1995 – 2001

Year		1995	1996	1997	1998	1999	2000	2001
Number of meetings		5	6	5	2	7	4	2
Total number of requests ¹		18	68	31	23	45	32	16
Outcome of the requests considered during that year	No. (%) of requests approved	16 (89)	59 (87)	20 (65)	20 (87)	26 (58)	19 (59)	7 (44)
	No. of requests not approved	0	8	9	2	9	2	3
during that year	No. of requests pending ²	2 (11)	1 (2)	2 (6)	1 (4)	10 (22)	11 (34)	6 (38)
	Number (%) of requests which were decided without delay (%) ³	15 (83)	61 (90)	19 (61)	22 (96)	28 (62)	15 (47)	8 (50)
Approved category	'non-stock'	2	24	14	6	1	1	0
	'special'	14	34	6	11	22	6	0
	formulary non-protocol		1		3	2	3	1
	protocol regulated ⁴	-	-	-	-	-	9	5
	trials/studies					1		1
Total Cost (Lm) (x 1,000)		77	157	85	124	134	216	19

¹ total number of requests for different drugs discussed during the year. Each 'new drug' has only been counted once within each year.

² requests remaining pending a decision at the end of the respective year

³ without delay means that a decision was made at the first consideration by the DTC

⁴ this category did not exist until 2000

SOURCE: Minutes of meetings of the DTC

The percentage of requests that were approved dropped from 87% in 1998 to 44% in 2001. In the same period the percentage of requests that remained pending at the end of the respective year increased. The number of drugs approved as 'non-stock'

decreased to nil in 2001. On the other hand in 2000 and 2001 there were approvals for formulary approved protocol-regulated drugs for the first time (a new category).

Table 5.4 provides data on approval of drugs on an individual patient basis from 1995 to 2001. The 'new policy for the introduction of new drugs of 1999' specified that the approval of drugs as non-formulary was to be stopped and that all new drugs were to be approved as formulary. Drugs that were approved as protocol-regulated still required a request for each individual patient. The number of approvals for patients continued to increase steadily, from 14,129 in 1998 to 27,578 in 2001.

Table 5.4 Approval of drugs for individual patients from NHS hospitals (1995 – 2001)

Year	1995	1996	1997	1998	1999	2000	2001
Number of different drugs approved for individual patients	272	281	321	328	320	368	376
Total number of approvals for individual patients	4,596	7,034	11,226	14,129	17,370	21,837	27,578

The I Charts for the percentage of requests approved and for the percentage of requests which were decided without delay which were presented in Chapter 3 up to 1998 were updated with the data for 1999 to 2001 from Table 5.3 and are presented as Figure 5.1 and Figure 5.2 respectively. The mean, the control limits and the warning limits for the individual charts were maintained as they were before 1999 (the values for 1999 to 2001 were not included in the calculation) so that any changes in approval trends before and after 1999 could be compared.

Figure 5.1 Individual chart for percentage of requests approved (1991-2001)

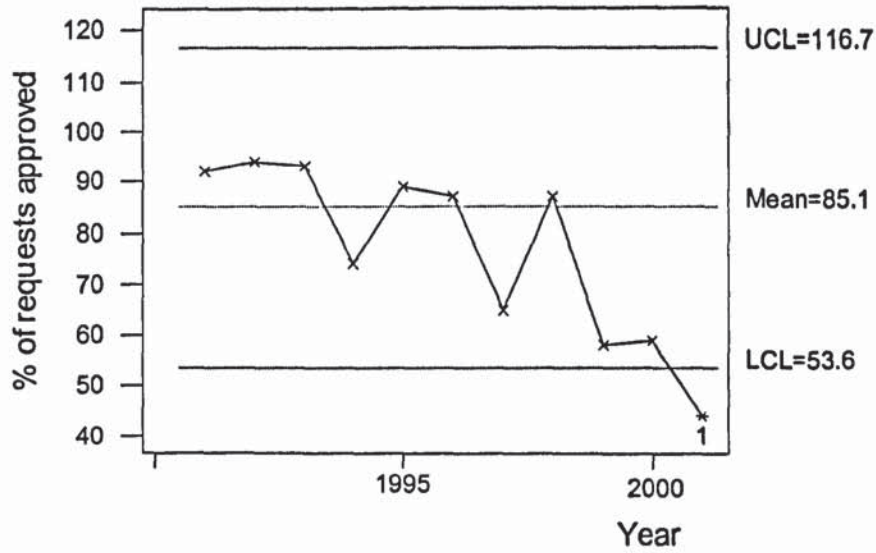
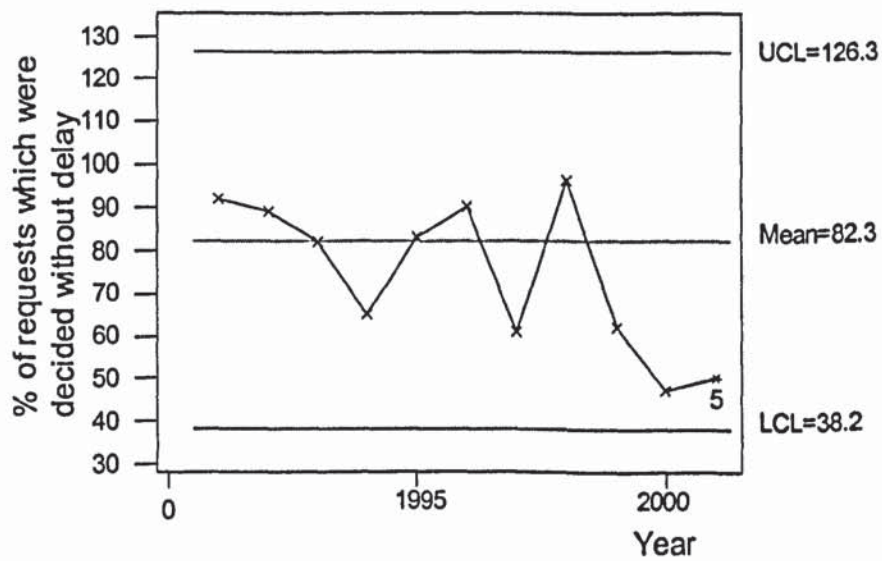
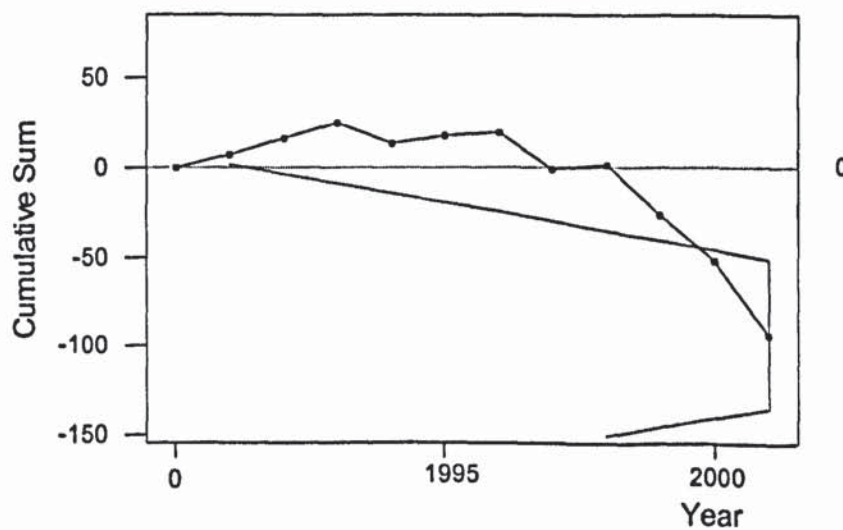


Figure 5.2 Individual chart for the percentage of requests decided without delay (1991-2001)



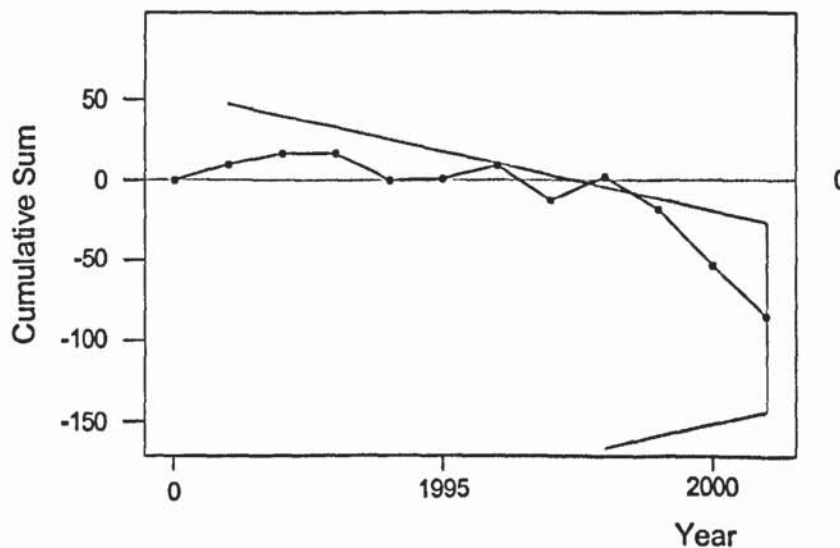
As can be seen in Figure 5.1, the lower warning limit (2 sigma below the mean) was set at 64.1 and the lower control limit (LCL) at 3 sigma below the mean was set at 53.6. Therefore the values for 1999, 2000 and 2001 (58, 59 and 44 respectively) were all below the lower warning limit. The value for 2001 was even below the lower control limit indicating that some assignable cause of variation was present from 1999 to 2001. This variation was confirmed by the visual change in slope of the CuSum chart for the same data as shown in Figure 5.3. The slope was horizontal up to 1999 but from 1999 onwards there was a clear visual shift downwards in the slope of the CuSum chart, confirming that the changes in the process average occurred from 1999 onwards. The V mask placed on the value for 2000 and 2001 cut the previous trace of the CuSum chart confirming that there was a significant change in the process during these years.

Figure 5.3 CUSUM Chart for the percentage of requests approved (1991-2001)
V masked at 2001



In the I Chart for the percentage of requests decided without delay (Figure 5.2), the values for 1999, 2000 and 2001 (62, 47 and 50 respectively) were within the lower control (3 sigma) limit of 38.2. The values for 2000 and 2001 were outside the lower warning limit (at 2 sigma below the mean) at 52.9. The CuSum chart showed the same trend as that for % of request approved and was horizontal up to 1999 and then shifted downwards showing a change in the process average as from 1999. The V mask at the values for 1999 and for 2000 did not cut the trace however the V mask placed at the value for 2001 cut the trace, as shown in Figure 5.4, confirming a significant variation in process from 2001.

**Figure 5.4 CUSUM Chart for the percentage of requests decided without delay
V masked at 2001**



5.4.1.3 Prospective follow-up of requests discussed by the DTC from July 1999 to December 2001

The information from the requests for new drugs and for update of the formulary that were considered by the DTC during the period July 1999 to the end of 2001 was collated for the individual drugs. The categories used to classify the information and a summation of the information for the drugs considered is presented in Table 5.5.

Out of 54 drugs requested, 41 requests were for 'new drugs'. Most of these (31) were for drugs which were not available in the NHS, 7 requests were for drugs which were available but were requested for a new indication and 3 requests were for the use of samples or trial drugs. 13 requests were for update of the formulary, 4 of which were for drugs that were not available on the NHS but were requested to replace drugs that were no longer available, for example methylergometrine was replaced by ergometrine. 9 requests for update of the formulary were for drugs that were already available but for which different dosage forms or strengths were being requested.

A number of preparations used to be prepared extemporaneously and these are being procured ready-made wherever possible (mainly as specials). Patients who required deoxycoformicin injections and botulinium A toxin used to be sent abroad for treatment. These drugs were now approved within the NHS, as it was cheaper to provide this treatment in Malta. Certain drugs such as donepezil tablets were required for conditions that were not approved for treatment on an out-patient basis. Two requests where there was no entitlement were approved on a humanitarian basis, these

included sufentanil forte injections and antipsychotics such as citalopram, sertraline and reboxetine.

Table 5.5 Summary details of 'new drug' and formulary update applications considered by the DTC during the action evaluation (July 1999 – December 2001)

Requests for new drugs and for update of the formulary		Type of request		% of total
		'New drugs'	Formulary update	
Number of drugs considered by DTC n=54		41	13	
Status of drug with respect to drugs available on formulary	Not available within NHS	31	4	65
	Available, new indication	7	0	13
	Available, different preparation	0	9	17
	Not approved but available as sample or trial drugs	3	0	5
Innovation of the drug with respect to treatment available for the disease on the formulary	No other drugs available for the disease	3	0	6
	Sub-groups of patients are less responsive to available drugs	19	0	35
	Disease responsive to available drugs	16	8	44
	No entitlement to free medicines for the disease	2	0	4
	Replacement of available drug/ preparation	1	5	11
Therapeutic improvement of the drug relative to the nearest alternative drug available on NHS	Major	1	0	2
	Moderate	14	3	31
	Minor	18	6	44
	Same	5	4	17
	Less	0	0	0
	Not applicable	3	0	6
Cost increase relative to nearest available drug	Major increase (>25%)	5	0	9
	Moderate increase (10 – 25%)	13	1	26
	Minor increase (< 10%)	10	8	33
	Same	7	4	20
	Decrease in cost	3	0	6
	Not applicable	3	0	6
Final approval given by Director General	Approved	24	9	61
	Not approved	17	4	39

Licensing

Of the 41 new drugs requested 11 (27%) were licensed by the European Medicines Evaluation Agency (EMA). 5 of these were approved for reimbursement (angiotensin II receptor antagonists (open specification)), botulinum toxin type B, leflunomide, etanercept and basiliximab) while 6 were not approved (mycophenolate, entacapone, ribavirin, infliximab, docetaxel and verteporfin).

Guidelines

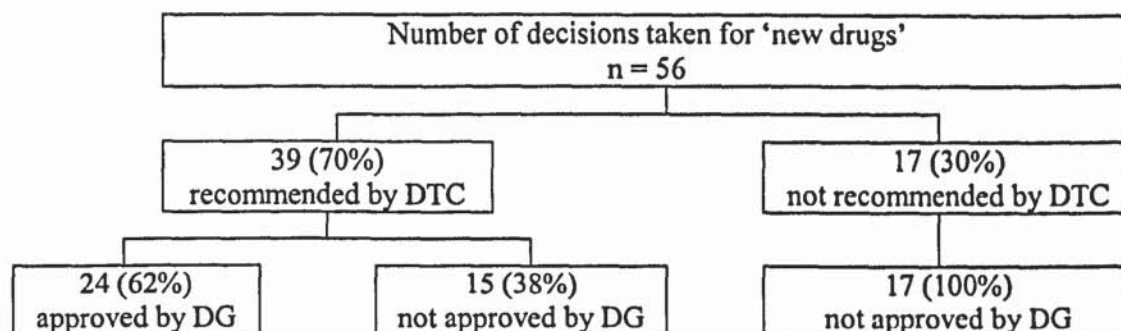
Of the new drugs discussed, National Institute for Clinical Excellence (NICE) guidelines were available for the following drugs:

- taxanes were approved by NICE for breast and ovarian cancer and were not approved in Malta
- ribavirin was recommended by NICE but was not approved in Malta
- cox II inhibitors for osteoarthritis were recommended by NICE and also approved in Malta
- etanercept for rheumatoid arthritis was approved by NICE and was also approved in Malta
- donepezil was approved by NICE but was not considered for reimbursement in Malta because there was no entitlement to free medicines on Schedule V for dementia

Figures 5.5 and 5.6 provide details of the 71 decisions taken for the 54 different drugs considered by the DTC. A drug may have been considered by the DTC more than once. As shown in Figure 5.5, 56 decisions were taken for the 41 'new drugs' considered. The DG did not overturn any application that was not recommended by

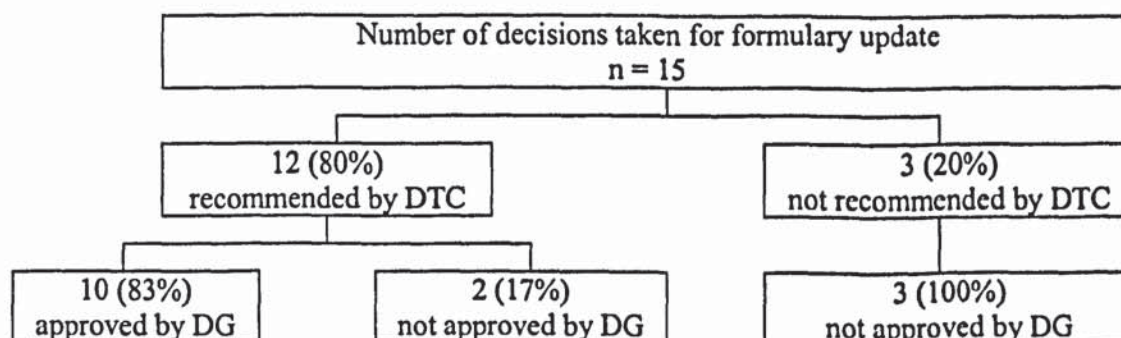
the DTC. Out of 39 'new drug' recommendations by the DTC, 15 (38%) were not approved by DG.

Figure 5.5 Drug and Therapeutics Committee (DTC) and Director General (DG) decisions for 'new drugs' during action evaluation period (July 1999 – December 2001)



As shown in Figure 5.6, 15 decisions were taken for the 13 drugs considered for formulary update. 2 out of the 12 (17%) DTC recommendations for formulary update were not approved by the DG.

Figure 5.6 Drug and Therapeutics Committee (DTC) and Director General (DG) decisions for formulary update during action evaluation period (July 1999 – December 2001)



5.4.1.4 Case studies to illustrate key issues relevant to the managed entry of new drugs

The cases were a convenient sample, chosen because they illustrated particular aspects and provided insight into the managed entry of new drugs into the NHS in Malta. The prospective cases were followed up to December 2001 where appropriate.

The following cases are numbered to facilitate cross-referencing when presented within the key areas identified from the 'General logic model'.

Case 1: low-molecular weight heparin (LMWH). The supply of unfractionated heparin in pre-filled syringes was stopped. The DTC had to recommend alternative treatment. Setting of an open specification for one LMWH proved difficult.

Case 2: fentanyl patches. A request to conduct a clinical trial was received. The Department of Health asked for the inclusion of a clause on the patient consent form which clearly stated that the Department was not liable to supply stock of the drug once the trial supply was stopped. The policy for clinical trials was discussed.

Case 3: implementation of the formulary chapter for cardiology. Cardiology was the first chapter of the formulary to be revised after the DG approved the process in 1999. The senior consultant was a major participant. The licensing status of drugs within the EU was considered during the decisions taken.

Case 4: drugs for the treatment of hepatitis C. Demonstrated the problems until entitlement for this treatment was approved on Schedule V in 1998 and the plans for monitoring of treatment that were set at that time.

Case 5: treatment of HIV. Initially was only approved for patient who acquired HIV through contaminated blood products supplied through the NHS, but was approved for all patients following pressure from media and interest groups.

Case 6: hyperlipidaemia. After long debate about the entitlement to free treatment for prophylaxis, just before the election of 1998 this treatment was approved. A protocol for the use of statins was set including strict criteria for the eligibility of treatment. The protocol was to be strictly vetted by pharmacists, but this was not possible due to lack of manpower.

Case 7: proton-pump inhibitors. Drugs for *Helicobacter pylori* eradication were not approved unless there was active peptic ulceration due to criteria for entitlement on Schedule V.

Case 8: taxanes. Paclitaxel was initially approved on a named-patient basis but following the policy for the introduction of new drugs of 1999, the drug was approved with a protocol for the treatment of ovarian cancer. Docetaxel was not approved within the NHS in Malta, in spite of it being recommended by NICE. A patient who was prescribed docetaxel took the DG to court. The court supported the policy for the introduction of new drugs of 1999. In December 2001 the case was still pending a ruling on the appeal.

Case 9: imatinib. A good example of pressures by the media and individual patients to introduce a new drug on the NHS.

Case 10: entacapone. Although the drug was licensed by the EMEA, the DTC considered that there was limited evidence on the safety and efficacy of the drug and the recommendation was postponed, pending further data.

Case 11: C-1 esterase inhibitor concentrate. The preparation available for the drug contained blood derivatives that did not fit the criteria for the safety of blood products adopted by the NHS.

Case 12: cisapride. The national decision on the action to be taken due to reports of ventricular arrhythmias with cisapride was taken by the Gastro-intestinal sub-committee of the DTC. In the meantime EMEA was to take a decision for the EU.

Case 13: riluzole. Riluzole was approved within the NHS in 1998, following a political decision to include motor neurone disease on the Schedule V list. Later the neurologist reported that “the response to treatment was unimpressive”. Attempts to stop treatment with this drug within the NHS proved difficult.

Individual details of each of these cases is provided in Appendix IX for further information.

Presentation of information from the case studies within the key areas identified from the 'General logic model'

1. Availability of medicines

At times the DTC was forced to consider alternative drugs because of cessation of manufacturing by the pharmaceutical industry. This was exemplified by the discontinuation of unfractionated heparin and the subsequent need for the DTC to consider an alternative (case 1).

The case of fentanyl patches (case 2) demonstrated problems arising from the merger of pharmaceutical companies. In this case the local representative for the product remained the same but the local agent changed.

2. Medicines registration

Not all the drugs within a therapeutic class were licensed similarly. For example only one of the angiotensin II receptor antagonists was licensed for congestive heart failure (case 3) and the different preparations of low molecular weight heparin varied widely in their licensed indications (case 1).

3. Access to medicines through the NHS

The request to conduct a clinical trial of fentanyl patches in Malta was an example of the 'use' of clinical trials as a form of promotion, to introduce a new drug (case 2). This case stimulated the development of a policy for the conduct of clinical trials within the NHS. The Ethics Committee that considered this trial did not accept the disclaimer clause that the Department of Health was not responsible for continuing to supply stocks of the drug once the trial material was finished. Another measure to introduce a new drug into the NHS employed by the industry was the offer to supply ribavirin free of charge together with the stock of interferon for the treatment of hepatitis C (case 4).

The cases demonstrated a number of problems with the implementation of the legislation for entitlement to free medicines. The supply of treatment for hepatitis C (case 4) and for HIV (case 5) were debated at length because these conditions were not on the Schedule V list. This debate resulted in delay in approving the treatment on the NHS. The requests for medicines for hypercholesterolaemia (case 6) and for *H. pylori* eradication (case 7) highlighted the issue that medicines for prophylaxis were not covered within Schedule V.

The media, patient groups and individual patients continued to exert pressure on the NHS to introduce new drugs. A cross section of the cases show that in the last months before the general election of 1998 there was a surge of pressure to approve the pending requests. These pressures led to approval of a number of drugs which up to then were still being debated. The drugs were approved with a protocol (in some cases

with a specific request form in line with the protocol). Statins (case 6) and treatment for hepatitis C (case 4) were approved, subject to strict criteria for monitoring.

Pressure from patients and the media continued after the election. In the case where a consultant request for docetaxel for the treatment of breast cancer was refused (case 8) the patient herself took the Department of Health to court claiming that her right to life (as guaranteed in the Constitution of Malta and in the European Convention for Human Rights) was not being ensured. This case and the issue of prioritisation and allocation of resources were also intensively covered and discussed within the press. The outcome was that the courts accepted the principles of the policy for the introduction of new drugs. Although the patient has since died, the case is still under appeal and the final outcome will establish case law in this area.

In the case for imatinib (case 9) the patients and their families participated in a number of television programmes. Personnel from the DTC and the DG were invited to take part in such programmes where the patients would also be present. The invitations were declined. It remains very difficult to explain the concepts of rationing and of allocation of resources via the media, particularly where individual cases are emotively presented.

A number of patients were prescribed new drugs before they were approved on the formulary. The patients started buying the treatment through their own funds or through support from the Community Chest Fund (a national charitable fund) – as demonstrated by the cases for docetaxel (case 8) and for imatinib (case 9).

4. Selection of drugs on the NHS

The cases illustrated that since July 1999 there were attempts to incorporate evidence within the decision process, particularly information on the licensing status of the drug, and information on safety and efficacy. The information on the licensing status and the information on efficacy from the European Public Assessment Reports (EPARs) started being given a high importance by the secretariat of the DTC. In the case for taxanes (case 8) presentation of the clinical trial data from the EPAR was quite reassuring that this was the 'best available data'. In the compilation of the case for imatinib (case 9) the efficacy data of the EPAR was presented in detail because this case resembled that of the taxanes.

Use of the information on the EPARs from EMEA showed that a number of drugs were approved by EMEA for exceptional circumstances. In such cases the information available from the clinical trials was usually very limited. For example when docetaxel was approved by EMEA in 1995, the information from Phase III clinical studies was not yet available. Additional data was submitted later (case 8). The same happened in the case of imatinib. EMEA gave a positive opinion on this product based on extrapolated data (case 9). It was difficult to postpone a decision on the premise that there was lack of good evidence of efficacy when this evidence was considered to be acceptable for marketing authorisation. It was often queried by consultants as well as by the media and patients how drugs that were licensed were not automatically introduced within the NHS. There was a clear confusion between efficacy as considered for Market Authorisation and effectiveness as considered in DTC decisions.

Matters were complicated by comparison of what was being done in Malta with the appraisals from organisations outside Malta, particularly the NICE for England and Wales. In the case of taxanes (case 8) NICE was evaluating taxanes at the same time of the court case in Malta. The patient's legal representative during the court case referred to the NICE guidance. NICE issued guidance to the NHS on the use of taxanes for the treatment of breast and ovarian cancer in May 2000 (National Institute for Clinical Excellence, 2000). There was a lot of speculation in the medical press before this guidance was issued. There was an appeal against the NICE guidance filed by the drug company and by non-governmental organisations. The appeal panel did not agree with the original guidance which resulted in approval by NICE. The decision of the DTC in Malta was highly criticised because in the public view docetaxel had not been approved in Malta but had been approved by NICE.

Due to this court case the DTC members and secretariat started becoming more considerate of the approval of indications during medicines registration. The secretariat presented the information on the licensed indications of the drugs considered. In the case of the angiotensin II receptor antagonists (case 3) there was the problem that only one of the drugs in the therapeutic class was licensed for congestive heart failure. The legal implications and responsibility in the use of products for unlicensed indications was recognised. Some consultants considered the licensing information to be a barrier that provided an excuse for DTC not approving some of their requests.

It was difficult to ensure efficacy of treatment and even more difficult to prioritise between different products. In the case of cancer treatment (case 8 and case 9) the

outcome measures were usually morbidity and mortality and the final question often ended up being whether it was worth paying so much money for a limited number of months of survival. At times the outcome of treatment was more subjective and was not so well defined such as in the case of entacapone (case 10).

Marketing authorisation at an early stage produced problems with establishing safety. In the case of entacapone (case 10) the safety profile was not established when the drug was first discussed by the DTC.

5. Procurement, distribution and supply

Following incidents of supply of contaminated blood products through the NHS in the past there was major concern regarding contamination of products containing derivatives of blood. Products that did not contain blood (or derivatives) were generally preferred. An example of this is the case for C-1 esterase inhibitor concentrate (case 11).

One of the major changes which effected the procurement process was the policy of setting of specifications for a therapeutic class rather than for a specific product, as was done in the case of statins (case 6) and for angiotensin II receptor antagonists (case 3). It was difficult to obtain data on therapeutic equivalence between drugs in the same therapeutic group, which compounded the adjudication process. As shown by the case of preparations of low molecular weight heparin (case 1) the preparations were different in many ways, which caused difficulty in setting specifications.

6. Rational use and monitoring

Although when alfa-interferon was approved for hepatitis C in June 1999 there was great emphasis placed on the monitoring which had to be done (case 4), this did not happen in practice and up to the end of December 2001 there were no reports of follow-up and of outcome.

