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How and why do developed countries vary in reclassifying medicines from prescription to non-prescription?

Natalie J. Gauld

A thesis submitted in fulfilment of the requirements for the degree of Doctor of Philosophy, The University of Auckland, 2013
Abstract

Background
Since the 1980s, many countries have reclassified medicines from prescription-only supply to non-prescription, e.g. to widen access to medicines and help manage health resources. However, countries vary in the medicines they have available without prescription. Having a pharmacy-only or pharmacist-only classification of medicines has been suggested to help medicines reclassify but no research has considered the range of factors contributing to international variation in reclassification.

Aims
The primary aim of this thesis was to understand why developed countries vary in reclassifying medicines from prescription to non-prescription. A second aim was to assess the variation in reclassification between selected countries.

Methods
The research used a heuristic qualitative methodology, which engaged the researcher as a key component of the research. Five core countries (New Zealand, Australia, the United Kingdom, the United States and Japan), and four supplementary countries (Singapore, Canada, Denmark and the Netherlands) were selected for study. Semi-structured interviews were conducted in these countries with key informants on medicines reclassification. Document analysis supplemented analysis of the interview transcriptions. A tool was developed and implemented to compare countries’ progressiveness in reclassification through ‘innovative’ reclassifications.

Results
Sixty-five interviews were conducted with 79 key informants. A unique blend of factors contributed to each country's reclassification progressiveness, but particular barriers or enablers typically occurred in two or more countries. Important enablers included: positive government policy; supportive regulator and a committee open to reclassification; having a pharmacist-only or pharmacy-only schedule; and trust in pharmacy and consumers. Key barriers included: absence of pharmacy-only or pharmacist-only schedule; risk-averse regulator and/or committee; negative medical or consumer groups; and high reclassification cost. Individuals and politics could encourage or hinder reclassification. Company factors and sales potential affected industry’s desire to drive reclassification. Sales potential depended on factors including: population size; advertising; market exclusivity; prescription reimbursement; pharmacy support; brand strength and patent expiry. Local, regional and global effects on reclassification occurred.

Conclusions
This study provides multi-dimensional international benchmarking for reclassification progressiveness. In documenting and explaining international variation in reclassification, it exposes opportunities for change and improvement in policies and practices that may widen consumer access to medicines.
Peer Reviewed Output

Papers derived from this thesis


Other related papers published or under review during completion of this thesis

Kelly F, Gauld N, Shaw J. Barriers to positive policy change that aims to increase access to medicines through reclassification: the case of oseltamivir in New Zealand. (under review).


Related Work

During this research project I submitted applications to reclassify individual medicines to the Medicines Classification Committee in New Zealand as follows:

2010: Topical calcipotriol

2011: *Vibrio cholera* and enterotoxigenic *Escherichia coli* vaccine (oral)

2012: Influenza vaccination

2012: Trimethoprim (through specially trained pharmacists, under strict criteria)

2012: Prolonged-release melatonin (unsuccessful as yet)

2012: Tetanus, diphtheria and pertussis vaccination (awaiting outcome)
Acknowledgements

I owe much gratitude to many people who have enabled me to do my PhD thesis.

My husband Matthew provided amazing support, had faith in me and accepted the enormous impact this research has had on our family. His computer support and proof-reading were exemplary. My children, Lauren and Brenna, have had the PhD throughout such a large part of their lives, and I appreciate their understanding. We will have weekends back again. I am also grateful to my parents, Barbara and Brian, whose genes, strong work ethic and encouragement have got me to this point.

Associate Professor Stephen Buetow’s excellent timely advice and encouragement, and wealth of knowledge were tremendous. I could not have had a better main supervisor.

Dr Fiona Kelly provided a valuable pharmacy (and Australian) perspective, and much useful and knowledgeable feedback.

Dr Linda Bryant, Dr Stewart Jessamine and Assoc Prof Lynne Emmerton made time to review large sections of the thesis and provided valuable advice. Professor Nahoko Kurosawa was an integral part of the Japanese section, facilitating my interviews, reviewing my chapter and answering my many questions.

Without the generosity of the participants in sharing their time and vast knowledge with me, this information could not have been collected. What was unexpected was how very welcome they all made me in visiting them for interviews. Many have kindly been available for further questions or checked chapters. Jeltje Luinenburg searched for dates for me for reclassifications in the Netherlands allowing me to complete my chart. I hope I have done justice to the information all participants have shared with me.

I thank David and Julie Rees-George, and Cheryl Hook for their support through after-school or holiday child-care.
Co-Authorship Form

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<table>
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**Certification by Co-Authors**

The undersigned hereby certify that:

- the above statement correctly reflects the nature and extent of the PhD candidate's contribution to this work, and the nature of the contribution of each of the co-authors; and
- in cases where the PhD candidate was the lead author of the work that the candidate wrote the text.

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Last updated: 25 March 2013
# Table of Contents

Abstract ........................................................................................................................................... i
Peer Reviewed Output ................................................................................................................ iii
Related Work .................................................................................................................................. iii
Acknowledgements ....................................................................................................................... iv
List of Figures .................................................................................................................................. xiii
List of Tables .................................................................................................................................. xiv
Glossary ........................................................................................................................................... xvi

Chapter 1. Introduction .................................................................................................................. 1
  1.1. Context of this research .......................................................................................................... 1
  1.2. This thesis ............................................................................................................................... 2
  1.3. Aims ....................................................................................................................................... 2
  1.4. The structure of this thesis ..................................................................................................... 3
  1.5. My role ................................................................................................................................... 3
  1.6. Research funding .................................................................................................................. 3

Chapter 2. Conceptual framework and literature review ............................................................. 4
  2.1. Introduction ............................................................................................................................ 4
  2.2. Conceptual framework .......................................................................................................... 4
    2.2.1. Pragmatism .................................................................................................................... 4
    2.2.2. Systems thinking and comparative approach ............................................................... 4
    2.2.3. Multilevel approach ...................................................................................................... 5
  2.3. Literature Review .................................................................................................................. 7
    2.3.1. Self-care and self-medication ....................................................................................... 7
    2.3.2. Medicines reclassification ............................................................................................ 10
  2.4. Summary of this Chapter ....................................................................................................... 34

Chapter 3. Methodology and Methods ......................................................................................... 35
  3.1. Introduction ............................................................................................................................ 35
  3.2. Methodology ........................................................................................................................ 35
    3.2.1. Multi-level approach .................................................................................................... 35
    3.2.2. Case study methodology ............................................................................................... 36
Chapter 4. New Zealand

4.1. Introduction ................................................................. 51

4.2. Background ................................................................. 51

4.2.1. Influence from the UK and Australia, including Trans-Tasman Harmonisation .......... 51

4.2.2. Health in NZ .......................................................... 51

4.2.3. The Medicines Classification Committee ................................................. 53

4.3. Primary data sources .................................................... 53

4.4. Reclassifications in NZ .................................................. 53

4.4.1. The early 1990s wave of reclassifications ................................................. 53

4.4.2. Reclassifications in NZ 2000-2012 ......................................................... 56

4.5. Participants’ considerations of NZ’s position in reclassification .................................. 59

4.6. Overriding themes from interviews ............................................. 60

4.6.1. Small size ..................................................................... 60

4.6.2. Kiwi ‘can do’ attitude ..................................................... 61

4.6.3. Individuals influencing reclassification .................................................. 61

4.6.4. Trust .......................................................................... 62

4.6.5. Financial motivators ....................................................... 63
Chapter 9. Japan

9.1. Introduction ................................................................. 182
9.2. Background ................................................................. 183
9.3. Reclassifications 2003-2012 ........................................ 184
9.4. Broad themes ............................................................... 188
  9.4.1. Doctor influence .......................................................... 188
  9.4.2. Financial motivation .................................................... 188
  9.4.3. Culture, history and beliefs .......................................... 188
  9.4.4. Politics ........................................................................ 189
  9.4.5. Pharmacy factors .......................................................... 190
  9.4.6. Global effects .............................................................. 190
  9.4.7. Conservative approach ............................................... 191
  9.4.8. Summary of over-riding effects .................................... 191
9.5. Results by stakeholder or factor ........................................ 192
  9.5.1. Government ............................................................... 192
  9.5.2. Regulator, committee and process ................................ 192
  9.5.3. Schedules ................................................................. 195
9.6. Findings by stakeholder or factor ...................................... 167
  9.6.1. Government ............................................................... 167
  9.6.2. The regulator, committee and process ............................. 167
  9.6.3. Behind-the-Counter Category ........................................ 169
  9.6.4. Pharmaceutical company factors .................................... 172
  9.6.5. Health system and pharmacy ........................................ 174
  9.6.6. Consumers ................................................................. 176
  9.6.7. Doctors ...................................................................... 176
  9.6.8. Advertising ................................................................. 177
  9.6.9. Reclassification ahead .................................................. 177
  9.6.10. Discussion ................................................................. 178
9.7. Summary ......................................................................... 187
List of Figures

Figure 2-1 Conceptual Model................................................................................................................................................. 6
Figure 2-2 USGAO review of availability of 14 selected medicines in 1995................................................................. 29
Figure 2-3 USGAO findings of medicines availability in 2007, and Gilbert, et al. findings of availability in 2003.................................................................................................................................................. 29
Figure 3-1 Overview of methods used for individual countries.................................................................................................. 40
Figure 4-1 Innovative prescription to non-prescription reclassifications in NZ 2000-2012.............................................. 56
Figure 4-2 Innovative reclassification considerations and outcomes in NZ 2000-2011*.............................................. 59
Figure 4-3 Overview of factors affecting company decisions on reclassifications in NZ.............................................. 72
Figure 5-1 ‘Innovative’ reclassifications in Australia from 2000-2012................................................................. 90
Figure 5-2 Appendix H advertising considerations for pharmacist-only medicines in Australia 2000-2011*......................... 90
Figure 5-3 Innovative reclassification considerations in Australia 2000-2011*................................................................. 91
Figure 5-4 Factors affecting company decisions to reclassify medicines from prescription to non-prescription in Australia................................................................................................................................................. 105
Figure 5-5 Effects of pharmacy behaviour on reclassification (coding red for barrier and green for enabler) in Australia.................................................................................................................................................. 107
Figure 5-6 Factors contributing to pharmacist behaviour in Australia and effects of that behaviour on reclassification.................................................................................................................................................. 108
Figure 6-1 Innovative reclassifications in NZ and Australia 2000-2012* ......................................................................... 121
Figure 6-2 Innovative reclassification considerations in NZ and Australia 2000-2011 ................................................. 121
Figure 7-1 Company considerations for reclassification in the UK................................................................. 152
Figure 8-1 Key barriers to behind-the-counter availability in the US .................................................................................. 171
Figure 8-2 Company factors in the US market.................................................................................................................. 173
Figure 9-1 Process of reclassification in Japan.................................................................................................................. 193
Figure 9-2 Factors affecting pharmaceutical company reclassification decisions in Japan.................................................. 197
Figure 9-3 Influence of drugstores and pharmacies on category one medicines................................................................. 200
Figure 11-1 The trilogy of overarching factors causing variability in reclassification in developed countries.................................................................................................................................................. 224
Figure 11-2 Total number of innovative reclassifications across five core countries 2003-2012 ........................................ 229
Figure 11-3 Innovative reclassifications in five core countries 2003-12 .............................................................................. 230
### List of Tables

Table 2-1 Potential consumer and societal benefits and risks of reclassification ........................................14  
Table 2-2 Comparative studies pertinent to reclassification ........................................................................28  
Table 2-3 Conclusions of comparisons of effect of scheduling on medicines’ availability .........................30  
Table 3-1 Countries and regions by level contributed to the research .....................................................35  
Table 3-2 A comparison of my approach versus the typical heuristic approach[350, 358] ..............................37  
Table 3-3 Non-prescription medicine schedules in researched countries ..............................................41  
Table 3-4 Demography of included countries and health system ............................................................42  
Table 3-5 Countries studied in this research compared with previous research ....................................43  
Table 3-6 Examples of Significant Improvement Used in Assessing Priority Reviews ............................49  
Table 4-1 Demographic and health measures for NZ .............................................................................52  
Table 4-2 Examples of down-scheduling recommendations, NZ 1990 ..................................................54  
Table 4-3 Examples of reclassification decisions (1991-1993), NZ .........................................................55  
Table 4-4 All prescription to non-prescription reclassifications 2000-2012 in NZ ....................................57  
Table 4-5 Innovative reclassifications and attempted reclassifications in NZ 2000-2012 ...................58  
Table 4-6 Barriers and enablers arising out of the ‘small size’ theme ....................................................60  
Table 4-7 Summary of key financial incentives and impediments to reclassification in NZ from interviews ........................................................................................................................................63  
Table 4-8 Pharmacy-related barriers and enablers for reclassification ..................................................74  
Table 5-1 Demographic and health measures for Australia .....................................................................86  
Table 5-2 All prescription to non-prescription reclassification approvals in Australia* 2000-2012 ......89  
Table 5-3 Innovative reclassification attempts in Australia 2006-2012 ...................................................92  
Table 6-1 Committee differences between Australia and NZ .................................................................119  
Table 6-2 Innovative reclassifications in NZ and Australia 2000-2012 .................................................120  
Table 6-3 Trans-Tasman differences and similarities in reclassification ...............................................124  
Table 6-4 Oseltamivir considerations compared for NZ and Australia ...................................................131  
Table 7-1 Key aspects of the UK market .................................................................................................141  
Table 7-2 Key UK prescription to non-prescription reclassifications 2003-2012 ....................................142  
Table 8-1 Key aspects of the US market .................................................................................................162  
Table 8-2 Key reclassifications in the US 2003-2012 ..........................................................................163  
Table 9-1 Key aspects of the Japanese market ........................................................................................183  
Table 9-2 Categories of medicines in Japan from 2009[77, 605, 608] ......................................................184  
Table 9-3 Key reclassifications in Japan 2003-2012 .............................................................................186  
Table 9-4 Pharmacy or drugstore factors impinging on reclassification ..............................................202  
Table 10-1 Key aspects of the Netherlands and Denmark .....................................................................209  
Table 10-2 Interviews used for Europe, Singapore and Canada .............................................................210  
Table 10-3 Enablers and barriers for reclassification in Singapore ......................................................221  
Table 10-4 Enablers and barriers to reclassification in Canada (based on two interviews) .................222
Table 11-1 A decade of first-in-world innovative reclassifications in core countries (2003-2012)......230
Table 11-2 Innovative reclassifications by date 2003-2012 in five core countries..................231
Table 11-3 Comparison of timing of selected reclassifications across countries up to and including 2012 ..............................................................................................................................................232
Table 11-4 Comparison of key enablers and barriers across the five core countries* ................234
Table 11-5 Variable effects of pharmacy factors on reclassification............................................244
**Glossary**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>ACMS</td>
<td>Advisory Committee on Medicines Scheduling</td>
</tr>
<tr>
<td>ASMI</td>
<td>Australian Self-Medication Industry</td>
</tr>
<tr>
<td>BTC</td>
<td>behind the counter</td>
</tr>
<tr>
<td>CHM</td>
<td>Commission of Human Medicines (UK)</td>
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<tr>
<td>CHMP</td>
<td>Committee for Medicinal Products for Human Use (Europe)</td>
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<tr>
<td>EHC</td>
<td>Emergency hormonal contraceptive (‘Plan B’ or the morning-after pill)</td>
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<td>EPA</td>
<td>eicosapentaenoic acid</td>
</tr>
<tr>
<td>EU</td>
<td>European Union</td>
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<tr>
<td>FDA</td>
<td>Food and Drug Administration (US)</td>
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<tr>
<td>GP</td>
<td>general practitioner</td>
</tr>
<tr>
<td>MCC</td>
<td>Medicines Classification Committee (NZ)</td>
</tr>
<tr>
<td>MHLW</td>
<td>Ministry of Health, Labour and Welfare (Japan)</td>
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<tr>
<td>MHRA</td>
<td>Medicines and Healthcare products Regulatory Agency</td>
</tr>
<tr>
<td>NDAC</td>
<td>Non-prescription Drugs Advisory Committee (US)</td>
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<td>NDPSC</td>
<td>National Drugs and Poisons Schedule Committee</td>
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<tr>
<td>NRT</td>
<td>nicotine replacement therapy</td>
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<tr>
<td>NSAID</td>
<td>non-steroidal anti-inflammatory drug</td>
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<tr>
<td>NZ</td>
<td>New Zealand</td>
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<tr>
<td>OTC</td>
<td>over-the-counter</td>
</tr>
<tr>
<td>PAGB</td>
<td>Proprietary Association of Great Britain</td>
</tr>
<tr>
<td>PAFSC</td>
<td>Pharmaceutical Affairs and Food Sanitation Council (Japan)</td>
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<tr>
<td>PGD</td>
<td>Patient Group Directions</td>
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<tr>
<td>PGEU</td>
<td>Pharmaceutical Group of the European Union</td>
</tr>
<tr>
<td>PMDA</td>
<td>Pharmaceutical and Medical Devices Agency (Japan)</td>
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<tr>
<td>QCPP</td>
<td>Quality Care Pharmacy Program</td>
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<td>Rx</td>
<td>prescription</td>
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<td>S2</td>
<td>Schedule 2 (pharmacy-only; Australia)</td>
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<td>S3</td>
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<tr>
<td>TGA</td>
<td>Therapeutic Goods Administration (Australia)</td>
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<tr>
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<td>Trans-Tasman Harmonisation</td>
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<tr>
<td>UK</td>
<td>United Kingdom</td>
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<td>US</td>
<td>United States</td>
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<td>USGAO</td>
<td>United States Government Accountability Office</td>
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Chapter 1. Introduction

1.1. Context of this research

Self-care is an integral part of human life – it is what people do to manage illnesses or keep well. Self-medication is part of self-care, and has been practised for over 4,000 years.[1]

Developed countries face an ageing population with increased burden of chronic illnesses and a shrinking tax base to fund the increasing costs of health care.[2, 3] Delays in access to primary medical care occur in some countries, particularly Canada and the United States (US),[4, 5] and in many developed countries most doctors believe that their health system does not work well.[4] Healthcare reforms, e.g. in the US and Ireland, are further likely to increase the work demands on doctors.[6, 7] A substantial proportion of patients with chronic conditions report insufficient time or communication with the doctor,[8] suggesting unmet need.

Even in developed countries, many people do not always access the medicines they need; e.g. in the US in 2005, only 38% of people at medium risk of cardiovascular disease were prescribed statins.[9] Significant statin under-treatment also occurs in the United Kingdom (UK).[10] Reasons for non-access may include under-treatment by doctors,[11, 12] lack of screening,[12] or difficulty accessing health professionals who control supply of the medicines.[13] Patients often have difficulty paying for health care[14] and the cost or time taken to get a prescription medicine can cause adults to miss taking prescription medicines for a period of time, or substitute non-prescription medicines.[15]

More desirable forms of self-care have been identified by the World Health Organization (WHO) as potentially helping to manage such problems.[3, 16] In the UK, for example, government policy has attempted to increase self-care, by using the ‘expert patient’, minor ailment schemes (shifting minor ailments from doctors to pharmacy), patient group directions (PGDs) and non-medical prescribers.[17] Another self-care initiative involves reclassifying (sometimes called switching or deregulating) medicines, including from prescription to non-prescription.[17]

Reclassification can allow patients to become more active in their healthcare decisions and reduce the burden on doctors.[18] Countries have driven reclassification of medicines for reasons that include improving access; e.g. in France with reference to the emergency hormonal contraceptive (EHC).[19]

Reclassification has also been promoted to help contain medicine costs, as in Denmark,[20] and Sweden.[21] The cost savings for health funders and/or consumers may be substantial, e.g. in 1992 in the US, Temin estimated savings in physician visits of US$70 million a year from reclassifying cough and cold remedies.[22] The pharmaceutical industry has also turned to the non-prescription market (and reclassification) because, as prescription market growth has slowed and prices have come under pressure, the opportunity exists to retain sales after patent expiry.[23]
Reclassification is not without risk, including inappropriate use or abuse, risk of adverse events, and potential for delayed diagnosis of a serious condition.[24] However, oftentimes the risks appear not to eventuate, e.g. in Denmark following the H₂-antagonist reclassification in 1989.[20, 25] Evidence of widespread harms of recent reclassifications has not been seen.[26, 27] The UK, the most active country in reclassification in the last decade, has not reversed any of its recent reclassifications, and recently reiterated its government policy on reclassification of medicines.[28]

However, reclassification varies,[21, 26, 29] even between highly developed countries with some similarities (such as among European countries).[21] This variation has been apparent to me in my 20-year involvement as a pharmacist, committee member and researcher in the area of reclassification primarily in New Zealand (NZ).

Research between countries suggests that the variation in reclassification is unrelated to criteria for reclassification,[30-32] but that a pharmacy-only or pharmacist-only reclassification may facilitate reclassification.[31-33] However, countries with similar schedules can also vary in non-prescription availability of medicines,[31] so other factors appear to be involved. Although suggestions have been made regarding variation between the US and UK, for example,[34] research is needed to elucidate the reasons behind the variation among highly developed countries.