The protocol for the use of statins (case 6) was also intended to establish tight controls over the use and consequently the expenditure on statins. The protocol specified that the Lipid Committee was to vet all such applications. Initially there was monitoring of all requests for statins and this also involved random checking of the information on the request form with the information within the individual patients' case notes. This monitoring slackened after 4 months because of the lack of manpower. There was also an intention to vet all requests for proton-pump inhibitors in the treatment of peptic ulceration (case 7) but once again this failed to be followed through due to lack of manpower.

The pharmacovigilance issues related to cisapride (case 12) led to restricted use of the drug. It was difficult to objectively decide on the policy to adopt at a national level. It was important to reduce risk to patients, but the risks needed to be considered against the benefits of the drug, particularly for indications where there was no alternative treatment. In Malta a committee of consultants took the decision.

Riluzole (case 13) was the only drug that was approved on the NHS and was then stopped because of the limited evidence for its benefits in clinical practice. Initially

riluzole had been introduced because of pressure from patients and after political update of the Schedule V list of disease conditions, which now included motor-neurone disease. It was difficult to implement a reversal of the initial approval decision. Some patients who were on riluzole did not want to stop treatment and the drug was continued for these patients. Although it was decided not to approve new patients to commence riluzole, this decision was difficult to implement in practice and exceptions were made.

5.4.2 The change process

5.4.2.1 Organisational change

By the end of 1999 the planned reorganisation of the NFM section of the GPS had progressed well. The senior pharmacists at the NFM section started concentrating on formulary management activities and delegated all routine administrative duties. The fact that the four senior pharmacists were put in an office together helped them to develop the formulary management role and to support each other. As these pharmacists had not worked in the clinical field before, the secretariat of the DTC supported them in that area. The duties of the pharmacy technicians were well defined and this increased their sense of responsibility. When monitoring of certain activities on an individual basis (for example the issue of out-of stock lists per pharmacy technician and follow-up of the lists) started, some pharmacy technicians felt threatened. However, those who worked well were pleased with the recognition when the monitoring highlighted their good performance. The fact that the monitoring data

for the individuals was kept within the NFM section and only the global figures were given to the authorities was less threatening for the pharmacy technicians.

Government policy for adoption of EU legislation and for the implementation of the system for medicines registration dictated the priorities for organisational development within the GPS for 2000. A plan was set with tight time-scales. The GPS was 'divided' into an operational unit (NFM, stores and distribution) and a regulatory unit (the MRAU). However the GPS still remained as one department under the same director.

Excellent progress had been made during 1999 in line with planned changes to the NFM section as described above. However, following division of the GPS into two units a new principal pharmacist was appointed to the NFM. This new pharmacist stopped the planned changes and indeed reversed most of the progress made to date. He dictated that pharmacists only do "professional work related to procurement". Moreover the communication between the pharmacy technicians and the pharmacists was severely broken because there was a distinctive separation between the routine (administrative) and the 'professional' aspects of work and the pharmacists were only responsible for the latter. The principle of teamwork and of shared responsibility at NFM was lost. The participation of the senior pharmacists in formulary management activities was stopped.

During the division of the GPS, the GPS considered that it was not within their remit to provide secretariat support to the DTC. This made the position of the researcher very difficult as she had been appointed as secretary to the DTC by the DG. Despite

this difficulty the researcher continued to provide support to the DTC and took every opportunity to build partnerships between the GPS and the DTC. For example the EPARs, which were usually kept at the MRAU of the GPS were used by the DTC to provide information for the evaluation of new drugs. In addition the GPS consulted the DTC and its sub-committees on clinical issues relating to pharmacovigilance, for example to make recommendations regarding the pharmacovigilance issues concerning cisapride (case 12).

The director of the GPS embarked on a twinning project with the Medicines Control Agency (MCA) of the UK for the implementation of the legislation relating to drug registration. It was planned to build a system for medicines registration on the model of the MCA. The difficulties with implementing a system for medicines registration and for pharmacovigilance in line with EU legislation in Malta included limitation in terms of experienced assessors, scientific experts and pharmaceutical inspectors; the extent of the work involved to review the large number of products on the market and the effect of medicines registration on the price of medicines in Malta.

The MRAU was strengthened with staff and a new team was formed. Initially this team coordinated well together. The role of the new pharmacists demanded technical input and a high level of responsibility and initiative. Some of the pharmacists were not prepared for this type of challenge as this was a total departure from prevailing attitudes within the GPS. Some pharmacists complained that they were being given responsibilities above their post. These pharmacists then refused to go abroad for meetings and conferences. The change process still went on but there was a constant

and escalating opposition to change. This opposition resulted in slowing down of the progress of change.

By 2001 the collaboration between the action researcher and the pharmacists within the regulatory section could not continue because the situation reached a point where all change was being opposed. The setting of the regulatory functions and the action research were continued at a higher level with the director of the GPS. Consequently the pharmacists within the GPS (with the exception of the director) started to oppose the research. The pharmacists knew that the action research was still going on, although they were no longer participants in it. There was increased direct collaboration with the DG, particularly regarding matters concerning medicines policy, including the work of the DTC.

The Malta Chamber of Pharmacists (which at that time was the union as well as the professional body for pharmacists) was brought into the dispute between the pharmacists and the director of the GPS. The pharmacists within the GPS wanted the new regulatory unit and the director to be totally separated from the GPS. In April 2001 the pharmacists at the GPS went out on strike action to put pressure on the authorities to bring about full separation. The lobbying included a plan for a new director for the GPS. It is important to note that the organisational changes implemented by the director led to this conflict and not the planned change within the action research. The researcher ended up having to defend her position with the union. The president of the union supported the researcher and the research, but at the same time the president was pressurised by the majority of the union members to oppose the setting up of a separate section for medicines policy, as proposed by the researcher.

To overcome this dispute in June 2001 the DG removed the regulatory unit from within the GPS. Moreover a new section, the National Medicines Policy and Audit Unit (NMPAU) was set up within the Health Division independent of the GPS. This section was responsible for the DTC and for medicines policy. This development was proposed by the researcher as part of the action research. In July 2001 there emerged three separate departments, the existing government pharmaceutical services (GPS), a revised and re-staffed medicines regulatory unit (MRU) and a new national medicines policy and audit unit (NMPAU) were established.

Although the pharmacists in the hospitals were excited about the hospitals becoming autonomous from the Health Division (because they considered that this would bring better working conditions), they were reluctant to start taking up the increased accountability and responsibility for medicines use. There was a feeling that the responsibility for the budget was being shifted. On the other hand some people on the regulatory side felt that they were being disempowered.

5.4.2.2 Policy change

The adoption of the EU legislation with respect to pharmaceuticals required the setting of new legislation for Malta. The MRU (formerly the MRAU) was responsible for the new legislation related to pharmaceuticals. A legal firm (which was not familiar with the area of pharmaceuticals) was assigned the drafting of the new Medicines Act. The draft legislation was not acceptable. Subsequently the MRU and the DG familiarised themselves with the EU directives and regulations and re-drafted the Medicines Act, with the support of the legal advisor within the Department of Health. The exercise of writing the legislation was very time consuming.

The policy for the pricing of medicines in Malta was not prioritised during the exercise for planning and prioritisation for change that was presented in Chapter 4 because at that time it was considered that this policy could only be set if there was political backing. When later ministers discussed the implementation of the provisions of EU legislation with regard to medicinal products it was recommended that further consideration should be given to the possible implementation of a pricing policy prior to the implementation of the provisional licensing system. This provision was included because it pre-empted the introduction of a provisional licensing system and the inevitable introduction of a registration fee, which may result in an increase in drug prices in Malta. A draft pricing policy was therefore set through collaboration between the Consumer and Competition Division and the Health Division. Whilst a proposal was presented to ministers, by December 2001 no progress had been made.

As was identified previously in the descriptive evaluation, entitlement to free medicines and the policy for reimbursement were politically sensitive issues. After the election of 1998, as they promised during the election campaign, the government removed the 50c prescription charge. Some time later the same government implemented a change in the policy for entitlement. The list of drugs on the Schedule II 'Pink Card' was restricted to formulary drugs without a protocol, rather than to all the drugs available within the NHS as it was before. However patients (Schedule II, 'Pink card' holders) already started on non-formulary drugs were allowed to continue to receive them. There was no consultation over this amendment and it resulted in a number of anomalies.

Some consultants still submitted requests for non-formulary drugs for Schedule II 'Pink card' holders. They insisted that it was not within their remit to inform patients of the change in the policy for entitlement. Health care professionals argued that this policy was discriminatory to implement at a fixed point in time as it led to inequity for new patients. A working committee was set up to investigate alternatives and to make recommendations for the review of the system for entitlement to free medicines. A document was finalised by mid-2000 and was presented to the Minister of Health and the Minister of Finance. No action had been taken by the end of 2001.

The proposals for the revision of the current policy for the introduction of new drugs were discussed with the DG and were accepted. This revised 'policy for the introduction of new drugs of 1999' was circulated to all concerned and it was strictly implemented by the DTC with strong and consistent support from the DG.

The court case regarding taxanes (case 8) supported the 'policy for the introduction of new drugs of 1999' and did not consider it to be discriminatory, although an appeal ruling is still pending. Following the court case there was renewed support for implementation of the policy and whenever there was pressure on the DTC to bypass the policy, the court case was quoted.

The revision of the formulary was to proceed in line with the policy of 1999. The formulary was to include all the drugs available on the NHS. Drugs that were not listed on the revised formulary were not available within the NHS and needed to be officially introduced through the new procedure for introduction of new drugs. Thus following the revision, drugs were either on the formulary and therefore available to

all patients who fitted the protocol or they were not on the formulary and not available. The 'non-formulary' category was removed.

Following the new 'policy for the introduction of new drugs of 1999', it was still mandatory to set protocols for all new drugs. The DG insisted that he was still the service provider and therefore set the policy for implementation of drug protocols. When the hospitals become autonomous they would become responsible for monitoring of prescribing and for the restriction of costs. Accordingly the DG stressed the need for prescribing according to protocols.

Some consultants viewed drug protocols as informative but did not consider them prescriptive or mandatory. Implementation of prescribing policies was therefore a major point of contention. There were frequent incidents in this regard, for example the DTC encountered requests with information that the prescribing was according to protocol and then on checking the patient's file found that it was not. In such situations the requests were sent back to the consultant with a note of refusal and no further action was taken. Due to time constraints it was difficult to check more than a few requests against individual patient files. However, this type of monitoring created antagonism between the consultants and the DTC.

The policy for the use of samples within the NHS was discussed at several DTC meetings. With the greater awareness of medicines registration there was increased concern of legal liability. The Health Division was concerned that if samples were used within the NHS and something happened to the patient, the Health Division could be sued. Consent forms were therefore suggested as a safeguard. The DTC

considered that enforcing a policy to prevent the use of samples would have created a lot of antagonism with the consultants and industry and recommended that the use of samples was allowed as long as it was at the full responsibility of the consultant concerned. By the end of December 2001 the policy for the use of samples was not yet finalised. Questions about the legal issues remain answered.

The draft of the National Drug Policy (NDP) Document for Malta that was presented in May 1998 was shelved mainly because all resources were concentrated on developing EU legislation. The setting up of the NMPAU in mid-2001 created the opportunity for the setting of a NDP for Malta. Support for the setting of a NDP was obtained through the Biennial Collaborative Agreement between the Ministry of Health in Malta and the World Health Organisation (WHO) for 2002 – 2003. The support of the WHO was considered beneficial to provide expertise for the setting of the policy and also for the drafting of the final document. Participation of foreign experts at seminars in Malta was recommended to help the introduction of particular policies considered to be politically sensitive. This is ongoing and it is planned that the process for setting the NDP will include consultation with all relevant stakeholders.

5.4.2.3 Change in the processes for the selection of new drugs into the NIIS

The action research supported a cyclical process of reflection and action to enable gradual improvement of the processes for the selection of new drugs into the NHS in Malta. An increased input to the decision process during DTC meetings was maintained through the incorporation of objective information by the secretariat and

through intervention by the chairman and the secretariat during discussion at meetings.

One of the first challenges was to include evidence that would support decision-making. When the Internet became available within the GPS in 1999 information was much more accessible. The main constraint was that of time, as the time for compilation of summary information was limited. During the compilation of the information for paclitaxel and docetaxel extra effort was put in because of the ongoing court hearings (case 8). This experience focused the pharmacists of the DTC secretariat on the need for concise, up to date, evidence-based information to support the decision making of the committee.

During the action evaluation, information on the EU registration of the drug for the indication for which it was requested was considered. This policy pre-empted the introduction of a registration system in Malta in line with EU registration. On the other hand not all drugs that were registered within the EU were reimbursed in Malta. Some consultants complained that EU registration should not be taken into account at this stage (not mandatory yet) and felt that this was just an excuse to reject their requests.

Most of the requests for new drugs were for drugs that had been licensed within the EU for quite some time and were not yet available within the NHS in Malta. Only 27% of the drugs considered during the prospective follow-up were approved by the centralised procedure of the EMEA. Medical representatives were usually asked to

submit the licensing information of the products that were not licensed through EMEA. The information from EMEA was also available on the website.

Consideration of the status of registration of the product within the EU gave an insight to problems that could be encountered with the introduction of registration in Malta. Some products were being imported in Malta in export packs and the indications listed on the package insert of the export pack were not in line with those on the summary of product characteristics. Moreover some products were not licensed for the same indications in all countries of the EU.

Another new policy adopted for the process of selection of new drugs into the NHS was that of approval of therapeutic classes rather than of particular drugs. This policy was mainly promoted by the secretariat of the DTC. The chairman of the DTC and the members frequently supported it. The main aim of this policy was to increase cost-effectiveness, because there was more competition at the level of drugs within the same therapeutic group. This policy counteracted the exclusivity of the local agents in the tendering process. It also favoured the supply of generic products. On the other hand this policy introduced the problem of having to determine the therapeutic equivalence between different drugs in the same therapeutic class and also the problem of the possibility of having a different drug on the formulary every three years (with every new tender). The main opposition to this policy came from the pharmacists in the national formulary management section of the GPS, because they considered that this policy was going to complicate the adjudication process for them. At times medical representatives questioned the criteria for therapeutic equivalence used by the DTC for the comparison of products.

If a drug had an established use, it was more likely to find information and established guidelines for its use, such as the availability of guidelines from the Scottish Intercollegiate Guidelines Network (SIGN). Most of the consultants in Malta studied their speciality in the UK and therefore follow the UK system of practice. Guidelines from official organisations were often amended and used by the consultants and by the DTC to set local guidelines.

The setting up of a template for protocols helped to standardise the information presented in the protocols and to ensure that key points were not missed. The template was prepared from the information collected in the descriptive evaluation and was used routinely during the action evaluation. The template was updated when considered necessary. For example during the introduction of sirolimus it was realised that the template did not include requirements for therapeutic drug monitoring, and these were subsequently added on. Although most of the protocols specified that there was to be monitoring of treatment with protocol-regulated drugs and that approvals of new drugs were granted on condition that there needed to be regular feedback about the outcome of treatment, monitoring was not being conducted. From July 1999 to the end of December 2001 there was only one report on the outcome of treatment with a protocol-regulated drug.

Pharmacoeconomic studies, were occasionally submitted with the requests for new drugs. These were generally compiled by the pharmaceutical industry and were of limited use as they did not take the perspective of the NHS in Malta. The cost-effectiveness data presented by the secretariat at the DTC meetings reflected the projected impact to the NHS such as whether a drug was additional to the NHS or if it

replaced another drug. The secretariat of the DTC did not have time and resources to do detailed modelling of treatment and outcomes, but it was clear that any projections had to take account of the local situation. From experience, when one drug replaced another, although the consumption of the new drug started to increase as soon as it was available, there was a time lag before the consumption of the replaced drug started to decline.

The process of selection of new drugs had to be done within national policies such as the policy for entitlement to free medicines and needed to consider local prioritisation for the allocation of the drug budget. The members of the DTC consistently resisted the consideration of prioritisation and of allocation of resources whenever this issue was brought up during the discussion for the selection of new drugs. Most of the members of the DTC felt that their remit was 'clinical' and it was up to the DG to decide on rationing.

The members of the DTC also found difficulty in discussing certain criteria of cost-effectiveness. This was a difficult concept to apply in practice. Consultants considered it to be unethical to decide whether it was worth paying so much money to save so many months of life. At times when the chairman of the DTC and the secretariat brought up elements of cost-effectiveness during the discussion there was direct opposition from the other members of the DTC.

Since 1998 none of the members of the DTC had voluntarily declared a potential conflict of interest. During the change process it was not deemed feasible to enforce such new measures on the members of the committee because they had been on the

committee for a long time and they may consider such measures to be threatening. However, if a new committee was to be set up, principles such as declaration of potential conflict of interests should be applied from the beginning.

In the prospective follow-up of requests discussed by the DTC from July 1999 to December 2001 the number of requests that needed to be reconsidered following additional information was increasing, causing a rise in the work of the DTC secretariat. The detailed comments and/or responses to DTC recommendations by the DG were used to build a baseline and increased awareness of all the required information prior to the meetings. The secretariat often had to keep chasing consultants to send the required information. Medical representatives and patients also tried to exert pressure to hasten the process.

Availability of data on the websites of organisations such as EMEA and NICE caused some problems to the secretariat of the DTC. There were instances where the secretariat did not have enough time to keep abreast with all the updates on these websites. Keeping up to date entailed dedicated time for browsing. There were instances where the patient was aware of additional information on a particular website before the secretariat of the DTC. For example in the case of imatinib (case 9) a patient knew that the appraisal by NICE was finalised before the secretariat realised this development. This patient even contacted NICE directly.

5.4.3 Description of the processes for the managed entry of new drugs into the NHS in Malta as in December 2001

The information from the methods used in this evaluation was used to construct a new logic model to represent the managed entry of new drugs into the NHS in Malta as in December 2001. This model, 'Descriptive model 2', is presented in Table 5.6 in the same way as 'Descriptive model 1' was previously (Chapter 3). The main changes in 'Descriptive model 2' as compared to 'Descriptive model 1' are highlighted.

Table 5.6 'Descriptive model 2' of the managed entry of new drugs into the NHS in Malta as in December 2001

Resources		Activities	Outputs	Customers reached	Outcomes
Structural and human	Inputs to support				
Local agents	National policy for clinical trials did not exist. New legislation (being drafted) will contain provision for clinical trials.	Promote new drug to consultants.	Consultants are informed of new drugs and are encouraged to prescribe new drugs.	Consultants	Consultants request that the drug is introduced within the formulary of the NHS.
Medicines Regulatory Unit (MRU) (replaced the MRAU and is independent of GPS)	Keep database of CPP's. No adverse drug reaction (ADR) reporting system.	Submit a certificate of pharmaceutical product (CPP) to MRU . Issues license to agent to enable importation. Database of licensed drugs maintained.	MRU give receipt for CPP. Agent gets license.	MRU Local agents	Agent gets license to import the drug.

Changes in 'Descriptive model 2' from 'Descriptive model 1' are highlighted in bold.

CPP= certificate of pharmaceutical product; MRU= medicines regulatory unit; MRAU= medicines regulatory affairs unit; GPS= government pharmaceutical services

Table 5.6 Continued

Resources	Inputs to support human	Activities	Outputs	Customers reached	Outcomes
Government/Minister for Social Security in discussion with Minister for Health	Entitlement to free medicines governed by legislation and implemented through the Schedule V list and through the Schedule II 'Pink card' system. Drugs available to 'Pink card' holders were restricted to formulary drugs without a protocol. Prioritisation through ad hoc decisions by DG.	Political support for update of entitlement criteria. Enforcement	Only drugs listed on the formulary are provided free, based on disease (Schedule V) and / or personal entitlement (Schedule II 'Pink card'). Drugs that are not on the formulary are not provided through the NHS.	Consultants DTC Pharmacies Patients	NHS provides free drugs that are not protocol-regulated to all entitled patients. Protocol-regulated drugs are available on Schedule V only. Protocol-regulated drugs are supplied on a named (individual) patient basis.
Consultants within the NHS	Policy for the introduction of new drugs revised in 1999. The formulary contains all drugs available within the NHS. Protocols and guidelines for prescribing new drugs contain more information	Consultant makes request to DTC for new drugs to be included on formulary. Drugs are approved on a named-patient basis only in exceptional cases.	The request is sent to DTC secretariat. No formal confirmation of request is given to consultant.	DTC secretariat no longer within GPS, now forming part of the NMPAU.	DTC secretariat presents the information including the licensing status of the drug within the EU and evidence on efficacy, clinical- and cost-effectiveness of the drug as available.

Changes in 'Descriptive model 2' from 'Descriptive model 1' are highlighted in bold.

DG= Director General; DTC= Drug and Therapeutics Committee; NHS= national health services; EU= European Union; NMPAU= national medicines policy and audit unit

Table 5.6 Continued

Resources		Activities	Outputs	Customers reached	Outcomes
Structural and human	Inputs to support				
DTC		Considers information including licensing status of the drug. Minutes of DTC meetings are sent to DG.	DG ratifies or rejects decision or requests further information before making decision.	DG	Drug is approved, rejected or decision left pending.
DG	Drug budget allocation. Formulary being revised	Reimbursement within NHS for new formulary drugs always linked to a protocol.	Drug is added to formulary. Protocol-regulated drugs are approved on the formulary and supplied on a named-patient basis.	DTC	
DTC		DTC notifies GPS of approval.	GPS start procurement for drug or therapeutic class as appropriate.	GPS	
GPS		Tenders arranged in order of price within therapeutic class for equivalent doses.	Lowest price with CPP accepted.	Local agent/ foreign wholesale dealer	GPS source the product through a tendering process. Some tenders are issued with open specifications for a therapeutic class.
Local agent/ wholesale dealer		Importation of drug.	Drug supplied to GPS.	GPS	GPS receives drug

Changes in 'Descriptive model 2' from 'Descriptive model 1' are highlighted in bold.

DTC= Drug and Therapeutics Committee; DG= Director General; GPS= government pharmaceutical services; CPP= certificate of pharmaceutical product

Table 5.6 Continued

Resources		Activities		Outputs	Customers reached	Outcomes
Structural and human	Inputs to support GPS		GPS should inform DTC of availability of drug.	DTC may get to know that the drug is now available.	DTC	Drug available within NHS.
				DTC updates the web-formulary if appropriate.	HMMU	Drug can be prescribed for all patients who satisfy criteria of the protocol.
				DTC informs prescribers and pharmacists through a circular.	Hospital/out-patient pharmacy	
Consultant	Formulary and prescribing guidelines	Issues a prescription for formulary drug to patients. For protocol-regulated drugs a named-patient request is written.	Prescription given to patient. Request issued to hospital Medicines Management Unit.	Stock distribution.	Patient	Patient gets the drug dispensed. Patient must wait for approval of protocol-regulated drug before treatment can start. No need to wait for procurement of stock.
Hospital Medicines Management Unit (HMMU)		HMMU checks request against protocol criteria and takes advice re concerns from DTC	Letter of approval sent to patient or non-approval sent to consultant		Patient Consultant	Patient receives approval for protocol-regulated drug or patient notified of non-approval by consultant

Changes in 'Descriptive model 2' from 'Descriptive model 1' are highlighted in bold.
GPS= government pharmaceutical services; DTC= Drug and Therapeutics Committee; HMMU= hospital medicines management unit

Table 5.6 Continued

Resources		Activities	Outputs	Customers reached	Outcomes
Structural and human	Inputs to support Patient	Dispensing of drug from pharmacy.	Drug available for patient.	Government pharmacies	Patient starts treatment through the NHS.
Patient/ carer		Administration of medicine.	Patient takes the medicine as recommended by the prescriber. Patient does not comply.	Patient	Aim is improved symptoms, rational use, and health-related outcomes.

External influences:

1. Political picture: The Nationalist government that was elected in 1998 was still in government.
2. Government policy: there was progress towards EU accession in terms of new legislation, but legislation was now being drafted.
3. Policies of the Department of Health: the separation of operational and regulatory structures and functions was slow.
4. The same Director General was still in post, since February 1999.
5. National health-related policies: a National Drug Policy document was being drafted.
6. Pressures by different stakeholders including consultants, medical representatives, politicians, patients and the public still continued.

5.5 DISCUSSION

The aim of this chapter was to promote the development of a more systematic approach for the managed entry of new drugs into the NHS in Malta using an action research methodology. Action research was conducted for the period July 1999 to December 2001. A number of positive changes were achieved.

Action research is itself an intervention for change. The action research was initiated as planned and prioritised in the exercise for planning and prioritisation for change described in Chapter 4. During this action evaluation the planning was continued in line with the opportunities for change that were created. The action research progressed as a series of 'spirals' as described by Cormack (2000). The changes within different components within organisation, policy and processes progressed at different rates. At times the different reforms were slow or even static and then suddenly started to accelerate rapidly.

The action evaluation described in this chapter showed that in action research the choice of action and the way it was implemented could influence the nature of the change. As predicted from the experiences of change in other countries (World Health Organisation, 1997a) the political developments that were going on in Malta created opportunities for reforms. Action research was found to be a suitable method to bring about reforms when the opportunity became available. The case of the NHS in Malta was dynamic and interventions were adopted if considered best to maximise improvement. For example, when there was an opportunity to set up the NMPAU, the required planning and action were implemented to bring about this change.

Opportunities for change were incorporated within the planning and the action was chosen accordingly.

One of the main factors that effected the change process was the conflict that built up between the director and the pharmacists of the GPS. This rift resulted in resistance to the changes that were proposed by the director and in delay in the introduction of the EU legislation. The pharmacists at the GPS applied pressure, including strike action supported by the union. This is a good example of Lewin's force field analysis which conceptualised organisational change as a process shaped by interaction of driving forces for change with restraining forces impeding change (Garside, 1998). In July 2001, this conflict resulted in the setting up of an independent MRU and a new section, the NMPAU. Thus this conflict within the GPS catalysed a major reform which would otherwise not have been considered and had a positive impact on the action research.

The researcher was a practitioner within the practice and also a participant in the action research. Cormack (2000) explained that the fact that the researcher is part of the research situation is one of the main differences between action research and more traditional forms of research, which usually take care to ensure that the researcher is neutral and does not bias the research situation. This property of action research makes this method particularly useful as a tool for practitioners who want to bring about change in their practice. The experience of this action evaluation supported Waterman's observation and showed that carrying out action research over and above routine work was a commitment for the researcher/practitioner, particularly as it was continuous and over a long period of time from July 1999 to December 2001

(Waterman, 1996). The involvement and the subjectivity of the researcher often results in criticism of the validity and reliability of action research. Titchen explains that the validity of action research rests with the researcher's honesty and integrity and that appropriate standards of rigour against which the success of change can be assessed must be utilised within an overall research framework which remains faithful to the interests and needs of practice (Titchen, 1995). The researcher did not join the pharmacists at the GPS in their conflict with the director, as this was considered the best action in the interest of the practice.

The conflict within the GPS affected the collaboration of the pharmacists within the GPS with the research. Initially the pharmacists at GPS collaborated as participants in the research. However when the conflict developed the pharmacists at the GPS interpreted the researcher's lack of commitment to join the conflict as a mechanism to maintain the authorities' support for the research. This effected the researcher's relationship with colleagues at the place of work. This difficulty in maintaining a collaborative relationship between researcher and participants during action research was also highlighted by Meyer (1993).

The action research was written up in the form of a narrative in its contextual detail. Meyer explained that the relevance of this narrative and its validity were in the experience of the reader and in the applicability to him (Meyer, 2000). This is not the traditional way of presenting results. One of the main difficulties in the writing up is to make the personal values and beliefs of the researcher explicit so that the reader can identify them. Another problem is to keep the narrative as anonymous as possible.