Regional effects on reclassification are occurring in Europe,[20] including a centralised reclassification procedure, allowing a single application for all 27 member states.[35, 36] In the antipodes, an even stronger regional effect started in the mid-1990s, namely Trans-Tasman Harmonisation (TTH). NZ and Australia have been attempting to harmonise medicines classification ever since. No published literature investigates the TTH medicines classification initiative, and little literature investigates regional effects on reclassification.

1.2. This thesis

My research question therefore is:

How and why do highly developed countries vary in reclassifying medicines from prescription to non-prescription?

1.3. Aims

Specifically my study attempts to assess variation in the reclassification of medicines between selected highly developed countries, at three levels: international (macro-level), regional (meso-level) and country (micro-level).

At each level of analysis, my aims are:

International (macro-level):
1.4. The structure of this thesis

This thesis is organised into chapters that respond to these aims. It includes micro-level country-specific chapters, a meso-level chapter (Australia-NZ), and a macro-level chapter (international comparison). Micro-level chapters are provided for each of five core countries (namely NZ, Australia, UK, US, Japan), and a final micro-level chapter reviews reclassification from four other countries (Denmark, the Netherlands, Singapore and Canada). Given the TTH regional effects, both the NZ and Australian micro-level chapters include an analysis in 2000-2012 prescription-to-non-prescription reclassifications, allowing exploration of effects of TTH (and other factors) over time. My meso-level analysis then compares and contrasts the NZ and Australian findings and discusses them in light of the literature. For the ease of the reader, the meso-level chapter is placed immediately after the chapters on NZ and Australia, and before the micro-level chapters of the remaining countries. The macro-level chapter then compares findings from the micro- and meso-levels, before the conclusion.

Since this project required an assessment of variation in reclassification, and a measure of progressiveness in reclassification, a new tool was developed, as outlined in Chapter 3. This tool is used throughout the micro-level chapters, in the meso-level chapter, and in the macro-level chapter in order to indicate the level of progressiveness in by country in medicines reclassification.

1.5. My role

The research presented in this thesis is my own. I conceived the idea, conducted interviews, and transcribed (most), analysed, and reported them. My supervisors, Assoc. Prof. Stephen Buetow, Dr Fiona Kelly and Dr Linda Bryant, and advisors, Dr Lynne Emmerton and Dr Stewart Jessamine provided suggestions. I developed the tool to measure progressiveness in reclassification (using three supervisors to help face and content validate the tool. Prof. Nahoko Kurosawa assisted with Japan.

1.6. Research funding

This research was partially funded by the New Zealand Pharmacy Education and Research Foundation, and post-graduate research grants from the University of Auckland.
Chapter 2. Conceptual framework and literature review

2.1. Introduction

This chapter sets the scene for the original, empirical research reported in this thesis. It will describe and explain my overall conceptual framework which organizes the ideas and beliefs supporting and informing my study. The framework serves as a kind of ‘travel map’ that depicts the paths I have followed to address my study aims. A review of relevant literature informs the route taken.

2.2. Conceptual framework

My conceptual framework draws on systems theory to compare and understand recent international experiences in medicines reclassification. This variation is suggested to result from actions that have been taken in spheres of influence hierarchically defined by systems operating at and across the micro-, meso- and macro-levels and fitting on a subjective-objective continuum. This multilevel comparative and integrative perspective draws on the metatheory of pragmatism.

2.2.1. Pragmatism

Pragmatism aims to produce “current, workable solutions to real-world problems”.[37] It uses the methods that can best answer the research question, commonly mixing quantitative and qualitative methods.[37, 38] This methodological focus therefore commits to the production of useable knowledge from studies of actions in their practice context. This commitment is “subtle realist” in assuming the existence of an objective truth ‘out there’ in the world, knowledge of which is always tentative and based on probabilities. Reality is represented subjectively from a particular perspective influenced strongly by the values of the researcher. As a health professional and pragmatist, I recognise that the answer I find to my research question will be provisional and affected by my involvement.

2.2.2. Systems thinking and comparative approach

Pragmatism provides a coherent basis for systems thinking that focuses on relationships within and across different spheres of influence on the reclassification of medicines. The task of understanding these relationships led me to adopt a comparative approach. This approach has long been used to find and explain macro-social variation quantitatively or (more commonly) qualitatively,[39, 40] with research comparing geographical units on the basis of their political, social or legal systems.[41] Social processes and events need the context of their environment,[42] which comparative research emphasises[39] through comparison of whole cases.[40] Ragin described two main approaches, case-oriented and variable-oriented.[43] The case-oriented approach examines selected cases in-depth within their own context, including various features of the case rather than isolated variables. The complexity of the comparisons limits this approach to a small number of cases. Each case is
considered alone, and then compared with other cases explicitly focusing on what causes diversity between them (in outcomes and/or circumstances).[40, 43] The variable-oriented approach simplifies the data into variables that describe more thinly a typically larger number of diverse cases, allowing more generalisations. Mixing the approaches can yield ‘truth tables’ (a matrix of cases and variables).

The comparative approach can be used to generate theories or models applicable to unexamined cases, to validate theories or models, or to identify peculiarities in different cases.[42] My research is using it to identify peculiarities in cases that seem associated with the progressiveness of reclassification of medicines in that country, and to generate themes transferrable to other countries.

Comparative research is common in health, e.g. in pharmaceutical pricing,[44, 45] primary care services,[14, 46] pharmacy,[47] and health reforms.[48] Comparative reclassification research includes a comparison of policy and criteria in multiple countries,[32] and effects of scheduling on availability across different countries.[31, 49, 50] Others have examined reclassifications of particular medicines, comparing a single medicine across two or more countries,[19, 21] or multiple medicines across the same[51] or different countries.[29]

2.2.3. Multilevel approach

While comparative research is common at the micro-level or macro-level alone,[52] research at either level requires assumptions about the other level.[53] Problems with macro-micro comparisons [52, 54] include reductionism and dualism,[55] and arguments that one level is more important than the other.[53] Difficulty in linking the two levels,[56] and diversity in defining them,[53] sometimes prompt researchers to acknowledge intermediate levels.[54] Particularly in complex systems in which different levels have different effects and there is interplay between levels, the meso-level can provide a transitional step.[57] Nevertheless, multi-level research is required to justify the relevance of, and link, each level or context,[57] as done below.

Globalisation is increasing connectivity and global consciousness,[58] with goods, services, people, information and ideas flowing across borders.[59] Increasing connectivity between nation-states and regions forms part of this process.[58] Therefore, I examine international variability in reclassification at the levels depicted in Figure 2-1. This figure elaborates Ritzer’s Integrative (micro-macro) Theory of Social Analysis,[60] by suggesting that actions, beliefs and perceptions at a nation-state (individual country) micro-level influence the regional meso-level and the macro-level of the developed world. This influence takes place in terms of culture, values and norms, which feedback from the macro-level to regional and individual country levels. Perceptions, beliefs, culture and norms (on the subjective side) are posited to influence objective variables – actions, laws, processes, and vice versa. The modifications to Ritzer’s Model include the additional middle layer and an indication of the focus of the research by using darker shading on areas examined most, indicating a deliberate concentration on the subjective aspects of this research. Key research in this field to date has been predominately objective: Bowden[30] and Achanta[32] have examined documents to ascertain variability in reclassification processes (although Achanta conducted interviews); and US Government
Accountability Office (USGAO)[49, 50] and Gilbert, et al.[31] have used medicine availability measurements to examine effects of medicine schedules of each country on non-prescription availability of medicines. With subjective aspects under-researched to date, my research used in-depth interviews to elucidate contributors to variability in reclassification that may fall outside documented processes and actions.

A strongly subjective approach, with some collection of objective data, fits my study’s pragmatic and qualitative heuristic approach, and helps close the research gap exposed in my literature review.

*Colour coding in the chart above depicts concentration of work to best answer the research question.*
2.3. Literature Review

Figure 2-1 provides overall structure to how this study was conducted. However, it is not intended to provide a way of organising the literature that follows on self-medication, scheduling and reclassification, and reasons for reclassification. The review considers benefits and risks of reclassification and selected aspects of pharmacy, consumers and companies relating to reclassification. It then focuses on variation between countries, including research that compares differences between and within countries. My focus on highly developed countries is reflected in the literature reviewed. I provide additional literature discussion in each chapter to set the scene.

2.3.1. Self-care and self-medication

Self-care is "what people do for themselves to establish and maintain health, prevent and deal with illness."[16][p2] This term encompasses nutrition, hygiene, lifestyle, environmental factors, socioeconomic factors and self-medication, and includes prevention and management of long-term illnesses, and managing minor symptoms. Certain governments, particularly in the UK,[17] have encouraged self-care, mindful of increasing health costs.

Self-medication has been defined as "the selection and use of medicines by individuals to treat self-recognised illnesses or symptoms",[16][p3] including herbals and traditional products. However, responsible self-medication requires that medicines have proven safety, quality and efficacy, and are indicated for self-recognisable conditions or for some chronic or recurrent conditions following initial medical diagnosis.[16] I use the term self-medication to describe use of registered non-prescription medicines, according to this understanding. I use the term non-prescription medicine to mean a registered medicine not legally requiring a prescription. I assume that self-medication can extend to conditions recognisable through a pharmacist consultation,[61] though some countries lack pharmacist-only or pharmacy-only schedules.

2.3.1.1. History of self-medication

Medicinal herbs, minerals and animal products have been used for millennia.[1] Apothecary shops existed in Persia around 850 AD. Unable to afford doctors, most people self-treated, sometimes aided by an apothecary. Pre-packaged proprietary (secret formula) medicines emerged in England and Europe in the 17th century.[62] Medicines evolved in the 19th century with ready-made medicines and tonics for self-medication, and enthusiastic claims of effects were rife.[63] Advances in medical knowledge and pharmaceuticals in the 20th century[64, 65] alongside affluence and subsidised doctor visits and pharmaceuticals in many countries revolutionised health care. By the 1960s, doctor-centred care peaked in many countries and self-medication became unpopular.[64]

A decade later, self-care and self-medication began to regain popularity internationally with greater consumer education levels, knowledge and interest in their health.[16] There was also a nascent shift from constructing doctors as the ‘authority’ towards patient-centred care.[64, 66] The 1980s continued this development and saw many countries begin to reclassify medicines from prescription to non-
prescription, partly to save costs.[20, 64] Increasing self-management occurred e.g. doctors visits for colds approximately halved in the US from 1976 to 1989,[22] and has continued to.[67] The UK particularly embraced self-care, including improved use of pharmacies,[17] partly to help manage healthcare resources.[26]

Self-care and self-medication are an important part of healthcare, and without them the health system would not cope.[68]

### 2.3.1.2. Prevalence of minor ailments and self-medication

Globally, 90% of people feel unwell at least once every four weeks, with around 25% self-treating with a non-prescription medicine.[69] Recent consumer self-reporting supports this view.[70, 71] In the US, in 2011, 79% of consumers reported taking a non-prescription medicine from one or more of seven common categories studied.[72] Non-prescription medicine use is also common in children.[73, 74] For example, in the US 19% of children under 12 years had used analgesic/antipyretic agents in the previous seven days.[75]

### 2.3.1.3. Medicine schedules

Availability of self-medication depends on legal restrictions to supply according to schedules of availability, which vary between developed countries.[27]

Three non-prescription tiers occur in NZ, Australia and Canada as pharmacist-only, pharmacy-only and general sales categories.[76] Pharmacist-only requires pharmacist involvement in supply to consumers (in a pharmacy), while pharmacy-only requires that only licenced pharmacies supply the medicine. General sales availability typically allows sales anywhere, although some countries impose further requirements (e.g. lockable premises). The Netherlands has pharmacy-only, drugstore and pharmacy-only, and general sales availabilities.[77] Japan recently changed to pharmacist-only, drugstore and pharmacy-only, and general sales (restricted to licensed shops).[77] Dutch and Japanese drugstores require a trained registered person on-site.

The UK, Singapore and many European countries have two non-prescription tiers: pharmacy-only and general sales.[77, 78]

Several countries have a single tier with three different versions. Italy allows sales in non-pharmacy outlets with a pharmacist.[77] Many European countries, e.g. Spain, Greece and Austria have a single category which prohibits supplies of non-prescription medicines outside of pharmacies.[77] The third version is a single non-prescription classification that allows sale anywhere and no official pharmacy-only or pharmacist-only category. Used in the US, this scheduling was also implemented in Portugal in 2005.[77]

The pharmacist-only category is uncommon internationally. Aronson believes such a category (which may include strict criteria for supply) would benefit the UK by enabling complex classifications.[79] Oseltamivir in NZ exemplifies such supply, with strict criteria managing potential concerns.[80, 81]
pré cis of the evidence around pharmacist-only and pharmacy-only is important, but outside of the scope of this literature review. For ease of the reader, I have used pharmacist-only, pharmacy-only, and general sales throughout this thesis rather than the exact phrase legislated in each country.

Little published research has investigated the different impacts of the various schedule models[82] even though several countries have recently changed (e.g. Portugal, Japan, Netherlands),[77] or considered changing (e.g. Australia,[83-85] and the US[49, 50]) their systems. Researchers conducting an extensive project to evaluate Australian scheduling suggested that scheduling internationally is not research-based.[86] Part of this project is considered under comparative research below (Gilbert, et al.,[31] 2.3.2.12) Another part researched pharmacy non-prescription interventions, finding a 0.6% professional intervention rate across pharmacist-only and pharmacy-only sales. Around a fifth were deemed (by a panel) to avoid an emergency doctor visit or serious harm.[82] They estimated the net benefit of current Australian scheduling of around Aus$2.61 billion (US$2.68 billion).[86] A low pharmacy response rate could bias towards high-performing pharmacies, and interventions may have been under-reported. The economic analysis has not been peer-review published, and one author disagreed with the findings.[87, 88] The Pharmacy Guild of Australia, which has an interest in retaining pharmacy scheduling, distributed the funding.

Little research compares pharmacy and non-pharmacy supply. Porteous, et al., found inappropriate use of non-prescription analgesics in people purchasing medicines from a pharmacy, from general stores or getting prescription analgesics.[89] However, this finding may be contaminated by education in previous pharmacy encounters, for example. Mystery shopping in Sweden found advice inappropriately given (and sometimes dangerous) in general sales stores, but less commonly in pharmacies.[90] One study in 42 stores found better advice on use of ginger and folic acid in pregnancy from pharmacy than health food shops, but reported that ginger supply in pharmacy could improve.[91]

A 'third class of drugs' or 'behind the counter' (BTC) has been debated for years in the US,[33, 92] and was formally considered in the 1980s.[92] and by the USGAO in 1995[49] and 2009.[50] The 2009 report concluded "pharmacist-, infrastructure- and cost-related issues" need resolution before a BTC category could be instigated.[50] Proponents of BTC reportedly believed consumers would save money on drugs and doctor visits and that pharmacists could assist consumers and make appropriate doctor referrals.[50] Many patients[15] and pharmacists are supportive,[93] believing it would improve access to medicines. Opponents believed costs could increase if BTC drugs were not reimbursed, were concerned that BTC may become the default category limiting access, and that pharmacists are not trained in diagnosis and cannot access patient information such as laboratory test results. This report was sparse in methodology and results, and did not mention the earlier Australian work. BTC arose again in a Food and Drug Administration (FDA) hearing in 2012,[94] but no further progress in the area has been obvious.
Some industry commentators report that medicines sales are higher under more liberal arrangements than where people are unable to self-select.[95] Indeed, omeprazole[23, 96] and H₂-antagonists[97] have sold more in the US than the UK.

2.3.2. Medicines reclassification

Alongside the trend to self-medication has been a liberalisation of medicines for self-care using reclassification through the various schedules.

2.3.2.1. Definitions

WHO and the World Self-Medication Industry (WSMI) define reclassification (or switching or deregulation) as the move in classification (or scheduling) of a medicine from prescription to non-prescription status.[26, 98] Reclassification and switching can also mean moving down from one non-prescription category to another (e.g. pharmacy-only to general sales).[61] Sometimes the term Rx-to-OTC (prescription to over-the-counter) switch,[95] or OTC switch[99] is used to show the change from prescription to non-prescription. In the UK, POM-to-P switching (referring to Prescription-Only Medicine to Pharmacy Medicine) is commonly used.[61, 100] The Australians favour ‘down-scheduling’ to describe movement to less restrictive classifications,[76] and use ‘de-scheduling’ primarily to describe movement to unscheduled (or general sales).[84, 101, 102]

Less commonly, medicines move upwards in classification or scheduling, e.g. terfenadine moving from pharmacy-only to prescription medicine after QT-prolongation became evident.[27] Industry has termed this reverse switch,[26, 77] but Australians prefer ‘up-scheduling’.][103, 104]

Throughout this thesis I have predominately used the term reclassification in the context of prescription to non-prescription reclassification. Occasionally it is used to mean other movements, as should be obvious from the context. I have occasionally used down-scheduling or up-scheduling as defined above. Given OTC can mean all non-prescription medicines,[27] or just general sales availability,[50] I have avoided using OTC switch or Rx-to-OTC switch. Occasionally I use the term OTC for brevity to mean non-prescription medicine.

2.3.2.2. Examples and a brief history of reclassifications

Reclassification has taken a roller coaster ride since the early 1970s. Early reclassifications included sedating antihistamines in the 1970s,[105] and ibuprofen[105] and terfenadine[100] in the 1980s. In the US, the FDA’s OTC review reclassified many medicines, and probably contributed to the subsequent industry interest.[63] The late 1980s to mid-1990s saw considerable reclassification activity in many countries including Denmark,[20] the US,[105] the UK,[106] NZ[30] and Australia.[34]

The government-driven Danish H₂-antagonist reclassification in 1989[20] was a seminal point in reclassification. Research undertaken as a requirement of this reclassification, demonstrated that such a reclassification could occur safely.[20] Denmark was highlighted as a model for the world.[20] Optimism for reclassification surged internationally,[107-111] particularly given industry incentives of
huge US growth of products after reclassification,[92] expiring patents and slowing drug development.[65]

US enthusiasm dwindled from the mid-1990s as fewer reclassifications became approved[34] and growth slowed.[95] Statin reclassifications were rejected.[112] Government policy and ground-breaking reclassifications sustained the UK enthusiasm longer.[34, 113] World-first reclassifications included simvastatin, tamsulosin, and azithromycin.[114-116] However, since the mid-2000s, reclassification has slowed in the UK,[100, 117] and US,[112] and Europe.[118]

Chronic-care
Reclassifying medicines for chronic conditions has received international attention.[26, 64, 119-121] For example, UK stakeholders identified reclassification candidates (2001/2002) including many chronic medicines.[121] Simvastatin and tamsulosin have since reclassified in the UK.[115, 122] However, these and other chronic care medicines generally have not been reclassified in other developed countries,[123] with statins rejected multiple times in the US.[112] Although it was predicted that the 1.8 million UK consumers taking statins pre-reclassification could increase by up to 8 million,[124] simvastatin performed poorly post-reclassification.[115]

Controversy
While some reclassifications seem to generate little comment, other considerations attract controversy,[64] e.g. H2-antagonists in NZ[125] and Canada,[126] and simvastatin[115] and trimethoprim and nitrofurantoin[120, 127] in the UK.

The EHC reclassification in the US was extremely controversial. Even before the reclassification, EHC prescriptions were not dispensed by some pharmacists or in some pharmacies (for moral/religious reasons).[128, 129] Wal-mart pharmacies only stocked the EHC for dispensing after legal action and media exposure.[130] The EHC availability attracted concerns about promiscuity and a misunderstanding about its effect (some people believe life begins at fertilisation and the EHC provides an abortion).[130] The EHC consideration became highly political, leading to the reclassification being rejected against the advisory committee’s recommendation, although it was later approved.[19, 131-133] Despite support from many medical groups and consumer groups, the approval took five years, four or more applications, and legal action. Eventually questions from Congress members prompted a GAO investigation, and the US President endorsed the reclassification (to some criticism).

Regional and international influences (meso-level and macro-level)
Regional influences on reclassification emerged during the 1990s and 2000s. The European Union (EU) has shown an increasing presence, growing in size (now 27 members) and importance economically and governmentally, including medicines regulation and reclassification.[77] In 1991, Juul[45] noted that the European influence was likely to prevent further government-driven reclassifications in Denmark. Around a decade later, the mood in Europe became positive, with political support[26, 134, 135] and the promise of centralised reclassification – with just one
reclassification application required for the whole EU market.[77] However, European reclassification has not lived up to the promise. Only two medicines have successfully reclassified centrally between 2004 and 2012, (pantoprazole and orlistat).[100]

Australia and NZ have gone further in regionalisation through TTH. Both countries aim to harmonise the classifications of medicines (generally to the less restrictive schedule of the two countries).[136] TTH of medicines’ classifications began in the late 1990s.[137] Initially all scheduled medicines in both countries were reviewed with differences identified and considered by the classification committees in each country. If one committee agreed to harmonise with the other country’s scheduling the classification was resolved, if not, the medicine would remain unharmonised and then return for committee discussion at a later date. Scheduling changes in one country are automatically considered by the committee in the other country. A joint medicines regulator, the Australia and NZ Therapeutic Goods Agency, is planned for implementation in 2016. Although TTH was described in 2003 as ground-breaking,[138] this initiative has not been studied.

International effects are also seen. Regulatory authorities may expect applications for reclassification to include classification status elsewhere, e.g. in Canada,[139] the UK,[140] and NZ.[141] A decision by a regulatory authority to reclassify upwards can have a ripple effect across other developed countries e.g. cough-cold products in young children[142, 143], reflecting increasing connectivity between nation-states resulting in global impacts.[58] Following the reclassification of $H_2$-antagonists in Denmark in 1989, these medicines reclassified within a few years in multiple countries.[126, 144]

2.3.2.3. Mechanisms for reclassification

Generally reclassification is initiated by a pharmaceutical company’s application, although occasionally regulatory authorities have down-scheduled medicines[21, 30, 98] Regulator-driven up-scheduling or changes in requirements for non-prescription supplies occurs if new safety concerns arise,[27, 98] e.g. codeine misuse.[145]

WHO noted in 2000 that “in many cases the process will involve a review of existing data and experience and not the performance of new clinical trials or investigations, though the latter may occasionally be necessary.”[146][p5] However, US reclassifications in a new therapeutic class typically require actual use, self selection and label comprehension trials.[112] In the UK, the Medicines and Healthcare products Regulatory Agency (MHRA) also works with companies to identify gaps that require data generation.[61]

Many developed countries have a specific process for reclassification,[26] although only a little research has been done in this area.[31, 32, 112] Some regulators provide significant background work on a reclassification, e.g. the UK[61] and US,[112] and Australia provides an evaluation report.[147] Typically a committee advises or decides on reclassifications. For example, the FDA’s Non-prescription Drugs Advisory Committee (NDAC) and a relevant prescription advisory committee jointly meet on major reclassifications.[112] The UK uses the Commission of Human Medicines
(CHM) for ‘major’ applications.[61] NZ uses the Medicines Classification Committee (MCC) to advise on reclassifications (not only major ones).[148]

Developed countries tend to use similar criteria to evaluate reclassifications.[30-32] although the US excludes the possibility of a pharmacist’s intervention in helping self-diagnosis and safe use.[50] Additionally, criteria and policy have previously been identified by Bowden[30] and Achanta.[32] Therefore, I will not compare and contrast these criteria, but simply discuss key WHO criteria.

WHO Guidelines report that “Regulatory assessment of a change from prescription to non-prescription status should be based on medical and scientific data on safety and efficacy of the compound and rationality in terms of public health.”[146][p4] WHO has three essential criteria a reclassified medicine needs to meet:

1. Low inherent toxicity (e.g. no reproductive toxicity, genotoxicity or carcinogenicity)
2. Appropriate indication for self-medication. Use should not unduly delay medical diagnosis and treatment
3. No undesirable properties, e.g. unfavourable adverse event profile, medical monitoring of therapy, significant abuse risk, or potentially serious interactions with common medicines

WHO suggests the following factors may help: high product usage; marketed on prescription at least five years (noting that this requirement varies by country); and its adverse events give no cause for concern, and their frequency has not been increasing unduly. The WHO clearly requires judgements to be made, e.g. requiring “acceptable level of risk from inappropriate use”. The mechanisms of US reclassification is well-outlined in US case studies of reclassifications, for the EHC,[133] non-sedating antihistamines,[149-151] nicotine replacement therapy (NRT)[152] and statins.[153] Reviewing these studies highlights the reliance on actual use studies in the US. The FDA typically provides a list of considerations for the committee, although the committee appears to divert into other areas, particularly consumer cost and BTC availability.

2.3.2.4. Non-sponsor reclassifications and government policy

Government-driven down-scheduling occurs occasionally. Over 50 ingredients reclassified by 1980 under the US ‘OTC Review’ process in which panels reviewed medicines for effectiveness and safety, and suggested reclassifications.[63, 154] Denmark reclassified 20 medicines in 1984 or 1989,[20] and NZ followed with an unknown number in the early 1990s.[30] In the late 1990s, Sweden reclassified omeprazole (but rejected another 12 medicines),[21] and France reclassified the EHC in 1999.[19] Cost appeared to motivate the Swedish and Danish reclassifications.[20, 21] Although Bowden considered Denmark to be leading in reclassification, in 1991, further regulator-driven reclassifications in Denmark were thought unlikely given European influence.[20] Not all regulator- or government-initiated reclassifications go well. The 1982 US reclassification of orciprenaline (metaproterenol) was reversed six months later following medical criticism and congressional pressures.[154] Governments
can also encourage reclassifications as in the UK.[28, 34, 117, 155] where targets (number of reclassifications) were set.[117] Japan and Europe have also had positive policy.[26]

Third-parties have rarely attempted to reclassify medicines. In 1998 in the US, Wellpoint (a health funder) famously attempted to reclassify the non-sedating antihistamines through a Citizen Petition.[29, 149, 150] Despite a positive advisory committee recommendation, these medicines remained prescription-only until the sponsor reclassified them. A Citizen Petition also started the EHC consideration in the US in 2001, but a sponsor became involved in 2003.[133] In NZ in 2010, a pharmacy retail group successfully reclassified topical calcipotriol.[156]

### 2.3.2.5. Benefits and risks of reclassification

Table 2-1 summarises benefits and risks to consumers and society from reclassification.

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<td>Consumer convenience</td>
<td>Misdiagnosis or delayed diagnosis</td>
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<td>More timely access to medication</td>
<td>Use of suboptimal therapy</td>
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<td>Lower health funder costs</td>
<td>Increased consumer costs</td>
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<td>Lower consumer costs</td>
<td>Adverse effects</td>
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<tr>
<td>Educational opportunity for consumers</td>
<td>Use with contraindications or precautions</td>
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<td>Decreased doctor workload</td>
<td>Failure to recognise or report adverse effects</td>
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<td>Greater choice of treatments</td>
<td>Drug interactions</td>
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<td>More effective or more appropriate treatments</td>
<td>Loss of medical control</td>
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<td>Self-reliance</td>
<td>Incomplete medical records/doctor unaware of all medicines a patient is taking</td>
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<td>Active consumer role in own healthcare</td>
<td>Reduced screening</td>
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<td>Reducing absenteeism</td>
<td>Unnecessary use</td>
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<td>Potential for more guideline-adherent supply</td>
<td>Double-dosing of the same medicine</td>
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<td>Reduce illegal sales of prescription medicines</td>
<td>Loss of surveillance data</td>
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<td>Reduce potential for internet purchase (including counterfeit products)</td>
<td>Dependence and abuse</td>
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<td>Resolve important areas of non-treatment</td>
<td>Increased resistance to antimicrobials</td>
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<td>Change in patterns of infections</td>
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<td>Inappropriately prolonged use</td>
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<td>Health system costs from severe adverse effects or prescribing changes</td>
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<td>Inadequate or excessive dosage</td>
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<td>Increased health inequity</td>
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<td>Consumer perception of low harm</td>
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<td>Neglect of lifestyle changes</td>
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Many benefits and risks have not been quantified or even confirmed. Other benefits or risks have strong evidence, e.g. misuse of codeine-containing medicines.[145, 170, 171] Benefits and risks (particularly cost savings for consumers and funders) may depend on the health care model. Benefits most often discussed are: consumer convenience; cost savings; timely access and empowerment. Risks often raised are safety-related, including inappropriate use and misdiagnosis, and fragmentation of care.

Benefits of improved health
Some reclassifications may increase the usage of medicines with population benefits, e.g. NRT[172] to help smoking cessation and reduce smoking-related health risks, and EHC to reduce abortions.[19] Such reclassifications may align with clinical guidelines[173] and encourage consumers to take a more safe[158] and active role in self-medication, which can be important when early treatment works best, e.g. oseltamivir for influenza,[174] and the EHC.[175] However, some commentators have suggested limited benefits from the NRT,[176] and EHC usage did not increase for women in Great Britain[177] (although it doubled in the US).[178]

Some reclassifications may improve usage of medicines or enable health screening. Ibuprofen was reclassified in Sweden to encourage consumer use instead of aspirin for safety reasons.[158] Failure of sildenafil to reclassify in Europe lost the opportunity to address risky internet usage of unregistered medicines (according to Kelly)[100] and to screen middle-aged men for cardiovascular disease.[179]

Health risks
Reclassifications introduce medicine-dependent risks: adverse events may occur with correct use, or with inappropriate use, including use with contraindications or outside labelled indications or directions.[180-182] Misdiagnosis may occur, leading to unnecessary use or delayed medical care e.g. Ferris, et al. found many US women purchasing a vaginal antifungal did not have vaginal candidiasis alone.[183]

WHO guidelines for reclassification suggest tolerance to some risk, but do not define an “acceptable level of risk from inappropriate use”.[146][p19] Furthermore, many risks are not unique to self-medication[98, 184] and some predicted risks do not eventuate, e.g. with H2-antagonists,[20] NRT,[172] oseltamivir[81] and the EHC.[177] Harms have occasionally emerged post-reclassification, e.g. terfenadine up-scheduled following the discovery of potentially fatal QT-prolongation.[27] However, few post-marketing surveillance studies have occurred after reclassification, and voluntary reporting surveillance is imperfect.[185] Risks of misdiagnosis, and inappropriate use following a new reclassification, would not emerge through voluntary reporting of adverse effects. Adverse effects may be under-reported if unrecognised, or a doctor is not consulted or informed of the self-medication. Reclassification research could help identify uncommon effects,[185] inform future reclassifications, and support pharmacy staff in screening and advising patients.

Tools such as limiting dose and pack size, labelling, restricting supply to pharmacy and protocols for supply may minimise risk.[80, 98] Pre-reclassification studies assist in considering safety.[112] Bond and Hannaford stated that reclassification only occurs after “sound evidence of safety” is provided, but
Oster, et al. (1990) believed that such decisions occur under “substantial uncertainty.”[186][p835]. While some academics and industry observe that evidence does not suggest public health problems are occurring from reclassifications[26, 27, 187] and reclassification reversals are rare,[26] some epidemiological studies highlight important risks which should be considered carefully.

**Other consumer and society benefits**

Pharmacy can deliver health care closest to the patient,[7] at a reasonably convenient time, without an appointment. Therefore, apart from improved health, consumers may experience, through reclassification, improved convenience, cost savings, and reduced time off work [15]. Empowerment may motivate consumers to participate more actively in their health care.[163, 188] Three UK qualitative projects on reclassification around the same time found mixed views. Smith and Newbould detected low support for reclassification in consumers,[189] but Hibbert, et al.[190] and Bissell, et al.[191] found consumers largely positive, appreciating the convenience and empowerment of medicines being reclassified.[190] Swedish and Australian women supported the EHC reclassifying,[192-195] but English consumers generally opposed simvastatin reclassifying.[165]

**Other consumer or society risks**

Consumers are not medicines’ experts, and a plethora of brands and advertising can be confusing.[196] Consumers may use suboptimal therapy without sufficient knowledge or because they choose to ‘make do’ rather than see a doctor.[197] Reclassification may affect lifestyle, e.g. using simvastatin instead of lifestyle changes, or having unprotected sex. However, the latter did not appear to increase post-reclassification in Great Britain; and nor did regular contraception change.[177] Prescription funding may cease for the medicine reclassified,[110] increasing consumer costs and creating health inequity.[198]

**Benefits of reduced doctor visits**

The potential reduction in doctor visits is often cited, and regularly appears in economic analyses (see below). For example, in the US, doctors’ visits for cold remedies halved with cough/cold remedy reclassifications,[22] and decreased 72% for vaginal candidiasis.[199] Reducing doctors’ consultations for minor ailments should help manage the burgeoning healthcare demand [200]. It may reduce pressure on doctors[27] providing them with more time to manage complex patients, among other things. Reducing the burden on doctors is particularly important where shortages exist, or demand is expected to increase, e.g. Ireland with universal health care.[7]

However, some studies have not shown doctors’ visits to fall. Andrade found US doctors’ visits remained static despite reduced prescriptions for H₂-antagonists in chronic users,[201] against the prediction of Oster, et al. pre-reclassification.[186] Similarly, the UK chloramphenicol reclassification saw only a 16% drop in prescription usage, [202] despite OTC supplies equivalent to 67% of prescription eye drops.[203] Banks reported that ‘doctor dependency’ remains in the UK.[204]

The benefits of reduced doctor visits probably vary by country and by medicine, and sometimes appear overstated, e.g. by Temin in 1983.[205] However, at least some reclassifications have saved doctors’ visits, which is likely to help meet future healthcare demands.
**Risks of reduced doctor visits**

Misdiagnosis has been reported with self-medication, e.g. with vaginal antifungals (although Finnish doctors still supported the reclassification).[183, 206] However, risks may exist pre-reclassification, e.g. 6% of Finnish antacid users had warning symptoms before H2-antagonists reclassified.[207] Reclassifications may affect opportunistic health promotion and counselling about lifestyle,[163] e.g. sexually transmitted infection checks with EHC.[7] Patients may not inform their doctor of OTC medication they are taking, or be asked about it.[208] Tamsulosin provides an important risk in cataract surgery, but a general practitioner (GP) referral letter could exclude pharmacy-supply.[209]

UK consumers buying reclassified medicines retained medical contact.[210] US women self-medicating with oral contraceptives from Mexico kept good doctor contact for preventative screening.[211] Conversely, 38% of US purchasers of phenazopyridine (a urinary analgesic) substituted the medicine for a doctor’s visit, sometimes despite important warning symptoms.[197]

Reduced doctors’ visits can be an important benefit of reclassification. Concomitant risks are important, but need to be considered in light of existing self-care.

**Saving health funders’ and society money**

Societal savings estimates vary from negligible1 with famotidine in Canada (Tasch, et al., 1996) [212] and omeprazole in the UK,[213] to US$70 million per year for cold remedies (Temin, 1992)[22] and US$400 million for hydrocortisone in the US.[205] Temin calculated from doctor visit data US$70 million per year in savings from doctor visits, transport and time from reclassifying cold remedies. In 1990, Ryan and Yule estimated UK societal savings of £2.0 million (US$3.05 million) for 1987 for hydrocortisone 1% and around £3-4 million (US$4.6-6.1 million) per year in 1985-1987 for loperamide.[214] Carlsten, et al. found US$30 – 400 million savings per year for 16 reclassifications (1980-1992) in Sweden. [158] Health funders can save by moving costs to consumers, with little overall savings (excluding consumer time).[201, 212]

Predicted savings may not eventuate. The intended UK£90 million (US$137 million) per year health funder savings from 1980s Danish reclassifications[215] were re-estimated in 1991 at US$1.5 million per year, excluding doctor visits.[20] The medicine, methods used, assumptions made, and market factors will affect estimates.[20, 205] Prices typically drop in the US,[110, 205] but rise in the UK and France.[110]. Additionally, removing reimbursement in some countries can prompt doctors to substitute other products, increasing health funder costs.[168]

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1 Including consumer cost
Other risks

Tinetti suggested a US lovastatin reclassification could motivate further reclassifications of treatments for asymptomatic conditions, conceivably continuing “until only a few highly toxic medications remain under the control of prescribing physicians.”[160][p2728] US committee members rejected oral aciclovir for genital herpes, considering a reclassification may set a precedent for oral antimicrobials.[216] Commentators suggested chloramphenicol could set a precedent in the UK,[202] but the subsequent trimethoprim and nitrofurantoin withdrawals[127] suggest that did not occur.

2.3.2.6. Pharmaceutical companies

Pharmaceutical companies drive most reclassifications.[98] Sponsors’ benefits include increased sales,[27] and the ability to set pricing.[198] Occasionally they oppose reclassification, withdrawing reclassified EHC in Denmark in the late 1980s,[20] and opposing the NZ calcipotriol reclassification,[156] and the US non-sedating antihistamines reclassification.[150]

In 1985, the US-based Haverkost described reclassification as “a marketing man’s dream”.[217][p135] He believed success of reclassified medicines was more likely compared with other new product launches, and reclassifications could fund research and development for new medicines. By 1993, nine of the 10 best-selling US OTC medicines were reclassified medicines.[111] Reclassification lost favour as growth slowed and reclassifications became difficult, and by 1997-1999, 40% of the top-growing US OTC brands were reclassified medicines.[95]

However, since 2008, OTC medicines have outgrown prescription medicines, re-stimulating pharmaceutical company interest.[218, 219] Global sales are US$109 billion per year ex-manufacturer,[219] with growth arising from widening distribution channels (e.g. supermarket sales), strong OTC brands, and emerging markets.

In 1980, industry considered likely market growth, profit growth, and the superiority over existing OTC products in evaluating potential reclassifications.[66] Other drivers included: threats to the product’s prescription market (e.g. a new product). Reclassifications are often timed for patent expiry,[23, 117, 220] but sometimes occur earlier,[66, 119, 221] particularly given the first product in a category to reclassify may gain the most, as seen with vaginal antifungals in Sweden.[222]

Industry benefits for US reclassification can be large, but other countries can vary. In the US omeprazole quickly grew to US$40 million per month,[23] versus well under £1 million (US$1.5 million) per year in the UK.[96] Topical hydrocortisone 1% sales increased modestly post-reclassification in the UK,[214] in contrast to trebling in US sales.[205] In two years, post-reclassification sales increased by an average of 36% for Swedish medicines,[2] before levelling.[158]

In the UK, Thomas and Noyce suggested advertising, pricing (versus prescription) and pre-reclassification exposure influenced post-reclassification sales.[223] I suspect ‘unmet need’ was important, as clotrimazole vaginal products grew modestly overall, but aciclovir cream grew over

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2 Those that reclassified between 1980 and 1992
200%. Marketing strategy is also important, with similar medicines or even the same active ingredient in different brands experiencing different growth in Sweden[158, 224] and the US.[119] Aiding potential sales for companies, medicines are ‘experience’ products, whereby consumers want certainty of quality (from a brand), and tend not to change products easily.[23, 196] With relatively low knowledge, people rely on brands and advertising.[225] Thus, the brand may last well post-reclassification with less generic pressure than prescription products.[119]

Criticism of industry in reclassification occurs primarily around advertising. US commentators have reported aggressive or intense advertising[119, 226] exaggeration of benefits,[92] and insufficient risk information.[227] In Australia, an advertising breach stimulated removal of orlistat advertising approval.[228-230] Critics have suggested advertising could increase inappropriate post-reclassification usage or demand,[22, 163, 198, 231, 232] (‘pill for every ill’), and consider consumers need balanced information.[160, 206] Rizzo, et al. suggested that negative findings from reclassification studies may not be published.[233]

2.3.2.7. Consumers and reclassification

An exhaustive review of consumers and self-medication is outside of the scope of this review. I refer the reader to Taylor’s recent reviews,[68, 187, 234] and note continuing gaps in understanding consumer self-medication.[187] Instead I will provide a flavour of the data regarding consumers and reclassification. Pre-reclassification usage research, such as US actual use studies,[235] and studies of pharmacist supplies under patient group direction or in a doctor-authorised scheme (e.g. for the EHC)[236-238] have been excluded. They are informative to a reclassification decision, but may not reflect the final reclassified environment. Consumer views were discussed under 2.3.2.5.

Sources of information

Information sources for purchasers of reclassified medicines include: the pharmacist, doctor, friend/family, and advertising, of varying importance.[210, 224, 239] In Sweden for hydrocortisone, “journals” were initially most important, but over time, pharmacist recommendation became more important.[224] Doctors were mentioned about a quarter of the time for English purchasers of recently reclassified medicines[210] but 5% for diclofenac in NZ, where advertising was more important.[239]

Knowledge

Although increasing consumer knowledge has increased self-medication interest,[16] low health literacy is a significant problem internationally, particularly in older people, those with low education or low income, and minorities.[240] It has been associated with worse health outcomes, and reduced ability to manage medicines, understand medicine labels and take medicines correctly. For example, many Italian consumers found OTC labelling difficult to understand, particularly those with lower education levels.[241]

Self-medication knowledge can be limited.[169] US consumers had low awareness of precautions with reclassified non-steroidal anti-inflammatory drugs (NSAIDs),[242] and limited ability to diagnose
vaginal candidiasis, with potentially serious health outcomes.[183, 243] The 85% growth in vaginal antifungal supplies in the US post-recategorisation[243] thus suggests misdiagnosis may be common. Some UK consumers appear unaware of risks of non-prescription medicines (believing a medicine ‘off the shelf’ must be safe),[190, 191] and lack awareness of non-prescription schedules.[244] While some UK consumers believe a reclassified medicine has some risk being previously prescription-only,[189, 244] Bissell, et al. found most purchasers of reclassified medicines concentrated on benefits rather than risks.[244]

In Finland, Sihvo suggested that women needed more balanced information than advertising provided, given misdiagnosis with vaginal antifungals, and suggested that pharmacy staff provide more information.[206] However, UK consumers were confident they could manage conditions they had successfully managed multiple times previously (‘lay expertise’).[191] Sinclair found many ibuprofen purchasers had previously discussed the condition they were treating with their doctor.[182]

Ruiz suggests educating consumers and health providers to manage the potential for drug interactions, in particular encouraging consumers to tell their doctor of OTC medicine use and doctors to ask about it.[169] Consumers also need education about OTC medicines not being risk-free.[169]

**Usage**

Across several different countries, researchers have found that younger,[210, 226, 245] wealthier,[245, 246] and better educated[210, 224, 245] consumers are more likely to buy reclassified medicines. This may be reflective of self-medication purchasers in general in some countries, e.g. non-prescription analgesic users in Scotland.[89] It may also reflect cost barriers in some countries to accessing reclassified medicines.[80, 194, 247] In the US, Caucasian people, and people with chronic conditions were more likely to take reclassified medicines.[248]

In a self-medication review, Taylor noted experiences of reclassified medicines suggest reasonable consumer use.[187] UK reclassified medicines purchasers often viewed using them as a routine activity to manage minor health conditions.[244] However, inappropriate use is also seen as highlighted in section (2.3.2.5).