In addition to the action research, other methods were used to provide information for the change process and to generate new knowledge that could be used in the planning and implementation of further change. Some methods continued from the descriptive evaluation presented in Chapter 3. The document and records research was maintained, with the difference that it was current and could therefore be used for planning future change as well as for the description. The follow-up of the activity of the DTC in relation to 'new drug' applications, allowed longitudinal evaluation. The participant observation was incorporated as part of the action research.

A number of case studies were used to demonstrate particular aspects of the managed entry of new drugs into the NHS in Malta. The information from some of the cases for example from the case for taxanes (case 8) and from the case for imatinib (case 9), both of which were anticancer treatments, converged in a number of aspects. The cases gave an insight into the implications of the changes that were occurring and enabled corrective action when considered necessary. For example, the setting of specifications for therapeutic groups rather than for specific drugs was creating problems with the procurement process (case 1, case 3, case 6) and this led to a review of the way that the specifications were set during the process for selection of new drugs.

The prospective follow-up of requests discussed by the DTC from July 1999 to December 2001 was used to bring about change in the process for the selection of new drugs. This exercise pre-empted some requirements that would need to be implemented once Malta adopted medicines registration in line with EU legislation. This prospective follow-up was also intended to generate knowledge that would be

useful in preparation for the requirements specified by EU legislation. Information was obtained about the different factors to be considered in the steps of the selection process. This information may be used to standardise the selection process and bring about further improvement. This prospective follow-up yielded much more information than the previous retrospective analysis of the minutes and correspondence of the DTC described in Chapter 3.

Some data from the different methods was triangulated. Triangulation showed that there was discrepancy between what consultants had indicated in the questionnaires conducted in Chapter 3, and what they did in practice. This supported Gillham's observation that a common problem encountered in triangulation is that there is often a discrepancy between what people believed and what they did (Gillham, 2000). Although cost-effectiveness was ranked significantly higher in the questionnaire of 1999, the prospective follow-up showed that consultants did not often consider this factor when requesting new drugs. Consultants requested new drugs even if there was an alternative cheaper preparation available within the formulary. 44% of requests during the prospective follow-up were for drugs that were considered by the DTC to be equivalent to formulary alternatives. Therapeutic equivalence was a relative term and consultants and members of the DTC often interpreted the clinical significance of differences (between drugs within the same therapeutic group or for the same indication) in diverse ways.

Gillham's observation on triangulation was also confirmed by the data available on the conduct of clinical trials (Gillham, 2000). The request to conduct a clinical trial of fentanyl patches on a small number of patients for a short period of time within the

NHS in Malta demonstrated what Kessler *et al.* (1994) called 'seeding' trials. 'Seeding' trials are company-sponsored trials that serve little or no scientific purpose and which do not support the stated research goal. Although 54% of consultants (1999 consultant questionnaire) were aware that post-marketing scientific studies were a disguised form of promotion, they still embarked on 'seeding' trials. One concern was that the Ethics Committee approved 'seeding' trials as if they were clinical trials.

For organisational change and policy change it was easy to determine whether a planned change was implemented or not and whether the planned outcome was achieved. For example the policy for the introduction of new drugs was changed and no more new drugs were approved on an individual patients basis. The MRU was separated from the GPS and the two departments were totally autonomous from each other.

For the process of selection of new drugs it was more difficult to determine whether the planned change was achieved and to evaluate the outcome of any change. The plots of the measurement data for the indicators of the process for the selection of new drugs within the NHS showed that there was a significant decrease in the % of requests that were approved and in the % of requests that were decided without delay. This variation was what Deming (1993) explained as a 'special cause' variation, whereby there were circumstances not regularly present in the system that influenced variation. The qualitative information could be used to investigate what these 'special causes' were. One change that could effect these indicators was the 1999 revision in the policy for the introduction of new drugs. Since the implementation of this policy, drugs were no longer approved on a named-patient basis, but were considered to be

introduced on the formulary. The decision to include drugs within the formulary required consideration of additional factors to what had been considered previously, such as alternative drugs already listed within the formulary, difference in cost to alternatives, and possibly cost-effectiveness. A second possible reason for decreased rate of approvals was the fact that there was a newly appointed DG. Thirdly the intervention through the action research could have had an impact on the rate of approval.

The prospective follow-up provided further insight into possible causes of changes in the process for approval. Although 65% of the drugs requested were not available on the NHS, only 2% showed a major therapeutic improvement, the remaining 98% showed moderate, minor or no improvement. This information also gave an insight into the outcome of such recommendations with 24% of requests recommended by the DTC not subsequently receiving approval by the DG. Although the equivalent figure is not available before 1999, most of the requests for drugs on a named-patient basis used to be approved because they were considered on an individual level. Often reasons why the DG did not approve such recommendations included the need for justification of the increase in cost with respect to alternatives and direction for amendment of protocols, particularly with respect to details for monitoring of drug treatment. Therefore although the interventions by the new DG could effect the rate of approval and the delay in approval, all of the interventions could be justified and helped to strengthen the processes.

It is important to consider the relevance of indicators used, particularly their relation to the outcomes of the process. Although the revised policy decreased the rate of

approval, it removed the inequity that resulted from approval of non-formulary drugs and may have improved the cost-effective use of drugs. Thus the percentage of requests approved and the percentage of requests decided without delay were simply indicators of process they represented and did not reflect the quality in terms of therapeutic and economic outcomes of the process of selection of new drugs. It is recommended that outcomes that reflect the type of decisions that are made are included within the process.

The main limitation that still remained with the process of selection of new drugs was that a protocol was still being set for all new drugs approved. Although protocol-regulated drugs were now considered as formulary, a patient request still needed to be submitted to the pharmacy for each patient. In 2001 pharmacists in public hospitals vetted 27,578 individual patient requests. This volume of requests rendered the process for audit of protocols within routine work impossible to achieve. The case studies showed that the use of protocol-regulated drugs was not being monitored. This problem is a priority in the planning of further change. However the need to set up such audit to ensure the implementation and monitoring of policies for prescribing, may be difficult and slow to accomplish in practice. The pharmacists currently doing excessive administrative work should be utilised for more clinical activities that support rational prescribing and drug use. The prospective follow-up showed that 35% of requests for new drugs were considered to be useful for specific sub-groups of patients. Ideally protocols should be limited to such drugs. Moreover rather than having a patient request sent to pharmacy for vetting, alternative methods for implementation and monitoring of prescribing should be considered.

It is difficult to independently measure the impact of the action research on the managed entry of new drugs into the NHS in Malta. The case is dynamic and generated change. It is not possible to distinguish to what extent the changes were due to the action research or due to external factors, although the actions implemented did have a direct impact on the changes.

Another benefit from the action research was the information generated about the experience of bringing about the changes and about the different processes for the managed entry of new drugs. The knowledge can be utilised to inform the planning and implementation of further change in the managed entry of new drugs into the NHS in Malta and perhaps changes in other areas of healthcare. This insight into the managed entry of new drugs may also be utilised to inform the processes involved in the managed entry of new drugs into the NHS of other countries.

5.6 SUMMARY

An action evaluation was conducted from July 1999 to December 2001. The aim of this evaluation was to promote the development of a more systematic approach for the managed entry of new drugs into the NHS in Malta using an action research methodology.

Action research was implemented as an intervention to bring about change. This progressed in a series of spirals of planning and action. The action produced change, which in turn led to further planning. The changes in different processes developed at different rates. The experience of bringing about change was presented as a narrative within the context of this case study.

There was no attempt to control the case. Change was not only due to the intervention but was influenced by the dynamics of the environment and by external factors. Not all change was an improvement. It was not possible to distinguish which changes were due to the intervention, the changes that originated from external factors and what resulted from the combination of both.

Overall a number of positive changes were achieved in the managed entry of new drugs into the NHS in Malta during the action evaluation and these are evaluated and described in Chapter 6.

CHAPTER 6:

OUTCOME EVALUATION

6.1 INTRODUCTION

A descriptive evaluation of the managed entry of new drugs into the National Health Service (NHS) in Malta was conducted. Initially a 'General logic model' was developed to represent the framework for the managed entry of new drugs in countries of the European Union (EU). This 'General logic model' was used to build 'Descriptive model 1', which presented the relevant processes within the managed entry of new drugs into the NHS in Malta as in June 1999. This descriptive evaluation was presented in Chapter 3. An action evaluation was then conducted from July 1999 to December 2001. An exercise for planning and prioritisation for change was conducted at the beginning of the action evaluation and was presented in Chapter 4. During the action evaluation, which was presented in Chapter 5, action research was conducted as cycles of planning and action and served as an intervention for change. At the end of the action evaluation the managed entry of new drugs into the NHS in Malta as in December 2001 was presented using 'Descriptive model 2'. Consequently an outcome evaluation was required to describe and evaluate the changes that took place during the action evaluation. This outcome evaluation is presented in this Chapter.

As described by Ovretveit (1998) outcome evaluations concentrate on discovering the outcomes or impact of an intervention. In this research the outcome evaluation was conducted following the action evaluation. The action evaluation did not intend to

measure the effectiveness of action research as an intervention for change. During the action evaluation the aim was to achieve the best change and no efforts were made to control external factors likely to effect change. Where the opportunity arose, these external factors were influenced to support the planned change.

6.2 AIM AND OBJECTIVES

The outcome evaluation was conducted to identify and evaluate changes in the processes for the managed entry of new drugs from baseline (June 1999) to December 2001.

The objectives were to:

1. describe the main changes that happened during the period of the action evaluation
2. identify factors that supported or hindered these changes.

6.3 METHODOLOGY

The main changes that occurred during the period of the action evaluation were identified through comparison of 'Descriptive model 2' with 'Descriptive model 1'. The outcome of the changes that were proposed during the exercise for planning and prioritisation of change described in Chapter 4 was followed through 'Descriptive model 2'.

Results are presented under the headings organisation, policy and processes as before.

6.4 RESULTS

6.4.1 Organisation

A major goal was accomplished in terms of organisational change when in July 2001 the Government Pharmaceutical Services (GPS), which up to then incorporated all the pharmaceutical functions of the NHS were restructured into independent departments. The GPS remained responsible for operational functions and the Medicines Regulatory Unit (MRU) was set up, autonomous of the GPS, with responsibilities for medicines registration and pharmacovigilance. A new section, the National Medicines Policy and Audit Unit (NMPAU), was established as part of the Health Division housing the secretariat of the Drug and Therapeutics Committee (DTC) and with a remit including the National Drug Policy (NDP).

In December 2001 the system for medicines registration in line with EU legislation was still being set. The system for pharmacovigilance was still not operational. As there was no system for medicines registration, licensing for importation was still being based on the use of Certificates of Pharmaceutical Products (CPPs) issued through the World Health Organisation (WHO) certification scheme on the quality of pharmaceutical products moving in international commerce (World Health Organisation, 1997b).

The changes that were planned during the planning exercise in Chapter 4 to establish policy functions of formulary management within the national formulary management section of the GPS started progressing during the action evaluation but were reversed

when a new pharmacist was put in charge of this section. When the NMPAU was set up, this provided a new department with a focus on development of medicines policy.

The NMPAU also supported the planned developments in the remit of the DTC as a regulatory committee with responsibilities for the managed entry of new drugs into the NHS and for the setting of policies for drug use within the NHS. The action evaluation demonstrated that changes that were possible within the current organisational framework of the DTC were limited. For the DTC to be able to take up its role in the processes for the selection of new drugs to the level required by EU legislation, particularly for the implementation of the Transparency Directive (Council Directive, 1988), further organisational change, including a revision in the composition and remit of the DTC is required.

The proposed changes to ensure implementation and monitoring of medicines policy and to support prescribing within the hospitals of the NHS depended mainly on the progress of the hospitals in becoming autonomous service provider units. By the end of December 2001 progress in this area was minimal. The lack of organisational support within the hospitals blocked or compromised further changes. The DTC was still involved in functions that should have been handed over to hospitals. In spite of the new 'policy for the introduction of new drugs into the NHS of 1999', the protocols for protocol-regulated drugs and other prescribing policies were still being implemented coercively within the hospitals of the NHS. There was no alternative structure to support the implementation and monitoring of prescribing policies. This remains a key area of organisational change to support quality assurance of the processes.

6.4.2 Policy

The new medicines legislation that was being drafted 'The Medicines Act' progressed slowly, one reason being that the legal firm that was commissioned to do the work was not capable of doing the task. The MRU and the Health Division had to redraft the legislation, over and above their other duties.

During the action evaluation there were two initiatives to update other parts of the national legislation. During the exercise for planning in Chapter 4 it was recommended that the policy for entitlement to free medicines be revised. This change was considered feasible and a report was compiled by the Health Division and presented to the Minister. Although during the exercise for planning it was not considered feasible to set a national pricing policy, during the action research there was a political request for the drafting of a national pricing policy. The national pricing policy was needed to control the likelihood of an increase in the prices of medicines in Malta following the introduction of fees for medicines registration. A report was presented to the relevant Ministers. Both of these reports were still pending political approval in December 2001.

The main change in policy that was accomplished was the implementation of a new 'policy for the introduction of new drugs into the NHS of 1999'. Consequently no additional drugs received approval within the non-formulary category for specific patients. The categorisation of drugs available within the NHS was changed. All drugs that were available within the NHS were to be listed within the formulary. Some

formulary drugs were to have a protocol for use. Approval was granted for the revision of the formulary in line with these criteria.

By December 2001 the final decision for prioritisation during the process for the selection of new drugs into the NHS was still being taken by the Director General (DG) on consideration of the recommendations of the DTC. As drugs were no longer being approved for individual patients and were only approved as formulary, the demands on the prioritisation decision were increased. One particular case whereby a request for the introduction of docetaxel for the treatment of breast cancer was not approved resulted in a court hearing. The court ruling supported the new 'policy for the introduction of new drugs of 1999' and the method of prioritisation. In December 2001 an appeal of the decision was still pending.

Following the court case the Health Division became more concerned with potential problems of liability. The policy for the use of samples raised the issue of the responsibility of the Health Division when stocks of samples were supplied to patients by consultants working within the NHS. Moreover patients who were being started on treatment with samples expected to continue on this treatment, particularly if they were doing well. The DTC was pressurised to approve this continuation of treatment on the NHS. Following discussion it was decided that the use of samples within the NHS was to be stopped.

During the exercise for planning in Chapter 4, it was recommended that a NDP be set for Malta, however at that time this change was not prioritised because it was considered that all the resources would be focused on the setting up of the new

legislation. When the NMPAU was set up, the NDP was again prioritised and plans were made for the setting up of this policy.

6.4.3 Processes

The plans for change in processes in the exercise for planning and prioritisation for change in Chapter 4 focused on the process of selection of new drugs into the NHS. During the action evaluation changes were made in these processes to develop them in line with the requirements of EU legislation. These requirements included consideration of the licensing status of the new drugs requested within the EU and a need for transparency within decision making.

The action research showed that the processes for the selection of new drugs into the NHS were not isolated. During the action research it was attempted to develop links between the processes for selection of new drugs into the NHS and other processes of 'Descriptive model 1'. For example recommendations were made to support the setting of specifications for the process of procurement, particularly when approval within the NHS was for a therapeutic group, rather than for a drug. The process for the setting up of protocols for new drugs was improved and protocols were being set with the intention of supporting prescribing. Consultants from the relevant specialties were involved in the setting of protocols to ensure ownership.

As there was no system for the registration of medicines yet, requests for new drugs were still submitted by consultants working within the NHS. In an attempt to consider the essential components of the 'General logic model' the registration of the drug

within the EU started being considered as part of the process for selection of new drugs. Information on the efficacy, clinical effectiveness and cost-effectiveness (where available) of the drug was presented to support the discussion of requests. At times there was not substantial evidence of efficacy and effectiveness, even for drugs that were already licensed. The calculation of costs was generally done by the secretariat of the DTC, taking the perspective of the NHS in Malta. Pharmacoeconomic studies submitted with requests for new drugs were not found to be useful because they were usually compiled by medical representatives and emphasised the perspective of the industry. Attempts by the secretariat and chairman of the DTC to incorporate the consideration of prioritisation within the decisions of the DTC were not successful and were resisted by members of the committee.

The changes in the process for the selection of new drugs into the NHS increased the demands and the scrutiny on the process. Some NHS consultants considered that inclusion of the licensing status of products and of specific indications was an additional hurdle to the reimbursement decision. The media, patient groups and individual patients exerted pressure to get new drugs introduced within the NHS. Consultants and patients criticised the DTC when it did not recommend drugs that were licensed or drugs that were recommended by other organisations such as the National Institute for Clinical Excellence (NICE).

6.5 DISCUSSION

Ovretveit explained that some outcome evaluations have been criticised for adopting one view of what is a valued outcome, often the view of those in power (Ovretveit, 1998). Within this thesis the outcome evaluation adopted the perspective of what was considered to be the best for the practice.

The descriptive evaluation presented in Chapter 3 showed that from 1995 to 1999 there had been little change in the managed entry of new drugs into the NHS in Malta. The policy for the introduction of new drugs that was introduced in 1993 was coercively implemented, in spite of the problems of inequity and inefficiency that it was generating. This outcome evaluation aimed to identify what changes were accomplished during the period of the action evaluation and to analyse the factors that effected change. Some of the changes, for example the new 'policy for the introduction of new drugs in 1999' proceeded as planned during the exercise for planning of change presented in Chapter 4. Some changes progressed better than was originally planned. For example, the changes within the organisation of the national formulary management section of the GPS that were planned in Chapter 4 did not succeed, but better changes were achieved through the setting up of the MRU and the NMPAU as departments independent of the GPS. These changes were possible due to opportunities created through the case including political developments and the strike action by the pharmacists at the GPS. Some planned changes, for example the revision of the legislation for entitlement to free medicines, did not happen.

The case was dynamic and as such this effected the process and feasibility for change. Moreover external factors, particularly the political developments had an impact on the progression of change. As expected from observations of the effects of political reforms on changes in other countries (World Health Organisation, 1997a), the political developments in Malta supported major reform. Government policy to join the EU required the adoption of EU legislation and this resulted in need for new medicines legislation in Malta and the need to introduce a system for medicines registration. The appointment of a new DG supported major reform in policy including the revision of the policy for the introduction of new drugs and related policies such as the revision of the formulary. Having a new DG had the advantage that he was not involved in the setting of the old policies and therefore was less likely to oppose such changes. Moreover because of the increased pressures on the NHS from patients, there was increased sensitivity to issues that could lead to litigation. Therefore the inequity arising from the implementation of the policy for the introduction of new drugs of 1993 and the possibility of being sued because of the use of samples of medicines within the NHS prioritised and supported change in both of these policies.

The process for joining the EU led to major changes in Malta. Some people considered that one of the greatest advantages of Malta's joining the EU was that the country would have to adopt certain 'essential' legislation, such as medicines registration, which would have otherwise continued to be ignored or blocked. Moreover adoption of EU legislation brought about major revision in the national legislation which was well warranted. The implementation of EU legislation and the need to set supportive structure was seen by some as an opportunity for creating new

posts and positions of power. For example the planned organisational framework for medicines registration and the setting of a new Medicines Regulatory Authority were going to require a lot of financial resources and these would have to be recuperated from the fees set for the registration of medicines. The fees for registration were going to be high and this would have increased the prices of medicines for patients. The politicians wanted to set a national policy for pricing of medicines in order to control the prices of medicines for patients, before the introduction of medicines registration. It was important that any changes implemented were planned within the resources of Malta after considering the full impact of the changes. This example of the impact of the introduction of fees for registration showed that changes in one part of the system had effects in other processes within the system. Therefore the impact of changes needed to be considered at different levels within the logic model.

The overall aim of the research was to develop a systematic approach to the managed entry of new drugs into the NHS in Malta. The use of logic models the 'General logic model' and 'Descriptive models 1 and 2' demonstrated that logic models were a useful tool. The logic models enabled visualisation of the links that existed between the different processes, and the lack of association where related processes were isolated. The use of 'Descriptive model 1' and its progression during the action evaluation supported the planning and implementation of change and explicitly captured the direct outcomes of the changes as well as the impact of the changes on other processes of the managed entry of new drugs.

The action evaluation achieved some improvement towards a more systematic approach to the managed entry of new drugs into the NHS in Malta. For example,

limitation of consideration of approval of new drugs to medicines and for indications that were already registered within the EU system was expected to improve the safety and efficacy of the medicines approved within the NHS in Malta (Routledge, 1998). The improvement in the process of setting of protocols for new drugs, including the increased involvement of users, and the use of evidence for the setting of protocols were intended to support more rational prescribing. Evidence has previously shown that guidelines are most likely to be adopted in practice when dissemination and implementation strategies are multifaceted and incorporate specific features such as involvement of the end user (Grimshaw *et al.*, 1995; Feder *et al.*, 1999).

It was difficult to measure the extent and the outcome of the actions that were implemented in practice. The measurement of the impact of these changes requires long-term follow-up and needs to be studied within the environment of the case study for Malta. Moreover as medicines registration has not yet been introduced in Malta, the situation is still in flux. Although only drugs which had medicines registration were being approved into the NHS, because products were procured generically by the GPS, there was no guarantee that the products that were supplied through the NHS were registered within the EU. The document research in Chapter 3 showed that the importation of products using a CPP did not prevent problems of bioequivalence. The linkage of the logic model showed that the problem of procurement of products of insufficient bioequivalence extended down to the patients and could therefore effect the outcome of patients' treatment. 'Descriptive models 1 and 2' showed that problems within the processes depicted by these models generally effected patient treatment and its outcome.

The action evaluation confirmed aspects from the theory for change presented in the literature. The failure in bringing about minor reorganisation within the national formulary management section of the GPS and the success of the major reform that took place confirmed Berwick's recommendation that organisation change should be aimed at bringing about change of an organisation rather than change within the organisation (Berwick, 1996). The policy reform achieved confirmed that previously described by Reich (1995), for policy reform to succeed, policy makers must develop methods to understand, analyse and then manipulate the political conditions in favour of policy reform.

While during the action evaluation changes were implemented in the process for the selection of new drugs by actions from the secretariat, the chairman of the DTC and the DG there was no strategy to promote behavioural change in the members of the DTC. The changes that were implemented were mainly coercive. Although the licensing status of the drugs requested was being considered during the process for the selection of new drugs into the NHS, the members of the DTC were not really convinced that consideration of licensing was of additional clinical benefit. The members of the DTC had been in post for a long time and it was difficult for them to accept that the process for the selection of new drugs needed to be changed. The experience of the action evaluation showed that for changes in the process for selection of new drugs to be more sustained it was necessary to implement strategies that promoted behavioural change in the members of the DTC. As confirmed by the systematic review conducted by Bero *et al.* (1998), passive dissemination of information is generally ineffective at altering practice, no matter how important the issue. The resistance to behavioural change was shown in other areas of the action

evaluation. For example, there was slow progress in the adoption of implementation and monitoring of prescribing policies within the hospitals. Because of this resistance to behavioural change, when the new policy for the introduction of new drugs was implemented the DG still insisted that a request was to be submitted for each patient requiring a protocol-regulated drug.

The action evaluation showed that whilst it was relatively easy to change policy if there was support from the relevant authorities, the challenge was in the implementation of new policy. Implementation of new policy required change in behaviour or change in organisational culture, which were frequently difficult. The need for change in behaviour or in organisational culture resulted in resistance to change. For example, the court case for taxanes originated because it was considered that the implementation of the revised policy for the introduction of new drugs went against the 'national culture' which was that the NHS was to provide all treatment that patients needed. This 'national culture' was clearly evident during the interviews with patients and from the focus group discussions presented in Chapter 3. The proposals for change in the legislation on entitlement to free medicines were probably not implemented by the politicians because they were considered to be politically unfavorable and would cause opposition from the public. Even though the proposals were submitted at the beginning of the new government, when it was considered to be more politically feasible to introduce change in policy the proposed changes were still considered to be politically unfavorable. This example confirmed Reich's observation that policy reform is a political process because it seeks to change who gets valued goods in society (Reich, 1995).

The implementation of action research to change the processes for the selection of new drugs into the NHS was intended to improve these processes and make them more compatible with the requirements for adoption of EU legislation. The action evaluation pre-empted the problems that would be encountered with the implementation of EU legislation. The consideration of the licensing status of the drug and of the indication within the EU was considered by some consultants working within the NHS to be an extra obstacle. Consultants ranked licensing low when they were asked to rank factors that they considered when prescribing new drugs within the consultant questionnaire (Chapter 3). During the revision of the formulary chapter for cardiology (case presented in Chapter 5), some consultants insisted on their right to prescribe drugs for unlicensed indications. The need to consider the licensing status of drugs and the responsibilities of consultants when they use drugs for unlicensed indications needs to be more explicit.

The fact that the DTC did not approve all of the drugs that were registered by the EU was also a point of contention for both consultants and patients. Although there were no set criteria, the DTC in Malta considered cost-effectiveness as part of the decision for reimbursement. Maynard and Bloor (1997) recommended that cost-effectiveness should be considered in the UK. The authors referred to cost-effectiveness as the “fourth hurdle”, as it was considered to be in addition to the consideration of quality, safety and efficacy which are the criteria considered in medicines registration. Australia considers cost-effectiveness during reimbursement decisions, based on cost-effectiveness evaluations submitted by the industry. However the consideration of cost-effectiveness in Australia was considered to delay access to medicines (Clear and Grobler, 1998). If Malta continues to consider cost-effectiveness during the process

for the selection of new drugs into the NHS, clear criteria will be required for its determination and the process will need to be fully transparent. Another problem encountered during the action evaluation was lack of information at the time of DTC decisions for some of the drugs. Dent and Hawke (1997) also highlighted this problem.

Following the action evaluation it was planned that the processes for the selection of new drugs within the NHS continued to be managed and improved through the establishment of the NMPAU. The existence of a specific organisational structure and designated personnel to support the DTC and the new policy for the introduction of new drugs and for the setting of prescribing policies strengthened the processes for the selection of new drugs into the NHS in Malta. The main challenge for further planning for change in these processes is the implementation of EU legislation including medicines registration and the adoption of the Transparency Directive (Council Directive, 1988).

It is recommended that the composition of the DTC be revised. A new composition is required to provide the resources necessary and to meet the additional demands imposed through the implementation of the EU Directives. The decision for the selection of new drugs would have to be achieved within the set time limits and increased transparency is required for decision-making, particularly in the consideration of cost-effectiveness and of prioritisation. It is recommended that a revised composition of the DTC contains members in addition to NHS consultants such as doctors, healthcare workers, a pharmacologist, a health economist and possibly a member of the public. Once the new DTC is established, it would be of

benefit to implement interventions to inform and promote behavioural change with the final membership. Grol (1997) showed that different types of intervention can be used to promote behavioural change amongst healthcare professionals and to support the implementation of research findings in clinical practice. Oxman and colleagues concluded that although there were no “magic bullets” for improving the quality of healthcare, a range of interventions were available, that if used appropriately, could lead to substantial improvement in clinical care (Oxman *et al.*, 1995)

Now that the different pharmaceutical organisations and functions within the NHS are separate, each department will need to set a plan for further improvement. The plans for change will need to be based on the current baseline. In areas where the organisational set up, the policies and the processes are well established it is recommended to set systems for continuous quality improvement. The setting up of the organisational framework and the processes required for the implementation and monitoring of policies for rational and cost-effective use of drugs is going to be within the remit of the autonomous service providers and the personnel within them. This is going to be a major challenge for the NHS in Malta, particularly as it involves a radical change in organisational culture.

6.6 SUMMARY

This outcome evaluation described the main changes that occurred during the action evaluation that was presented in Chapter 5 and identified factors that influenced change.

Change was accomplished through the implementation of action research, which was an intervention for change and through the influence of external factors, particularly the political developments during the period, which supported reform.

The main change that was accomplished within the organisational framework to support the managed entry of new drugs into the NHS in Malta was the separation of the pharmaceutical departments of the NHS. Medicines regulation and pharmacovigilance were under the remit of the MRU. These functions were not yet fully established by December 2001. A new section, the NMPAU, was set up which was responsible for medicines policy and the work of the DTC. The NMPAU started developing a NDP for Malta.