Reclassification sometimes simply shifts consumer procurement from prescription to non-prescription, minimising concerns about overuse or unnecessary use. For example, in the two years following the EHC reclassification, EHC usage in Great Britain remained static, but about a third of women sourced it from pharmacy instead of the doctor or other sources.[177] In Sweden, less than 20% more packs of vaginal antifungals were supplied seven years after the reclassification than in the year before the reclassification, but 93% of women moved to pharmacy-supply.[222]
Chapter 2

Consumer politics
Sometimes different consumer groups have supported and opposed the same US reclassifications, e.g. the EHC[133] and statins.[153] Politics on the EHC reclassification had more impact in the US (2.3.2.2)[19, 133, 249-251] than the UK,[19] despite legal challenges in the UK.

2.3.2.8. Community pharmacy and reclassification
Pharmaceutical distribution is controlled through pharmacy to balance safety and access.[252] Pharmacy varies in different countries according to scheduling, ownership rules, healthcare funding (e.g. prescription subsidy arrangements), history, and culture.[252-254] Significant differences even occur between European countries.[47]

Pharmacy is changing. Dispensing mass-produced medicine has replaced compounding and pharmacy’s status has lowered.[16, 252, 255] Pressures include constricted prescription costs, and competition.[253, 256] Pharmacy has consequently ‘reprofessionalised’, aided by pharmacy’s accessibility,[252] pharmacist training,[254, 257] and concerns about managing an ageing population.[252, 254] In some countries, pharmacy has extended e.g. into repeat prescribing, medicines management,[252] health promotion,[258] and supplying reclassified medicines.[190] Pharmacy organisations often develop protocols and training to support reclassifications,[24, 259, 260] and pharmacists willingly up-skill.[80, 261, 262]

Pharmacy may benefit from reclassification, with increased use of pharmacists’ professional skills,[26, 263] sales, and credibility.[264] However, pharmacists’ views on reclassification vary by medicine, country and over time. Surveys in the late 1980s or early 1990s in the UK,[265] US[266, 267] and Australia[30] showed pharmacist reluctance for reclassification, and little support for reclassifying cimetidine or the oral contraceptive, but greater support for terfenadine and 1% hydrocortisone. In the US, reclassification to general sales could lose pharmacy sales,[66, 267] while in Australia, some pharmacists worried that down-scheduling to general sales may follow the initial reclassification.[30] In 1994, most UK pharmacists supported reclassifying nasal beclometasone, ocular chloramphenicol, and cimetidine, and nearly half supported the EHC.[268] UK pharmacists considered the reclassifications increased their clinical role and enhanced their professional status.[269] This positive attitude may reflect influences from strong government policy on reclassification, and earlier reclassifications may have engendered confidence.

Pharmacy supported the EHC reclassifying, e.g. in Sweden (2004),[192] the UK (2001),[263] and Canada (2008, 2011).[260, 270] However, US pharmacists varied, e.g. 97% supporting EHC reclassification from Walgreens chain stores’ pharmacists in San Francisco (surveyed 2002),[271] 6% from South Dakota pharmacists (surveyed 2003),[272] and 17% from Rhode Island community pharmacists (surveyed 2004). In the US, pharmacists’ views were likely influenced by the national debate about pharmacists’ rights to refuse to dispense the EHC,[128] ongoing politicking,[19] and perhaps the lack of BTC category worrying pharmacists about consumer self-management. Likely

3 Not all medicines considered in all surveys; the US studies had low response rates
influences in South Dakota included a state tightening of abortion law, pharmacists having low EHC knowledge, and many pharmacies not stocking the EHC. However, in Rhode Island most had dispensed the EHC but still did not want reclassification. The Walgreens study comprised a select group, most of whom had received training, had good knowledge, had dispensed the EHC, and half were involved in an EHC study.

UK pharmacists were unconvinced about reclassifying simvastatin, both soon after reclassification[247] and five years later,[273] worrying about efficacy, complexity, and medical records,[273] possibly influenced by negative media.[115] Few Canadian community pharmacists (surveyed 2007-2009) agreed with reclassifying simvastatin (10%), or omeprazole (37%) but moderately supported fluticasone (54%).[274] Pharmacists from Idaho, US were more enthusiastic with 81% for nasal corticosteroids and 42% for statins, using BTC availability.[93] Canadian concerns about loss of funding for patients[274] may have contributed to the US-Canada difference.

Community pharmacists are sometimes seen as retailers rather than health professionals,[252, 275] and consumers have reported poor supervision of support staff, and lack of advice,[190] or privacy.[194] Doctors may resist pharmacy’s expanding role,[255, 276] though this may be improving,[276] and some pharmacists do not want (or feel confident with) such a role.[255, 276, 277] Pharmacists may face increased liability.[125] Insufficient time in pharmacy has been raised by academics,[278] pharmacists[165, 279] medicines counter assistants,[280] and doctors.[114, 124, 281, 282] However, busyness or workload has not affected performance.[283-285] Other concerns include intrusive pharmacy questioning[259] and lack of diagnostic skills.[114, 120] Concerns about a pharmacy quasi-monopoly with pharmacy-only medicines have occurred, e.g. in Australia, the US and Finland.[88, 286, 287]

Pharmacy performance varies in mystery shopping,[278, 288-292] vignettes,[293] and observation,[76, 294, 295] and patient studies suggest some inadequacies.[180, 182, 206, 296] In the US, Tinetti (the Chair of the NDAC considering the lovastatin reclassification) doubted pharmacists would always provide professional counselling in a BTC situation.[160] Consultation is less common where a specific product is requested,[283] or for self-selected products,[295] and depends on the medicine.[297] Pharmacy support staff (and their training) vary by country, but may include pharmacy technicians and medicines counter assistants (sometimes called pharmacy assistants). UK medicines counter assistants managed 84% of requests for reclassified medicines autonomously.[280] Higher rates of pharmacist involvement were observed in NZ in 1999 (21%)[295] and in Australia in 1982 (28%)[298] and 2006 (28%),[76] possibly owing to the pharmacist-only schedule, or because each study included only 10-15 pharmacies. Some pharmacist-only supplies (primarily medicines potentially abused or diverted) had no consultation (7%) or were conducted by a pharmacy assistant (38%), reflecting poor practice. The supervising pharmacist may believe certain pharmacy assistants are competent in preventing abuse or misuse, but the 7% no consultation rate disappoints.

Confidence in supplying reclassified medicines is common for pharmacists,[260, 262, 299] and UK medicines counter assistants (with training and specific educational material).[280] However,
consumers do not always welcome advice or questioning[194, 280] and may give the expected response to procure the product quickly.[280] Sometimes consumers do not go to the doctor when referred.[296] However, 84% of consumers recruited at Swedish pharmacies later reported completely following the pharmacists' advice (although recall was not checked).[300]

Medical profession discomfort about pharmacy has long existed.[257, 301] Some doctors believe commercial pressures bias pharmacists,[276, 302] but commercial pressures were reportedly not evident in UK pharmacy practice,[303] or with oseltamivir supplies in NZ.[80, 81] UK pharmacists rejected requests for simvastatin[261] and tamsulosin^4.[304] Low sales of many reclassified medicines e.g. simvastatin[115] in the UK and H2-antagonists in Denmark,[20] may reflect similar trends.

Despite many criticisms, pharmacy remains an accessible, frequently used resource for medicines and advice, with highly trained pharmacists readily available without a consultation fee. Even in the US where there is no pharmacy category, most consumers reported the pharmacist is a very important source of drug information,[248] and found them helpful in supplying the EHC.[305] Many pharmacists perform well on mystery shopping,[297, 306, 307] They mostly performed as well as GPs in herpes labialis vignettes,[308] and were more conservative than doctors in migraine.[309] Consumer reports with the EHC were largely favourable.[305, 310] NZ oseltamivir research indicated a responsible pharmacist approach.[80, 311]

Drug-related problem interventions occurred in 1.9 per 1000 non-prescription purchasers in Sweden,[312] and 5.7 per 1000 unit sales in Australia.[82] Variation may arise from a different sales mix, self-selection variation, or a pharmacist shortage in Sweden.[284] The therapeutic condition influences referral rates and pharmacist involvement; a small UK study reported no referrals for headlice, and 8% for vaginal symptoms.[313] A larger NZ study using similar methodology found a similar doctor referral rate for vaginal symptoms (9.1%).[314]

In most countries pharmacy plays an important role in reclassification, however improving performance by some pharmacists and pharmacy staff may help further reclassifications.

2.3.2.9. Doctors and reclassification

Medical support for reclassification sometimes occurs,[183, 259, 315] and UK medical organisations have contributed to MHRA stakeholder reclassification discussions.[24, 155] However, doctors have voiced concerns about medicine reclassifications,[92, 114, 125, 126, 316-319] particularly for long-term conditions.[114, 166, 302] Concerns include adverse events,[120, 166] inadequate screening,[120, 166, 281] and ineffective dose for simvastatin.[166]

Medical views can affect reclassifications, e.g. the US reversal of orciprenaline (metaproterenol),[154] and the UK trimethoprim and nitrofurantoin reclassification withdrawals.[127] Friedman, et al (1992) believed that the physician-heavy decision-making process in the US slowed reclassifications.[320]

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^4 This study is limited by the small number of surveys, low response rate (36%) and sampling (one pharmacist per pharmacy in a region in England)
However, reclassifications can progress despite strong medical opposition. In the 1990s, NZ gastroenterologists threatened a media campaign if H$_2$-antagonists reclassified,[125] yet these medicines have since become general sales.[321] A similar situation occurred in the UK.[302]

Physician attitude may vary between organisations and countries and over time.[302, 322] The Australian Medical Association declared that a busy pharmacy was the wrong environment for EHC supply and that the reclassification should be reversed.[316] In contrast in the US, although some medical groups opposed the EHC reclassification, many medical organisations supported it.[133, 323] Although restricted by variable response rates and regional sampling, four English GP surveys (1983-2004) found chloramphenicol acceptance of 24% in 1992 increased to 80% in 2004.[302, 324-326] Increased support was attributed to the lack of known issues arising with previous reclassifications, acceptance of reclassification,[302] and increasing doctor workload.[24] Minimal support for ranitidine reclassification and high support for vaginal antifungals occurred in Finland (1999) and two US regions (1993), despite some doctors reporting self-treatment deficiencies with vaginal antifungals.[164, 322, 327]

Chronic condition treatments (e.g. antihypertensives) attract little medical support.[302] Doctors disagreed with simvastatin reclassifying in the UK[9,165] and the US[6,328] with concerns including inappropriate use, insufficient consumer monitoring and follow-up. US doctors worried that patients could discontinue prescription lipid lowering agents to self-medicate. However, most consumers would want to talk to doctors before starting a non-prescription statin,[328, 329] so this concern may be unwarranted. GP support helps reclassification success,[330] with the simvastatin failure partly attributed to medical concern.[115]

Negativity to reclassification is unsurprising given that doctors see consumers when self-care fails,[92, 164, 320] but not when it works.[331] Doctors may be influenced by having seen sub-optimal consumer behaviour, but Madhavan and Gore suggested doctors’ concerns about patient decision-making ignores studies suggesting much patient decision making is reasonable.[331] These US-based researchers proposed that advertising may disenfranchise doctors, and that doctors may worry that patients may feel cheated, or doubt the doctor’s credibility if prescribed a non-prescription medicine. Others have suggested that doctors may dislike change and losing control with reclassification,[302] or note a long-standing doctor-pharmacist divide.[257, 301] Liaw and Peterson reported concerns about extending pharmacist domains “revolve around professional authority and practice, remuneration and patient care”.[301][p272-3]

Other commentators have raised medical remuneration,[92, 110, 320, 331] possibly supported by research.[322, 331] Deletraz-Delporte and Stanford believed doctors’ attitudes to reclassification varied between EU member states according to their funding.[110] Three US physician organisations (two in allergy areas) strongly opposed reclassifying non-sedating antihistamines.[149] Furthermore, four committee members voted against the reclassification because they believed benefit-risk could

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5 Post-reclassification survey with a low response rate
6 Doctors on a panel (n=200) likely to see patients with high cholesterol were surveyed
not be assessed for OTC use without actual use studies. Given the consumer safety advantage compared with OTC sedating antihistamines⁴³ patch protection' seems possible.

2.3.2.10. Reclassifications in different countries

This section considers some of the key factors commentators (mainly from industry) have suggested contributes to variation in reclassification between countries.

Regulator or government policy has arisen often in the US and UK. Francesco suggested in 1995 that the UK was becoming more active than the US in reclassification partly because of positive UK policy, but also because of the US committee, and a "coolness" from the FDA to reclassification.⁴⁴ In 2010, Hemwall further opined that the FDA and its advisory committees were risk-averse.⁴⁵ Others have also reported the UK government support for reclassification and positive regulator policy over many years.⁴⁶, ⁴⁷, ⁴⁸, ⁴⁹, ⁵⁰, ⁵¹, ⁵², ⁵³ However, the FDA has appeared proactive in other reports, e.g. suggesting reclassification candidates in 2001.⁵⁴ and holding meetings to consider reclassification issues.⁵⁵, ⁵⁶, ⁵⁷ US proactivity appears less successful than in the UK, with statins rejected in the US⁵⁸ and a slowdown in US reclassification in the 2000s.⁵⁹

Political support has also been considered to help the reclassification process elsewhere.⁶⁰ In 1999, Eberwein believed that the EU's political support for reclassification (including chronic disease treatments) would facilitate reclassification and increase the importance of self-medication within healthcare.⁶¹ However, this has not eventuated.⁶² Francesco proposed that the Europeans and Americans differed in perspective.⁶³ Under US law, a medicine should only be restricted to prescription-only status if medical supervision or controlled access were required, while the Europeans defaulted to prescription. It is unclear whether this facilitates reclassification in the US, given the difficulties reclassifying non-sedating antihistamines⁶⁴ and the EHC.⁶⁵

McCreedy, from the MHRA, reportedly observed that the UK's ability to use pharmacy safeguards was not possible in some European countries, and suggested confidence in pharmacy helped UK reclassification.⁶⁶ Kelly (2012) further opined that lack of trust in pharmacy contributed to the European reticence to reclassify.⁶⁷

Use of special studies is typical in first-in-class US reclassifications,⁶⁸, ⁶⁹, ⁷⁰ (except non-sedating antihistamines),⁷¹ and Soller suggests that the FDA's framework (including studies) allows a "predictable and consistent approach" to reclassifications.⁷² However, the FDA and/or its advisory committees have been criticised for inconsistency by industry⁷³ and academics.⁷⁴, ⁷⁵, ⁷⁶ It is unclear why Soller differs from the others, given his long-standing commentary on US reclassification and reading of multiple meeting transcripts.⁷⁷, ⁷⁸, ⁷⁹

Companies may vary in driving reclassification in different countries. Francesco suggested that US companies were reticent versus UK companies (but not why).⁸⁰ Lyon (2001) reported European companies were more reluctant than US companies because consumers could not self-select medicines and European medicine reimbursement affected the self-medication market.⁸¹
Additionally, some European countries restricted use of the pharmaceutical brand, also affecting sales success post-reclassification. Others have also mentioned the European reimbursement barrier.[110] A further factor helping US sales is three years of exclusive rights to market a product in the US (i.e. no generic competition) versus one year exclusivity in Europe, and none in some other countries.[26]

In 2013, Kelly reported that Europe is slowing UK reclassification because of the requirement for medicines registered centrally to reclassify centrally.[100] Like others,[110] Kelly reported that Europe contained varied cultures and medical practices. Lyon considered strong pharmacy and medical lobby in some European countries hinders non-traditional reclassifications.[95]

The commentators responsible for these views typically have had strong 'insider' knowledge from years of experience in their market. However, while very well-informed, most commentaries take an industry perspective. Their view is not necessarily that from other stakeholders, such as the regulator, the consumer, the pharmacist, or the doctor. However, commentators have suggested reasons for differences in reclassification between the UK, the US and Europe. There is a need to understand what the views from other stakeholders are, to more formally evaluate the differences, and to look beyond these three markets that receive the most attention.

2.3.2.11. Summary of medicines reclassification

This section has provided an overview of reclassification, including some history, benefits and risks, and the key stakeholders. It has highlighted strong activity from the UK in particular, and pockets of activity elsewhere. Activity varies over time, and many differences between countries were reported, although these have occurred mainly at the UK-US-Europe interfaces, or within Europe, rather than other countries.

2.3.2.12. Comparative literature on reclassification

Comparisons between countries have shown reclassification varies,[19, 21, 31, 32, 49, 50] and the WSMI (2009) highlighted the UK, Germany, Australia and the US as the most progressive countries in the area.[26] Regulators[333] and industry[100] appear proud of the UK's 'leadership' in this area.

Comparative literature on reclassification, either across countries or within a country, is the most relevant to this research. Some comparisons have considered one or two variables such as scheduling,[31, 49, 50] or reclassification policy or criteria[31, 32]) or multiple countries’ reclassification of a single medicine.[19, 21]

WSMI tables7 showed marked differences in medicines availability between countries, but were limited by gaps, obsolete products and some omissions, and uncertain accuracy. Comparing the WSMI tables (dated 19 December 2008) with NZ regulator information, I found 20 discrepancies for NZ (personal communication with the AESGP on 15 July 2009). USGAO reported discrepancies against regulatory agency information also.[50] Additionally, if comparing the WSMI tables for a

7 The industry website tables were replaced by a search function by medicine around 2012
country, there are no allowances for the fact that one country may have more ‘me toos’ reclassified than another, providing little or no extra benefit to consumers.

Soller identified first-in-class switches[112] which uniquely push the boundaries of OTC availability, to differentiate these reclassifications from the easier ‘me-toos’. In drug development, a first-in-class medicine has a novel mode of action, whereas a ‘me-too’ uses an existing mode of action.[337] However for reclassification, first-in-class switches may not push boundaries, and follow-on switches could push boundaries. Topical griseofulvin (reclassified in the UK) has a different mechanism of action to the already-switched azoles and polyenes,[332] but does not push boundaries. A reclassification of diclofenac, allowing 150 mg per day (full dose)[332] after the ibuprofen low-dose switch, would probably push boundaries in most countries, yet would be deemed a follow-on switch. A non-prescription medicine with a new indication previously untreated in the non-prescription arena may push boundaries, e.g. domperidone, for nausea and vomiting.[338] Finally, some medicines have no clear class, such as ketotifen (an antihistamine and mast cell stabiliser) and acetylcysteine (a mucolytic and nutritional).[332] A tool is needed to consider incremental patient benefit.

2.3.2.13. Between country variation

Even reasonably similar developed countries differ in availability of medicines without prescription.[21, 31, 49, 50] Table 2-2 reports details of comparative studies relevant to my research.
## Table 2-2 Comparative studies pertinent to reclassification

<table>
<thead>
<tr>
<th>Author</th>
<th>Countries</th>
<th>Objective</th>
<th>Method</th>
</tr>
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<tbody>
<tr>
<td>Bowden, 1993</td>
<td>Australia, NZ, US, UK, Canada, Denmark</td>
<td>Literature review for thesis comparing recent reclassifications and criteria for reclassification</td>
<td>Document analysis</td>
</tr>
<tr>
<td>USGAO, 1995</td>
<td>Canada, Italy, Australia, Netherlands, Denmark, EU, France, Germany, UK, US, Sweden, Switzerland</td>
<td>To ascertain the costs and benefits of a pharmacist-only or pharmacy-only class of drugs for the US</td>
<td>Literature review, interviews and document analysis. Comparison of classifications of 14 selected drugs (past or mooted reclassifications) across countries except France and Italy</td>
</tr>
<tr>
<td>Achanta, 2002</td>
<td>US, UK, Canada, Australia, Japan</td>
<td>To: examine the regulatory environment of OTC medicines; the application of US policy of OTC medicines; explore views on critical questions for the US on regulatory aspects of OTC medicines</td>
<td>Document analysis (five countries), 18 interviews (across four countries), and 18 public statements reviewed, 473 internet surveys (pharmacy academics), three individual US case studies</td>
</tr>
<tr>
<td>Cohen, 2003</td>
<td>Sweden, US</td>
<td>To compare omeprazole reclassification decisions in two countries</td>
<td>Case study using documents and other sources. WSMI table comparison</td>
</tr>
<tr>
<td>Cohen, et al., 2005</td>
<td>UK (simvastatin), Sweden (omeprazole), US (loratadine)</td>
<td>To compare three unusual reclassifications</td>
<td>Commentary using quasi-case studies of unique reclassifications in three countries</td>
</tr>
<tr>
<td>Gilbert, et al., 2006</td>
<td>Australia, Canada, France, NZ, US, UK</td>
<td>To compare scheduling arrangements in six countries and how these arrangements affect consumer availability of medicines</td>
<td>Comparison using data from WSMI tables for 119 medicines considering influence of scheduling on availability. Document analysis to compare criteria for scheduling used in each country</td>
</tr>
<tr>
<td>Armstrong, 2006</td>
<td>US, Canada, France, UK</td>
<td>To investigate government, political and social forces affecting reclassification in four countries</td>
<td>Comparison using document analysis of reclassification of EHC in four countries</td>
</tr>
<tr>
<td>Nguyen, et al., 2006</td>
<td>US</td>
<td>To compare decision-making processes of the FDA’s Non-prescription Drugs Advisory Committee</td>
<td>Comparative case study of three reclassification attempts within one country, through document analysis and video from one meeting</td>
</tr>
<tr>
<td>USGAO, 2009</td>
<td>US, Australia, Italy, the Netherlands, UK</td>
<td>To report on arguments supporting and opposing a US BTC drug class; to ascertain the impact of scheduling on availability; to report issues important to the establishment of a BTC drug class</td>
<td>Comparison using data from WSMI tables showing non-prescription availability for 86 medicines across five countries. Comparison of 1995-2007 reclassifications in three countries. Literature review, reports and meeting minutes. Interviews for each country</td>
</tr>
</tbody>
</table>

BTC = Behind the counter; WSMI = World Self-Medication Industry; OTC = Over The Counter; EHC = Emergency Hormonal Contraception; USGAO = United States Government Accountability Office
Observers and researchers agree that variation exists. However, country progressiveness depends on the countries examined, medicines selected, perspective, and the methodology. Cohen found the US had 50% more medicines available off-prescription than Sweden, but comparisons of more countries provide greater interest. I have adapted findings by USGAO and Gilbert, et al. into Figure 2-2 and Figure 2-3 to highlight variation in findings. The US can appear less progressive in reclassification than other countries, or similar to (or more progressive than) other countries. USGAO in 1995 found the US in the middle and the Netherlands and UK liberal. USGAO (using 2007 data) found Australia and the UK most liberal and US, Italy and the Netherlands similarly restrictive. Gilbert, et al. (using 2003 data) found NZ the most liberal and the US the most restrictive with the UK in the middle. The difference in findings could impact on conclusions.

**Figure 2-2 USGAO review of availability of 14 selected medicines in 1995**

![Figure 2-2](image)

Source: Adapted from USGAO, 1995

**Figure 2-3 Findings of medicines availability from USGAO and Gilbert, et al.**

USGAO findings from 2007 (86 medicines) Gilbert, et al. findings from 2003 (119 medicines)

![Figure 2-3](image)

Source: Adapted from Gilbert, et al., 2006, and USGAO, 2009
These graphs (Figure 2-2, Figure 2-3) exclude the comparisons of restrictions to availability within non-prescription medicines, i.e. how many medicines were general sales versus how many were more restricted. The USGAO and Gilbert, et al. found the US had more medicines with general sales availability than all other countries examined,[31, 50] a fact that the USGAO weighted strongly. It is informative to compare the conclusions from the three projects (Table 2-3).

<table>
<thead>
<tr>
<th>Research and publication date</th>
<th>Researchers’ country</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>USGAO 1995</td>
<td>US</td>
<td>“There is no clear pattern of increased or decreased access to drugs as nonprescription [sic] products where a pharmacist or pharmacy class exists.&quot;[p3]</td>
</tr>
<tr>
<td>Gilbert, et al., 2006</td>
<td>Australia</td>
<td>“…the presence of several different schedules within the non-prescription schedules appears to allow greater direct access to medicines by consumers.&quot;[p100]</td>
</tr>
<tr>
<td>USGAO 2009</td>
<td>US</td>
<td>“…it is unclear whether the presence of restricted nonprescription [sic] drug classes increases drug availability.&quot;[p20]</td>
</tr>
</tbody>
</table>

I suspect that the differing conclusions arose from medicine selection, country selection, weighting by researchers to different measures, timing and inherent biases. For example, timing and medicines selection could have contributed to the strong contrast for the Netherlands comparing 1995 to 2007.

The 1995 USGAO’s comparison is particularly flawed. Its 14 medicines included six NSAIDs (and aspirin) and two H2-antagonists, but aspirin does not fulfil the selection criteria, and many past reclassifications or mooted reclassifications were not included. Inclusion of many NSAIDs, when the US had been particularly active in reclassifying NSAIDs potentially skewed results.

Both the 2009 USGAO report and Gilbert, et al. used data from WSMI tables (for over 200 medicines). WSMI table deficiencies are mentioned above. The USGAO checked regulator data,[50] while Gilbert, et al. checked only the Australian data (which was accurate).[31] Both research groups removed medicines which the WSMI tables indicated were not available in all selected countries. USGAO removed 24 more that regulatory agency information showed were not approved in some selected countries. Gilbert, et al. had 119 medicines (including some multiple dose forms) remaining; USGAO had 86 remaining. This selection is convenient but somewhat arbitrary, and countries with more ‘me-toos’ reclassified will look better without incremental consumer benefit. While researchers’ comparisons show that countries vary, further conclusions, e.g. which country is more progressive than another, or effect of scheduling on availability, may be limited.

The countries chosen affect the outcomes. USGAO (2009) included two countries with similar quantities available off-prescription to the US despite having a pharmacy or pharmacist controlled category, whereas Gilbert, et al. had no countries rating the same as the US (Figure 2-3). The USGAO (2009) started with the 11 countries considered in 1995,[49] and excluded seven countries
that had not evaluated their drug classification since that time. The Australian researchers started with the 35 countries in the WSMI tables, but only examined countries with detailed descriptions of scheduling processes and availability of experts to answer questions, of which there were six.

In 2009, the USGAO conducted a second comparison, examining all medicines reclassified between 1995 and 2007. Australia down-scheduled the most (n=193)\(^8\) with fewer down-scheduling in the UK (n=50), and US (n=31). However, all down-scheduling was included (e.g. pharmacy-only to general sales). TTH in Australia could affect unused ingredients (unmentioned in the report), and again there is no accounting for 'me-toos'. This comparison seemed to influence the USGAO very little, who did not discuss what it meant or why it might have occurred, perhaps suggesting that it did not suit their direction, or was not deemed important.

In reaching their conclusions, the US-based study appeared to weight general sales availability highly while the Australian-based study weighted the prescription:non-prescription divide highly. In other words, the US seemed to think high general sales availability (as in the US) meant better access, while the Australian-based researchers seemed to think low numbers on prescription (as in Australia) meant better access. This may reflect status quo bias based on the country's current scheduling, or the US consumer rights culture.[339] The 1995 USGAO report notes that “consumers have the power to choose their own nonprescription [sic] drug regimen by comparing different products on such items as dosing, side effects and price”.\(^49\)[p40] The Australian researchers perhaps had a pharmacy bias, and concerns about open availability that consumers might not have. Funding channels perhaps introduced a further bias.

These three projects compared non-prescription availability of medicines across a relatively small number of countries to ascertain effects of one variable, scheduling. Commentators have suggested other factors involved that may vary by country.[30, 34, 95] Thus it appears that availability of medicines varies by country, possibly with some influence of scheduling but also other factors. Furthermore, comparisons between countries in medicines availability need careful study.

Factors other than scheduling, such as criteria for reclassification, policy and politics, have also been researched. Achanta, Bowden, and Gilbert, \textit{et al.} found reclassification criteria were similar across selected countries (although Achanta reported some inconsistent application). Bowden (1993) found similar information requirements for reclassification across six countries.[30] However, he considered that poorly defined requirements and insufficient clarity about weighting of information (such as labelling) could introduce subjectivity and allow political and social influences. Achanta considered the US should also have better defined requirements but the other countries were well-defined,[32] (Notably, Soller took an opposite view in the US considering absolute definitions should be avoided).[340] Bowden, Achanta and Cohen reported regulator-initiated down-scheduling could occur in some countries but not all.[29, 30, 32] Achanta reported that while the scientific principles for reclassification were “remarkably similar” across the US, UK, Canada, Australia and Japan, “the end results of each classification system are highly variable.”[p69]

\(^8\) Alongside 67 up-schedulings as noted by the authors
In 2001, Achanta found US pharmacy academics considered their regulatory environment for OTC medicines deficient, unlike academics in the UK, Canada and Australia, perhaps because the US has no official pharmacist-controlled category.[32] A low response rate (7-17%), and narrow range of participants limits his findings. Achanta used 18 key informant interviews in the US, UK, Canada and Australia and public statements from 18 stakeholders to consider regulatory issues the FDA was exploring.[341] Regulator-driven reclassifications received mixed support, as did a BTC model in the US. The study findings are limited from an international perspective given the unevenness in numbers and participant characteristics, e.g. two Australian participants versus nine US participants. Achanta also described three unusual FDA reclassification considerations, reporting how challenges were addressed but did not compare the three.

Cohen compared the Swedish government-driven omeprazole reclassification with the rejected US sponsor-driven omeprazole attempt.[21] In some contrast to Achanta[32] and Bowden[30], he found variation in regulatory requirements (no actual use trials in Sweden), efficacy considerations, and labelling considerations.[21] Sweden noted an absence of evidence that the medicine was unsafe, while the US worried there was no evidence of safety as an OTC. Cohen found Sweden’s omeprazole decision inconsistent with its history of rejecting medicines that had reclassified elsewhere. Concomitant with the first-in-world omeprazole reclassification, it rejected 11 medicines reclassified elsewhere in Europe. He suggested cost savings may have contributed to this anomaly. This fits with Bowden’s concerns about lack of definition and clarity of weighting allowing judgement variations.[30]

Nguyen, et al. (who compared three US reclassification considerations) reported that insufficient definition in meeting procedures, affected consistency of discussion.[51] A lack of official principles to steer the evaluation; omissions and ambiguity in FDA-drafted questions; and sometimes not answering these questions in the meeting contributed to inconsistency. Cost and access were raised in all considerations, even though cost apparently should not be discussed. Nguyen, et al. reported a committee member suggested that the statin dose should be higher, and at a following meeting declined to approve a higher statin dose for cost reasons. This research provides insight into committee variation. The researchers suggested training committee members and improving the FDA questions, recording member voting for accountability, and structured committee processes.

Armstrong observed that politics hindered the EHC reclassification in the US, aided the government-driven reclassification in France, and had little effect in Canada or the UK (despite a High Court challenge).[19]

Armstrong, Nguyen, et al., and Cohen show the importance of case study comparisons for explaining reclassification variation. However, many countries do not publish transcripts or minutes from committee meetings. Although not formal research, Brass and Hiatt in 2012 suggested improvements to FDA Advisory Committee meeting process (not limited to reclassifications).[336] The commentary reported inadequate preparation by members, insufficient expertise, and use of anecdotes and experience rather than evidence. Suggested improvements included carefully selecting committee members.
members, correcting misinformation during the meeting, providing members with feedback, and (like Nguyen, et al.), [51] member training and improving FDA questions. The experiences of Brass and Hiatt as participants in multiple meetings may have provided greater insight than reading transcripts.

2.3.2.14. Methods and approach used in researching the process of reclassification

Considering the conceptual framework outlined earlier (see 2.2), only one of the comparative reclassification studies truly takes a macro-level approach, the Gilbert, et al. study. [31] Armstrong’s EHC comparison, [19] the USGAO reports [49, 50] and Achanta’s work [32, 341] take a US-centred approach. Armstrong’s conclusion mentions the non-US countries once in four paragraphs. Cohen’s comparisons [21, 29] had limited scope rather than providing macro-level research.

Comparative reclassification researchers have used various methods (Table 2-2), and tended towards an objective rather than subjective approach. USGAO (2009) used document analysis, literature, interviews and WSMI data with an objective-subjective mix. [50] Gilbert, et al. analysed documents and WSMI data in a very objective approach. [31] Cohen took a largely objective approach, using documents and a brief survey of US health funders. [21, 29] Armstrong’s paper takes a very legal perspective using document analysis limiting the opportunity for subjectivity. [19] Achanta used an electronic survey, case studies (summarising meeting transcripts and some submissions) and a mix of interviews (responses to statements) and examination of public statements. [32] The cross-country comparison of stakeholders’ views by Achanta and Rhodes had limitations in participant selection, and relied on publicly-available statements from half of the stakeholders limiting findings.

A more subjective approach arose in the single case study from Kurko, et al. [232] Insights from the interviews provided background information and perceptions that were important in understanding how the Finnish NRT reclassification to general sales had occurred. Interviews and documents were complementary and provided triangulation. Three other case studies rather unusually used the perspective of an involved party (an ‘insider’). [20, 115, 156] providing insight beyond what documents could contribute. Juul supplemented his knowledge with research findings and sales data.

2.3.2.15. Other comparative health studies

Comparative research between countries can provide bench-marking and/or explain differences in health-related areas. Two such studies use a mix of document analysis and interviews to understand differences and reasons behind the differences. Franken, et al. considered drug reimbursement across five European countries (their own and four selected on diversity) using analysis of policy documents, literature and 37 interviews with key informants. [342] Abraham and Davis used a subjective-objective approach to compare drug safety withdrawals in the UK and US. [343] Their extensive document analysis provided a comparison of all withdrawals for 22 years by year withdrawn and the document analysis supplemented with interviews with 73 key informants gave insight into the differences between the countries that caused the higher rates of withdrawals in the UK than the US.
2.3.2.16. Summary of comparative research

Comparative reclassification research provides useful insights into reclassification processes, within a country and across countries. Cross-national research has examined from two to 11 countries using different methodology. While such research has provided an indication as to the variation that can be seen between countries, there is a need for a better tool for comparison than the WSMI table count.

Multiple factors may affect reclassification, but have not been formally investigated across multiple countries. Additionally, no formal research has considered NZ and Australia in light of Trans-Tasman Harmonisation. Since this harmonisation affects consumer access to medicines in one or (more likely) both countries, research is needed to consider implications of this regional effect.

Research techniques used in comparative reclassification research have varied considerably. Case studies from insiders and a mix of interviews and document analysis have provided in-depth research as is required to meet the aims of this study (1.3).

2.4. Summary of this Chapter

I have produced a conceptual framework for the study and reviewed literature relevant to reclassification of medicines on the international (developed world) stage. My focus has been on comparative reclassification research or other research that informs the factors involved in reclassifying medicines. Variation in reclassification occurs, probably for a multitude of reasons, but no formal research has yet been conducted to ascertain the key reasons across developed countries.
Chapter 3. Methodology and Methods

3.1. Introduction

Chapter 2 outlined my conceptual framework including a comparative, multi-level model and literature review. This current chapter presents the qualitative methodology and methods that I have used to operationalise that model to describe and account for international variability in medicines reclassification. I primarily use multi-level and heuristic methodologies.

3.2. Methodology

3.2.1. Multi-level approach

My ‘macro-meso-micro’ model compares reclassification within global, regional and national spheres or levels of influence, as wielded for example by multi-national pharmaceutical companies.[344, 345] My macro-level analysis is defined here as spanning highly developed countries. It looks at experience of barriers to, and enablers of, reclassification across nine countries (see Table 3-1) in the context of the international trends they help to produce.

<table>
<thead>
<tr>
<th>Country</th>
<th>Micro-level</th>
<th>Meso-level</th>
<th>Macro-level</th>
</tr>
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<tbody>
<tr>
<td>NZ</td>
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<td></td>
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<tr>
<td>Australia</td>
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<td>UK</td>
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<td>US</td>
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<td>Japan</td>
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<td>Singapore</td>
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<td>Netherlands</td>
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<td>Denmark</td>
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<td>Canada</td>
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<tr>
<td>European</td>
<td></td>
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<tr>
<td>International</td>
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</tbody>
</table>

N.B. The size depicts the level of analysis and contribution of each country or region

Developed and developing countries differ in medicines usage.[346] Emerging markets have less regulated drugs, and poorer regulation enforcement.[169] Thus, developing countries and emerging markets have been excluded from this study to provide an underlying similarity.

Meso-level analysis is suggested to include regional spheres of influence from forces including TTH, and European effects.[35] My meso-level focuses on reclassification in Australasia given the
uniqueness of TTH. The regional level was recognised by both USGAO[50] and Achanta,[32] in including information from the EU. Lastly my micro-level analysis considers to varying degrees the individual experiences of five countries – NZ, Australia, UK, US and Japan. NZ is examined over a longer period to understand the background to its current innovation in reclassification, as little background is available academically. Additionally, I have the greatest experience in NZ.

3.2.2. Case study methodology

Case studies have been used widely in reclassification research.[19, 21, 51, 115, 149, 150, 152, 153, 232] Additionally, multi-level comparative research typically uses individual countries as cases. It explores them within their own environment, then compares the cases with other cases.[40] I have followed this model, but I have also nested cases within these individual cases, and within the meso-level. At the macro-level the many interviewed participants provide breadth rather than depth.[347] In contrast, the analysis at the micro-level, including the nested case studies, provides depth to a selected area of this research to complement the rest of the work.[347] These nested case studies provide specific reclassification examples to illustrate some of the barriers and enablers to reclassification, and the medicine-specific nature of some of these barriers. Most of my case studies are instrumental case studies, used to illustrate an issue or particular finding.[348, 349]

3.2.3. Heuristic approach

My macro-meso-micro level analysis involves a heuristic approach. Following Moustakas, this qualitative approach embraces the knowledge and active input of the researcher, who has a high level of personal involvement and interest in the topic.[350, 351] Derived from phenomenology, it uses methods such as in-depth interviews to deepen the researcher’s understanding of the nature and meaning of their own lived experience of the study phenomenon.[350] Studies using the heuristic approach usually centre on emotions and intensely personal experiences,[350, 351] with self-searching important in the methodology.[351-353] In contrast, this research is less about emotions, and is less intense or personal, (Table 3-2) but it draws reflexively on my everyday, personal experience as an ‘insider’ to engage deeply with my subject.[354]

Moustakas’ heuristic methodology appears uncommon, being unmentioned in Denzin and Lincoln’s extensive Handbook of Qualitative Research.[355] Embase and Medline revealed few examples of this research approach in medicine; one was Nuttall’s work in psychotherapy, the other a knee arthritis study by a researcher with this condition.[354, 356] However, reclassification is my lived experience, and some participants shared a similar interest in and enthusiasm for the same topic, which often provided a connection from sharing our experiences.[351, 352]

I drew on my ‘insider’ knowledge of medicines reclassification. Like Peck and Seeker, the ‘insider’ approach probably helped me to access key informants.[357] My knowledge and experiences were integral to the conduct, direction and findings of the research. However, as with Peck and Seeker, I was mindful that my own assumptions and experiences could lead me to jump to conclusions rather than accurately interpret participants’ constructions.[357] To manage this, I triangulated with
documents and provided case studies, and used a participant in each key country to read the relevant chapter.

Table 3-2 A comparison of my approach versus the typical heuristic approach[350, 358]

<table>
<thead>
<tr>
<th></th>
<th>Standard heuristic approach</th>
<th>My heuristic approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Closeness to data</td>
<td>Connectedness and relationship</td>
<td>Connectedness and relationship</td>
</tr>
<tr>
<td>What is described</td>
<td>Portrays meanings and personal significance</td>
<td>Portrays meanings but not personal significance</td>
</tr>
<tr>
<td>Method</td>
<td>Extended interviews with up to 10-15 participants providing in-depth information stopping when they reach a natural close[351]</td>
<td>A mix of extended interviews stopping when they reach a natural close, and shorter interviews. Supplementary document analysis.</td>
</tr>
<tr>
<td>Analytical processes</td>
<td>Creative synthesis including the researcher’s intuition and inferences</td>
<td>A mix of distillation and creative synthesis including the researcher’s intuition and inferences</td>
</tr>
<tr>
<td>Reporting</td>
<td>Individuals are portrayed as whole persons</td>
<td>Individuals have reduced visibility owing to confidentiality and the large sample size</td>
</tr>
</tbody>
</table>

3.2.4. Reflexivity

This section reflects on my background, both to explain the heuristic approach and to give insight into how my background shaped my perspective on issues in this area including potential biases. This research has been a reflexive process, reflecting on how the interview discussion affects my perspective on reclassification.