The policy for the introduction of new drugs was changed in 1999. All drugs were approved on the formulary and the system for approval of drugs as non-formulary was stopped. Related policies including the formulary were also revised. The new DG was instrumental for this reform in policy. The proposals submitted for revision of the legislation for entitlement to free medicines and for the introduction of a national pricing policy still awaited political approval.

Some improvement was achieved in the processes for the selection of new drugs into the NHS in Malta; particularly these processes were linked to other processes to achieve a more systematic approach. It was considered that the remit and composition of the DTC needed to be revised to establish the structure to support the level of decision making and of operations required for the implementation of EU legislation. It was recommended that action should be taken to bring about change in the behaviour of the final membership.

In addition to the changes in the system for the managed entry of new drugs into the NHS in Malta presented in this outcome evaluation, the case study also aimed to increase knowledge. The knowledge generated from the case study included knowledge about the use of different types of evaluation in the developmental perspective, change management and the use of action research as an intervention for change and knowledge to support a more systematic approach to the managed entry of new drugs into the NHS. This knowledge was useful to make generalisation that could be applied to achieve further improvement in the practice in Malta and also in other countries. Further reflection on the case study methodology and elements of the systematic approach that may be generalisable to EU countries is discussed in Chapter 7.

CHAPTER 7:

GENERAL DISCUSSION

By February 1999 there was little improvement in the processes for the introduction of new drugs into the national health services (NHS) in Malta from what was previously presented (Vella, 1995). The formulary was last published in 1986. Since 1995 the policy for the introduction of new drugs of 1993 continued to be implemented coercively and no monitoring was undertaken. In the meantime most new drugs were approved as non-formulary. Non-formulary drugs were classified as either 'special' (mainly approved with a protocol that specified the department or the criteria for which the drug could be used) or as 'non-stock' (approved for specific patients). Whenever a non-formulary drug was required a request needed to be completed for each individual patient.

Problems due to the policy for the introduction of new drugs continued to increase leading to inequity and to an unsustainable situation. The most significant problem was that the approval of drugs on a 'non-stock' basis kept on increasing. There were no criteria for the processing of 'non-stock' requests and there was a high risk of external influences, leading to inequity in access to drugs through the NHS. Such external influence included lobbying by/or on behalf of individual patients and special interest groups such as the industry and direct intervention by politicians. The number of patient requests for non-formulary drugs increased from 4,596 in 1995 to 14,129 in 1998. The volume of requests for non-formulary drugs increased the administrative burden. Although the authorities insisted that the information submitted by consultants

on the requests was to be audited with the patients' notes, the volume of work involved rendered such audit impossible.

The processes for the introduction of new drugs in Malta were still isolated and there was minimal linkage with related processes. Malta still lacked a system for medicines registration and the decision for the introduction of new drugs did not consider the licensing status of indications for drugs. The legislation for entitlement to free medicines through the NHS was updated politically without consultation. The support for rational drug use was limited and the emphasis of the protocols set for 'special' drugs was to control rather than to inform prescribing.

The question for this research was whether it was possible to develop a systematic approach to the managed entry of new drugs into a NHS, using Malta as a case study. It was considered that the political developments that were going on in Malta would support reform. A case study of Malta was conducted and has been presented in chapters 3 to 6. This case study showed that it was possible to bring about improvement in the processes for the managed entry of new drugs into the NHS in Malta and a more systematic approach was achieved. Following this research, the changes will need to continue to develop.

One of the greatest criticisms of case study research is the level of generalisability of the case study findings (Yin, 1994). Cormack (2000) explained that the aim of case study research is to make a generalisation based on the plausibility of the link between the characteristics of the phenomena being studied.

7.1 THE CASE STUDY OF MALTA

The development of a systematic approach to the managed entry of new drugs into the NHS in Malta required major revision of the processes that were in place in June 1999. Research coordinated by the World Health Organisation (WHO) Action Programme on Essential Drugs studied the experience of developments in the National Drug Policies (NDPs) in 12 developing countries. WHO set out to identify strengths, weaknesses and political dimensions of pharmaceutical policy formulation and implementation within each country. The WHO study showed that radical changes were more likely to happen when there were political windows of opportunity and change in the global political environment. When such opportunities presented themselves it was possible to implement quick and widespread reforms (World Health Organisation, 1997a).

Malta had just had a change of government in September 1998 and the developments that followed the election were therefore considered to be conducive to change. The nationalist government that was elected in September 1998 had a mandate for European Union (EU) accession. Malta therefore started the process of adoption of EU legislation, part of which specifically provided for a system of medicines registration. Moreover the government had a policy of decentralisation of service provision to hospitals and the development of a regulatory function within the Health Division. In addition a new Director General (DG) was appointed in February 1999.

The processes for the managed entry of new drugs were studied within the environment of the 'case' that is the NHS in Malta. As the case was difficult to

specify and was likely to change whilst the evaluation was being conducted, particularly as an intervention for change was being implemented, a developmental evaluation was done. The evaluation was conducted in three steps (pre, during and post intervention). A descriptive evaluation was conducted pre-intervention, which incorporated an evaluability assessment. The evaluability assessment involved the identification of common processes within the framework for the introduction of new drugs into NHS in countries of the European Union (EU) and the presentation of these processes using a logic model. The descriptive evaluation used a logic model to describe the processes for the managed entry of new drugs into the NHS in Malta as in June 1999 and identified the main problems with the processes in place at that time (Chapter 3). Consequently, an exercise of prioritisation and planning for change was conducted (Chapter 4). This was followed by an action evaluation, which was conducted for the period July 1999 to December 2001 using action research as an intervention for change (Chapter 5). The change was then evaluated using an outcome evaluation (Chapter 6).

It was not possible to distinguish whether the changes were solely due to the intervention (the action research), or external factors or both. In most instances the changes were due to a combination of these factors. The evaluation was not intended to determine the effectiveness of the action research in isolation. The action research had an impact on the change process mainly through the planning for change and also through the actions implemented. The external factors supported and catalysed the changes.

From the time of the study by Vella (1995) to June 1999 there had been little change in the processes for the managed entry of new drugs in Malta and the descriptive evaluation showed that no systematic approach existed at that time. Major components of the system were missing, for example there was no system for medicines registration and where processes did exist they were not linked. The outcome evaluation in December 2001 showed that change had been achieved in organisational, policy and processes. Moreover there was an increase in the linkage between different processes making the approach more systematic.

The most important policy change achieved was the new 'policy for the introduction of new drugs of 1999'. This new policy allowed drugs to be approved within the formulary but no longer as 'non-stock'. Approval of drugs on an individual patient basis was limited to exceptional cases. This policy of 1999 served as a catalyst for changes in other policies. The formulary (which was last published in 1986) was to be revised and published on the intranet. This new 'policy for the introduction of new drugs of 1999' was supported during the court case for docetaxel (case 8, Chapter 5).

The main organisational change achieved was the separation of the functions of the GPS and the setting up of the National Medicines Policy and Audit Unit (NMPAU). The prospective follow-up of requests discussed by the Drug and Therapeutics Committee (DTC) from July 1999 to December 2001 that was conducted during the action evaluation, generated information which was used to improve the processes for the selection of new drugs into the NHS. These can also be used for further development of this process in line with the requirements set by EU legislation and in coordination with other related processes.

The setting up of the NMPAU was considered to be a major change in support of the development of a systematic approach for the managed entry of new drugs into the NHS in Malta. The NMPAU was also responsible for the setting up of a NDP for Malta. The need to extend the systematic approach from the area of the managed entry of new drugs to other fields of pharmaceutical policy was forthcoming. As illustrated by the logic model the different areas of pharmaceutical policy are linked together and are interdependent.

7.2 FACTORS FROM THE CASE STUDY OF MALTA THAT INFORM CASE STUDY RESEARCH AND DEVELOPMENTAL EVALUATION IN HEALTHCARE

Gillham (2000) highlighted that one of the properties of the case study is its specificity and defined a 'case' as "a unit of human activity embedded in the real world, which can only be studied or understood in context, which exists in the here and now, that merges in with a context so the precise boundaries are difficult to draw". The political changes, the reforms within the NHS and the external pressures from the industry and patients were an integral part of the case in Malta and were incorporated as part of the case study. It was not possible to control the case. The change process and the intervention for change were conducted within the environment of the case. Where applicable, the reforms and external factors were used to catalyse the process for change. On the other hand where reforms and external factors were considered to cause difficulties in the process of change, action was implemented where possible to counteract these problems.

Norris (1998) conducted a retrospective case study to show the effects of the introduction of EU legislation on the national legislation in Norway. Because the case study was conducted in Norway, most of the issues discussed were specific to Norway. The national legislation in Norway was totally different from the national legislation of Malta and therefore the details discussed in the case study of Norway did not apply to Malta. Similarly, the case study of Malta identified a number of characteristics that were specific to Malta. These included the small size of the population of the island, the lack of major pharmaceutical industry, the political and organisational culture. In addition the system for reimbursement in Malta involved no co-payment and was implemented through a positive list and a centralised system for the procurement and distribution of medicines through the NHS which was unique.

The case study has been found to be ideal to study the complexity of real life phenomena. Ovretveit (1998) explained how the type and design of the evaluation needed to be chosen according to the phenomenon that was being evaluated. The developmental perspective in evaluation is appropriate for evaluating certain types of phenomena such as services, policies, health reforms and interventions to organisations where other types of evaluations such as experimental or economic evaluations are often not possible (Ovretveit, 1998). Both the case study of Norway and the case study of Malta describe a reform within a real life complex system and use a developmental evaluation. In the case study of Norway, Norris (1998) used the descriptive case study method which was conducted retrospectively. The case study of the managed entry of new drugs into the NHS in Malta was aimed at bringing about change and therefore an action evaluation approach was used. The case study of Malta

was therefore conducted prospectively allowing an intervention (action research) to be applied to bring about change within the case.

Plsek and Greenhalgh (2001) described most health care systems as complex adaptive systems with boundaries that are not rigid. Plsek and Greenhalgh explained that the management of complexity was important for the implementation of improvement in healthcare as most systems were complex and therefore needed to be defined. The complexity of systems can also make problem solving more difficult and may lead to unexpected actions in response to change (Plsek and Greenhalgh, 2001).

The 'managed entry of new drugs within the NHS in Malta' was a complex system. In order to perform an evaluation the system needed to be represented. The experience of the description of the complex system and its application for bringing about change in Malta could be useful to other researchers planning developmental evaluations. The research on NDP by WHO described above (World Health Organisation, 1997a) used two main research tools: standardised NDP indicators for assessment of NDP performance and political mapping for the analysis of NDP formulation and implementation processes. The literature described the use of logic models as a tool to schematically describe programmes (Chapter 2). Dwyer and Makin (1997) explained how logic models are used to provide an evaluability assessment (to assess whether a programme is evaluable) and to integrate programme planning and evaluation. Although the logic model was derived from the field of management it has also been used in healthcare (Julian *et al.*, 1995).

In the case study of Malta, the logic model was shown to be a versatile tool and particularly useful for the inductive approach of the developmental evaluation. The first step of the evaluation necessitated an evaluability assessment to confirm the feasibility of describing the complex system and to direct the description of the managed entry of new drugs into the NHS in Malta at baseline before the introduction of the intervention. The information on the situation in EU countries from the literature was used for the evaluability assessment. A logic model of the general framework for the managed entry of new drugs into the NHS in Europe was outlined and the main processes and the interactions between them were identified. Although as described by Kanavos and Mossialos (1999) the 15 national markets of the EU countries are very different, the general framework adopted by the countries is quite standard. This logic model from the literature, the 'General logic model' was not considered to be prescriptive, but was used as a starting point to build the descriptive model for the managed entry of new drugs into the NHS in Malta as in June 1999.

The logic model approach managed to provide an overview of the complex system identifying the organisational structure, the resources and the processes involved. This model also collected information on the 'logic' that showed the linkages between the different processes. For the practice of the managed entry of new drugs into the NHS in Malta the lack of a systematic approach was considered to be a major problem. The fact that the logic model explicitly showed the links involved in the system was considered to be a major advantage of the logic model over the use of indicators (World Health Organisation, 1997a). Whilst an indicator showed if a particular organisational process was present or not, the logic model provided additional detail of how such processes were linked to the process of selection of new drugs into the

NHS. A system for medicines registration was one of the processes which influenced the process of selection of new drugs into the NHS. These links formed the basis for planning and prioritisation of the required changes, which were to be implemented during the action evaluation.

7.3 THE USE OF ACTION RESEARCH AS AN INTERVENTION FOR CHANGE

Research suggests that most quality improvement interventions have highly variable effects that depend heavily on the context in which they are used and the way they are implemented (Walshe and Freeman, 2002). Action research was chosen in preference to other interventions for change specifically because the problems identified before the intervention was planned showed that reform was required. Systems for quality improvement could only be introduced once the processes were in place. Moreover it was considered that the opportunities for change that existed within the case supported reform. By December 2001 a number of major improvements were achieved. In the areas where reform was accomplished for example in the GPS and in the NMPAU the next step will be to introduce systems for continuous quality improvement. The experience of the action research will be used to inform choice, suitability and the application of action research as an intervention for change.

Walshe and Freeman (2002) suggested that the approach to quality improvement used in an organisation probably mattered less than how and by whom it was used. It was recommended by Walshe and Freeman that organisations should choose an intervention carefully and then persevere to make it work. Walshe and Freeman

proposed that future research into quality improvement interventions should be directed more at understanding how and why they work rather than measuring whether they work (Walshe and Freeman, 2002). Although these recommendations by Walshe and Freeman were made when the case study for Malta was finalised, they support the methods used within the action evaluation. Once action research was chosen as the intervention for change, it was maintained throughout the action evaluation because it was considered to be a versatile intervention that could respond to different types of opportunities for change.

Theory for change stresses on the need to aim for the achievement of major change rather than limited changes (Berwick, 1996). During this action research there were a number of opportunities that supported major change. Without these opportunities the possible changes during the action evaluation would have probably been limited to minor improvements in the processes for the selection of new drugs. The main external factor that supported change was the election of a new government in 1998. This government had an agenda for EU accession and for the decentralisation of NHS provision that dictated division of regulatory and operational functions. A major internal factor that supported change was the appointment of a new DG who was prepared to take changes beyond what was originally planned for the action evaluation. The rebellion within the GPS led to more ambitious change than anticipated, for example it created an opportunity for the setting up of the NMPAU. The benefit of the use of multiple actions in parallel was demonstrated within the case study.

Van Harten *et al.* (2000) noted that various features of the organisation can influence the development of the quality management system and suggest that it is necessary to provide for analysis of the influences from the environment and the interaction with the technology. The aim of the action evaluation in the case study on the managed entry of new drugs into the NHS in Malta was to implement an intervention to bring about reform in the practice that was quick. The research did not aim at evaluating the effectiveness of action research as an intervention and external factors were considered as part of the planning for change.

Van Harten *et al.* evaluated the introduction of a quality management system through a case study in a large Dutch rehabilitation hospital. The experience of this evaluation showed that the introduction of a quality management system (QMS) could be seen as a change process. The development of the QMS led to the conclusion that there was no well defined QMS to fit any kind of organisation. Just as in the case study for Malta, the case study in the Dutch rehabilitation hospital found that it was essential to conduct a pre-change diagnosis (van Harten *et al.*, 2002). Sluijs *et al.* (2001) found that some quality management activities are more closely related to the effectiveness of quality management than others. Cyclical quality improvement procedures, human resource management and the flexible attitude of employees showed the strongest relationship with improved quality management (Sluijs *et al.*, 2001). As shown through the case study for Malta action research was conducted in cycles of planning and action that could be timed and adapted in response to the opportunities for change.

The conceptual framework of theory-practice development described by Cormack (2000) was clearly demonstrated during the course of the action research. The

identification of a problem brought about planning, the planning decided upon the best action, the implementation of action brought about change, the change generated knowledge that was used for further planning. For example, the fact that there were over 14,000 requests for non-formulary drugs was identified as a problem. Planning for change showed that the approval on a named-patient basis was leading to inequity and inefficiency and that the best action was to reform the policy for the introduction of new drugs. It was unpredictable whether the DG would accept this planning for major reform. In fact the DG went further and set a new policy that specified that drugs were no longer to be approved outside the formulary. Once the policy was set the content was used to plan its implementation (the next cycle).

Although the planning of change was specific to the case, the principles adopted and the factors considered may be applicable to other action evaluation. The questions from the model for improvement by Langley *et al.* (1992) were used for the planning of change. The applicability of the individual questions varied depending on the change that was being considered. The questions were answered considering the theory for change and the evidence on effectiveness of different actions and different ways of implementing them, when and if such evidence was available. The process for prioritisation also considered the feasibility of change within the situation in Malta and the factors (internal and external) within the case that affected such change.

Watermann (1998) suggested that a strength of action research that demonstrated its validity was that the method addressed the tensions and difficulties that arose in practice. The action research of the managed entry of new drugs into the NHS in Malta demonstrated a number of difficulties that arose in practice. The changes

implemented by the director of the GPS to support the process for the introduction of EU medicines registration were not part of the planned intervention of the action research. However these changes were met by major opposition from the pharmacists within the GPS. This phenomenon is clearly explained by Lewin's force field analysis which conceptualises organisational change as a process shaped by the interaction of driving forces for change with restraining forces impeding change (Garside, 1998). When the director tried to alter the 'equilibrium' by bringing about change, the reaction of the pharmacists at the GPS was strong enough to shift the position to a new equilibrium which was different from that planned by the director. Ideally before implementing any change the new position should be agreed by both sides, but in practice this balance is often difficult to achieve.

The actions employed for change depended on process that needed to be changed, the improvement that was planned and the feasibility of applying the action. During action research the use of the Plan-Do-Study-Act (PDSA) cycle (Langley *et al.*, 1992), was found to be applicable for the implementation of certain actions but less appropriate to others (Chapter 4). As explained by Berwick (1996) the PDSA cycle describes inductive learning whereby an action is tested in the real world setting before it is employed. The PDSA cycle was found useful for implementing action in the processes of drug selection because the processes were cyclical and repetitive and therefore allowed the testing of the action in the real world setting. An action (for example inclusion of information on cost-effectiveness of alternative drugs) could be planned, studied and implemented for one drug. The knowledge gained from this cycle (for example the need to set the costs for equivalent treatment regimens) could be utilised when presenting the request for another drug.

For change in policy or change in organisation it is not possible to test the action. Before introducing new policy, the details should be discussed with various stakeholders, however once the policy is published it is difficult to make further changes, therefore implementation needs to be standardised. In the case of organisational change, there is little opportunity to take an action and to study it in practice before it is implemented, particularly for major changes. Once the change is implemented it may still be possible to learn from it and to apply this knowledge and experience the next time that a similar change is implemented, but such changes are not undertaken routinely.

Cormack (2000) described the flexibility and unpredictability of the process of action research. These attributes were clearly demonstrated by the action research for the managed entry of new drugs into the NHS in Malta. There were changes that started proceeding as planned and suddenly reversed back to the old situation or worse. The changes within the National Formulary Management (NFM) section within the GPS started progressing and suddenly reversed when a new pharmacist was put in charge. During the planning of this change it was known that the planned change was not really the ideal one, but this was the only feasible proposal. The theory of organisational change specified that it is necessary to bring about change of a system rather than change within a system (Berwick, 1996). However the only way of creating technical support for formulary management (which was a high priority for change) was through the reorganisation of the NFM section. When this change was halted by the new pharmacist in charge all progress on the formulary stopped. Some changes or opportunities for change were created by external factors. During the exercise for the planning for change major reorganisation and division of the GPS was

recommended. However, this change was not prioritised and the feasibility of this change ranked low because it was highly opposed by the Director of the GPS. When through the action of external forces this change became feasible, the planning was reconsidered and an intervention was implemented so that in addition to the sections for regulation and for operations, a third section was set up for medicines policy.

7.4 THE USE OF THE CASE STUDY FOR MALTA TO INFORM THE SYSTEMATIC APPROACH TO THE MANAGED ENTRY OF NEW DRUGS INTO NHS

In 1992 Norway signed the European economic agreement (EEA) and thus formed part of the European internal market. Norris (1998) presented a case study for Norway and explained the problems faced by this country when it had to implement EU legislation into its national legislation. Although the specific details of the case study by Norris were only applicable to Norway, the insight obtained from this case study was useful to a country such as Malta that was preparing for EU accession. In the same way the case study for the managed entry of new drugs into the NHS in Malta could generate knowledge that would be applicable to EU countries and to EU accession countries.

The literature contains mixed views on the benefits of a single market for pharmaceuticals. Markets inside the European Union and in other European countries are still quite heterogeneous (Kanavos and Mossialos, 1999). The organisation of the demand side and the purchasing processes are highly dependent on the existing financial schemes for health care services (World Health Organisation, 2000). Patients

may have different demands for the same problem and the cost of distribution of medicines varies from one country to another (De Pourville, 2001).

During the evaluability assessment of the case study for Malta (Chapter 3), a general logic model was developed to describe the managed entry of new drugs into NHS's in European countries. This logic model demonstrated that in spite of the heterogeneity between pharmaceutical markets in different European countries, there was a common general framework for the managed entry of new drugs into the NHS. This logic model illustrated that the managed entry of new drugs into NHS consisted of a main process – the process for selection of new drugs – which was linked to a number of other processes within the national pharmaceutical policy. The system for medicines registration and policies for pricing and reimbursement acted as inputs to the process of selection of new drugs into the NHS. The main output of this process was cost-effective use of the resources and rational use of the medicines supplied through the NHS.

The case study showed that Malta needed to develop a systematic approach to the managed entry of new drugs and to its national drug policy. A number of changes were being implemented in areas of the NDP in Malta and these needed to be coordinated to ensure that they all had a common goal. The establishment of the national medicines policy and audit unit in July 2001 provided the organisational structure and the required resources for the setting of a NDP. The Health Division in Malta embarked on the setting of a NDP.

Although NDPs were originally used to improve pharmaceutical policy in developing countries (World Health Organisation, 1997a), some developed countries have also found it useful to publish their policies in order to support a systematic approach to the use of pharmaceuticals. For example Australia, which has a well-developed system for pharmaceuticals and was the first country to include cost-effectiveness data in decisions about reimbursement (Langley, 1996), published a national medicines policy (Commonwealth of Australia, 1999a) and evaluated 'the quality use of medicines' component within this policy (Commonwealth of Australia, 1999b).

Even well developed European countries still have areas that need to be addressed within their national pharmaceutical policy and may benefit from the setting of a NDP that addressed the different areas related to pharmaceuticals systematically. Walley *et al.* (2000) made a case that the UK would benefit from a NDP. They pointed out that in the UK there were a number of policies that impinged on pharmaceuticals but there was no coherent, integrated NDP. They concluded that the lack of a single policy on drugs had caused problems, and attempts to resolve these difficulties had created new precedents and future problems, almost in the manner of case law. Walley *et al.* (2000) supported these conclusions with two examples of problems caused by the lack of a clear policy that defined national priorities based on the balance between meeting patients' needs and ensuring effective use of NHS resources in the UK. The first example was of the case of sildenafil (Viagra). Initially the secretary of state for health advised general practitioners not to prescribe the drug. The manufacturer challenged the action taken by the secretary of state in court and the outcome was that the drug was funded by the NHS for defined conditions only. The second example concerned the way in which recommendations by the National Institute for Clinical Excellence

(NICE) were made and implemented in respect of certain drugs such as zanamivir (Relenza), beta interferon and the taxanes (Walley *et al.*, 2000).

7.5 THE IMPLICATIONS OF ACCESSION INTO THE EU

The case study by Norris (1998) showed that European harmonisation obliged Norway to make major changes in its domestic legislation that were conflicting with the existing national policies and legislation. The author considered that European harmonisation represented an attempt to impose a set of policies based on a different world-view on a complex set of existing arrangements (Norris, 1998). Specific details from the case study for Malta showed that the implementation of EU legislation was bringing about major changes. EU countries already had most of the systems that were being introduced in Malta in place for a long time. For most EU countries there was a gradual build up of policies and therefore the changes followed one after the other. In the case of Norway and more so now in the case for Malta, substantial changes had to be implemented in a short time and these had to replace an existing system. This type of drastic change is difficult and needs to be managed effectively. Although accession into the EU will bring about benefits to Malta, the transition will also cause difficulties.

One of the major shortcomings identified at the beginning of the case study of Malta was that there was no system for medicines registration and for pharmacovigilance. The history of how such systems for drug regulation were developed as a result of misfortune (Routledge, 1998) were a good reason why Malta needed to introduce a system for medicines registration and pharmacovigilance.

In Malta a system for medicines regulation in line with EU directives was being introduced in a situation where there were no previous medicines regulations. During the interviews held with medical representatives in 1999 (Chapter 3), some individuals were glad that Malta did not have a system for medicines registration, because according to them registration was mainly a bureaucratic system. When the system for medicines registration was discussed, the local agents representing the pharmaceutical industry exerted pressure on the authorities and on politicians so that their perceived negative impacts of registration were minimised. One major concern voiced by the local agents was over the fees that were going to be introduced as part of medicines registration. The implications of the introduction of fees for medicines registration was also of concern from the public health perspective. The warning that small countries find the high fixed costs associated with medicines registration difficult to bear (Bennett *et al.*, 1997) was very applicable to Malta. The major sources of income for regulatory authorities in EU countries were the fees that they received particularly for reference member state status within the mutual recognition procedure (Abraham and Lewis, 1999). It was unlikely that with its limited resources and with its lack of any innovative pharmaceutical industry, Malta was going to be in a position to compete for regulatory work with the other EU countries.

Another concern from the point of view of pharmaceutical public health was that the introduction of EU medicines registration could reduce access to 'essential' medicines in Malta. A larger market size was shown to be associated with less time lag for medicines registration (Wu *et al.*, 1998). Whilst medicines licensed through the EU centralised procedure are registered in all EU countries, medicines licensed through the mutual recognition procedure are only licensed in the countries chosen by the

industry. Because of the small market size (the population is less than 400,000) drug companies may not consider it worthwhile to submit applications for medicines to be registered in Malta, particularly if Malta sets a high registration fee, and there may be reduced access to essential medicines, particularly those with a small volume of use. Within the EU legislation, once a product is registered in a country, it can be imported by anyone licensed to import medicines. After accession 'parallel importation' should be easier than the situation today. However in practice 'parallel importation' may not have a high impact on the prices of medicines in Malta because the market volume is small. Up until now the DG has made exceptions with a view to protecting the availability of essential products in Malta, for example in cases where no local agent imported a particular drug in Malta, the GPS acted as an importer. Malta can control some internal factors such as the registration fees to protect its public health. However once EU legislation is implemented, the Superintendent of Public Health in Malta is restricted to the level of exceptions and concessions that can be made to ensure that access to medicines in Malta is not compromised. The EU will need to address any specific problems arising once Malta and other small countries join the EU.

A concern within EU countries (Kanavos and Mossialos, 1999) that will need to be addressed in Malta in line with EU accession is the cross-boarder issues in the provisions of services. In the case study of the request for taxanes to treat breast cancer presented in Chapter 5, the patient had gone to the UK for a private consultation and was prescribed docetaxel, which was not available within the NHS in Malta. A number of Maltese patients go abroad, particularly to the UK, for treatment and for consultation. If a patient goes abroad privately, the NHS in Malta is not bound to continue treatment and may give an available alternative from the formulary. The

EU legislation on cross-boarder issues may lead to Maltese patients taking advantage of this legislation and of the differences between systems of health services in other EU countries to get treatment abroad.

The adoption of the EU system for medicines registration presents a number of advantages to EU countries. Five years from the inauguration of the EMEA, the new system saves member states time and effort in assessing marketing authorisation applications and ensures a homogenous regulatory policy throughout the EU. Pharmaceutical companies submit one application and avoid the procedures and bureaucracies in the 15 member states (Garattini and Bertele, 2001). Once Malta forms part of the EU, it will be able to benefit from these advantages.