I started by being aware of what I knew and had experienced, and what I thought about reclassification of medicines as well as what I needed to find out; with this awareness I was then able to “...deepen and extend the understanding through the eyes and voices of others.”[358][p17] My learning in this research has been iterative,[359] earlier interviews have shaped the selection of later countries (e.g. adding Japan) and participants, and the content and conduct of later interviews.[358]

3.2.4.1. Biography in relation to reclassification

I first became interested in medicines reclassification in the early 1990s when, as a young pharmacist working in community pharmacy, I was excited by the professional opportunities presented by the wave of reclassifications in NZ. The reclassifications enabled me to use my training, increase my knowledge, provide effective medicines to healthcare consumers and treat people previously referred to doctors. Since that time I have worked in a range of community pharmacies, and spoken at length with community pharmacists in NZ, Australia, the UK, Singapore and France about reclassification. Educationally I have provided information on non-prescription medicines and reclassification to pharmacy assistants, pharmacy students and pharmacists through academic providers, pharmacy organisations and trade publications. I have also assisted researchers as an ethics committee member for four years. In industry I worked on the launch of diclofenac tablets after reclassification.
My Master’s degree explored the usage of diclofenac tablets post-reclassification[180, 360], and my further reclassification research includes two oseltamivir studies[80, 81] and a case study.[156] As an MCC member (2004-2009), I searched literature, and communicated with pharmacists and experts about reclassifications under consideration. I communicated with regulators and/or members of the relevant committees in the UK, Australia and Singapore, and observed at an Australian classification meeting (2007). Since 2010, I have submitted reclassification applications in NZ. In 2011, I was consulted on a European reclassification attempt and attended a European Committee for Medicinal Products for Human Use (CHMP) meeting.

3.2.4.2. Perspectives

Set against this background, I largely support reclassification. As a consumer, I appreciate the benefits doctors provide, but find visiting the doctor for myself and my children difficult for urgent matters, given the time taken and the inflexibility of the doctor’s availability. I prefer a patient-centred approach to the traditional paternalistic doctor-centred model. As a taxpayer, I favour funding important and serious conditions rather than conditions that can be self-managed or managed with pharmacy or nursing assistance (where consumers have this capability). I believe that further reclassification of medicines from prescription to non-prescription will assist health workforce issues in NZ[361] and elsewhere. I occasionally use medicines (conservatively) for myself and my family.

I have viewed variable practice in pharmacy, and know from simulated patient research, both academic[289, 291, 362] and non-academic,[288, 363-365] that pharmacists and pharmacy assistants vary in performance of their professional duties, as do doctors.[12, 366, 367] I am concerned that non-prescription medicines can be treated as ordinary items of commerce by pharmaceutical companies, pharmacy and consumers. I believe improving pharmacy performance, and treating medicines responsibly will maximise future reclassification opportunities.

I am a well-educated, middle-class European New Zealander in good health. Most participants were also middle-class, well-educated and European. Consumer organisations and countries with non-European cultures were included to provide others with a voice.

3.2.4.3. Potential biases

I have several potential biases from work, funding and my ethical obligations.

I was employed in industry in the 1990s. During my PhD I worked on a small industry-funded research project (2011), and a minor, unrelated industry project, and consulted to a company in 2011 on a potential European reclassification. In 2012 I consulted to two pharmaceutical companies on NZ reclassifications. I received a travel grant from Roche in 2008 to present oseltamivir research, and during that travel period I conducted interviews for my PhD. Pharmacybrands (a pharmacy retailer) funded my time working on reclassifications. I contracted on a project in 2010 for NZ medicines’ regulator, and was a government appointee to two Ministry of Health committees.
I have the bias of being a pharmacist. As a pharmacist my ethical obligation to consider the consumer's best needs is ingrained. As a New Zealander I may look at NZ with rose-tinted glasses. I hope that the insights from my experiences will enable me to see it as it is, including its deficiencies, and observe potential advantages in other systems that might be used to improve the NZ system.

In summary, I may have sympathies towards industry, pharmacy, the regulator, consumers and NZ. This research reports what may influence reclassification in different countries largely from the perspectives of key people involved internationally. I believe that limited opportunity exists for gain for any group out of my findings, and that my broad-ranging insights should inform the research. I have sought participants whose experiences, opinions and perspectives differ from mine. I have used documents and participant feedback on findings to help provide triangulation.[350, 358]

3.2.5. Methods

Figure 3-1 summarises the methods I have used to examine international variability in reclassification. I was a bricoleur,[350, 368] in using whatever tools I thought would work to achieve my task. Tools included interviews, document analysis, observation, participation, and case studies, all within a heuristic framework. My use of these specific methods varied with the level of analysis.

To enable a meaningful comparison between the countries, I devised a new tool, that of ‘innovative’ reclassifications to reduce the clutter of ‘me-too’ reclassifications, particularly in the TTH environment. This comparison was used at all levels of analysis. I also developed the ‘first-in-world’ innovative reclassification tool to compare the most progressive countries. Themes arising from the micro-level were compared and contrasted across countries to provide a meso-level of analysis, and ultimately insight into macro-level barriers and enablers across all selected countries, which contribute to the progression or hindrance of reclassification.

3.2.6. Consultation and ethics

For the interviews, the methodology and initial question guide were developed by the researcher with input from two supervisors (Dr Linda Bryant and Associate Professor Felicity Goodyear-Smith10). Māori consultation was unused because most participants were based in other countries, and the few NZ participants were considered unlikely to be of Māori ethnicity. Ethical consultation took place with the University of Auckland Human Participants Ethics Committee, with minor changes required and the study approved in August 2008, approval number 2008/304, prior to conducting interviews. Subsequent amendments were approved by the Committee.

10 Supervisor in the first year
3.2.7. Identification of the countries involved

Figure 3-1 shows the countries selected. Countries were selected using theoretical and pragmatic criteria[369] from a list of countries ranking highly (45 or above) in the United Nations Human Development Index; this index provides a measure of health, education and living standards for each country.[370] This threshold was expected to ensure the chosen countries[350] were similar in terms
of education and health, and their level of socioeconomic development and functioning. The individual developed countries were purposively selected for the research as information-rich cases.\[350\]

A difficulty of comparative research is that, rather than being independent, cases ‘borrow’ some of the traits being compared from another case, effectively providing two examples of the same case.\[369\] The ‘borrowing’ may arise from historical similarities, or ideas diffusing across different countries with globalisation. Examples specific to reclassification include the H2-antagonist reclassification that rippled across the world,\[20, 125, 126, 371\] and pharmacy models evolving from Britain in former British colonies. The strongest example of borrowed traits affecting reclassification is TTH. Suggested solutions to cross-contamination include (1) maximising diversity in nations selected and/or (2) identifying culturally clustered countries, selecting cases that are outside of this cluster or are similar, and then deliberately providing a more limited comparison.\[369\] In this research, I have done both. I have selected Commonwealth countries: NZ, Australia, Singapore, Canada, and the UK. I have deliberately selected diversity also, with the US, European countries and Japan adding diversity in pharmacy evolution, scheduling systems, health funding systems and cultures (Table 3-3, Table 3-4).

Three countries have small population sizes, three are medium sized, and three are large. I have included countries with recent first-in-world reclassifications (UK and NZ) and countries with a more conservative approach, based on my knowledge. There were constraints nevertheless to maximising variability.\[350\] Selecting a sample that has most of the combinations and permutations of the sampling factors represented was impossible to achieve within the limitations of variation, e.g. the single unrestricted non-prescription schedule in the US is highly unusual.

**Table 3-3 Non-prescription medicine schedules in researched countries**

<table>
<thead>
<tr>
<th></th>
<th>Pharmacist-only</th>
<th>Pharmacy-only</th>
<th>Drugstore or pharmacy</th>
<th>General sales</th>
</tr>
</thead>
<tbody>
<tr>
<td>NZ</td>
<td>●</td>
<td>●</td>
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<td>USA</td>
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Table 3-4 Demography of included countries and health system

<table>
<thead>
<tr>
<th>Geographical location</th>
<th>Population</th>
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<tbody>
<tr>
<td></td>
<td>Low (&lt;10m)</td>
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<tr>
<td>Americas</td>
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<tr>
<td></td>
<td>Canada</td>
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<tr>
<td>Asia</td>
<td>Singapore*</td>
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<tr>
<td>Oceania</td>
<td>New Zealand</td>
</tr>
<tr>
<td>Europe</td>
<td>Denmark</td>
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*The US and Singapore are the only two countries in the table not to have effective universal health care[372]*

NZ and Australia were chosen because of TTH. The UK was chosen as the so-called world ‘leader’ in reclassification,[24, 333] with universal healthcare and a common prescription-pharmacy-general sales classification system. In contrast, the US has had few recent reclassifications,[112] non-universal health care, and unusual scheduling.[50] The US is politically important[350] owing to the large non-prescription market.[77] Japan was selected as an Eastern country with a pharmacist-only schedule and new drugstore and pharmacy category.[350] Reclassifying topical aciclovir (2007) and vaginal antifungals (2008),[77] years after many other countries suggested it was conservative.

Denmark was active in government-driven reclassification over 20 years ago (like NZ).[30] but no longer appears progressive in reclassification.[123] Like Australia, Canada has a medium population size, universal health system and three non-prescription medicines schedules, yet has fewer non-prescription medicines, inconsistent with the view that pharmacist-only and pharmacy-only schedules enable reclassification.[31] The Netherlands has a pharmacy and drugstore schedule like Japan. Like the UK, the Netherlands has free doctors’ visits and capitation funding for doctors.[14] Singapore has widespread doctor-dispensing[11], a non-universal health system, an unusually low health spend as a percentage of GDP, and a mix of Western and Chinese medicine.[373]

In sampling countries, I wanted to build on previous research (Table 3-5). For example, Denmark was considered by Bowden[30] and the 1995 GAO report,[49] so it was chosen when looking for a disconfirming case for NZ. Most previous research had focused on Western countries. I expanded into Eastern cultures in case cultural variation affected reclassification, using both a large country (Japan), and Singapore as a small country with a Western-Eastern mix.

At the micro-level of analysis, NZ and Australia receive high attention. Both countries publish detailed meeting records for triangulating interview findings. I have expert knowledge of NZ developments in medicines reclassification and have watched the reclassification environment in Australia since 2004. With my NZ experience and heuristic approach, I have conducted a ‘lens’ or ‘keyhole’ analysis that uses NZ as a lens through which to interpret developments in reclassification in and beyond this national setting.

11 According to my visits to community pharmacies in Singapore in 2005.
### Table 3-5 Countries studied in this research compared with previous research

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*Achanta examined processes across all countries marked, but excluded Japan from interviews

My meso-level analysis focuses on NZ and Australia, which have been uniquely attempting to harmonise their medicines scheduling since the late 1990s.[136, 374, 375] Australia is a natural comparator with NZ. Australia and NZ have similar in life expectancies at birth, education and living standards,[370] universal access to health,[376] and spend per GDP on health,[370] and both have British-derived pharmacy systems,[377, 378] and similar non-prescription medicine schedules (Table 3-3). Both countries use largely the same evidence for reclassification decisions (based on my experience), yet recent differences in scheduling include salbutamol,[379] sumatriptan, [380] and oseltamivir.[104] The meso-level presents a unique opportunity to explore factors contributing to variation between two similar countries.

The macro-level analysis examines experiences of reclassification across nine countries. This comparative analysis incorporates and builds on the micro- and meso-level analyses by identifying commonalities and differences across all the countries (cases) examined.[40] Each country is taken in its own context and compared with the other countries, in terms of outcomes, and barriers to and enablers of reclassification. Even where the outcomes are similar, the means of arriving at these outcomes can vary, and so reasons behind the outcomes are at the forefront of the research.
3.2.8. Participant recruitment

Within each country, views were sought from key informants with a national perspective. Further informants were sought for their pan-Australasia, pan-European, multi-country or global perspective.

Participants were identified from my prior knowledge, or by contacting appropriate organisations, e.g. the medicines regulator in each selected country and identifying the person most involved with medicines reclassification. Occasionally snowball sampling occurred, where participants suggested others to interview.[350] Professor Kurosawa assisted in selecting Japanese participants.

Participants were usually directly involved in reclassification somehow, or were the appropriate spokesperson for their organisation. Informants came from medicines regulators; pharmaceutical industry; pharmacy, consumer or doctor organisations; and academia. Some participants were current or previous members of committees considering reclassification. Early interviews revealed which types of informants were most useful to talk to in other countries; for example, consumers’ and doctors’ organisations were less informative than others more involved in reclassification. After initial contact, the information sheet and consent form were sent, and an interview was arranged.

3.2.9. Interviews

Following informed consent, I conducted interviews face-to-face, by telephone or by Skype. Interviews were audio-recorded, except for five US interviews for which notes were taken (one because of background noise, and the others at participant request). Brief field notes were made immediately after the interviews. All interviews occurred on a single occasion, except one which was face-to-face then telephone (owing to time constraints). Occasionally, extra information was sought by email. Interpreters were used for three interviews conducted in Japanese.

Literature, and findings from previous conversations12 or interviews, the country studied and the participant’s role, were used iteratively[359] to inform the development of questions for each interview. The questions sought commonalities and differences potentially contributing to the level of reclassification in each country. In NZ and Australia, meeting records and my own involvement in reclassification influenced interview questions.

After reflecting on the first 10 (semi-structured) interviews I evolved to the conversational style true to the heuristic methodology, allowing each interview to take its own path of conversation.[358] This approach allowed spontaneity in asking questions and exploration of areas according to the participant’s responses,[358] and provided a more connected experience. While I attempted to include all vital topics,[350] that was not always possible. Sometimes concentrating on a particular area (owing to participant responses or experiences)[358] meant non-coverage of other areas, limiting comparability between participants.[350]

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12 For example, from visits to regulators or pharmacy organisations before commencing my PhD
Chapter 3

Most questions were open-ended to encourage rich responses.[350] Later interviews sometimes sought confirmation or disconfirmation of developing ideas from earlier interviews. The heuristic approach treats the interviewer and interviewee as sharing equal interests in knowledge generation and transfer. Sharing experiences creates a connection, and stimulates disclosure by the interviewee.[358] The conversational approach allows ‘testing’ of ideas among co-equals.[381] He noted that both the interviewee and interviewer “…could be expected to check the clarity, reasonableness and sense of reality of the views of the other”. While providing rich information, the conversational interview nevertheless has multiple challenges – no two interviews ask the same questions, analysis takes more work than structured interviews and questions needed to be formulated quickly within interviews.[350] affecting the question quality.

Panel 3-1 Lines of inquiry

Basic lines of inquiry usually included questioning the participant about:

- His/her role/the organisation’s role in medicine reclassification
- Where he/she considered their country sat in reclassification from prescription to non-prescription compared to other developed countries, and why this was
- Contributing factors to the differences between their country and other countries in classification decisions
- Barriers to reclassification in their country
- Enablers to reclassification in their country
- Which country he/she thought was advanced in reclassification and what they thought made it different from their country (if known)
- Views on why NZ and Australia sometimes make different decisions (for relevant participants)
- Views on non-sponsors driving reclassification, e.g. government or pharmacy organisations
- Views on the classifications used for medicines in their country
- Views on market exclusivity for medicines that are reclassified

Most questions asked for participants’ opinions and judgements, e.g. “where do you think Australia sits internationally in reclassification?”, or “what do you think about the idea of market exclusivity for a medicine if a company puts in a reclassification application?” No questions in the interview guide were explicitly and specifically about feelings (unlike usual heuristic methodology),[358] but participants sometimes revealed emotions, such as frustration or disbelief. Some questions asked about experiences, for example, “what happened with the sumatriptan reclassification?”

I felt that rapport and trust were quickly built before or during most interviews, in part through sharing information and using country-specific terminology (e.g. ‘OTC switch’ in Japan). Rapport and trust were sometimes difficult on telephone interviews, and with some representatives from consumer organisations and regulators. Using a spontaneous approach may be more influenced by interviewer effects and biases,[350] so I asked open questions about the barriers and enablers of reclassification prior to much sharing of information.
A small koha (gift) was provided at the end of face-to-face interviews. Participants could review their transcript, and withdraw or modify interview content. To protect participants, participants’ quotes have not been numbered but given by background. Quotes that could be sensitive were de-identified. One NZ telephone interview was withdrawn following recorder failure. Another person from the same organisation had already been interviewed. I transcribed most interviews and used a transcriber for other interviews. I checked all transcripts against the recording.

3.2.10. Interview analysis

The heuristic approach typically involves immersion in the material to obtain a thorough understanding of both participants as individuals and the group as a whole.[358] I read and reviewed interviews throughout the data collection period. I then worked through one country at a time, reading and rereading each individual transcript, summarising each interview, compiling key points onto a large piece of paper and coding sections in Nvivo 9 (by theme), then working through the themes returning to each interview in its entirety and comparing the different findings. I also brought in relevant comments from participants outside of the country. Where documents were used (primarily NZ and Australia) I compiled summaries, extracts and comparative charts (see 3.2.11) alongside the interviews. I developed a composite depiction which reflected the group and individuals including descriptions, diagrams and quotes.

For the meso-level of analysis, I immersed myself in the two country chapters, the comparative data I derived from interviews, and extracts from the meeting minutes for selected medicines or meetings. I checked back on interviews and meeting reports throughout the process. Only after preparing a portrait of each of the five key countries, and findings from the supplementary interviews, did I tackle the macro-level. I revisited key factors for each section (NZ, Australia, Meso-level, UK, US, Japan, supplementary interviews) then returned to the original data to immerse myself in the macro-level and derive a composite depiction, all the time returning to interviews or to NVivo codings to find the voices.

I have continued to communicate with some of the participants, by email and at conferences. While email communications have only occasionally (with permission) added data, they have helped my immersion in the area and provided clarity and understanding around some of the issues. For Japan, Professor Kurosawa acted as co-researcher, and listened to interviews, read transcripts, and provided input into analysis.

3.2.11. Document Analysis

Meeting records for NZ and Australia were analysed for prescription to non-prescription reclassifications’ numbers and dates in NZ and Australia; to ascertain reasons for rejections; and to inform case studies. Australian records were examined for advertising decisions. As key informants’ “…perspectives are necessarily limited, selective and biased”,[350] documents provided additional information and triangulation.
The minutes or records released for the National Drugs and Poisons Schedule Committee (NDPSC), Advisory Committee on Medicines Scheduling (ACMS) and MCC meetings are reliable and valid as official documents of committee meetings. Small omissions and errors are possible given the duration of the meetings and the volume or summary nature of some records. For orlistat in Australia in October 2006 the NDPSC agreed to reconsider advertising at the next meeting, and the Chair later decided the scheduling should also be reviewed. The next meeting records reported that the committee had decided to reconsider advertising and scheduling. Other omissions could include off-the-record comments, an indication of discussion intensity, speaker identification, and submissions from interested parties. In Australia, the applicant is confidential and submitters were, until recently. In NZ, applicants are identified, submitters are sometimes identified, and most of the application and Medsafe report (when prepared) are on the Medsafe website.

As NZ experienced unusual non-sponsor driven activity, including government-driven reclassification and TTH during the 1990s, MCC documents for 16 meetings were reviewed from 1990 to 1999. They provided decisions and reasons for decisions, and indicated the influence of TTH, evolution of the committee, and involvement of various stakeholders in NZ.

NZ and Australia were compared over 13 years (2000-2012), in line with available records and trends in reclassification rates. Twenty-four meeting minutes for NZ and 37 records of meetings for Australia were reviewed (an estimated 3,000-4,000 pages). All meeting records were scanned through twice (for accuracy) with notes taken. Prescription-to-non-prescription reclassifications and rejections were analysed, tabulated, and compared between Australia and NZ, and against recent reclassified medicines from the UK. Complementary medicines, excipients, nutritionals and redundant medicines were excluded. Information was extracted for case studies as necessary, read multiple times, compared with interview or other information as appropriate, and reported. Although even documents can be affected by the researcher’s hand, much information in meeting records was clear-cut, or was quoted to convey the exact meaning minuted.

Other documents were used as required, including regulatory websites, government reports, media reports, reclassification applications and agendas. Interview findings usually guided document use; for example, orlistat arose often, so relevant documents were sought. The project scope limited the extent of document usage; it was not feasible to outline the process of reclassification for each country. Reclassification, process, data requirements and criteria considered were reviewed by Achanta, so are not repeated here. Reclassified medicines and year of reclassification were obtained from regulator websites, industry websites, industry bodies or pharmacy organisations.

3.2.12. Other data collection and triangulation

Data triangulation was achieved by comparing data across different levels, micro-, meso-, and macro-levels, and using different methods. Document analysis for NZ and Australia supported the interview findings and provided confidence that the other interviews in other countries were probably also reliable. My involvement in NZ provided rectangularisation.
Investigator triangulation, where multiple researchers provide input[350] was necessarily limited. In
the heuristic approach the investigator becomes part of the research,[358] and using investigator
triangulation could impair this process. However, my supervisors and advisors provided sceptical peer
review to check if my position was supported by the evidence provided. I used three pharmacists (LE,
FK and LB) to talk through my ideas and check my decisions in developing and using the innovative
reclassification model. Professor Kurosawa provided input into my analysis on Japan.

3.2.13. Case Study methods

Multiple small case studies are nested within the individual countries (cases) or the meso-level to
illustrate and triangulate other findings, a common occurrence in extended qualitative research.[350]
For some case studies, supporting documents were sought to provide more detail that may have
informed the committee. For example, the Coroner’s report for potassium chloride was accessed, and
information on the orlistat advertising complaint and mystery shop was included in the findings.

3.2.14. Innovative Reclassifications

When comparing reclassifications between countries, deficiencies occur with the method used by US
GAO[49, 50] and Gilbert, et al.[31] as outlined in my literature review (2.3.2.14). First-in-class
reclassifications, used by Soller[112] also is difficult to apply and may not provide a measure of
uniqueness as defined (see 2.3.2.12).