The current system in Malta of having new drugs requested for reimbursement by consultants increases the possible influence of the industry on consultants. This pressure by the industry was verified through the consultant questionnaires and through the interviews with consultants reported in Chapter 3. It is recommended to change the current system where drugs are considered for reimbursement on requests from consultants. The implementation of the Transparency Directive (Council Directive, 1988) will require that medicines be considered for reimbursement as soon as they are registered.

Drug regulation in Europe may not properly support public health needs. Garattini and Bertele (2001) noted that despite the fact that the mission of the European Medicines Evaluation Agency (EMEA) was “to promote the protection of human health and of consumers of medicinal products”, EMEA was located in an industrial directorate of

the European Commission (Directorate General Enterprise) rather than the health directorate. Garattini and Bertele remarked that if public health issues were paramount, EMEA approval of new drugs would depend on their benefits to patients, and would be granted only for well-defined indications after extensive research. Garattini and Bertele (2001) highlighted concerns including the fact that the EMEA receives part of its funding from the industry, and that the composition of the Committee for Proprietary Medicinal Products (CPMP) is not homogenous and that some CPMP members advise the industry. Some of these concerns were also shared by Juillard (2002) who highlighted the potential conflict of interest that arose from having a regulatory 'industry' funded largely by the pharmaceutical industry.

The current system for reimbursement and for the control of spending of drugs in Malta, particularly the centralised supply side controls, which is one of the exceptional properties of the system in Malta, may not be acceptable to the Commission. The Commission communication on the single market in pharmaceuticals (European Community Communication, 1998) has already alluded to the fact that some mechanisms used to increase the viability of health care systems may unnecessarily distort the operations of the pharmaceutical market and lead to a reduction in the competitiveness of this sector.

7.6 GENERAL ASPECTS OF THE MAIN PROCESSES OF THE MANAGED ENTRY OF NEW DRUGS INTO NHS

Wallerstein (1997) concluded that national legislation on the financing of healthcare was difficult and slow to change. This observation was supported by the case study for

Malta. The Health Division had set proposals for the revision of the legislation for entitlement to free medicines (Laws of Malta, 1987) and presented recommendations for the setting of a new pricing policy that would safeguard the prices of medicines once medicines registration was introduced. These changes required political endorsement and were not yet implemented by the end of December 2001. The setting up of a New Medicines Act to include EU legislation in Malta provided an opportunity for a general update of national medicines legislation. The Medical and Kindred Professions Ordinance, that formed the core legislation for pharmaceuticals, dated back to 1901 (Laws of Malta, 1901) and although it was amended a number of times the setting of new legislation was needed. The case study of Malta illustrated that if the right opportunity arose (in this case the appointment of a new DG) then policies that did not require political approval, such as the policy for the introduction of new drugs, could be changed.

The lack of equity resulting from the approval of 'non-stock' drugs for specific patients as a result of the policy for the introduction of new drugs of 1993 was considered to be of great concern. Maynard (1996) explained that rationing care by rules that differed, were incoherent and implicit lead to inefficiency and inequity. The inequity in the managed entry of new drugs in the NHS in Malta was the result of approval of drugs for individual patients without standard criteria.

When a new policy for the introduction of new drugs was introduced in 1999 it specified that all new drugs be approved as formulary and that all patients who were eligible to receive them (through entitlement and in line with the set protocols) were supplied with the drug through the NHS. The Court case for taxanes did not find the

policy of 1999 to be discriminatory and accepted the fact that while the state was obliged to make 'adequate provision for medical care', it was not obliged to supply all drugs. This case is still under appeal. Moreover, the policy of 1999 was also in line with the revised concept of "new universalism" for access to health care of the World Health Organisation (WHO). This proposed that governments must ensure that good healthcare is accessible to everyone, but they should not attempt to provide all possible treatments (Brown, 1999).

In spite of the developments in improving equity within the system for the supply of medicines within the NHS in Malta, the problem of prioritisation and allocation of resources was not tackled. In December 2001 the situation with regard to prioritisation was still as described in 1999 and implicit ad hoc rationing by the DG was still being used to prioritise treatment. The literature acknowledges priority setting as a complex interaction of multiple decisions at various levels that cannot be reduced to a purely technical exercise (Leese, 1996; Klein, 1998). Although the case for public participation in difficult health care choices has been studied, no explicit set of priorities have been proposed (Stronks *et al.*, 1997).

The issue of prioritisation in terms of limited resources for the supply of medicines through NHSs is a widespread problem. Countries have tackled this problem differently. Israel adopted a system that allowed ranking of drugs according to their costs and clinical importance (Shani *et al.*, 2000). Towards the end of the 1990s 'postcode prescribing' had become a key issue for the NHS in the UK. Access to certain treatments and services differed between health authorities and controversies emerged over supply of a wide range of treatments, including beta interferon for

multiple sclerosis. England and Wales tackled this problem through the establishment of the National Institute for Clinical Excellence (NICE) in April 1999. NICE guidance was to produce a common currency of effectiveness for the NHS to inform and assist decision-making about treatment and health care at all levels (Select Committee on Health, 2002). In practice the establishment of NICE has not resolved the issue of 'postcode prescribing' which remains in the UK.

The case study of Norway (Norris, 1998) specifically mentioned the level of transparency and accountability that was required for reimbursement decisions as one of the changes that Norway had to introduce on becoming part of the European internal market. One of the main problems that will need to be addressed to increase the transparency of decision making in Malta is prioritisation. To date the DTC is still mainly considering the technical aspects of the evaluation. The problem of prioritisation and implicit ad hoc rationing by the DG that was described in 1999 (European observatory on health care systems, 1999) had still not been resolved by December 2001. It is recommended that the process for selection of new drugs into the NHS in Malta establishes clear criteria and starts addressing prioritisation as part of the recommendation of the DTC. Technology assessment must relate to such political decisions as resource allocation (Banta and Andreasen, (1990). In Malta a possible advantage is that there is only one decision for all the islands which removes the complications arising from varying decisions for prioritisation within the same country as in the UK (Select Committee on Health, 2002).

One of the main criticisms of NICE since it was set up in April 1999 was the effectiveness of NICE in tackling the problem of prioritisation. Maynard (2001)

commented that NICE had approved all new pharmaceutical products and failed to articulate a hierarchy, or league tables, of incremental cost-effectiveness. Consequently NHS expenditure was inflated and resource allocation was distorted (Maynard, 2001). Moreover there was still variation between the recommendations of NICE and those of Health Authorities. NICE recommended the use of donepezil and other anticholinergic drugs for Alzheimer's disease, whereas the South and West Committee, using similar evidence, did not. The Trent Working Group on Acute Purchasing was also cautious about these drugs (Dent and Sadler, 2002).

The action evaluation in Malta showed that the process of selection of new drugs was subject to a number of pressures. The decisions or recommendations of other committees or bodies (particularly of NICE) were frequently compared to the recommendation taken by the DTC. A source of pressure experienced during the prospective follow-up were individual patients, particularly through the court case for docetaxel (case 8, Chapter 5) and through televised interviews and appeals, the media and politicians. Moreover in Malta, there were times when the decisions of the DTC regarding the adequacy of the available evidence (particularly regarding efficacy from clinical trials, effectiveness in clinical practice and relative efficacy compared to alternatives) were questioned by consultants submitting requests. During the consultant questionnaires in Chapter 3, consultants gave a significantly higher response in favour of the consideration of cost-effectiveness. However from the prospective follow-up of requests discussed by the DTC from July 1999 to December 2001 (Chapter 5), it was evident that consultants did not prioritise cost-effectiveness.

It is envisaged that when requests for new drugs start being submitted by the industry the controversy over the interpretation of the evidence will increase. Up to now the DTC has dealt solely with applications from consultants. In Malta there are no major manufacturing companies therefore political pressure from the industry has been comparably mild. This contrasts with the situation in some other countries where the industry has a substantial financial influence. A good example of this was when zanamivir's manufacturers, Glaxo Wellcome, challenged NICE's decision that zanamivir would not be available on the NHS and threatened to take the company's research abroad. Subsequently NICE reversed its decision on the drug. In the event NICE lost much credibility within the UK and worldwide (Smith, 2000).

From the experience of the case study, it is difficult to start patients on a drug in order to monitor clinical effectiveness of the drug in patients and then expect that patients' treatment will be withdrawn if the drug is not found to be effective in clinical practice. Riluzole had been introduced into the NHS in Malta because of lobbying by the Multiple Sclerosis Society (Dunn, 1998) and was later found not to be effective (case 13, Chapter 5). The patients who were started on this treatment and wanted to continue, could not be stopped. Moreover a rigorous study carried out in the US showed that withdrawal of 12 categories of drugs with questionable efficacy in a random Medicaid sample resulted in an increase in prescriptions overall (due to substitutions) many of which were undesirable (Freemantle and Bloor, 1996).

Although it is planned that when Malta accedes into the EU the registration of the currently available products will take place over four years, it is expected that there will be a high rate of registration until all the current products are processed. All the

products licensed by the centralised procedure of the EU will be automatically registered on accession. In an exercise carried out by the national medicines policy and audit unit at the end of December 2001, there were 172 products licensed by the centralised procedure (European Medicines Evaluation Agency, 2001). Of these products: 18 were approved into the NHS in Malta, 6 were not approved and 4 were still being discussed. The drugs that were not considered for reimbursement will all need to be evaluated by the DTC.

Malta needs to continue with the process of change in the system for the managed entry of new drugs into the NHS so that it will be in a position to meet the challenge of adoption of the EU legislation. The Scottish Medicines Consortium (SMC) which was set up to provide advice on newly licensed preparations in Scotland aims to cover all the licensed preparations. In order to be able to issue recommendations soon after licensing the SMC asks pharmaceutical companies to complete a New Product Submission form ahead of the product launch (Scottish Medicines Consortium, 2002). It is recommended that the DTC in Malta establish a similar process once the system for medicines registration is introduced.

Banta (1997) recommended that within the European Union those involved in health technology assessment in different countries should come together, compare methods and results and learn from each other. Banta considered that this co-ordination may reduce waste and duplication and will help to ensure that high priority issues are tackled. Banta suggested that diversity would be a particular strength of such a group. The author noted that the existing diversity between EU countries was not understood or documented and that the relationship between health technology assessment and the

health system in different countries had hardly been examined. Banta recommended that resources should be devoted to studying the relationships between health technology assessment and health systems in the member states of the EU (Banta, 1997). The research for Malta showed that case study research is a useful methodology to study this diversity and has provided information for Malta that may be generalisable to other European countries.

7.7 SUMMARY AND RECOMMENDATIONS

In February 1999, Malta was considered to have major problems with the managed entry of new drugs into the NHS. At that time, the country was going through a period of political change, which included adoption of EU legislation in preparation for EU accession. A case study of Malta was conducted to determine if it was possible to develop a systematic approach to the managed entry of new drugs into a NHS.

A developmental evaluation was conducted. A descriptive evaluation, which incorporated an evaluability assessment, was undertaken prior to implementation of the intervention. The descriptive evaluation detailed the managed entry of new drugs into the NHS in Malta as in June 1999 and identified the main problems at that time. A logic model was used to facilitate the description. The major problem identified was that the processes did not provide a comprehensive cover of the major areas of managed entry of new drugs, in particular there was no system for medicines registration, and the approach was not systematic. The policy for the introduction of new drugs of 1993 was never reviewed, was coercively implemented without any monitoring, allowed approval of non-formulary drugs and resulted in inequity.

Following identification of the problems and factors that effected the feasibility for change within the processes for the managed entry of new drugs, an exercise of prioritisation and planning for change was conducted. This considered a number of factors including knowledge about change-management, the external factors influencing the case and the feasibility of the proposed change. The planned changes targeted the organisation, policy and the processes for the selection of new drugs into the NHS. An action evaluation was conducted for the period July 1999 to December 2001 with the aim of developing a more systematic approach to the managed entry of new drugs into the NHS in Malta. Action research was used as an intervention for change. Opportunities due to external factors were used where possible to catalyse the ongoing changes.

The changes that occurred from July 1999 to December 2001 were assessed using an outcome evaluation. A number of improvements supporting a systematic approach were achieved. The policy for the introduction of new drugs was revised in 1999 and related policies were also revised. New drugs were only approved on the formulary thus reducing the problem of inequity. The formulary and related protocols underwent revision to provide the support required for the rational use of medicines available through the NHS. Although the system for medicines regulation was not yet in place, the licensing status and evidence about the medicines was incorporated during the process of selection of new drugs.

The insight and the information from the case study of Malta were used to generalise knowledge about elements of the systematic approach to the managed entry of new drugs that were applicable to EU countries. Generalisability was achieved regarding

the applicability of the methodology used particularly case study research and the use of action research as an intervention for change and for generating knowledge. The information from the case study for Malta was applied to aspects related to the managed entry of new drugs including national drug policies, the implications of accession into the EU and issues applicable to the processes for selection of new drugs into the NHS such as prioritisation and cost-effectiveness.

The following recommendations are proposed:

1. The changes within the NHS in Malta will need to continue and plans for further change need to be set. One of the main priorities is for organisational change within the service provider units. In areas where major changes have been achieved such as within the newly set national medicines policy and audit unit (NMPAU), standards for audit need to be introduced to ensure continuous quality improvement.
2. For implementation of the Transparency Directive the decisions for the introduction of new drugs into the NHS need to be more explicit in the criteria used for decision-making, particularly in relation to prioritisation. The knowledge and experience gained from the case study of the managed entry of new drugs into the NHS in Malta should be applied to continue to improve the quality of the decision processes. Until a system of medicines registration is in place, it is recommended to continue considering the licensing status of drugs within the EU. Any developments should be well planned and should be aimed at making the processes more systematic. The process for revision of the formulary should be

continued. The formulary should be revised every three years in addition to ongoing update when a new drug is introduced periodically. The composition of the DTC needs to be changed to enable it to perform the complex tasks involved in the selection of new drugs into the NHS, particularly when the Transparency Directive is adopted. It is proposed that the DTC is composed of 12 to 14 members: 6 clinicians (which should include general medicine, paediatrics and oncology), a physician from public health, a health economist, a specialist in pharmacology, 2 clinical pharmacists, a pharmacist from medicines policy and ideally 2 representatives from the public. The appointments should continue to be renewable annually but ideally the composition should be revised every three years. The process for setting of policy by the DTC should adopt a bottom up approach and involve the primary users responsible for the implementation.

3. Once Malta adopts the Transparency Directive (Council Directive, 1988), the process for the selection of new drugs into the NHS will need to be routinely audited. Audit must ensure that quality is maintained despite the pressures to conduct decisions within the time limits set by the Transparency Directive. The 'policy for the introduction of new drugs of 1999' should continue to be implemented and protected from any political influences or external pressures. A standardised procedure must be set for the approval of drugs as non-formulary in exceptional cases so that all requests approved through this procedure are justified.
4. The project of setting a NDP for Malta, should be continued. The process of developing the NDP should utilise the information and knowledge gained through the case study for the managed entry of new drugs into the NHS. A common

framework needs to be set for the different pharmaceutical functions within the NHS as well as for the private sector. The experience of setting a NDP for Malta may be useful to other European countries that might consider the setting up of a NDP.

5. It is recommended that Malta will continue to collaborate with the WHO on issues relating to pricing and reimbursement of medicines and on the sharing of information between countries, particularly information on the national prices of medicines.
6. The Health Division should continue to develop its role as a regulator within the NHS in Malta by continuing to support the national medicines policy and audit unit, which is a sub-section within it, and by expanding its role to include the co-ordination of other areas of health technology assessment in Malta. When Malta becomes a member of the EU it will be important to keep abreast and where possible participate in any developments that occur in the field of health technology assessment and in the process towards the single market for pharmaceuticals, especially as these developments may have specific implications for Malta because of its unique characteristics.
7. It is recommended that the knowledge gained from this case study for Malta is utilised for further research particularly for case study research, for bringing about change in practice and for further developments in the systematic approach to the managed entry of new drugs into NHS.

7.8 CONCLUSIONS

The case study was found to be suited to study the complexity of real life phenomena and to conduct developmental evaluations whereby the case under study is changing. To achieve a systematic approach towards the managed entry of new drugs it is necessary to identify the related processes and the proposed links between them. The logic model was found to be a suitable tool for describing the complex system, for supporting and for evaluating change. Action research was found to be an effective intervention to bring about quick reform as well as to implement more gradual improvement.

This research was effective in achieving a number of improvements within the processes for the managed entry of new drugs into the NHS and supported the development of a more systematic approach. However, the problem of inequity remains. Malta is not unique in this respect in that any healthcare system with limited resources will face challenges in this area. Rather than try to remove inequity the key is to increase the transparency of the decision making process which is facilitated by a systematic approach.

In this thesis it has been shown that some essential common elements exist in the framework for the managed entry of new drugs into the NHS in EU countries. It may be possible to coordinate aspects of the processes involved such as the technical aspects of health-technology assessment, however the problem of inequity remains for all EU countries because the healthcare systems, resources, cultural issues and politics for prioritisation in the majority of EU countries differ widely.

REFERENCES

ABRAHAM, J. and LEWIS, G., 1999. Harmonising and competing for medicines regulation: how healthy are the European Union's systems of drug approval? *Social Science and Medicine*, 48 (11), pp.1655-1667.

ACCOUNTS PAYABLE OFFICE OF THE GOVERNMENT PHARMACEUTICAL SERVICES, 1999. Statistics on expenditure on medical supplies. Gwardamangia, Malta: Government pharmaceutical services, Government Medical Stores.

BANTA, D., 1997. Introduction to the EUR-ASSESS report. *International Journal of Technology Assessment in Health Care*, 13 (2), pp.133-143.

BANTA, D. and BUCH-ANDREASEN, P., 1990. The political dimension in health care technology assessment programmes. *International Journal of Technology Assessment in Health Care*, 6, pp.115-123.

BATALDEN, P.B. and STOLTZ, P.K., 1993. A framework for the continual improvement of health care: building and applying professional and improvement knowledge to test changes in daily work. *Journal on Quality Improvement*, 19 (10), pp.424-445.

BELLMAN, L., 1996. Changing nursing practice through reflection on the Roper, Logan and Tierney model: the enhancement approach to action research. *Journal of Advanced Nursing*, 24 (1), pp.129-138.

BENNETT, S., QUICK, J.D., and VELASQUEZ, G., 1997. Public-private roles in the pharmaceutical sector – implications for equitable access and rational drug use. World Health Organization. WHO/DAP/97.12.

BERO, L.A., GRILLI, R., GRIMSHAW, J.M., HARVEY, E., OXMAN, A.D. and THOMSON, M.A., 1998. Closing the gap between research and practice: an overview of systematic reviews of interventions to promote the implementation of research findings. *British Medical Journal*, 317 (7156), pp.465-468.

BERWICK, D.M., 1996. A primer on leading the improvement of systems. *British Medical Journal*, 312 (7031), pp.619-622.

BLACK, N., 1992. Research, audit and education. *British Medical Journal*, 304, pp.698-700.

BLOOR, F. and FREEMANTLE, N., 1996. Lessons from international experience in controlling pharmaceutical expenditure II: influencing doctors. *British Medical Journal*, 312 (7045), pp.1525-1527.

BLOOR, K., MAYNARD, A., and FREEMANTLE, N., 1996. Lessons from international experience in controlling pharmaceutical expenditure III: regulating industry. *British Medical Journal*, 313 (7048), pp.33-35.

BOWLING, A., 1997. Research methods in health: investigating health and health services. Buckingham: Open University Press.

BROWN, P., 1999. WHO urges "coverage for all, not coverage for everything". *British Medical Journal*, 318 (7194), p1305.

BURKE, K., 2002. NICE may fail to stop "postcode prescribing," MPs told. *British Medical Journal*, 324 (7331), p191.

BURNFIELD, A., 1997. Interferon beta in multiple sclerosis. *British Medical Journal*, 314 (7080), p600.

CHISHOLM, J., 1999. Viagra: a botched test case for rationing. *British Medical Journal*, 318 (7178), pp.273-274.

CLEAR, P.R. and GROBLER, M., 1998. Regulating the pharmaceutical industry: Australian scheme disadvantages. *British Medical Journal*, 316 (7126), p227.

CLOSS, S.J. and CHEATER, F.M., 1996. Audit or research – what is the difference? *Journal of Clinical Nursing*, 5 (4), pp.249-256.

COMMONWEALTH OF AUSTRALIA, 1999a. National medicines policy. Commonwealth Department of Health and Aged Care, Canberra, Australia: Publications Production Unit (Public Affairs, Parliamentary and Access Branch).

COMMONWEALTH OF AUSTRALIA, 1999b. Report of the national indicators, evaluating the quality use of medicines component of Australia's national medicines policy. Commonwealth Department of Health and Aged Care, Canberra, Australia: Publications Production Unit (Public Affairs, Parliamentary and Access Branch).

CORMACK, D., 2000. *The research process in nursing*. Fourth edition, Oxford, England: Blackwell Science Ltd.

COUNCIL DIRECTIVE, 1965. Council Directive 65/65/EEC. Council Directive of 26 January 1965 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products. Brussels, Belgium: The Council of the European Economic Community. [online] <http://europa.eu.int/eur-lex> .

COUNCIL DIRECTIVE, 1988. Council Directive 89/105/EEC. Council Directive of 21 December 1988 relating to the transparency measures regulating the pricing of medicinal products for human use and their inclusion in the scope of national health insurance systems. Brussels, Belgium: The Council of the European Communities. [online] <http://europa.eu.int/eur-lex> .

CROPPER, S. and FORTE, P., 1997. The nature of decision support systems. *In*: S. CROPPER and P. FORTE, eds. *Enhancing Health Services Management – The role of decision support systems*. Buckingham: Open University Press, p 27.

DAVIES, H.T.O., NUTLEY, S.M.N., and MANNION, R., 2000. Organisational culture and quality of health care. *Quality in Health Care*, 9 (2), pp.111-119.

DEMING, W.E., 1993. *The new economics for industry, education, government*. Cambridge, Massachusetts USA: Massachusetts Institute of Technology, Centre for Advanced Engineering Study.

DENT, T.H.S. and HAWKE, S., 1997. Too soon to market. *British Medical Journal*, 315 (7118), pp.1248-1249.

DENT, T.H.S. and SADLER, M., 2002. From guidance to practice: why NICE is not enough. *British Medical Journal*, 324 (7341), pp.842-845.

DEPARTMENT OF HEALTH (MALTA), 1986. The formulary of the government pharmaceutical services. Valletta, Malta: Department of Health.

DEPARTMENT OF HEALTH (MALTA), 1998. Schedule V of the Social Security Act. Valletta, Malta: Department of Health, DH Circular No. 113/98, 30 July 1998.

DEPARTMENT OF HEALTH (MALTA), 1999. Policy on entitlement to free medicines. Valletta, Malta: Department of Health, DH Circular No. 193/99, 21 July 1999.

DE POUVOURVILLE, G., 2001. The heterogeneity of markets for drugs in Europe. *The European Journal of Health Economics*, 2 (1), pp.4-10.

DICKER, A. and ARMSTRONG, D., 1995. Patients' views of priority setting in health care: an interview survey in one practice. *British Medical Journal*, 311 (7013), pp.1137-1139.

DRUMMOND, M.F., 1998. A reappraisal of economic evaluation of pharmaceuticals, science or marketing? *Pharmacoeconomics*, 14 (1), pp.1-9.

DUNN, Miriam, 1998. Free medicines in the pipeline. *The Malta Independent*, 23 June 1998.

DWYER, J.J.M. and MAKIN, S., 1997. Using a program logic model that focuses performance measurement to develop a program. *Canadian Journal of Public Health*, 88 (6), 421-425.

ENTWISTLE, V.A., WATT, I.S., BRADBURY, R. and PEHL, L.J., 1996. Media coverage of the child B case. *British Medical Journal*, 312 (7046), pp.1587-1591.

EUROPEAN COMMUNITY COMMUNICATION, 1998. Commission communication on the single market in pharmaceuticals. Brussels, Belgium: European Community Communication 588 of 25 November 1998.

EUROPEAN MEDICINES EVALUATION AGENCY, 1996. The European medicines evaluation annual. London, England: The European Medicines Evaluation Annual Ltd.

EUROPEAN MEDICINES EVALUATION AGENCY, 2002. Medicinal products for human use. List of authorised products, European public assessment reports (EPARs). [online] <http://www.emea.eu.int/> [31st January 2002].

EUROPEAN OBSERVATORY ON HEALTH CARE SYSTEMS, 1999. Health care systems in transitions, Malta. Copenhagen, Denmark: WHO Regional Office for Europe.

FEDER, G., ECCLES, M., GROL, R., GRIFFITHS, C. and GRIMSHAW, J., 1999. Clinical guidelines: using clinical guidelines. *British Medical Journal*, 318 (7185), pp.728-730.

FERNER, R.E., 1996. Newly licensed drugs: should be on probation until their value is demonstrated. *British Medical Journal*, 313 (7066), pp.1157-1158.

FITZGERALD, L., 1999. Case studies as a research tool. *Quality in Health Care*, 8, p75.

FREEMANTLE, N. and BLOOR, K., 1996. Lessons from international experience in controlling pharmaceutical expenditure. I: influencing patients. *British Medical Journal*, 312 (7044), pp.1469-1471.

FREEMANTLE, N. and MASON, J., 1999a. Not playing with a full DEC: why development and evaluation committee methods for appraising new drugs may be inadequate. *British Medical Journal*, 318 (7196), pp.1480-1482.

FREEMANTLE, N. and MASON, J., 1999b. DEC methods for appraising new drugs: paper has errors and omissions. *British Medical Journal*, 319 (7215), pp.1006-1007.

GARATTINI, S. and BERTELE, V., 2001. Adjusting Europe's drug regulation to public health needs. *Lancet*, 358 (9275), pp.64-67.

GARSIDE, P., 1998. Organisational context for quality: lessons from the fields of organisational development and change management. *Quality in Health Care*, 7 (Suppl), pp.S8-S15.

GILLHAM, B., 2000. *Case study research methods*. London, England: Continuum.

GLENNIE, J.L., TORRANCE, G.W., BALADI, J.F., BERKA, C., HUBBARD, E., MENON, D., OTTEN, N. and RIVIERE, M., 1999. The revised Canadian guidelines for the economic evaluation of pharmaceuticals. *Pharmacoeconomics*, 15 (5), pp.459-468.

GORHAM, P., 1995. Cost-effectiveness guidelines. *Pharmacoeconomics*, 8 (5), pp.369-373.

GOSDEN, T., FORLAND, F., KRISTIENSEN, I.S., SUTTON, M., LEESE, B., GIUFFRIDA, A., SERGISON, M. and PEDERSEN, L., 2000. Capitation, salary, fee-for-service and mixed systems of payments: effects on the behaviour of primary care

physicians. The Cochrane Database of Systematic Reviews, Cochrane Effective Practice and Organisation of Care Group. [online] <http://www.cochrane.co.uk/> [8 June 2000].

GRIMSHAW, J., FREEMANTLE, N., WALLACE, S., RUSSELL, I., HURWITZ, B., WATT, I., LONG, A. and SHELDON, T., 1995. Developing and implementing clinical practice guidelines. *Quality in Health Care*, 4, pp.55-64.

GROL, R., 1997. Personal paper: beliefs, and evidence in changing clinical practice. *British Medical Journal*, 315 (7105), pp.418-421.

GROL, R., DALHUIJSEN, J., THOMAS, S., VELD, C., RUTTEN, G. and MOKKINK, H., 1998. Attributes of clinical guidelines that influence use of guidelines in general practice: observational study. *British Medical Journal*, 317 (7162), pp.858-861.

HAINES, A. and DONALD, A., 1998. Introduction. In: A. HAINES, and A. DONALD, eds. *Getting research findings into practice*. London, England: BMJ Publishing group, pp.1-9.

HAMPTON, R., 1983. The end of clinical freedom. *British Medical Journal Clinical Research Edition.*, 287 (6401), pp.1237-8.

HART, E., 1995. Developing action research in nursing. *Nurse Researcher*, 2 (3), pp.4-14.

HART, E. and BOND, M., 1995. *Action research for health and social care, a guide to practice*. Buckingham, England: Open University Press.

HART, E. and BOND, M., 1996. Making sense of action research through the use of a typology. *Journal of Advanced Nursing*, 23 (1), pp.152-159.

HOLTER, I.M. and SCHWARTZ-BARCOTT, D., 1993. Action research: what is it? How has it been used and how can it be used in nursing? *Journal of Advanced Nursing*, 18, pp.298-304.

INTERNATIONAL RESEARCH ASSOCIATES (EUROPE), 1998. Eurobarometer 49. June 1998.

JONSSON, E. and BANTA, D., 1999. Management of health technologies: an international view. *British Medical Journal*, 319 (7220), p. 1293, November 1999. [online] <http://bmj.com/cgi/content/full/319/7220/1293>.

JUILLARD, J., 2002. Reorienting European medicines policy. *Prescrire International*, June, pp.1-19.

JULIAN, D.A., JONES, A., and DEYO, D., 1995. Open systems evaluation and the logic model: program planning and evaluation tools. *Evaluation and Program Planning*, 18 (4), pp.333-341.

KANAVOS, P. and MOSSIALOS, E., 1999. Outstanding regulatory aspects in the European pharmaceutical market. *Pharmacoeconomics*, 15 (6), pp.519-533.

KEEN, J. and PACKWOOD, T., 2000. Using case studies in health services and policy research. In: C. POPE and N. MAYS, eds. *Qualitative research in health care*. Second edition, London, England: BMJ Publishing Group, pp.50-58.

KESSLER, D.A., ROSE, J.L., TEMPLE, R.J., SCHAPIRO, R. and GRIFFIN, J.P., 1994. Therapeutic-class wars – drug promotion in a competitive marketplace. *The New England Journal of Medicine*, 331 (20), pp.1350-1353.

KLEIN, R., 1998. Puzzling out priorities: why we must acknowledge that rationing is a political process. *British Medical Journal*, 317 (7164), pp.959-960.

KOECK, C., 1998. Time for organisational development in healthcare organisations. *British Medical Journal*, 317 (7168), pp.1267-1268.

LANGLEY, G.J., NOLAN, K.M., and NOLAN, T.W., 1992. *The foundation of improvement*. Silver Spring, Maryland: API Publishing.

LANGLEY, P.C., 1993. The role of pharmacoeconomic guidelines for formulary approval: the Australian experience. *Clinical Therapeutics*, 15 (6), pp.1154-1176.

LANGLEY, P.C., 1996. The November 1995 revised Australian guidelines for the economic evaluation of pharmaceuticals. *Pharmacoeconomics*, 9 (4), pp.341-352.

LANNIGAN, N.A., 1993. *Hospital drug formularies an indicator for quality*. The Clinical Resource and Audit Group. Edinburgh, Scotland: HMSO, Edinburgh Press.

LAPORTE, J.R., BAKSAAS, I., and LUNDE, P.K.M., 1993. General background. In: M.N.G. DUKES, ed. *Drug utilization studies, methods and uses*. Copenhagen, Denmark: WHO Regional Publications, European Series, No. 45, pp 5-22.

LAWS OF MALTA, 1901. Medical and kindred professions ordinance. Chapter 31.

LAWS OF MALTA, 1987. An Act to establish a scheme of Social Security. Chapter 318.

LEESE, J., 1996. Choosing between competing health priorities. *Pharmacoeconomics*, 9 Suppl. 3, pp.4-7.

MALEK, M. and LANGSDALE, T., 1994. Prioritising healthcare is an economic necessity. *Pharmacoresources*, 1172 (July), pp.3-4.

MAYNARD, A., 1996. Rationing health care. *British Medical Journal*, 313 (7071), p1499.

MAYNARD, A., 2001. Towards a Euro-NICE? *Eurohealth*, 7 (2), p26.

MAYNARD, A. and BLOOR, K., 1997. Regulating the pharmaceutical industry. *British Medical Journal*, 315 (7102), pp.200-201.

McLAUGHLIN, J.A. and JORDAN, G.B., 1999. Logic models: a tool for telling your programs performance story. *Evaluation and Program Planning*, 22 (1), pp.65-72.

MEYER, J., 1993. New paradigm research in practice: the trials and tribulations of action research. *Journal of Advanced Nursing*, 18, pp.1066-1072.

MEYER, J., 2000. Using qualitative methods in health-related action research. In: C. POPE and N. MAYS, eds. *Qualitative research in health care*. Second edition, London, England: BMJ Publishing Group, pp.59-74.

MOSSIALOS, E. and KING, D., 1999. Citizens and rationing: analysis of a European survey. *Health Policy*, 49 (1-2), pp.75-135.

MOULDING, N.T., SILAGY, C.A., and WELLER, D.P., 1999. A framework for effective management of change in clinical practice: dissemination and implementation of clinical practice guidelines. *Quality in Health Care*, 8, pp.177-183.

MUIR-GRAY, J.A., 1998. Evidence based policy making. In: A. HAINES, and A. DONALD, eds. *Getting research findings into practice*. London, England: BMJ Publishing group, pp.70-77.

NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE, 1999. Clinical guidelines and referral protocols. [online] <http://www.nice.org.uk/> [23rd December 1999].

NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE, 2000. Guidance on the use of taxanes for ovarian cancer. [online] <http://www.nice.org.uk/> [1st June 2000].

NOLAN, M. and GRANT, G., 1993. Action research and quality of care: a mechanism for agreeing basic values as a precursor to change. *Journal of Advanced Nursing*, 18, pp.305-311.

NOLAN, T.W. and PROVOST, L.P., 1990. Understanding variation. *Quality Progress*, 23 (5), pp.70-78.

NORRIS, P., 1998. The impact of European harmonisation on Norwegian drug policy. *Health Policy*, 43 (1), pp.65-81.

NUIJTEN, M.J.C., BRORENS, M.J.A., HEKSTER, Y.A., VAN DER KUY, A., LOCKEFEEER, J.H.M., DE SMET, P.A.G.M., BONSEL, G. and PRONK, M.H., 1998. Reporting format for economic evaluation. *Pharmacoeconomics*, 14 (2), pp.159-163.

O'BRIEN, B.J., NOVOSEL, S., TORRANCE, G. and STREINER, D., 1995. Assessing the economic value of a new antidepressant. *Pharmacoeconomics*, 8 (1), pp.34-45.

OVRETVEIT, J., 1998. Evaluating health interventions: an introduction to evaluation of health treatments, services, policies and organisational interventions. Buckingham: Open University Press.

OXMAN, A.D., THOMSON, M.A., DAVIS, D. and BRIAN, H.R., 1995. No magic bullets: a systematic review of 102 trials of interventions to improve professional practice. *Canadian Medical Association Journal*, 153 (10), pp.1423-1431.

PEARCEY, P. and DRAPER, P., 1996. Using the diffusion of innovation model to influence practice: a case study. *Journal of Advanced Nursing*, 23 (4), pp.714-721.

PETRIE, J.C. and SCOTT, A.K., 1987. Drug formularies in hospitals. *British Medical Journal*, 294, p919.

PLSEK, P.E. and GREENHALGH, T., 2001. The challenge of complexity in health care. *British Medical Journal*, 323 (7313), pp.625-628.

QUICK, J.D., HOGERZEIL, H.V., RANKIN, J.R., LAING, R.O., O'CONNOR, R.W., DUKES, M.N.G. and GARNETT, A., 1997. *Managing drug supply: the selection, procurement, distribution, and use of pharmaceuticals*. Second Edition, Connecticut, USA: Kumarian Press Inc.

READ, P., 1998. Regulating the pharmaceutical industry: authors seem to have misunderstood pharmaceutical price regulation scheme. *British Medical Journal*, 316 (7126), p226.

REICH, M.R., 1995. The politics of health sector reform in developing countries: three cases of pharmaceutical policy. *Health Policy*, 32, pp.47-77.

RICHARDS, R.G., 1996. Interferon beta in multiple sclerosis. *British Medical Journal*, 313 (7066), p1159.

RONSEN, R. and GABBAY, J., 1999. Linking health technology assessment to practice. *British Medical Journal*, 319 (7220), p. 1292, November 1999. [online] <http://bmj.com/cgi/content/full/319/7220/1292> .

ROUS, E., COPPEL, A., HAWORTH, J. and NOYCE, S., 1996. A purchaser experience of managing new expensive drugs: interferon beta. *British Medical Journal*, 313 (7066), pp.1195-1196.

ROUTLEDGE, P., 1998. 150 years of pharmacovigilance. *Lancet*, 351 (9110), pp.1200-1201.

ROVIRA, J. and ANTONANZAS, F., 1995. Economic analysis of health technologies and programmes. *Pharmacoeconomics*, 8 (3), pp.245-252.

RYYNANEN, O.P., MYLLYKANGAS, M., KINNUNEN, J. and TAKALA, J., 1999. Attitudes to health care prioritisation methods and criteria among nurses, doctors, politicians and the general public. *Social Science and Medicine*, 49 (11), pp.1529-1539.

SABIN, J.E., 1998. The second phase of priority setting: fairness as a problem of love and the heart: a clinician's perspective on priority setting. *British Medical Journal*, 317 (7164), pp.1002-1004.

SCALLY, G. and DONALDSON, L.J., 1998. Clinical governance and the drive for quality improvement in the new NHS in England. *British Medical Journal*, 317 (7150), pp.61-65.

SCALON, J.D., FREIRE, S.M., and CUNHA, T.A., 1998. Validation of models for predicting the use of health technologies. *Medical Decision Making*, 18, pp.311-319.

SCOTTISH INTERCOLLEGIATE GUIDELINES NETWORK, 1999. SIGN guidelines – an introduction to SIGN methodology for the development of evidence-based clinical guidelines. Edinburgh, Scotland: SIGN Secretariat.

SCOTTISH MEDICINES CONSORTIUM, 2002. Scottish Medicines Consortium Home Page [online] <http://www.htbs.co.uk/smc/> [23rd November 2002].

SELECT COMMITTEE ON HEALTH, 2002. National Institute for Clinical Excellence, second report. London: House of Commons, Health Committee Publications, 3 July 2002.

SHANI, S., SIEBZEHNER, M.I., LUXENBURG, O. and SHEMER, J., 2000. Setting priorities for the adoption of health technologies on a national level – the Israeli experience. *Health Policy*, 54 (3), pp.169-185.

SLUIJS, E.M., OUTINEN, M., WAGNER, C., LIUKKO, M. and DE BAKKER, D.H., 2001. The impact of legislative versus non-legislative quality policy in health care: a comparison between two countries. *Health Policy*, 58 (2), pp.99-119.

SMITH, R., 1999. NICE: a panacea for the NHS? *British Medical Journal*, 318 (7187), pp.823-824.

SMITH, R., 2000. The failings of NICE, time to start work on version 2. *British Medical Journal*, 321 (7273), pp.1363-1364.

STEVENS, A., MILNE, R., LILFORD, R. and GABBAY, J., 1999. Keeping pace with new technologies: systems needed to identify and evaluate them. *British Medical Journal*, 319 (7220), p1291, November 1999. [online] <http://bmj.com/cgi/content/full/319/7220/1291>.

STRONKS, K., STRIJBS, A.M., WENDTE, J.F. and GUNNING-SCHEPERS, L.J., 1997. Who should decide? Qualitative analysis of panel data from public, patients, healthcare professional, and insurers on priorities in healthcare. *British Medical Journal*, 315 (7100), pp.92-96.

TITCHEN, A., 1995. Issues of validity in action research. *Nurse Researcher*, 2 (3), pp.38-48.

TOGNONI, G. and LUNDE, P.K.M., 1993. Therapeutic formularies, essential drugs, drug utilisation studies. In: M.N.G. DUKES, ed. *Drug utilization studies, methods and uses*. Copenhagen, Denmark: WHO Regional Publications, European Series, No. 45, pp.43-53.

TORVATN, H., 1999. Using program theory models in evaluation of industrial modernisation programs: three case studies. *Evaluation and Program Planning*, 22 (1), pp.73-82.

TOWSE, A., 1998. Regulating the pharmaceutical industry: having rationing rules for new pharmaceuticals but not other treatments is senseless. *British Medical Journal*, 316 (7126), p227.

VAN HARTEN, W.H., CASPARIE, T.F., and FISSCHER, O.A.M., 2000. Methodological considerations on the assessment of the implementation of quality management systems. *Health Policy*, 54, pp.187-200.

VAN HARTEN, W.H., CASPARIE, T.F., and FISSCHER, O.A.M., 2002. The evaluation of the introduction of a quality management system, a process-oriented case study in a large rehabilitation hospital. *Health Policy*, 60, pp.17-37.

VELLA, P., 1995. *Introducing new drugs – current hospital practice*. M.Sc. thesis, The Queen's University of Belfast.

WALLERSTEIN, K.R.B., 1997. *Pharmaceutical pricing and reimbursement in Europe*. London: PJB Publications Ltd. SCRIP Reports.

WALLEY, T., 1998. National structures to facilitate good medicines management. In: R. PANTON and S. CHAPMAN, eds. *Medicines management*. London, England: BMJ Books.

WALLEY, T., EARL-SLATER, A., HAYCOX, A. and BAGUST, A., 2000. An integrated national pharmaceutical policy for the United Kingdom? *British Medical Journal*, 321 (7275), pp.1523-1526.

WALLEY, T., HAYCOX, A., and BARTON, S., 1997. Drug rationing in the UK national health service. *Pharmacoeconomics*, 12 (3), pp.339-350.

WALSHE, K. and FREEMAN, T., 2002. Effectiveness of quality improvement: learning from evaluations. *Quality and Safety in Health Care*, 11, pp.85-87.

WARDEN, J., 1999. NICE opens for business. *British Medical Journal*, 318 (7189), p962.

WATERMAN, H., 1995. Distinguishing between 'traditional' and action research. *Nurse Researcher*, 2 (3), pp.15-23.

WATERMAN, H., 1996. A comparison between quality assurance and action research. *Nurse Researcher*, 3 (3), pp.58-68.

WATERMAN, H., 1998. Embracing ambiguities and valuing ourselves: issues of validity in action research. *Journal of Advanced Nursing*, 28 (1), pp.101-105.

WENSING, M. and GROL, R., 1994. Single and combined strategies for implementing changes in primary care: a literature review. *International Journal for Quality in Health Care*, 6 (2), pp.115-132.

WETHERILL, G.B. and BROWN D.W., 1991. *Statistical Process Control – Theory and Practice*. London, England: Chapman and Hall.

WORLD HEALTH ORGANIZATION, 1988. *Ethical criteria for medicinal drug promotion*. Geneva, Switzerland: World Health Organisation.

WORLD HEALTH ORGANISATION, 1997a. *Comparative analysis of national drug policies in 12 countries*. Action Programme on Essential Drugs, World Health Organization, WHO/DAP/97.6.

WORLD HEALTH ORGANISATION, 1997b. *WHO certification scheme on the quality of pharmaceutical products moving in international commerce*. World Health Organisation, WHO/PHARM/82.4 Rev. 5.

WORLD HEALTH ORGANISATION, 2000. *The world health report 2000. Health systems: improving performance*. Geneva, Switzerland: World Health Organisation.

WORLD HEALTH ORGANISATION, 2001. *How to develop and implement a national drug policy*. Second edition, Geneva, Switzerland: World Health Organisation.

WU, W.K., WERTHEIMER, A.I., and HADSALL, R., 1998. The evaluation of new drug introduction in nine developed countries, 1970-1983. *Journal of Social and Administrative Pharmacy*, 15 (4), pp.296-308.

WYATT, J. and WALTON, R., 1995. Computer based prescribing: improves decision making and reduces costs. *British Medical Journal*, 311 (7014), pp.1181-1182.

YIN, R., 1994. *Case study research: design and methods*. Second edition, Thousand Oaks, California: Sage Publications, Inc.

APPENDICES

Appendix I: Research Ethics Committee Approval

L-UNIVERSITÀ TA' MALTA
Msida – Malta
SKOLA MEDIKA



UNIVERSITY OF MALTA
Msida – Malta
MEDICAL SCHOOL

REF. TAGMNA:
OUR REF:

REF. TIEGMEK:
YOUR REF:

RefNo: 13/99

13th January 1999

Ms Patricia Vella
C/o Dept of Pharmacy
St Luke's Hospital

Dear Ms Vella,

Please refer to your application submitted to the Research Ethics Committee in connection with your study entitled:

'DEVELOPMENT OF A MODEL TO SUPPORT THE PRACTICE FOR THE INTRODUCTION OF NEW DRUGS INTO THE GOVERNMENT HEALTH SERVICES IN MALTA'

I have been directed to inform you that at the last meeting of the Research Ethics Committee of the Faculty of Medicine & Surgery members agreed that approval be given for this research.

Kindly also note that ethical approval is valid for a period of two years after which a final brief report is to be submitted to Research Ethics Committee on completion of your study.

Yours sincerely,

J Borg
Secretary Medical School

c.c. Professor A Serracino Inglott – Chairman, Research Ethics Committee
Dr Frank Portelli – Lecturer/Anatomy Department
Mr M Zarb Adami – Senior Lecturer / Pharmacy Department

Appendix II: Questionnaire to Consultants (Questionnaire of 1999)

36, Main Street,
Mellicha SPB 14

15th June 1999

Dear Consultant,

As part of my MSc in Clinical Pharmacy post-graduate studies in 1994 I had carried out a project on 'Introducing new drugs - current hospital practice'. This project analysed the system for introducing new drugs in hospital and recommended changes where indicated. This questionnaire was sent to all consultants working within the Government Health Services in order to explore factors which motivated them to prescribe new drugs and to obtain their opinion on the practice at that time.

Now, five years later as part of further research on the subject, I am repeating the exercise using the same questionnaire with just very minor alterations and using the same methodology. I would like to compare the response of this questionnaire to those of the previous one and highlight any differences.

You are kindly requested to fill the questionnaire and to send it in the self-addressed envelope enclosed with it. All replies will be kept anonymous and will be dealt with in the strictest confidential manner. It will be appreciated if the questionnaire is sent at your earliest convenience, if possible by mid-July.

On the first page of the questionnaire, kindly mark whether you had participated in the study when it was carried out in 1994.

As part of my project I am also studying the local perspective on equity and prioritisation as related to the practice for introducing new drugs into the Government Health Services. I have set a short questionnaire about this aspect. It only involves very brief answers - mainly ranking and ticking and I would be grateful if you could do this exercise and send the reply with the questionnaire.

By filling the questionnaires you will be helping me with my project and you will also be able to suggest recommendations for improving the present system, if necessary. The final results of the questionnaires will be shown to all those who would be interested to see them.

Thank-you for your co-operation,

Yours sincerely

Patricia Vella
Pharmacist (Secretary Drug and Therapeutics Committee)

CURRENT PRACTICE FOR INTRODUCING NEW DRUGS INTO THE GOVERNMENT HEALTH SERVICES IN MALTA

Please tick in the brackets () or circle YES, NO or DO NOT KNOW as applicable. Kindly answer all sections of the questionnaire. If you find problems with answering a particular question please put your remarks next to that question and move on to the rest.

Had you filled this questionnaire when it was circulated in 1994? YES NO

Department:-

Anaesthesia	()	Dermatology	()
Medicine	()	Obstetrics and Gynaecology	()
Oncology	()	Paediatrics	()
Psychiatry	()	Radiotherapy	()
Surgery	()	Primary care	()
Other _____			

Speciality (if applicable) _____

For how long have you held the present post as consultant with the Department of Health in Malta? _____

Have you requested any new drugs during the last five years (1994 to date) YES NO

The Formulary of the Government Pharmaceutical Services

Do you have a copy ?	YES	NO
Is the formulary sufficiently updated ?	YES	NO
Are you involved in decisions re additions/deletions ?	YES	NO
Are you adequately informed of alterations?	YES	NO

The Antimicrobial Policy

Do you have a copy?	YES	NO
Do you follow its recommendations?	YES	NO

If NO, why not? _____

Does it give clear guidelines on the use of new antibiotics? YES NO

1. Factors affecting the prescription of new drugs

How do you usually get to know of a new drug ?

Please rank in ascending order, starting with 1 for the most likely source:-

- () medical journals
- () medical representatives
- () Internet
- () conferences abroad
- () conferences in Malta
- () non-medical literature
- () colleagues
- () other _____

Which do you consider as the most influential "*pressure to prescribe*" a new drug

Please rank in ascending order, starting with 1 for the most important:-

- () advertising - (direct mail, journals, medical representatives)
- () controls and regulations by health authorities
- () demands from patients
- () demands from pressure groups and society at large
- () media and press
- () limitations of the hospital formulary
- () medical opinion leaders
- () other _____

2. Influence by the pharmaceutical industry

Have you been offered financial or material benefits in order to influence the prescription of new drugs

YES NO

If YES, of what type were they :-

- purely financial YES NO
- sponsorship to participate in domestic or international symposia YES NO
- opportunity to publish papers YES NO
- other _____

Are symposia / scientific meetings organised by local drug firms in order to introduce new drugs:

- of good standard YES NO
- scientific YES NO
- educational YES NO
- too promotional YES NO

Are entertainment or other hospitality and any gifts offered kept to a modest level?

YES NO

3. Requesting new drugs - Submitting a request and the outcome

Which factors do you consider prior to prescribing a new drug

Please rank in ascending order, starting with 1 for the factor which you consider to be the most important:-

- licensed indications
- unlicensed use
- literature and information about it
- reports of clinical trials
- safety
- comparison with drugs available in hospital
- costs
- cost-effectiveness
- advantages in administration
- other _____

From where do you usually get information on new drugs prior to requesting them

Please rank in ascending order, starting with 1 for the most likely source:-

- medical journals
- Internet
- information supplied directly by drug companies
- conferences abroad
- conferences in Malta
- non-medical literature
- information supplied by the hospital Drug Information Unit
- information supplied by the Drug and Therapeutics Committee
- other _____

4. The Drug and Therapeutics Committee (DTC)

Do you feel represented on the DTC? YES NO

Do you feel well informed with the decisions of the DTC? YES NO

Do consultants have the opportunity to contribute in the setting up of DTC policies? YES NO

Are you aware of the new protocols set up by the DTC since the beginning of 1993 for the use of particular new drugs in hospital? YES NO

Have you been / are you involved in the setting up of any of the protocols for new drugs set up by the DTC? YES NO

If YES

are you satisfied with the proceedings of the sub-committee? YES NO

Has such participation created any problems-

- time YES NO
- commitment YES NO
- relationship with peers YES NO

If NO

Have you been asked to be a member of any DTC sub-committee? YES NO

Would you be willing to actively contribute in such a sub-committee? YES NO

If NO, why not? _____

5. Clinical Trials and Post-marketing scientific studies and surveillance

Have you taken part in clinical trials for any new drug prior to approval for its use on the market YES NO

Have you taken part in clinical trials for any new drug after it was licensed for use on the market YES NO

Have you used any new drugs for unlicensed indications ? YES NO

If YES, which drugs and for what indications?

Drug	Unlicensed indication
_____	_____
_____	_____
_____	_____

Should authorities be informed of pre- or post- marketing clinical trials? YES NO

If YES, which authorities should be informed? _____

Do you agree with the following statements:-
 Post-marketing scientific studies have been used as a disguised form of promotion YES, NO, DON'T KNOW

Samples of new drugs should not be used on patients without permission YES, NO, DON'T KNOW

If a patient is started on a new drug using samples, the DTC is not bound to approve the drug for the patient YES, NO, DON'T KNOW

Should there be a national adverse drug reaction reporting system in Malta YES, NO, DON'T KNOW

If NO, why not? _____

6. Role of the pharmacist

Which factors do you consider to be part of the role of the hospital pharmacist?

Supply of information about new drugs on request by consultants	YES	NO
Supply of information about new drugs as soon as they are introduced	YES	NO
Evaluation of new drugs as soon as they are introduced on the market	YES	NO
Discussion with the consultant when prescribing a new drug on the ward	YES	NO
Participation as a member in the sub-committees involved in the setting up of protocols for the approval and monitoring of new drugs	YES	NO
Participation as a member of the Drugs and Therapeutics Committee	YES	NO
Participation in the design, organisation, implementation and evaluation of clinical trials on new drugs	YES	NO
Evaluation of whether requests for new drugs are according to criteria set in the established protocols	YES	NO
Monitoring of response to new drugs	YES	NO
Organisation and participation in audit and drug-use evaluation studies	YES	NO
Involvement in adverse drug reactions monitoring and reporting schemes	YES	NO

Other _____

Should pharmacists be allowed access to patient notes in order to be able to perform the above duties? YES NO

7. Recommendations for alterations in the system for introducing new drugs within Government Health Services in Malta

Is the current system for introducing new drugs in hospital efficient YES NO

Problems with the present system for introducing new drugs:-

Which factors do you consider to be a problem with the present system for introducing new drugs?

Time-lag until the drug is approved	YES	NO
Availability of stocks of the drug	YES	NO
Paper-work involved	YES	NO
The number of requests which are sent back for additional information	YES	NO
The number of requests which are not approved	YES	NO
Subsequent approval of the drug after it is approved for the first time	YES	NO

The involvement of pharmacists in the processing of requests	YES	NO
Having requests for new drugs submitted to the DTC through the Head of Department	YES	NO
The availability of adequate information prior to requesting a new drug	YES	NO
The importance given to cost of the drug	YES	NO
The setting up of protocols for the use of new drugs	YES	NO
Other _____		

Appendix III: The Prioritisation Questionnaire to Consultants

1. For each of the following please tick (✓) the relevant answer:

	YES	NO	DNK
Is the current system for allocation of resources within the Government Health Services adequate?			
Is the present system for entitlement to free medicines (Schedule V and pink card) fair and reasonable			
Should there be any form of rationing in the practice for introducing new drugs into the Government Health Services?			
Should physicians within the Government Health Services be allowed to treat their patients with whatever they feel is the best drug for the individual without having to consider costs?			
Is rationing ethical?			

DNK= do not know

2. How should new drugs be introduced into the practice for introducing new drugs into the Government Health Services in Malta?

Please rank (1,2,3, etc) starting with number 1 as the most recommended, number 2 as the next recommended etc and putting 0 where not recommended:

All requests for new drugs should be approved without restriction	
Develop new ways of using existing resources more effectively	
Study cost-effectiveness as compared to existing drugs	
Set prioritisation within a limited budget	
Assess the significance and impact of the disease for the population	
Other:	

3. Who should be involved in the setting of priorities for the practice of introducing new drugs into the Government Health Services?




Please tick (✓) wherever relevant:

nobody	
the general public	
the individual patient	
representatives of patients	
clinical consultants	
Drug & Therapeutics Committee	
consultants in public health	
all medical officers	
policy makers	
politicians	
administrators	
drug representatives	
the press and the media	
Other:	

4. If a system for establishing prioritisation for which new drugs are to be introduced is implemented in the practice for introducing new drugs into the Government Health Services in Malta, which factors should be considered when setting this prioritisation?

1=should not be considered	2=is not important	3= I am not sure about	4=is important	5= must be considered
-----------------------------------	---------------------------	-------------------------------	-----------------------	------------------------------

For each factor please tick (√) the box which applies most (one box per factor). If you do not understand any of these factors kindly put a question mark (?)