To measure innovation in drug development, Smith and Schmidt used FDA priority reviews (for
registering new medicines) to measure significant advantage over existing medication,[384] but
regulators do not prioritise non-prescription medicines. Thus, a new measure is needed to show
progressiveness or innovation in switch.

I attempted to better define and work with first-in-class reclassifications by creating lists to fulfil the
criteria. On finding many anomalies, and wanting to consider consumer benefit, I created another
model, adapting the FDA priority criteria for new chemical entities[385] into a mechanism to identify
‘innovative’ reclassifications. My framework defines an innovative reclassification as one having the
potential to provide – in the treatment, prevention, or diagnosis of a disease – either:

(1) safe and effective therapy where no satisfactory non-prescription therapy yet exists in that
country; or

(2) a clinically-significant improvement compared to current non-prescription therapies in that
country.

The italics indicate my revisions to the FDA criteria.

Recognising the subjective nature of determining ‘clinically-significant improvement’, I modified
examples provided by the FDA (Table 3-6). The FDA bases its judgement on clinical trials or other
scientifically-valid research. In contrast, the scope of my project required me to use my own clinical
judgement followed by review by my pharmacist supervisors and advisors (LE, FK, and LB). I searched for evidence only for reclassifications that I considered borderline. For example, I considered oral single-dose famciclovir likely to enhance patient adherence over five-times-daily cream application, without seeking evidence. There was no disagreement across myself and the three reviewers of the final lists of innovative reclassifications, with a rationale for the decisions made.

<table>
<thead>
<tr>
<th>Table 3-6 Examples of Significant Improvement Used in Assessing Priority Reviews</th>
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<tr>
<td><strong>FDA priority review examples[385]</strong></td>
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<tr>
<td>Evidence of increased effectiveness in treatment, prevention, or diagnosis of disease;</td>
</tr>
<tr>
<td>• Elimination or substantial reduction of a treatment-limiting drug reaction;</td>
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<tr>
<td>• Documented enhancement of patient compliance; or</td>
</tr>
<tr>
<td>• Evidence of safety and effectiveness in a new subpopulation</td>
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Points 3 and 4 exclude formulation changes that are not usually switch issues, such as a gluten-free or a modified-release formulation. It also excludes combinations of medicines already available individually without prescription. It may include a substantially different route of administration that overcomes an important barrier for a significant-sized subpopulation.

3.2.15. First-in-World Innovative Reclassifications

For further comparison of the most progressive countries, first-in-world innovative reclassifications were used where possible. A first-in-world reclassification is a first reclassification of a medicine which has not been previously reclassified in any other developed country (typically called ground-breaking).[333] These reclassifications are significant if they are first-in-world ‘innovative’ reclassifications. This is a new descriptor, using the innovative reclassifications as defined above, and then reporting which developed country was the first to reclassify.

First-in-world reclassifications are often difficult to find in the available literature, and reclassification dates can vary (see 3.2.11). I have used information from applications for reclassification (where available), meeting records reporting reclassifications in a different country, media reports, or relied on my knowledge to identify first-in-world reclassifications. First-in-world innovative reclassifications in the results sometimes cannot be referenced, so should be read with caution.

3.2.16. Summary of methods chapter

In comparing countries in reclassification, I have used multiple data sources, methods, and levels. My heuristic approach has involved my taking a highly active role in the research; and I have contributed
to some decisions discussed within this thesis. I have examined individual countries in detail alone, and then in combination. This analysis has resembled a funnel approach – the most detail on NZ, then on Australia, with a combined Australasian comparison including case studies. Next, I took a less in-depth focus on the US, UK and Japan, before collecting a little information from Canada, Denmark, Singapore and the Netherlands and a few international experts, and lastly produced a composite description at the macro-level.

I have created new measures for comparing progressiveness in reclassification: ‘innovative reclassification’ and ‘first-in-world innovative reclassification’ to provide quantitative information to support the qualitative findings.
Chapter 4. New Zealand

4.1. Introduction

New Zealand (NZ) represents the most in-depth country, allowing examination of a small country that has become one of the most active developed countries in reclassification. I will expose the progressiveness through rectangularisation and in-depth variable and case analysis of 23 years of minutes, interviews with key informants and my own experience.

This chapter first sketches the NZ environment to provide context. Examining meeting minutes from the 1990s and 2000s provides history and the current position of NZ in reclassification. The interview findings (supplemented with meeting minutes) are explored thematically then under headings common to all countries, to facilitate comparison. Given the intense examination of NZ, a longer period is examined than for any other country, and multiple case studies are provided.

4.2. Background

NZ is not very important in the world. Containing only 2% of the world's land mass and 0.06% of the world's population, NZ is isolated, surrounded by 2000km of sea. NZ ranks highly on the United Nations' Human Development Index, fifth behind Norway, Australia, Netherlands, and the US, with good life expectancy and schooling duration. However, earnings per capita are the lowest of the top 25 countries of the Human Development Index.

Settled by Polynesian people around 1300 AD, Europeans discovered NZ in 1642. British colonisation occurred nearly two centuries later, making NZ a relatively new Western country. The current population is largely European (68%), with indigenous Māori (descendants of the original Polynesian settlers) 15%, Asians 9%, Pacific peoples 7%, and others.

4.2.1. Influence from the UK and Australia, including Trans-Tasman Harmonisation

Britain has influenced NZ since colonisation, for example through preparation of NZ's Pharmacy Act of 1880. Until the mid-20th century, Britain was NZ's most important trading partner and source of migrants, including chemists and druggists. NZ has looked more at the Asia-Pacific area as Britain joined the European Economic Community. However, NZ remains close to Britain, including in healthcare. NZ and Australia have always been close and have been attempting to harmonise medicines scheduling since the late 1990s with TTH in advance of a joint medicines regulatory agency for the two countries (see 2.3.2.2).

4.2.2. Health in NZ

NZ spend on health as a percentage of Gross Domestic Product (GDP), 10% in 2009, has increased considerably since 2000 (Table 4-1).
NZ socialised health in 1938, in a world first, subsidising GP consultations and medicines, and fully funding hospitals.[396] Thus, consumers consulted the GP rather than the pharmacy, and pharmacies then depended on doctors for business.[390]

Revolutionary economic reform in the 1980s quickly moved NZ from highly regulated to highly liberated (deregulated),[386, 387] and major health reform followed.[396] A fast-rising medicines bill motivated the 1993 formation of The Pharmaceutical Management Agency (Pharmac).[397] Resulting strict pricing measures, including tendering for sole supply of generic medicines, adversely affected the pharmaceutical industry. Subsequent health reforms have created a changeable health environment.[396] but pressure remains, with an ageing population, chronic conditions and a challenging economic environment.[398]

NZ has approximately 980 community pharmacies, mostly independently pharmacist-owned. Pharmacists are trained in a four-year university degree course followed by a one-year internship.[399] Pharmacy technicians are formally trained, but most pharmacy assistants are not.

Three non-prescription medicine schedules exist.[400] Pharmacist-only medicines can only be sold by a pharmacist in a pharmacy or hospital, the medicine cannot be accessed by the public, and the sale
is recorded. Pharmacy-only medicines can generally only be sold in pharmacies. General sales medicines can be sold anywhere.

4.2.3. The Medicines Classification Committee

The MCC advises the Minister of Health’s Delegate on medicine classifications, with the Delegate making final decisions. The MCC comprises six members: two persons nominated by the NZ Medical Association; two persons nominated by the Pharmaceutical Society of NZ; and two persons from the Ministry of Health, one of whom chairs the meetings. Medsafe, NZ’s regulatory authority for medicines, oversees the MCC.

Meeting agendas, reclassification applications and related Medsafe reports (if any) are published on the Medsafe website facilitating public consultation. Twice yearly the committee considers applications and submissions using set criteria and makes recommendations to the Minister of Health’s Delegate. Resulting minutes are published on Medsafe’s website.

4.3. Primary data sources

Data sources for the NZ research comprise: interviews with 15 key informants; MCC meeting papers including applications, agendas and minutes; other documents as required; and the researcher’s knowledge and experience.

Interviews comprised 10 key informants from NZ, and five people operating at a regional or global level with NZ insights. One additional NZ telephone interview with recording failure was excluded. NZ based participants came from three pharmacy organisations (n=3), two doctors’ organisations (n=2), a consumer organisation (n=1), industry (n=3), the regulator (n=1), and academia (n=1). One person represented two areas. Two participants (and I) had served on the MCC.

Omissions, occasional errors and missing documents (e.g. The Department Position Paper of 1989) for pre-2000 meetings affected the minutes’ accuracy. Therefore, I used the minutes to understand and describe 1990s reclassification, without providing a complete list of reclassifications.

4.4. Reclassifications in NZ

4.4.1. The early 1990s wave of reclassifications

In 1989, the Department of Health commissioned a Position Paper to review classifications of all medicines, including proposing some forward-thinking prescription to non-prescription reclassifications (Table 4.2). In a changing, deregulating environment, NZ embraced medicine

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13 Not found by the MCC secretariat when requested
14 The Department of Health later evolved into the Ministry of Health and then Medsafe became the medicines’ regulatory authority within the Ministry of Health
15 The position paper is no longer held by Medsafe
reclassification opportunities during the 1990s, and by 1993 was at the forefront of medicines reclassification internationally.[30, 403]

At a seminal meeting in 1990, the MCC considered these reclassifications and general policy. Members reviewed non-prescription medicine categories (the current three tier system), contemplated podiatrist prescribing; and considered a type of continuation prescribing system,[404] all representing advanced thinking for the time, but the MCC elected to retain the current systems.

**Table 4-2 Examples of down-scheduling recommendations, NZ 1990**

<table>
<thead>
<tr>
<th>Prescription pharmacist-only to</th>
<th>Prescription pharmacy-only to</th>
<th>Pharmacist-only pharmacy-only to</th>
<th>Pharmacy-only general sales to</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aciclovir (dermal)</td>
<td>Diclofenac (dermal)</td>
<td>Naproxen (dysmenorrhoea)</td>
<td>Terfenadine’</td>
</tr>
<tr>
<td>Antifungals (vaginal)</td>
<td>Indomethacin (dermal)</td>
<td>Mefenamic acid (dysmenorrhoea)</td>
<td>Pyrethrins</td>
</tr>
<tr>
<td>Hydrocortisone ≤1% (dermal)</td>
<td>Silver sulphadiazine (dermal)</td>
<td>Nicotine (transdermal patches)</td>
<td>Tolnaftate (dermal)</td>
</tr>
<tr>
<td>Hydrocortisone ≤1% + anaesthetic (rectal)</td>
<td>Nicotinic acid (unclassified to pharmacy-only)</td>
<td></td>
<td>Nicotine in chewing gum’</td>
</tr>
<tr>
<td>Hyoscine (transdermal)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miconazole (oral mucosa)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minoxidil (dermal)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mupirocin (dermal)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nystatin (oral mucosa)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sulfacetamide (ocular)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triamcinolone (buccal)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Source: Medicines Classification Committee minutes appendix, 7th meeting, 1990*

*Not gazetted, remained pharmacy-only[405, 406]*

Many proposed reclassifications in the Position Paper were enacted (Table 4-2). However the MCC declined to reclassify oral aciclovir, colestipol, mebeverine, pizotifen, and pirenzepine, and declined some pharmacy-only to general sales proposals, including ibuprofen.[404] Some medicines were up-scheduled (e.g. colchicine to prescription medicine), usually following Position Paper recommendations. Chloral hydrate, dicycloverine (dicyclomine), oral beta2 agonists and oxybutynin retained non-prescription status but up-scheduled later, generally under TTH.

Galvanised by the reclassification activity, pharmaceutical companies, the Pharmaceutical Society, the Pharmacy Guild and individuals suggested further reclassifications,[407, 408] resulting in ground-breaking reclassifications in 1991-1993 (Table 4-3). Some innovative reclassifications were rejected. The Pharmaceutical Society suggested chloramphenicol be reclassified,[406] but strong opposition from the Ophthalmological Society (whose advice was sought), and the NZ General Practitioners’ Association[405, 407, 409] led to a rejection. The decision seemed contentious as a pharmacist MCC member “... expressed a strong view that ... pharmacists were capable of making a diagnosis [in this area]...” and that she believed the arguments put forward were unsatisfactory. The chloramphenicol decision contrasts with the same committee’s decision to reclassify ocular sulfacetamide,[406] just
two years prior. The committee apparently considered the risk of reclassification higher with chloramphenicol, despite both medicines treating the same condition. There was no discussion about up-scheduling sulfacetamide given misdiagnosis concerns prevented chloramphenicol reclassifying.

Table 4-3 Examples of reclassification decisions (1991-1993), NZ

<table>
<thead>
<tr>
<th>Prescription to pharmacist-only reclassifications</th>
<th>Prescription to pharmacist-only rejections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciclopirox (nail lacquer)</td>
<td>Beclometasone (nasal)*</td>
</tr>
<tr>
<td>Cimetidine (initially declined, accepted 1993)</td>
<td>Chloramphenicol (ocular)</td>
</tr>
<tr>
<td>Clindamycin (dermal)</td>
<td>Hydrocortisone with natamycin and neomycin</td>
</tr>
<tr>
<td>Colestyramine</td>
<td>Inhaled beta-agonists (e.g. salbutamol)</td>
</tr>
<tr>
<td>Diclofenac (oral)</td>
<td>Midazolam</td>
</tr>
<tr>
<td>Famotidine (initially declined, accepted 1993)</td>
<td>Piroxicam (oral)</td>
</tr>
<tr>
<td>Ketoprofen (oral)</td>
<td>Polymixin and bacitracin +/- neomycin (dermal)</td>
</tr>
<tr>
<td>Metoclopramide with paracetamol (nausea in migraine)</td>
<td>Prochlorperazine (migraine)*</td>
</tr>
<tr>
<td>Mupirocin (dermal)</td>
<td>Trimethoprim</td>
</tr>
<tr>
<td>Quinine (for cramps)</td>
<td>Zopiclone</td>
</tr>
<tr>
<td>Ranitidine (initially declined, accepted 1993)</td>
<td></td>
</tr>
<tr>
<td>Sodium cromoglycate (nasal and ocular)</td>
<td></td>
</tr>
<tr>
<td>Tretinoin (dermal)</td>
<td></td>
</tr>
</tbody>
</table>

Source: Medicines Classification Committee meeting minutes
*Later down-scheduled [410, 411]

Notably, some reclassifications in the first wave (1990-1992) later reversed with new data suggesting teratogenicity (dermal tretinoin for acne reversed 1993),[403] and resistance (mupirocin, reversed 1999).[412] Several others reversed when reconsidered under TTH (4.4.2).

The early 1990s saw the process evolve, with the committee developing application requirements and reclassification criteria.[407] Simultaneously the Chair requested the committee use “... a more analytical manner in order to provide high quality recommendations of a uniform standard.”[407] Following industry complaints,[405, 406] sponsors’ opinions were considered; sponsor opposition contributed to trimethoprim[407] and nedocromil[410] rejections. Occasionally the committee down-scheduled despite company opposition, e.g. ranitidine.[403] By 1993 and 1994, Medsafe provided reports to assist MCC decisions,[403, 413] perhaps in light of these concerns. NZ was very advanced in considering the EHC in 1994, with politics involved (Panel 4-1). Medsafe-driven reclassifications were unusual from the mid-1990s. All MCC members changed in 1997,[414] followed by fewer innovative reclassifications.
Chapter 4

Panel 4-1 Emergency Hormonal Contraceptive reclassification in NZ

January 1994: the Ministry of Health publicly stated that the MCC would consider reclassifying oral contraceptives.[415]

May 1994 MCC meeting: the Family Planning Association supported the EHC reclassifying but would not pursue the matter. EHC and oral contraceptives would be discussed at further MCC meetings.

Nov 1994 MCC meeting: The Ministry report on Yuzpe EHC was incomplete, but discussed. The sponsor threatened withdrawing the product from NZ if reclassified. Further work and consultation was required. The oral contraceptive was also considered, with members supporting the intent to widen access based on a Ministry of Health report. Public consultation was planned.

Nov 1995 MCC meeting: The public consultation revealed strong support for Yuzpe EHC widened access. No further safety issues had arisen. The committee were reminded of the Minister of Health’s interest in improving access to contraception and reducing unwanted pregnancies. The MCC agreed the Yuzpe EHC should become available through pharmacists.

Apr 1996 MCC meeting: Considerable response to the EHC decision from pro-life organisations, individuals and politicians was reported. Ministry work still incomplete. No further mention of widening oral contraceptive access.

May 1997 MCC meeting: All six MCC members changed, and the EHC and oral contraceptives were dropped with no minute recorded.

May 2001 MCC meeting: EHC was considered again following a Medsafe proposal. The EHC had since changed to levonorgestrel alone and been reclassified elsewhere. The MCC agreed to make the EHC available through accredited pharmacy pharmacists and nurses.

Source: Medicines Classification Committee meeting minutes, and as referenced

EHC = Emergency hormonal contraceptive; MCC = Medicines Classification Committee

4.4.2. Reclassifications in NZ 2000-2012

Innovative reclassifications were quiet in 2000-2003 (Figure 4-1, Table 4-5, Figure 4-2).

**Figure 4-1 Innovative prescription to non-prescription reclassifications in NZ 2000-2012**

![Graph showing number of reclassifications by year from 2000 to 2012.]

Source: Medicines Classification Committee minutes

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16 Required special training
During 2000-2003, up-scheduling occurred through TTH (for example oxybutynin,[416] colestyramine, dicycloverine, insulin and clindamycin[417]), and the Minister’s Delegate overrode several MCC recommendations (see 4.7.2). The MCC members were not proactive in seeking applications owing to high TTH workload,[418] and sponsor applications fell in 2002-2003 (Table 4-5). These factors suggest the committee may have been conservative at this time, possibly reducing sponsor interest in reclassification. TTH workload or waiting for TTH to settle down may have prevented industry from driving reclassifications.

**Table 4-4 All prescription to non-prescription reclassifications 2000-2012 in NZ**

<table>
<thead>
<tr>
<th>Year of MCC decision</th>
<th>Innovative reclassification</th>
<th>Reclassification but not innovative</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>Desloratadine</td>
<td>Oxiconazole (vaginal)</td>
</tr>
<tr>
<td>2001</td>
<td>Levonorgestrel (EHC)</td>
<td>Triamcinolone (nasal)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Levocetirizine</td>
</tr>
<tr>
<td>2002</td>
<td>Beclometasone and fluticasone nasal extended indication</td>
<td></td>
</tr>
<tr>
<td>2003</td>
<td>Sodium picosulphate</td>
<td></td>
</tr>
<tr>
<td>2004</td>
<td>Fluconazole</td>
<td>Ketotifen (ocular)</td>
</tr>
<tr>
<td></td>
<td>Orlistat</td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>Aclometasone (dermal)*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Clobetasone (dermal)*</td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td>Sumatriptan</td>
<td>Paracetamol long-acting</td>
</tr>
<tr>
<td></td>
<td>Oseltamivir</td>
<td>Ibuprofen 400 mg</td>
</tr>
<tr>
<td>2007</td>
<td>Azelastine (ocular)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Butaconazole (vaginal)</td>
<td></td>
</tr>
<tr>
<td>2008</td>
<td>Omeprazole</td>
<td></td>
</tr>
<tr>
<td>2009</td>
<td>Famiclovir</td>
<td>Pantoprazole</td>
</tr>
<tr>
<td></td>
<td>Chloramphenicol (ocular)</td>
<td>Guaiphenesin slow-release</td>
</tr>
<tr>
<td></td>
<td>Zolmitriptan (nasal spray)</td>
<td>Lansoprazole</td>
</tr>
<tr>
<td>2010</td>
<td>Calcipotriol (dermal)</td>
<td>Rizatriptan wafers</td>
</tr>
<tr>
<td>2011</td>
<td>Vibrio cholera and enterotoxigenic Escherichia coli vaccine (oral)</td>
<td></td>
</tr>
<tr>
<td>2012</td>
<td>Trimethoprim (‘accredited pharmacists’)</td>
<td>Influenza vaccination (‘accredited’ pharmacists)</td>
</tr>
</tbody>
</table>

* Considered simultaneously, effectively one innovative reclassification (same class)

Source: Medicines Classification Committee meeting minutes

Innovative reclassifications rebounded in 2004 and 2005 (Table 4-5, Figure 4-1), including previously rejected moderate potency corticosteroids. The increased reclassifications from 2004, increased approval rate (Figure 4-2) and the MCC proactively suggesting possible candidates,[379, 419] suggests the MCC became more progressive again. The 2004 change of half of the MCC members (two doctors and a pharmacist),[420, 421] and/or Australia’s reclassification momentum (see 5.4) may
have contributed to this progressiveness. Reclassification applications also increased (Figure 4-2, Table 4-5), possibly from increased industry confidence in the MCC, TTH encouraging NZ applications, or just a natural cycle with industry; interviews support all notions. Committee suggestions of potential candidates may have prompted applications (as a participant confirmed).