When deciding on whether to introduce a new drug into the Government Health Services or not, this factor:	 1	2	 3	4	 5
1. Evidence about safety					
2. Evidence from clinical trials that drug has proven efficacy					
3. Evidence that the drug is effective in clinical practice					
4. If the drug is used for treatment or prophylaxis					
5. Alternative drugs available on the formulary					
6. Drug cures the disease					
7. Prognosis of the disease condition without treatment					
8. Drug prolongs length of life					
9. Drug improves quality of life					
10. Disease condition is on the Schedule V list					
11. Drug is for hospital use only					
12. Drug will be required on an out patient basis					
13. The cost (in Liri) of treatment with the drug					
14. The cost-effectiveness of the drug					
15. No other treatment available for the disease condition					
16. The total increased cost to the Department					
17. Cost per patient					
18. The number of patients who would require the drug					
19. The age of the patient/s benefiting from the drug					
20. How much an individual patient would possibly benefit					
21. The sex of the patient/s benefiting from the drug					
22. If the disease was acquired through the health system					
23. Whether the drug is requested for cosmetic purposes					
24. Whether the drug is requested for recreational purposes					
25. The disease is acquired through sex, drug abuse, smoking					
26. The reputation of the consultant who prescribed the drug					
27. Possible influence by the pharmaceutical industry					
28. Information about economic evaluation of the drug					
29. Whether it is ethical to use the drug					
30. Whether the indication for use is licensed or not					
31. If the drug is registered by the Health Authority					
32. Pressure for approval from the patient, family, politicians					
Other:					

Appendix IV: Form for Patient Interviews

Interviewing form for interviews with patients who collected medicines from the out-patient pharmacy at St Luke's Hospital

Inclusion criteria to be confirmed:

- Patient was collecting medicines for self
- Patient was taking non-formulary drugs
- Patient consented to be interviewed

Time when interview was started: _____

Age:	
Sex (M/F):	
Location:	
Date:	

The system for entitlement to free medicines

1. How are you entitled to free medicines	Pink card	
	Schedule V (yellow)	
	other	
2. Did you encounter any problems with getting your entitlement?	Yes	
	No	
3. If yes, what was the problem?	Delay with the issue of Schedule V	
	Disease condition not on Schedule V	
	Problems with the Department of Social Services	
	Others:	
4. Do you agree with the current system for entitlement to free medicines?	Yes	
	No	
5. Any recommendations for improvement of the system for entitlement to free medicines?	Yes	
	No	

Prescribing of non-formulary medicines

1. How many non-formulary drugs are you taking?			
2. Did you find problems with getting a covering letter or the request for renewal?	Yes		
	No		
3. From where did you get your covering letter made?	In-patient in hospital		
	Out-patient in hospital		
	Private visit to a doctor		
	Others:		
4. How long did it take to receive the letter of approval?	Up to 15 days		
	up to one month		
	Up to two months		
	Other:		
5. In the meantime what did you do until the approval was received? a. buy the drug from own pocket b. contacted someone to hasten approval c. stayed without the drug d. other:			
	Yes		No
	Yes		No
	Yes		No

Availability of stocks of medicine

1. Are the government pharmacies always well stocked with the medicines that you require?	Yes		
	No		
2. If the government dispensary was out of stock of your medicine, but this could be found in the private pharmacies, what would you do?	Take another medicine with the same effect		
	Buy the medicine from a private pharmacy		
	Other:		

The use of resources within the Department of Health (yes, no, do not know DNK)

	Yes	No	DNK
1. Are the financial resources allocated to the health care system properly utilised?			
2. Should doctors employed with the NHS take the price of medicines that they prescribe into consideration when prescribing?			
3. If two medicines achieve the same desired therapeutic effect, should doctors prescribe the cheapest one?			
4. Does the Department of Health need systems to monitor the expenditure on new drugs?			
5. Should requests for new drugs made by doctors be approved immediately without being discussed?			
6. Should the Department of Health look into new ways how the budget available could be used more efficiently?			

How should new medicines be introduced?

1. Who should decide which medicines are introduced into the NHS?	Individual consultant physicians	
	Group of consultants	
	General practitioners	
	Drug and Therapeutics Committee	
	Department of Health policy planners	
	Patient groups	
	Politicians	
	General public	
	Individual patients	
	Hospital pharmacists	
	Medical representatives	
2. When decisions are being taken regarding the introduction of new drugs into the NHS, which opinion do you agree with?	Any potentially useful medicine should be procured	
	The interests of an individual patient should be weighed against the interests of other patients	

Factors that are to be considered when introducing new drugs into the NIIS

What factors are to be considered when introducing new drugs into the NHS in Malta:

Time when the interview was finished: _____

Appendix V: Discussion Guide for Interviews with Medical Representatives

Aims of the interview and the researcher’s role were clearly explained YES/NO
 Respondent accepted to participate in the interview YES/NO

Profession: Pharmacist _____ Other _____

Time when the interview was started: _____

1. From your experience with the practice for the introduction of new drugs into the Government Health Services:

- a. what aspects of the practice do you consider to be problematic?
- b. what is the current situation/the problem?
- c. what would you recommend as the alternative situation?
- d. what action/s do you recommend for improvement of these aspects within the practice?

Problematic areas	Current situation	Recommended situation	Actions to improve the practice

Additional comments/recommendations:

Time when interview was finalised: _____

Appendix VI: Detailed Responses to the 1994 and the 1999 Questionnaires to Consultants

For the questions where consultants had to answer YES, NO or DO NOT KNOW (DNK), the responses are recorded as number of responses and as percentages in brackets (%).

Response to the questionnaires

The figures in Table A1 show the number of questionnaires sent to consultants, and the number and percentage of questionnaire responses received for 1994 and 1999. The last column shows the percentage of consultants who answered the questionnaire in 1999 and who confirmed that they had also responded to the questionnaire in 1994.

The overall response rate was 75% in 1994 and 66% in 1999.

Table A1: Response rates to consultant questionnaires by department (1994 and 1999)

Clinical Department	1994			1999			Percentage of respondents of 1999 who also responded in 1994
	No. sent	No. received	% received	No. sent	No. received	% received	
Anaesthesia	8	6	75	9	8	89	44
Dermatology	2	2	100	4	1	25	25
ENT	2	1	50	2	2	100	100
Medicine	13	11	85	14	13	93	79
Obs. & Gynae	6	2	33	7	2	29	71
Oncology	3	3	100	2	2	100	100
Paediatrics	5	4	80	8	3	38	25
Psychiatry	5	4	80	4	3	75	75
Surgery	17	12	71	17	12	71	76
Miscellaneous	2	2	100	3	0	0	0
Total	63	47	75	70	46	66	63

There was no significant difference in the number of consultants in each department and in the total number of consultants in the two groups. Pearson Chisquare analysis of frequency table: $p=0.94$ (not significant). The average duration of the respondents in the post of consultant was 10 years (range < 1 year to 31 years) in 1994 and 9 years (range < 1 year to 22 years) in 1999.

Tables A2 and A3 provide a summary of responses to questions regarding the Formulary and the Antimicrobial Policy respectively.

Table A2: Opinion of consultants regarding the Formulary

The Formulary	1994			1999			Pearson Chisquare
	YES	NO	DNK	YES	NO	DNK	
Do you have a copy?	41 (87)	06 (13)	00 (00)	24 (52)	22 (48)	00 (00)	0.0002*
Is the formulary sufficiently updated?	09 (19)	30 (64)	08 (17)	07 (15)	26 (57)	13 (28)	0.85
Are you involved in decisions regarding additions/ deletions?	14 (30)	29 (62)	04 (08)	20 (43)	26 (57)	00 (00)	0.29
Are you adequately informed of alterations?	24 (51)	18 (38)	05 (11)	15 (33)	30 (65)	01 (02)	0.03*

* Significant ($p<0.05$)

Table A3: Consultant responses about the Antimicrobial Policy

The Antimicrobial Policy	1994			1999			Pearson Chisquare
	YES	NO	DNK	YES	NO	DNK	
Do you have a copy?	36 (77)	09 (19)	02 (04)	22 (48)	24 (52)	00 (00)	0.001*
Do you follow its recommendations?	28 (60)	10 (21)	09 (19)	21 (46)	24 (52)	01 (02)	0.01*
Does it give clear guidelines on the use of new antibiotics?	24 (51)	07 (15)	16 (34)	15 (33)	11 (24)	19 (41)	0.11

* Significant ($p<0.05$)

Tables A4 and A5 provide responses to questions regarding factors affecting the prescription of new drugs by consultants.

Table A4: Ranking by consultants of how they usually get to know of a new drug

How do you usually get to know of a new drug?	Ranking (1= highest rank)		Mann Whitney (p value)
	1994	1999	
medical journals	1	1	0.81
medical representatives	2	2	0.11
Internet *	Not included	6	Not applicable
conferences abroad	3	3	0.09
conferences in Malta	5	5	0.42
non-medical literature	6	7	0.09
colleagues	4	4	0.73

* The Internet was added in the questionnaire of 1999.

Table A5: Ranking by consultants of what they consider to be the most influential "pressure to prescribe" a new drug

Which do you consider as the most influential "pressure to prescribe" a new drug?	Ranking (1=highest rank)		Mann Whitney (p value)
	1994	1999	
advertising (direct mail, journals, medical representatives)	2	2	0.75
controls and regulations by health authorities	4	3	0.23
demands from patients	5	5	0.79
demands from pressure groups and society at large	6	6	0.16
media and press	7	7	0.75
limitations of the hospital formulary	3	4	0.38
medical opinion leaders	1	1	0.79

* Significant (p<0.05)

Tables A6, A7 and A8 provide details of consultant responses on the influence of the pharmaceutical industry.

Table A6: Consultant responses to the question of whether they have been offered financial or material benefits to influence the prescription of new drugs

Have you been offered financial or material benefits to prescribe new drugs?	1994			1999			Pearson Chisquare
	YES	NO	DNK	YES	NO	DNK	
	13	34	00	15	31	00	0.60
	(28)	(72)	(00)	(33)	(67)	(00)	

Table A7: Number of consultants claiming that they were given benefits by the pharmaceutical industry

What benefits were given by the pharmaceutical industry?	Number of consultants		Pearson Chisquare
	1994	1999	
purely financial	1	0	0.26
sponsorship to participate in symposia	13	14	0.19
opportunity to publish papers	1	5	0.12

Others: free samples, small gifts, subscription to journals, journal and book tokens

Table A8: Consultants' opinion about symposia on new drugs organised by the pharmaceutical industry

Are symposia on new drugs:	1994			1999			Pearson Chisquare
	YES	NO	DNK	YES	NO	DNK	
of good standard?	37	04	06	38	04	04	0.97
	(79)	(08)	(13)	(82)	(09)	(09)	
scientific?	31	08	08	34	08	04	0.87
	(66)	(17)	(17)	(74)	(17)	(09)	
educational?	35	03	09	35	06	05	0.35
	(75)	(06)	(19)	(76)	(13)	(11)	
too promotional?	18	21	08	16	24	05	0.58
	(38)	(45)	(17)	(36)	(53)	(11)	
Are entertainment and gifts offered modest?	42	02	03	40	01	05	0.60
	(89)	(04)	(07)	(87)	(02)	(11)	

Tables A9 and A10 give consultant responses to questions concerning factors that they consider prior to prescribing a new drug and from where they obtain information.

Table A9: Ranking of factors that consultants consider prior to prescribing new drugs

Which factors do you consider prior to prescribing a new drug?	Ranking (1= highest rank)		Mann-Whitney (p value)
	1994	1999	
licensed indications	7	7	0.67
unlicensed use	8	9	0.12
literature and information about it	3	3	0.60
reports of clinical trials	2	1	0.75
safety	1	2	0.18
comparison with other drugs available	4	4	0.83
costs	5	8	0.03 *
cost-effectiveness	9	5	0.00 *
advantages in administration	6	6	0.90

* Significant (p<0.05)

Table A 10: Ranking of sources from where consultants obtain information on new drugs prior to requesting them

From where do you get information on new drugs prior to requesting them?	Ranking (1=highest rank)		Mann-Whitney (p value)
	1994	1999	
medical journals	1	1	0.36
Internet **	Not included	4	Not applicable
information from drug companies	2	3	0.02 *
conferences abroad	3	2	0.01 *
conferences in Malta	4	5	0.64
non-medical literature	7	7	0.03 *
information from Drug Information Unit	5	6	0.90
information supplied by the DTC	6	7	0.61

* Significant (p<0.05)

** The Internet was added in the questionnaire of 1999.

Table A 11 gives consultant responses to a series of questions about the Drug and Therapeutics Committee (DTC)

Table A 11: Consultants' opinion about the DTC and its operations

Questions to consultants about the DTC	1994			1999			Pearson Chisquare
	YES	NO	DNK	YES	NO	DNK	
Do you feel represented on the DTC?	16 (34)	31 (66)	00 (00)	15 (33)	31 (67)	00 (00)	0.88
Do you feel well informed with the decisions of the DTC?	19 (40)	28 (60)	00 (00)	07 (15)	39 (85)	00 (00)	0.007 *
Do consultants have the opportunity to contribute in the setting up of DTC policies?	23 (49)	22 (47)	02 (04)	15 (33)	30 (65)	01 (02)	0.09
Are you aware of the new protocols set since 1993 for the use of new drugs?	19 (40)	28 (60)	00 (00)	19 (41)	27 (59)	00 (00)	0.93
Have you been / are you involved in the setting up of any of the protocols for new drugs set up by the DTC?	14 (30)	33 (70)	00 (00)	16 (36)	29 (64)	01 (02)	0.56
If YES - are you satisfied with the proceedings of the sub-committee?	06 (44)	04 (28)	04 (28)	13 (28)	02 (05)	30 (67)	0.13
Has such participation created any problems with time?	05 (36)	06 (43)	03 (21)	08 (17)	08 (17)	30 (65)	0.82
Has such participation created any problems of commitment?	05 (36)	06 (43)	03 (21)	05 (11)	11 (24)	30 (65)	0.45
Has such participation created any problems with your peers?	04 (29)	07 (50)	03 (21)	02 (04)	14 (31)	30 (65)	0.14
If NO - have you been asked to be a member of any DTC sub-committee?	01 (03)	27 (82)	05 (15)	01 (02)	30 (65)	15 (33)	0.94
Would you be willing to actively contribute in such a sub-committee?	17 (52)	12 (36)	04 (12)	21 (46)	08 (17)	17 (37)	0.27

* Significant ($p < 0.05$)

Tables A12 and A13 give consultant responses about clinical trials and post-marketing scientific studies and surveillance.

Table A 12: Consultants responses on participation in clinical trials

Participation in clinical trials	1994			1999			Pearson Chisquare
	YES	NO	DNK	YES	NO	DNK	
Have you taken part in clinical trials for new drugs <i>prior</i> to approval on the market?	14 (30)	31 (66)	02 (04)	10 (22)	33 (72)	03 (06)	0.41
Have you taken part in clinical trials for any new drug <i>after</i> it was licensed on the market?	15 (32)	31 (66)	01 (02)	15 (33)	31 (67)	00 (00)	1.00
Have you used new drugs for unlicensed indications?	07 (15)	38 (81)	02 (04)	14 (31)	31 (67)	01 (02)	0.08
Should authorities be informed of pre- or post- marketing clinical trials?	39 (82)	04 (09)	04 (09)	33 (72)	07 (15)	06 (13)	0.27

Table A 13: Consultants' views on the use of samples and on adverse drug reaction (ADR) reporting

Do you agree with the following statement?	1994			1999			Pearson Chisquare
	YES	NO	DNK	YES	NO	DNK	
Post-marketing scientific studies have been used as a disguised form of promotion	31 (66)	07 (15)	09 (19)	25 (54)	10 (22)	11 (24)	0.31
Samples of new drugs should not be used on patients within NHS without permission	27 (58)	18 (38)	02 (04)	24 (52)	19 (41)	03 (07)	0.69
If a patient is started on samples, the DTC is not bound to approve the drug	32 (68)	08 (17)	07 (15)	36 (78)	02 (04)	08 (18)	0.05
Should there be a national ADR reporting system in Malta?	46 (98)	00 (00)	01 (02)	43 (93)	03 (07)	00 (00)	0.08

Table A 14 gives the consultants' opinion on the role of hospital pharmacists.

Table A14: Consultants' responses to factors that they consider to be part of the role of hospital pharmacists

Is this within the role of the hospital pharmacist?	1994			1999			Pearson Chisquare
	YES	NO	DNK	YES	NO	DNK	
Supply of information about new drugs on request by consultants	42 (89)	03 (07)	02 (04)	45 (100)	00 (00)	00 (00)	0.08
Supply of information about new drugs as soon as they are introduced	41 (86)	03 (07)	03 (07)	38 (85)	07 (15)	00 (00)	0.19
Evaluation of new drugs as soon as they are introduced on the market	27 (57)	13 (28)	07 (15)	26 (58)	19 (42)	00 (00)	0.36
Discussion with the consultant when prescribing a new drug on the ward	38 (81)	07 (15)	02 (04)	37 (82)	08 (18)	00 (00)	0.78
Participation as a member in the DTC sub-committees	42 (89)	00 (00)	05 (11)	43 (96)	02 (04)	00 (00)	0.17
Participation as a member of the DTC	43 (91)	00 (00)	04 (09)	44 (98)	01 (02)	00 (00)	0.33
Participation in conducting clinical trials on new drugs	40 (85)	02 (04)	05 (11)	39 (87)	06 (13)	00 (00)	0.17
Evaluation of whether requests for new drugs are according to protocols	35 (74)	07 (15)	05 (11)	37 (82)	08 (18)	00 (00)	0.89
Monitoring of response to new drugs	27 (57)	14 (30)	06 (13)	34 (76)	11 (24)	00 (00)	0.32
Organisation and participation in audit and drug-use evaluation studies	40 (85)	02 (04)	05 (11)	40 (89)	04 (11)	00 (00)	0.43
Involvement in ADR reporting schemes	43 (92)	01 (02)	03 (06)	41 (91)	04 (09)	00 (00)	0.18

Tables A 15 and A16 give consultants' views of the system for introducing new drugs and of factors that consultants considered to be problematic at that time.

Table A 15: Consultants' opinion on the system for introducing new drugs

Is the current system for introducing new drugs in hospital efficient?	1994			1999			Pearson Chisquare
	YES	NO	DNK	YES	NO	DNK	
	08 (17)	30 (64)	09 (19)	01 (02)	42 (93)	02 (05)	0.007 *

* Significant ($p < 0.05$)

Table A 16: Consultants' views on problems within the system

Is this factor a problem with the present system?	1994			1999			Pearson Chisquare
	YES	NO	DNK	YES	NO	DNK	
Time lag until the drug is approved?	33 (70)	05 (11)	09 (19)	41 (96)	01 (02)	01 (02)	0.07
Availability of stocks of the drug?	29 (62)	08 (17)	10 (21)	37 (86)	05 (12)	01 (02)	0.25
Paper work involved?	33 (70)	05 (11)	09 (19)	34 (79)	07 (16)	02 (05)	0.63
The number of requests which are not approved?	13 (28)	20 (42)	14 (30)	23 (54)	19 (44)	01 (02)	0.19
Subsequent approval of the drug after it is approved?	24 (51)	10 (21)	13 (28)	25 (58)	15 (35)	03 (07)	0.47
The involvement of pharmacists in the processing of requests?	07 (15)	26 (55)	14 (30)	02 (05)	38 (88)	03 (07)	0.04 *
Having requests for new drugs submitted to the DTC through the Head of Department?	20 (43)	16 (34)	11 (23)	15 (35)	27 (63)	01 (02)	0.08
Available information prior to requesting a new drug?	12 (25)	23 (48)	12 (26)	07 (16)	34 (79)	02 (05)	0.08
The importance given to the cost of the drug?	28 (60)	10 (21)	09 (19)	30 (70)	12 (28)	01 (02)	0.82
The setting up of protocols for the use of new drugs?	16 (34)	19 (40)	12 (26)	18 (42)	24 (56)	01 (02)	0.80

* Significant ($p < 0.05$)

Appendix VII: Detailed Responses to the Prioritisation Questionnaire Sent to Consultants in 1999

Table A 17: Consultants' responses (YES, NO, DO NOT KNOW) to questions regarding entitlement to free medicines and prioritisation. Replies are given as number and as percentage (n=43)

	YES	NO	DNK
Is the current system for allocation of resources within the Government Health Services adequate?	03 (07)	29 (67)	11 (26)
Is the present system for entitlement to free medicines (Schedule V and 'Pink card') fair and reasonable?	10 (23)	30 (70)	03 (07)
Should there be any form of rationing in the practice for introducing new drugs into the Government Health Services?	30 (70)	10 (23)	03 (07)
Should physicians within the Government Health Services be allowed to treat their patients with whatever they feel is the best drug for the individual without having to consider costs?	12 (28)	29 (67)	02 (05)
Is rationing ethical?	25 (58)	12 (28)	06 (14)

Table A 18: Consultants' ranking to different options on how new drugs can be introduced into the practice for introducing new drugs into the NHS in Malta?

(The higher the score, the higher the rank)

	Score	Rank
All requests for new drugs should be approved without restriction	71	5
Develop new ways for using existing resources more effectively	192	2
Study cost-effectiveness as compared to existing drugs	218	1
Set prioritisation within a limited budget	188	3
Assess the significance and impact of the disease for the population	182	4

Consultants' responses on who should be involved in the setting of priorities for the practice of introducing new drugs into the Government Health Services

Top five (in rank order): Drug and Therapeutics Committee, clinical consultants, policy makers, consultants in public health, representatives of patients.

Table A 19: Consultants' ranking of factors which should be considered when establishing prioritisation for the introduction of new drugs into the Government Health Services

1=should not be considered	2=is not important	3= I am not sure about	4=is important	5= must be considered	
When deciding on whether or not to introduce a new drug into the Government Health Services, this factor:				mean score of evidence	Rank *
02. Evidence from clinical trials that the drug has proven efficacy				4.9	1
03. Evidence that the drug is effective in clinical practice				4.9	1
01. Evidence about safety				4.8	3
09. Drug improves quality of life				4.6	4
29. Whether it is ethical to use the drug				4.5	5
14. The cost-effectiveness of the drug				4.4	6
07. Prognosis of the disease condition without treatment				4.3	7
15. No other treatment available for the disease condition				4.2	8
30. Whether the indication for use is licensed or not				4.2	8
06. Drug cures the disease				4.2	8
20. How much an individual patient would possibly benefit				4.2	8
05. Alternative drugs available on the formulary				4.1	12
08. Drug prolongs length of life				4.0	13
13. The cost of treatment with the drug				4.0	13
16. The total increased cost to the Department of Health				3.9	15
17. Cost per patient				3.8	16
04. If the drug is used for treatment or prophylaxis (prevention)				3.8	16
18. The number of patients who would require the drug				3.7	18
28. Information about the economic evaluation of the drug				3.6	19
31. If the drug is registered by the Health Authority				3.4	20
23. Whether the drug is requested for cosmetic purposes				3.3	21
24. Whether the drug is requested for recreational purposes				3.1	22
19. The age of the patient/s benefiting from the drug				3.0	23
11. Drug is for hospital use only				2.8	24
12. Drug will be required on an outpatient basis				2.7	25
27. Possible influence by the pharmaceutical industry				2.4	26
25. The disease was acquired through sex, drug abuse, smoking				2.3	27
22. If the disease was acquired through the health system				2.2	28
10. Disease condition is on the Schedule V list of chronic illness				2.1	29
26. The reputation of the consultant who prescribed the drug				1.8	30
32. Pressure for approval from the patient, family, politicians				1.8	30
21. The sex of the patient/s benefiting from the drug				1.2	32

* Ranking order starting from the highest rank

Appendix VIII: Detailed Responses Collected during the Interviews with Patients

100 patients were interviewed, therefore the number of replies was equivalent to percentages. Interviews took from about 20 to 45 minutes.

Age: median age 54 (range 26 to 82)

Sex: 53 males, 47 females

Information on where the non-formulary drugs were first prescribed by consultants

58 patients had their non-formulary drugs prescribed when they visited their consultant at the Outpatients' Department at St Luke's Hospital. 34 patients had non-formulary drugs first prescribed while they were in-patients in hospital and then this treatment was continued after discharge. 8 patients had their drugs initially prescribed when they visited a consultant privately.

Entitlement to free medicines

88% of patients encountered inconveniences until they received the entitlement to free medication – mainly through delays in receiving the Schedule V card.

94% of patients were pleased with the current policies for entitlement to free treatment, however 76% of patients still believed that the system for entitlement could be improved.

The number of non-formulary drugs prescribed to patients

The majority of patients (51) had 3 or more of the drugs that they were taking which were non-formulary and thus required an approval. 27 patients were taking 2 non-formulary drugs and 22 patients were taking 1 non-formulary drug.

Tables A 20 and A21 give details of the time taken for the patients to receive the approval for non-formulary drugs and what the patients did in the meantime.

Table A 20: Time (weeks) for which patients had to wait before they received their first approval for non-formulary medicines

Time (weeks)	< 2	2 - 4	5 - 8	> 8
No of patients	17	57	24	2

Table A 21: Details of what the patients did until they received their approval for non-formulary drugs

In the meantime, until the approval was received the patient:	
Bought the medicine from his own pocket	68
Contacted someone who could hasten the issue of the permit	5
Stayed without the medicine	4
Other:	
Remained taking the previous medication	15
Was given a month's supply of drugs from the NHS	8

62 % of patients said that they did not have problems with the issue of a re-approval for non-formulary drugs.

Availability of stock

63% of patients said that dispensaries of the government health services were adequately stocked. When asked what they did if a drug was out of stock from the Government Health Services 57 patients stated that they would buy it from a community dispensary, 31 patients said that they would take other medicines with the same therapeutic effect and 12 gave other replies.

Table A 22: Patient responses to questions about prioritisation

Use of resources within the Department of Health	YES	NO	DNK
1. Are the financial resources allocated to the health care system properly utilised?	22	57	21
2. Should doctors employed with the government health services take the price of the medicines that they prescribe into consideration when prescribing?	74	18	8
3. If two medicines achieve the same desired therapeutic effect, should doctors prescribe the cheapest one?	87	5	8
4. Does the Department of Health need systems to monitor the expenditure on new drugs?	84	11	5
5. Should requests for new drugs made by doctors be approved immediately without being discussed?	40	46	14
6. Should the Department of Health look into new ways how the budget available could be used more efficiently?	88	5	7

Patients ranked that decisions for the introduction of new medicines into the government health services should be taken by (top five): individual consultant physicians, a group of consultants, general practitioners, the Drug and Therapeutics Committee and patient groups.

When asked to choose between two alternative principles for decisions regarding the introduction of new drugs, 29 patients decided that any potentially useful medicines should be procured while 71 patients were of the opinion that the interests of an individual patient should be weighed against the interests of other patients.

When asked which factors are to be considered when introducing new drugs into the Government Health Services, the top five factors spontaneously given by patients were:

high safety, no side-effects, the drug works, the drug is of good quality, the cost of the drug, other treatment that is available for the disease.

Appendix IX: Details of Case Studies to Illustrate Key Issues Associated with the Managed Entry of New Drugs into the NHS in Malta

Case 1: low molecular weight heparin (LMWH)

The local agent representing the foreign manufacturer for unfractionated heparin informed the government pharmaceutical services (GPS) that the manufacturing company had stopped the manufacture of unfractionated heparin in pre-filled syringes and therefore he would not be in a position to keep on supplying the product to the GPS. The GPS purchased over one year's stock of unfractionated heparin in prefilled syringes until a suitable alternative product could be identified and purchased.

During the 111th meeting of the Drug and Therapeutics Committee (DTC), LMWH was recommended and approved for the prevention and treatment of deep vein thrombosis (DVT). It was recommended to open the specifications to include dalteparin, enoxaparin and tinzaparin, as each of these were indicated for the treatment of DVT. It was not recommended to approve LMWH for the other indications of treatment, particularly as different LMWHs have different licensed indications. It was also noted that the dosage for the different LMWHs in terms of units varied and that they should be compared in terms of therapeutic equivalence.

The local medical representatives of the different manufacturers of LMWH followed the process of approval with care and requested meetings with various stakeholders including the Director General (DG), the secretariat of the DTC and the Chairman. One company also flew in the area managers from abroad.

A number of problems arose in the process of setting the specifications for LMWHs and these were discussed with various parties. The original decision for the introduction of LMWH was revised so that LMWH could be introduced gradually, the first step being prophylaxis. The introduction of LMWH for the treatment of DVT was to be delayed to a later stage.

Case 2: fentanyl patches

In October 1999 the medical representative (of the drug company) sent a copy of the Research Ethics Committee's approval for the final protocol of a clinical trial with fentanyl patches (Durogesic). The multicentre study was to run concurrently in other countries.

The secretariat of the Drug and Therapeutics Committee (DTC) sought clarification on the objectives of the clinical study as the drug was already licensed in Europe. Clarification was also sought on how patients would be recruited and what would happen once trial stock was finished. The DTC recommended that the patient consent form for the trial was to include a disclaimer of liability by the Department of Health and clarification that the Department of Health was not bound to continue supplying the drug free of charge once the trial was over.

The medical representative clarified that the objective of the trial was to give Maltese investigators the opportunity to have hands on experience with the preparation.

The Research Ethics Committee did not approve the inclusion of the disclaimer clause as set by the Department of Health. Consequently the consultant decided that he could not carry out the trial. He remarked "it is a pity that administrative quibbling deprived the department from a useful research grant and this has certainly not enhanced the reputation of the Department of Health in Malta".

Case 3: implementation of the formulary chapter for cardiology

When in 1999 the Director General (DG) accepted that the formulary be revised, the chapter for cardiology was the first to go through the process of revision and this exercise formed a pilot for the revision of the rest of the formulary.

The hospital pharmacists recommended that there should be a specific form for each protocol-regulated drug so that it could be ensured that the consultants provided all the required information (from the protocol) on the request. The chairman of the Drug and

Therapeutics Committee (DTC) considered that having a different form for each protocol-regulated drug would be too laborious for consultants to implement. One problem was the lack of availability of computers in all out-patient clinics.

As part of the revision of the formulary the protocols within each chapter needed to be revised. The existing protocol for angiotensin-converting enzyme (ACE) inhibitors and for angiotensin-II receptor antagonists (sartans) divided the ACE inhibitors into first line: captopril, enalapril and lisinopril (these were not protocol regulated) and second line perindopril and monopril (protocol-regulated). If a patient was intolerant to one of the ACE inhibitors in each category because of a 'dry, hacking cough', then an angiotensin-II receptor antagonist could be prescribed. At that time ACE inhibitors were divided into first-line and second-line to enable the introduction of perindopril and monopril.

When the protocol was being revised, the senior consultant cardiologist, who was involved throughout the process of revision, pointed out that there was no point in separating the ACE inhibitors into two categories. He insisted that there was no actual variation in the degree of coughing between the different members of this class. The consultants recommended that angiotensin-II receptor antagonists were to be prescribed after a patient did not tolerate any two of the 5 ACE inhibitors on the formulary. The choice of which ACE inhibitors were used was to depend on the prescribing habits of the consultants e.g. the cardiac surgeons preferred perindopril while the physicians started with enalapril or lisinopril. The cost of the different agents was worked out in terms of daily cost for the maintenance treatment. The issue was to be discussed at the DTC.

Another issue brought up during the revision of the protocols for cardiology was that some of the drugs included in the existing protocols were not licensed for the indications specified in the protocol. Up to a certain point in time the official licensing of indications was not being specifically considered by the DTC. However since July 1999 the licensing status of the drug and of its indication was included in all decisions of the DTC as shown by the following examples.

Example 1: Selective alpha-blockers

Doxazosin was not licensed for the treatment of CHF. Consequently the official formulary, which specified alpha-blockers as first line treatment for hypertension, were amended to the effect that doxazosin, or the whole class of peripheral alpha-blockers, were no longer to be considered as first-line antihypertensive therapy. The senior consultant cardiologist remarked that as a result of the warnings regarding doxazosin there had been a substantial diminution in the usage of the drug. However he recommended that doxazosin may still be used in specific cases of CHF when everything else had failed. He recommended that the use of this drug should be specified as being the decision of the caring physician.

Example 2: Angiotensin-II receptor antagonists

Angiotensin-II receptor antagonists were an alternative treatment for patients who had to discontinue treatment with ACE inhibitors because of persistent cough. Beyond this their role in hypertension remained to be established. They were licensed in the treatment of hypertension but were not licensed for the treatment of CHF. The senior consultant cardiologist recommended that angiotensin-II receptor antagonists should still be included in the protocol for CHF and pointed out that the angiotensin-II receptor antagonists were going to be licensed for the treatment of CHF in the near future. He remarked that most cardiologists felt that all patients with CHF should have the proven benefits of ACE inhibition. The 20% of patients who could not tolerate ACE inhibitors were to be given angiotensin-II receptor antagonists with the full knowledge that “as yet the lengthy process required by the FDA (USA) for licensing was still ongoing”. He recommended that it should be specified to the clinician that the use of angiotensin-II receptor antagonists in CHF was a decision for which consultants were entirely responsible.

The Director General (DG) specified that drugs should not be included in protocols/guidelines for unlicensed indications as legally the Department of Health could not take responsibility for recommending the prescription of drugs for unlicensed uses.

There are still no local guidelines for the use of products for unlicensed indications in hospitals of the national health services (NHS) in Malta.

The guidelines on 'The purchase and use of unlicensed medicines in hospital' from the Guild of Healthcare Pharmacists of the UK¹ specified that a clinician had the right to use any material for any purpose in the treatment of his own patients, although when he did so was entirely his responsibility. If a patient was harmed by a licensed medicine as a result of it being used for an unlicensed indication and not because of any defect in the product itself, then the prescriber may be liable for the resulting harm. A practitioner's medical defence union may require advance warning that unlicensed products were being prescribed. A hospital consultant having extensive knowledge of medicines used in a particular speciality could feel confident in using licensed medicines for unlicensed indications. This was to be fully explained to the patient's general practitioner, if a referral included a recommendation to continue to prescribe for an unlicensed indication. The general practitioner was not obliged to prescribe in such circumstances.

Case 4: drugs for the treatment of hepatitis C

In 1998 there was a growing public health concern regarding the increasing number of patients suffering from chronic hepatitis C in Malta. It was stressed that the larger the viral pool in the population, the greater the possibility that the virus would be transmitted. An exercise on the cost-effectiveness of treatment with alfa-interferon was commissioned.

Alfa-interferon was being requested on a named-patient basis. Some of the patients had contracted hepatitis C from blood products supplied through the national health services (NHS). These patients exerted pressure on the authorities, to start treatment without having to wait for the result of the cost-effectiveness exercise. The

¹ GUILD OF HEALTHCARE PHARMACISTS, 2001. The purchase and use of unlicensed medicines in hospitals. Policy Statement No. 006, Issued January 1997, Updated June 2001. [online] <http://www.ghp.org.uk/> [5th September 2001].

Department of Health was liable to provide treatment for these patients and treatment was started for this group. In the meantime some doctors and relatives of patients who did not qualify on these grounds started complaining. The latter patients consisted mainly of prison inmates and most of them were lost to follow-up once they got out of prison.

In February 1999 the cost-effectiveness exercise was finalised and it was recommended that treatment with alfa-interferon be given to patients who were hepatitis C carriers, as the literature and international experience suggested that treatment was cost-effective. The report proposed that there would be a genotyping exercise on 50 PCR positive patients to determine the prevalent strains of hepatitis C virus in Malta as genotype affects response to treatment. The protocol, a patient referral form and a sheet for monitoring clinical parameters were developed. It was proposed that one of the consultants involved would act as a co-ordinator to follow-up treatment of patients with hepatitis C. Up to the end of December 2001, there were no follow-up reports of outcomes submitted.

Case 5: treatment of HIV

The Drug and Therapeutics Committee (DTC) recommended a protocol for anti-HIV treatment during the 96th DTC meeting in September 1997. The authorities concluded that the protocol was acceptable but too expensive to implement. It was decided to limit treatment to haemophiliacs infected with HIV through the use of blood products, as the Department of Health was obliged to treat these patients. The DTC opposed this decision stating that it was discrimination which had ethical and medico-legal implications (DTC Correspondence, 1997). The Minister pointed out that HIV was still not included within the Schedule V list of chronic diseases. The DTC was instructed to comply until the position was revised.

The legal advisor within the Department of Health warned that the decision taken was difficult to defend and would be seen as discriminating. The National Advisory Committee on Aids Prevention and Control wrote to the Minister and strongly deplored this action as unethical and immoral since it “sentenced sufferers to death”. In the meantime, the media made it public that anti-HIV treatment was not approved.

Consequently the policy for protease inhibitors was approved to incorporate all HIV cases.

Because of the delay in treatment for HIV in Malta, all the patients were started off on multiple therapy and this reduced the risk of resistance compared to the use of single agents, as had happened in some countries where treatment was started early. However, in December 1998 the consultant caring for HIV patients requested that a new drug combination be available due to problems with viral resistance, as had happened in other countries (DTC Correspondence, 1998).

Case 6: hyperlipidaemia

Entitlement to free treatment with statins was debated for a long time. The main point of contention by the authorities was that statins were used for prophylactic therapy and not for treatment of a chronic condition and therefore patients were not entitled to free treatment through the Schedule V list of chronic diseases. At one point in early 1998 statins were no longer supplied on the Schedule V. This resulted in withdrawal of patients' entitlement to statin treatment free of charge. As patients' supply was stopped abruptly there was an accumulation of stocks of statins at the GPS stores.

Just before the election in September in 1998 it was accepted that statins were to be supplied on Schedule V. The protocol for lipid lowering agents became operational on 1st September 1998 and a circular was issued to that effect². The protocol for lipid lowering agents was the first protocol to be established in the form of treatment guidelines. This protocol was intended to enforce control over the use of statins. The Circular specified the role of different stakeholders (general practitioners, consultants, outpatient units, the ScheduleV office and the DTC) in the implementation of the protocol. It also specified that the lipid sub-committee of the DTC would vet applications for individual patients. A specific form, which included the criteria of the protocol, was prepared and consultants were to complete the relevant information. The form was self-carbonised and could be filled in triplicate: a copy was to be left in the

² Department of Health (Malta) Circular No. 120/98, 1998. Protocol for lipid lowering agents becomes operational on 1 September 1998. Valletta, Malta: Department of Health, 14 August 1998.

patient's file, a copy was to be sent to the Schedule V office and a copy was to be sent to the DTC.

In the 4 months following the approval of the protocol (September to December 1998) there were 508 requests for new patients and 486 renewals for statins. 245 of these requests for statins were sent back to the consultants because they were not in line with the protocol. A report of the number of requests sent back to individual consultants was presented at the lipid sub-committee meeting. In October, December and January an audit of several medical files of approved requests was undertaken against the protocol criteria. Reasons why patients' requests were not according to protocol included lack of evidence of risk factors within patient's file, no entries in the patient's file for a long period of time and insufficient information regarding the diagnosis of the indication. All the requests where it was claimed that the patient had familial hypercholesterolaemia were reviewed. Of the 48 files reviewed only 14 patients met the criteria.

Problems with the implementation of the lipid protocol included that in some cases the information on the requests forms received was inaccurate, illegible or incomplete. Consequently forms had to be sent back to consultants resulting in delay in starting treatment. It was not possible for the Biochemistry Laboratory to print two copies of the results of the lipid profile and therefore if the results were attached to the request that was sent to the DTC there was no copy in the patient's file (Minutes of the Lipid Sub-committee meeting held on 21/10/98).

The lipid sub-committee discussed a number of issues during 2000 – 2001. One point of concern was the setting of recommendations for the dose equivalence of different statin preparations to enable choice of the cheapest alternative from the open tender. In October 2000 the government pharmaceutical services (GPS) were in the process of adjudicating the tender for statins. The specifications at the time of the tender were open for either of fluvastatin 20mg, pravastatin 20mg or simvastatin 10mg. The previous tender was adjudicated on the basis of the World Health Organisation (WHO) Defined Daily Dose (DDD). However, following adjudication the local agent of MSD (representing simvastatin, Zocor) complained about the doses of equivalence used. The complaint emphasised that the WHO DDD was not intended for comparison

between different therapeutic agents. Consequently the lipid sub-committee agreed that the DDD was a research instrument and was not appropriate for determining therapeutic equivalence between drugs in the same group. It was recommended that the dose equivalence of statins would be determined from the doses of different statins required to achieve specific reductions in LDL cholesterol. A 25% reduction in LDL cholesterol was recommended as baseline, as this percentage was often quoted in studies.

One consultant recommended that the criteria to estimate coronary heart disease (CHD) risk in the protocol for statins of September 1998 should be revised to target the population most likely to benefit from treatment with statins. The lipid subcommittee decided that in spite of its limitations, the statin protocol of September 1998 was sustainable. It was decided to carry out a feasibility study at the Lipid Clinic to study eligibility of treatment comparing the current protocol with other methods for measuring CHD risk.

In 2001 the marketing and distribution of cerivastatin were suspended following reports of increased incidence of rhabdomyolysis, particularly when administered in combination with gemfibrozil. In Malta cerivastatin was available from private community pharmacies but was not supplied through the national health services (NHS) because it was not the statin being procured through the GPS tender.

Case 7: proton pump inhibitors

The entitlement to free medicines for patients infected with *Helicobacter pylori* was debated at length. In January 2001 the authorities instructed the Drug and Therapeutics Committee (DTC) that *H. pylori* eradication was not approved through Schedule V because this indication was considered to be prophylaxis. Consequently the DTC informed the gastro-intestinal (GI) sub-committee of the authorities' decision. Requests for non-formulary drugs for *H. pylori* eradication that were received by the DTC were not recommended, and were returned to the respective consultants.

The consultants did not agree with the authorities' decision. The entitlement through Schedule V depended on interpretation of 'chronic peptic ulceration'. It was recommended that the GI sub-committee, being the expert committee, made this determination. On the other hand it was noted that the Director General (DG) had absolute authority over the criteria for entitlement and could therefore over-ride any decision of the GI sub-committee. Consultants insisted that they were responsible for recommending treatment. It was then the remit of customer care services to explain to patients why they were not entitled to this treatment free. Consultants "refused to be part of a system whereby 'responsibility and authority were in conflict'".

The DTC was instructed to vet all requests for proton pump inhibitors (omeprazole). The requests for proton pump inhibitors for peptic ulceration were vetted against the patients' files and in a number of cases there was no evidence that the patient had peptic ulceration. The individual consultants were notified accordingly. The DTC discussed this problem with the relevant consultants. It was recommended that a copy of the endoscopy report confirming peptic ulceration should be attached to the requests for proton pump inhibitors.

Case 8: taxanes

Since 1995 paclitaxel (Taxol) was approved as non-formulary on a named-patient basis for patients suffering from carcinoma of the ovaries that recurred after two remissions with platinum therapy. In January 1999 paclitaxel was recommended by the Drug and Therapeutics Committee (DTC) but was not approved by the Director General (DG) (DTC 99, 1999). Subsequently approval on a named-patient basis for new patients was stopped.

By April 2000 three requests were received for individual patients for docetaxel (Taxotere) for breast cancer. The consultant oncologists were asked to submit a request for new drugs in line with the policy for the introduction of new drugs of 1999. In May 2000 one of these patients filed a case in court against the DG and the Minister of Health. The patient, who suffered from advanced breast cancer, went for treatment to a renowned referral centre in the UK privately where she was started on treatment with docetaxel. The case presented at court claimed that docetaxel was the

patient's only treatment option. It stated that although the health authorities in Malta knew that the treatment could save the patient's life, they refused this treatment because of the cost involved. The complaint stated that the Department of Health incorrectly informed the patient that docetaxel did not cure cancer but only prolonged life by a few weeks and therefore her claim that the drug could save her was erroneous and unfounded. Information was attached to the complaint showing that the drug could be 'life-saving'. The information consisted of the package insert of the drug and a photocopy of a page from a UK women's magazine claiming that "the NICE which was set up to decide which life-saving drugs should be used, says Taxol should be given to all cancer patients and that a similar drug Taxotere was given the green light". The case highlighted that the patient paid taxes and social security contributions like every body else and therefore was entitled to free medicines as much as everybody else. It was noted that other patients were treated with paclitaxel through the NHS and that while the Department of Health was claiming that the two drugs (paclitaxel and docetaxel) were totally different, the patient submitted information showing that they were "brand names" of the same pharmaceutical composition. The patient appealed to the DG (the defendant) to respect her right for life guaranteed in the Constitution of Malta and in the European Convention for Human Rights. The Department of Health restated that docetaxel did not cure cancer but extended life by a few weeks. Docetaxel and paclitaxel were two different drugs from within the same therapeutic group. The patient's right for life was only interrupted by the disease and not by the Department of Health. Social security contributions did not automatically entitle citizens to all medicines from public funds as they deemed necessary.

NICE issued its 'Guidance to the NHS on the use of taxanes for the treatment of breast and ovarian cancer' in May 2000³. Taxanes were recommended for ovarian cancer but not for breast cancer.

Following the publication of the guidance on the use of taxanes for ovarian cancer by NICE, the DTC recommended the request for paclitaxel as first-line treatment for ovarian cancer. This recommendation was approved by the DG.

³ NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE, 2000. Guidance on the use of taxanes for ovarian cancer. [online] <http://www.nice.org.uk/> [1st June 2000].

A case was also prepared for the introduction of docetaxel for breast cancer. The main source of information utilised was the information from the European Public Assessment Report (EPAR) for the product⁴. Docetaxel had been given a Market Authorisation (MA) by the EMEA in November 1995. In the initial assessment the Committee for Proprietary Medicinal Products (CPMP) recommended that the MA should be granted under exceptional circumstances (information from randomised Phase III clinical studies was not yet available at the time). In 1997 two Phase III randomised comparative trials were submitted by the MA holder and confirmed the favourable risk/benefit profile of docetaxel. Subsequently the CPMP issued its approval for docetaxel in January 2000. From the available studies it was also concluded that in alkylating failure, docetaxel did not effect the overall survival time or the time to progression. The introduction of docetaxel for breast cancer was discussed during the 107th DTC meeting in June 2000. The DTC decided to wait for further studies and did not recommend the request for docetaxel at that time. This was noted by the DG.

In the meantime an appeal against the NICE guidelines with regards to the decision on the treatment of breast cancer was filed by the drug company and by an organisation CancerBACUP. NICE's appeal panel ruled that NICE failed to act fairly and produced perverse guidance on the use of taxanes in breast cancer. Subsequently the NICE Guidance for the treatment of breast cancer was published on the 14th June 2000.

The information used in the NICE guidance corresponded with that used for the evaluation in Malta and the recommendations of the DTC were not changed. The NICE Guidance were being developed during the court case and were referred to during the hearing of the case. The recommendation of the DTC was compared to the final decision by NICE and was questioned.

On the 11th August 2000 there was a judgement made on the court case. Points from this court judgement were noted. It was clarified that it was not the remit of the court to pass an ethical, moral or political judgement on the operations of the defendant, but to give a legal judgement on the fact that the drug was not supplied through public

⁴ EUROPEAN MEDICINES EVALUATION AGENCY, 2000. Medicinal products for human use, European public assessment report for docetaxel. [online] <http://www.emea.eu.int/> [23rd May 2000].

funds. It was not the remit of the Court to decide whether the state was providing the best medical care. The Judge gave examples of case laws from abroad such as: R v Cambridge Health Authority 1995 and stated “The courts have only one function, which is to rule upon the lawfulness of decisions”.

The court noted that neither the Constitution of Malta nor the European Convention gave the right to free medical treatment. It was decided that in no way was the DG deliberately or recklessly taking any action against the patient’s right to life. The state was obliged to make “adequate provisions for medical care”. The court judged that the patient was not being denied adequate medical care, but a specific drug that in the opinion of the Department of Health was not justified at this stage. The Constitution also provides that “no one should be subjected to torture or to degrading treatment”. The court decided that the patient did not suffer any inhuman or degrading treatment.

The sentence was subsequently appealed and the appeal has been postponed several times. The patient has since died and by December 2001 the appeal had not yet been heard.

Case 9: imatinib

In March 2001 two requests were received from the Chairman of the Department of Radiotherapy & Oncology for imatinib, one for the use of imatinib for the treatment of chronic myeloid leukaemia and one for the treatment of gastrointestinal stromal sarcoma. Data was submitted with the requests. All the papers presented provided in vitro data and no in vivo data was available at that time.

Imatinib was not yet licensed by the European Medicines Evaluation Agency (EMA). No clinical trial data were available. The web-site of the NICE indicated that the appraisal for imatinib was still in progress and published the protocol being used for the appraisal. The case and the available information were discussed between the secretariat and the chairman of the DTC and it was decided to wait until there was a final decision by the EMA.

A specific case of a patient who was prescribed imatinib by his oncologist was sensationalised by the local media. The history of the patient's disease including details of his morbidity before treatment and of the "amazing progress in his blood picture" since starting treatment were given on television. The patient was hoping that the Department of Health would approve this medicine free through the NHS. The patient was given financial support by the Community Chest Fund (a national charity) to buy the first two boxes of medicine. The Department of Health responded to the media pressure by stating that the request for imatinib (Glivec) was being considered by the DTC and that evidence was being gathered for the case.

Because of these pressures it was decided to compile the case and present the case to the DTC even though the drug was not yet licensed. During the compilation of the case the consultant who submitted the requests was contacted for further information particularly regarding the number of patients who were eligible for the drug and the duration of therapy, which was not specified on the request. Once the appraisal was finalised it was sent to the consultant oncologist for his comments. In the meantime the media kept track of the progress of the request. By December 2001 the case was not yet discussed by the DTC because the DTC meeting that was scheduled for December was postponed, for unrelated reasons.

Case 10: entacapone

The request for entacapone was discussed during the 107th meeting of the Drug and Therapeutics Committee (DTC) in June 2000. At that time in view of the great individual variation reported in the response to treatment, and because the safety profile of the drug was not yet established, the DTC decided to defer the decision until more evidence was available. It was decided that should entacapone be found to be a drug of choice in clinical practice, more studies would be published shortly. The DTC recommended that the consultant neurologist should submit the request for entacapone, together with any updated information in six months' time.

In November 2001 the consultant neurologist submitted a further request and consequently the drug was re-considered by the DTC. The request recommended that this drug be prescribed solely by a consultant neurologist according to specified

criteria. The consultant stressed that the drug was licensed in Europe as well as the United States, stressing that the drug had passed the “rigorous scrutiny of the FDA”. The consultant neurologist pointed out that there were a few patients with severe Parkinson’s Disease who were purchasing the drug, in spite of its cost, as they felt that their quality of life had improved significantly. The consultant neurologist attested to this progress.

Further information was presented with the request: papers and a chapter from a neurology textbook. The information had been compiled by the medical representative of the product. The DTC considered that no additional information to what had already been presented in the first request was found. The consultant was invited to attend the next DTC meeting to present the case. This meeting was scheduled in 2002.

Case 11: C-1 esterase inhibitor concentrate

C-1 esterase inhibitor concentrate was requested for a named-patient suffering from acute attacks of angioedema. This request was discussed by the Drug and Therapeutics Committee (DTC) at the 92nd meeting in March 1997. The woman had refused to start prophylactic treatment with danazol because of probable side effects of this drug. The Chief Government Medical Officer (CGMO) requested that the patient sign a declaration that she refused treatment with danazol and that she was aware of the risks of viral transmission associated with the use of C-1 esterase inhibitor.

Recommendations of the Blood Product Advisory Committee (BPAC) were sought. In view of the fact that this drug was life saving a product was recommended, despite the lack of available information on the safety of the product. The product was obtained using voluntary paid donors. The BPAC requested that the patient be informed of the possible risks involved and that a consent form should be signed to confirm this. A protocol for the management of hereditary angioedema was prepared with specific forms to be kept in the patient’s file particularly as this was an acute condition and patients would need to be admitted urgently.

Case 12: cisapride

Janssen Cilag sent information detailing the rare but serious ventricular arrhythmias (VAs) reported during the use of cisapride (Prepulsid). The Drug Information and Pharmacovigilance Section of the Medicines Regulatory Affairs Unit (MRAU) received information from the company regarding action being taken by various health authorities. In the USA and Canada cisapride was put on a limited access programme so that only patients who met criteria for eligibility would have access to the drug. Concern about cardiac arrhythmias led to the initiation of a European review of the risks and benefits of cisapride. Germany invoked an article 12 procedure in July 2000. The European Medicines Evaluation Agency (EMA) was to reach a decision on the status of cisapride within the European Union (EU) within 120 days. This review was to consider what indications for cisapride, if any were justified. In accordance with the article all EU member states would be bound to implement this decision once it was taken. In the meantime all countries within the European Union (EU) reviewed the marketing status of cisapride. The marketing authorisation was suspended in the United Kingdom, Germany, and Luxembourg.

Data on usage of cisapride in different countries was presented. The company asked health authorities in Malta to categorise cisapride in the category of products that needed a controlled prescription. The Director General (DG) referred the issue to the gastro-intestinal (GI) sub-committee of the Drug and Therapeutics Committee (DTC) and requested that it submit scientific recommendations to the DG prior to him taking a final decision as to the marketing status of cisapride in Malta pending the decision from EMA.

The GI subcommittee considered that cisapride was a gastro-intestinal motility stimulant for which there was no alternative treatment. Within the national health services (NHS) cisapride was a protocol-regulated drug and therefore its use in the NHS was controlled. In the private setting cisapride could be prescribed by all medical practitioners. The possibility of restricting prescribing within private practice to 'specialists' was discussed extensively. It was pointed out that there was no definition of a 'specialist' according to the laws of Malta. It was debated whether legally prescribing by general practitioners could be restricted.

The different EU countries took a range of decisions from total restriction to no restriction at all. The GI subcommittee presented this variation to show that there was no clear evidence on which to base a final decision. It was considered that the risks were not major if the drug was prescribed according to the indications for use. It was recommended that prescribers should make a risk/benefit analysis and that if there were contra-indications the prescriber (be it a general practitioner, a surgeon or a medical consultant) was to take the responsibility of referring the case to the relevant cardiac specialist if deemed necessary.

By December 2001, a decision had not yet been taken by the EMEA.

Case 13: riluzole

Riluzole was initially approved on a named-patient basis in August 1998 after motor-neurone disease was added to the Schedule V list of chronic conditions immediately before the general election of September 1998. In 1999 Director General (DG) asked the consultant neurologist to submit a report on the outcomes of treatment with this drug.

Following pressure by the DG, and non-compliance by the consultant neurologist, the secretariat of the Drug and Therapeutics Committee (DTC) submitted a preliminary overview of the patients started on treatment with riluzole, their duration on treatment and whether they were still alive or had passed away.

In March 2000 the consultant neurologist informed the DG that he had stopped prescribing riluzole for motor neurone disease "as the response of treatment was unimpressive". He also informed the DG that he would be withdrawing riluzole from the patients already receiving this treatment. Consequently the DG recommended the withdrawal of the recommendations for riluzole and the deletion of the drug from the formulary. In April 2000 the government pharmaceutical services (GPS) were informed to stop procurement of the drug.

Some patients had already stopped treatment with riluzole on their own accord because they felt that they were not progressing, however two of the patients who were previously taking riluzole refused to stop treatment and requests were submitted by the consultant neurologist for re-approval. One of the patients and her family refused to stop treatment with the drug and put 'political' pressure on the national health services (NHS) to keep supplying the drug. The legal advisor stated that once started, treatment could not be withdrawn by the NHS. Moreover, stocks of riluzole (7000 tablets) were still available at the GPS and approvals for riluzole for these patients were granted, until stock lasted.