Table 4-5 Innovative reclassifications and attempted reclassifications in NZ 2000-2012

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Meetings (number)</th>
<th>Application source</th>
<th>Decision and date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alclometasone and clobetasone</td>
<td>3</td>
<td>Sponsor then TTH</td>
<td>Rejected 2000, Accepted 2005</td>
</tr>
<tr>
<td>Levonorgestrel (EHC)</td>
<td>1</td>
<td>Medsafe application</td>
<td>Accepted 2001</td>
</tr>
<tr>
<td>Inhaled salbutamol and terbutaline</td>
<td>2</td>
<td>TTH</td>
<td>Rejected 2001, sought more information 2005, nothing forthcoming</td>
</tr>
<tr>
<td>Omeprazole</td>
<td>5</td>
<td>Two sponsors</td>
<td>Reclassified in 2008</td>
</tr>
<tr>
<td>Fluocortolone/cinchocaine (rectal)</td>
<td>1</td>
<td>Sponsor</td>
<td>Rejected 2001</td>
</tr>
<tr>
<td>Fluconazole</td>
<td>2</td>
<td>Sponsor then TTH</td>
<td>Deferred then accepted 2004</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>2</td>
<td>Third party then sponsor</td>
<td>Rejected 2004, sought more information 2005, nothing forthcoming</td>
</tr>
<tr>
<td>Orlistat</td>
<td>2</td>
<td>Sponsor then TTH</td>
<td>Accepted 2004</td>
</tr>
<tr>
<td>Oseltamivir</td>
<td>2</td>
<td>Sponsor</td>
<td>Accepted 2006</td>
</tr>
<tr>
<td>Domperidone</td>
<td>2</td>
<td>Sponsor</td>
<td>Sought information 2006, not provided</td>
</tr>
<tr>
<td>Tranexamic acid</td>
<td>1</td>
<td>TTH</td>
<td>No sponsor interest, no consumer labelling, rejected 2006</td>
</tr>
<tr>
<td>Sumatriptan</td>
<td>1</td>
<td>Sponsor</td>
<td>Accepted 2006</td>
</tr>
<tr>
<td>Ocular fusidic acid</td>
<td>1</td>
<td>Sponsor</td>
<td>Resistance concerns, rejected 2007</td>
</tr>
<tr>
<td>Ocular chloramphenicol</td>
<td>4</td>
<td>MCC</td>
<td>Accepted 2009</td>
</tr>
<tr>
<td>Nasal zolmitriptan</td>
<td>1</td>
<td>Sponsor</td>
<td>Accepted 2009</td>
</tr>
<tr>
<td>Oral famciclovir</td>
<td>2</td>
<td>Sponsor</td>
<td>Accepted 2009</td>
</tr>
<tr>
<td>Topical calcipotriol</td>
<td>1</td>
<td>Third party (PBL)</td>
<td>Accepted 2010</td>
</tr>
<tr>
<td>Vibrio cholera and enterotoxigenic Escherichia coli oral vaccine</td>
<td>1</td>
<td>Third party (PBL)</td>
<td>Accepted 2011</td>
</tr>
<tr>
<td>Influenza vaccination</td>
<td>1</td>
<td>Third party (PBL)</td>
<td>Accepted 2012</td>
</tr>
<tr>
<td>Melatonin</td>
<td>2</td>
<td>Sponsor</td>
<td>Rejected 2012</td>
</tr>
<tr>
<td>Trimethoprim</td>
<td>1</td>
<td>Third party (PBL)</td>
<td>Accepted 2012</td>
</tr>
<tr>
<td>Colecalciferol 1.25 mg (monthly)</td>
<td>1</td>
<td>Committee</td>
<td>Unclear risk-benefit profile, rejected 2012</td>
</tr>
<tr>
<td>Diphtheria, tetanus and pertussis vaccine</td>
<td>1</td>
<td>Third party (PBL)</td>
<td>Sought further information 2012</td>
</tr>
</tbody>
</table>

Source: Medicines Classification Committee meeting minutes

TTH = Trans-Tasman Harmonisation; PBL = Pharmacybrands Ltd

While progressive from 2004, the MCC still rejected some reclassifications, such as fusidic acid (Table 4-5; Figure 4-2). Sometimes sponsors did not resolve MCC queries, e.g. simvastatin,
salbutamol and domperidone preventing reclassifications progressing. Despite many positive decisions, sponsor applications declined in 2008-2011.

Table 4-5 shows the changing source of reclassifications over time. TTH was relatively unimportant in ‘innovative’ reclassifications. Pharmaceutical companies drove about half of the considerations, the committee drove three considerations, and Pharmacybrands (a pharmacy retail group) drove most considerations from 2010. From 2000-2012 four reclassifications were first-in-world innovative reclassifications: oseltamivir; famciclovir; calcipotriol and trimethoprim.

Figure 4-2 Innovative reclassification considerations and outcomes in NZ 2000-2011*

From 2008 to 2011 no rejections occurred, but the following year (with the same committee as 2010 and 2011) three innovative reclassifications were not approved, suggesting that the 100% approval 2008-2011 was an anomaly. This committee approved trimethoprim in 2012, so these non-approvals do not herald a conservative shift. One 2012 rejection was the committee’s own candidate, colecalciferol, following a negative Medsafe report.

4.5. Participants' considerations of NZ's position in reclassification

NZ participants interviewed in 2009 and 2010, even those particularly involved in reclassification, seemed unaware that NZ was nearing the UK in reclassification progressiveness (see 11.4.1).

“Ten years ago, five years ago, I would say [NZ] were leading it. We’re probably more followers than leaders now.” Regulator [interview 2009]

Most interviews occurred after the first-in-world oseltamivir and famciclovir reclassifications, but before calcipotriol and trimethoprim. Possibly NZ was viewed as a follower because it followed the UK on sumatriptan and chloramphenicol, and Australia on orlistat and fluconazole, and lagged the US, UK
and Australia on omeprazole. Furthermore, two high-profile UK reclassifications (simvastatin and azithromycin) had not occurred in NZ.

4.6. Overriding themes from interviews

Seven main themes around reclassification emerged from the interviews. The most compelling themes were NZ being a small size and having a “can do” attitude. Further important themes included specific individuals’ influence, change, trust, financial motivation, and TTH. Inter-relationships between the themes commonly occurred.

These themes are discussed as an overview below (Sections 4.6.1-4.6.8), before further detail is provided broken down by the different parties and factors involved in the process (4.7.2-4.7.4) and demonstrating the interconnectivity of the different themes. Finally, participants’ suggestions for the future of reclassification in NZ are provided (Section 4.8).

4.6.1. Small size

“Population, volumes, we’re just too tiny here, too small.” Industry participant

Many facets of reclassification in NZ are small: the population; sales; pharmaceutical industry presence; pharmacy organisations; political influence; the regulator; and budgets and resources. Contrarily, while the small market should limit companies’ interest in reclassification, the smallness apparently contributes significantly to NZ’s current progressiveness. Being small and remote, NZ has developed a ‘can-do’ attitude, described as the next theme (4.6.2).

“…I would think NZ would have to be regarded as a general leader in this area, and that might be because of the relatively small, homogeneous nature of the population… We can do something quicker perhaps than some of the bigger countries.” Academic participant

<table>
<thead>
<tr>
<th>Barriers</th>
<th>Enablers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small volumes – low dollars, and NZ specific packaging difficult</td>
<td>Small (low) cost of reclassification</td>
</tr>
<tr>
<td>Small local offices for companies – lack resource</td>
<td>Small market is useful test market</td>
</tr>
<tr>
<td>Some pharmaceutical companies operate off-shore (unfamiliar or disengaged with NZ opportunities; unfamiliar with the NZ system)</td>
<td>Low level of politics</td>
</tr>
<tr>
<td>Small pharmacy organisations – limited resource for submissions or applications</td>
<td>Small regulator – pragmatic, flexible and open-minded (but individual-dependent)</td>
</tr>
<tr>
<td>Small, lean regulator – limited resource to drive reclassifications</td>
<td>Small homogeneous committee - can be flexible and open-minded (but individual-dependent)</td>
</tr>
</tbody>
</table>
The small size or absence of pharmaceutical companies hinders reclassification (see 4.7.4). However, a company may drive reclassification in NZ to help the Australian or global strategy with relatively low cost or difficulty compared with larger markets.

“…if it’s something that you want to do you can do it, see what happens in NZ, if it tanks it doesn’t matter, it’s nothing, we haven’t lost anything. If it goes great we’ve got experience then to provide to the Europeans, the FDA..... So I think being small actually helps...” Industry participant

Examples of early reclassification applications in NZ include oseltamivir, famciclovir and GSK attempting simvastatin shortly after the UK reclassification.

4.6.2. Kiwi ‘can do’ attitude

Several participants referred to NZ (‘kiwi’) culture, or a ‘can do’ type attitude. Being remote, New Zealanders have long needed to improvise when a need arises,[422] requiring self-sufficiency.

“…there’s still that sort of kiwi go get them type attitude that comes through. I think however, against that, we’re also quite careful within our decision making; it’s not reckless.” Industry participant

The process and minutes support a ‘can do’ mentality. Anybody can apply for a reclassification, and various individuals and organisations have done so over the years (Table 4-5). The MCC proactively suggested reclassification candidates[379, 423] and drove the 2009 chloramphenicol reclassification, and the regulator has developed applications (e.g. EHC Panel 4-1). Different mechanisms have enabled reclassifications, such as the mandatory training approach with the EHC,[416] and trimethoprim[173] and exemption to prescription under certain criteria, for calcipotriol and oseltamivir.[80] These mechanisms suggest committee and regulator flexibility. The ‘can do’ attitude and openness was not always present, with possible committee conservatism in 2000-2003 (see 4.4.2 and 4.7.2), and on some medicines (e.g. omeprazole took five meetings).

Applicants have innovated, in attempting first-in-world reclassifications, such as oseltamivir, and ocular fucidic acid, and unusual third-party reclassifications (e.g. calcipotriol).

The flexibility in approach and openness to ideas sometimes made NZ attractive to companies.

“…often companies will try NZ first and try to pull it through in NZ and at the same time go in Australia and time your application post-NZ’s decision, ok….... And try and pull it through that way.” Australian industry participant

4.6.3. Individuals influencing reclassification

The interviews revealed several individuals who influenced reclassification. The most mentioned individual (from both Australian and NZ interviews) was Dr Stewart Jessamine, the Chair of the MCC
since 1998,[424] and Group Manager of Medsafe. Participants considered Dr Jessamine enabled reclassification in NZ, and in Australia when he was an NDPSC member17.

“...I think Stewart is pragmatic... He'll listen to your argument ...he's not entrenched in 'oh well we've made that decision and that's it'.” Industry participant

Dr Jessamine’s reclassification influence started in 1993 when he joined Medsafe as a Medical Advisor, preparing reclassification applications and reports. He joined the MCC in 1997,[424] during a seemingly conservative period. This may suggest that an individual’s influence on reclassification may partly depend on other individuals involved, although presumably he was involved in the decisions to override MCC recommendations. Previous heads of Medsafe were also considered open-minded, probably also enabling reclassification, particularly during the active 1990-1993 period (see 4.4.1). Several participants (and I) considered the mix of individuals on the MCC influenced reclassifications.

Several participants referred to my role on the committee in a positive way, possibly because I was interviewing them. After finishing on the committee, I suggested Pharmacybrands drive reclassifications and have subsequently worked with Pharmacybrands on this.

4.6.4. Trust

Many participants discussed trust. The committee usually trusted pharmacy to generally do the right thing, and trusted the consumer to take a reasonable approach. The oseltamivir reclassification provides an exemplar of trust in pharmacy (see 4.7.5).

“...the question that the committee time and time again comes up with is how much do we trust pharmacy to do the right thing at the right time in the right situation? And what I would like to think in the last four or five years is that question is more likely answered in the positive than the negative.” Regulator participant (2009)

Trust was not blind faith, and varied between members (e.g. doctor members were concerned about chloramphenicol reclassifying) and over time (see 4.7.5).[425] The MCC’s interest in training material and consultation tools indicated the committee did not trust pharmacist to update themselves or ask consumers the right questions without it, and did not trust the applicant to prepare adequate materials. Apparently the committee trusted pharmacists to behave correctly after the materials and/or training were provided.

Participants (including industry) seemed to trust Medsafe and the MCC. However, one pharmacy participant believed Medsafe was very risk-averse, probably based on a recent spate of recalls. One participant speculated that the trust environment may relate to lack of liability with accident law in NZ, but others did not raise this.

17 Meeting attendance is not in the NDPSC records of reasons, but this membership was until at least 2007.
4.6.5. Financial motivators

Many financial motivators affect reclassification in NZ (Table 4-7), but a government desire to save funds did not arise. Given pharmaceutical companies typically drive reclassification, they need it to be financially viable, and largely it is not (see 4.7.4). Funding barriers, low prescription reimbursement prices and small market size limits the companies’ presence and interest in NZ (see 4.7.4). The small population size, and probably the low prescription copayment (4.7.6), lessen potential earnings post-reclassification, and can inhibit reclassification.

Table 4-7 Summary of key financial incentives and impediments to reclassification in NZ from interviews

<table>
<thead>
<tr>
<th>Enablers</th>
<th>Impediments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacy dispensary funding squeeze increases interest in retail and reclassification</td>
<td>Low volume reduces viability</td>
</tr>
<tr>
<td>Move to bulk-funding doctors may make them less resistant to reclassification</td>
<td>Low prescription dollars reduces company engagement</td>
</tr>
<tr>
<td>No application fee</td>
<td>Low cost prescriptions incentivise consumers to get medicines prescribed rather than self-medicating</td>
</tr>
<tr>
<td>Usually no need for special studies</td>
<td>Consumers expect to pay little for medicines</td>
</tr>
<tr>
<td>Movement from pharmacy-only to general sales may make pharmacy want more reclassifications from prescription to replace lost sales</td>
<td>Immediate generic entry (if off patent)</td>
</tr>
<tr>
<td></td>
<td>Pharmacy concentrating on the dispensary</td>
</tr>
<tr>
<td></td>
<td>Some patch protection (doctors and pharmacy)</td>
</tr>
<tr>
<td></td>
<td>Medsafe insufficient resource to continue to drive reclassifications</td>
</tr>
<tr>
<td></td>
<td>Pharmaceutical companies concentrating on the larger prescription market</td>
</tr>
</tbody>
</table>

"it’s really hard to see how a company can actually afford to make a commercially viable switched, OTC proposition, [because] effectively what you’re competing against is a $3 [US$2.55] cost to the patient…” Australian industry participant

However, the cost of reclassification in NZ is minimal compared with other countries, enabling non-sponsors to apply, for example Pharmacybrands.

4.6.6. Global influences

The MCC minutes reflected international influences on the MCC. The Danish H₂-antagonist reclassifications and subsequent research stimulated the MCC in 1992 to rethink their rejection of H₂ antagonists.[407] Reclassification applications need to include scheduling elsewhere, particularly in Australia, UK, USA and Canada.[401] From the mid-1990s, Australia became increasingly influential as TTH was considered (see 6.5.1). The US appears little in the minutes or interviews, although one participant noted: “the fact that the States [reclassified omeprazole] was a big signal that there wasn’t a lot of liability in it for us.”
The UK often influenced NZ reclassification. The MCC often attempted to align indications, pack sizes and/or dosing with that in the UK. The UK sumatriptan\citep{426} and chloramphenicol reclassifications reassured the MCC. Committee members’ suggestions for reclassification candidates were informed partly from UK reclassifications\footnote{Based on my committee experience}.

Global effects on industry encouraged and limited reclassification (see 4.7.4). Reclassification was enabled when it fitted the global strategy and reclassification material had been developed. Pharmacy organisations were aware of reclassifications in the UK and Australia.

**4.6.7. Change**

The concept of change frequently arose in interviews from different perspectives. Three participants used the term revolution in: empowering patients, pharmacy and patient care; having health professionals collaborating; and in funding different patient care models (such as minor ailments).

Change was noted to be easier in NZ than elsewhere.

> “We've got a political structure in NZ that does allow change to be affected very quickly, sometimes too quickly…” Pharmacy participant

The minutes revealed that the committee gradually evolved, changing processes (see 4.4.1) and, according to a participant, becoming more evidence-based. The committee encouraged change, proactively suggesting reclassification candidates, as did the regulator by preparing reclassification applications (particularly in the 1990s) and being available for industry discussions.

> “I think the Chair and the Chair's willingness to engage with industry and say come on let’s put in a submission, advocate for change, you know it’s risky but it’s required in the NZ environment because otherwise we’d have nothing to look at, basically.” Regulator participant

In 2011 and 2012, the MCC trialled applicants attending part of the committee meeting to improve clarity and transparency.\citep{423} In late 2012, the MCC started to review reclassification considerations including looking to the UK and Australia.\citep{427} This suggests the committee was continuing to evolve.

Change in pharmacy was commonly discussed, including up-skilling and increasing professionalism of pharmacy (see Section 4.8).

> “…I suspect you were getting the first generation of University trained degree pharmacists really coming into their own round about [the mid-1990s], and therefore there was a desire inside the profession to be more professional and basically that pharmacy was more than just counting pills. And that lent itself to that whole atmosphere of there being momentum for change…” Regulator participant
However, two participants noted some pharmacist reluctance to change, one attributing this to the security from dispensing income. Three participants considered a difficulty arose from some doctors being reluctant to accept new initiatives such as collaborative care. Changes could cause difficulties for pharmaceutical companies, particularly when driven by others.

“Changing the datasheet is a huge deal for a global manufacturer, to change that safety information has repercussions globally… it’s a safety issue.” Industry participant

“To have a change forced on you for your own product, a company would say ‘well it’s our product, why should we be forced to change something that we believe is right and we want it to stay this way.’” Industry participant

4.6.8. Australia and Trans-Tasman harmonisation

Australia strongly influenced reclassification through TTH and industry interest in reclassification. TTH effects raised considerations that would probably not otherwise have occurred, including up-scheduling during the late 1990s and early 2000s (4.4.1, 4.4.2). Australian decisions sometimes influenced MCC decisions, but these influences were not especially strong or important for innovative prescription to non-prescription reclassifications and did not arise in interviews.

Some companies submitted applications in NZ around the same time as Australia to help the Australian reclassification. However, because the NZ market demands small volumes, sometimes product availability will depend on availability in the Australian market to provide sufficient volumes. TTH is dealt with in the Australasian (meso-level) chapter (see 6.5.1).

4.6.9. Summary of overriding themes

Reclassification in NZ has clearly been highly influenced by the small market and global factors, many of which are financially based. The trusting, ‘can do’ environment and proactive, pragmatic individuals involved have contributed towards the progressiveness of NZ. It is interesting to see government interest is not in NZ’s overriding themes given it was highlighted in the UK’s progressiveness (see 2.3.2.10). See the macro-level chapter (Chapter 11) for further discussion on differences between countries.

Factors contributing to the seven inter-related overriding themes outlined above are now explored in more detail by stakeholder or factor

4.7. Findings by stakeholder or factor

4.7.1. Government

The NZ government appears to neither interfere in, nor promote reclassification. Politics received scant mention from interviews. One participant reported a pro-reclassification slant from two politicians in the 1990s, as confirmed in the MCC minutes (see 4.4.1).[403] Occasionally decisions
have been in line with government policy (NRT and EHC), and governmental policy pressure seemed likely in the NRT down-scheduling to general sales (see Panel 4-1, Panel 4-2).[428]

4.7.2. Regulator, committee and process

Medsafe can significantly influence reclassification in NZ. A third of the committee members (including the Chair) are Medsafe employees. Medsafe has driven down-scheduling and up-scheduling, provided reports on some reclassifications, and sometimes successfully recommended overriding MCC recommendations. Furthermore, Medsafe actions the reclassification decisions.

The 1989 regulator-commissioned review of classifications of most pharmaceuticals transformed reclassification in NZ (Section 4.4) and stimulated applications (see 4.4.1). This slowed from the late 1990s for resource reasons, but Medsafe drove the EHC reclassification in 2001,[416] and prepared a report for a proposed colecalciferol reclassification in 2011 following an MCC request.[173, 429]

Many participants considered the regulator enabled reclassification, being balanced or pragmatic (see 4.6.3), and with a flexible ‘can do’ attitude (4.6.2).

“Medsafe is small. [They] don’t have 25 people to look at a dossier and go ‘oh yeah, p17 says this we can’t do that’. They take a much more big picture view … They aren’t so fixed: ‘this is what I believe and I don’t care about what you say’.” Industry participant

An international participant observed that reclassification was enabled by the lack of requirement for special studies. High transparency in NZ enables reclassifications because the process is clear. However, industry noted competitors with generics and ‘me-too’ medicines benefited from transparency, preventing companies driving some reclassifications (see 4.7.4). The public availability of the application for reclassification before the MCC meeting caused industry concern.

“…you didn’t put the same submission into NZ as you did into Australia, because NZ’s got published…” Australian industry participant

This transparency facilitates ‘me-too’ applications (Table 4-4). Omeprazole took five meetings over seven years to reclassify,[426, 430-433] but pantoprazole,[425] and lansoprazole[434] quickly followed. Sumatriptan was reclassified in 2006,[426] using an extensively tested pharmacy tool.[309] With sumatriptan rejected in Australia (see Panel 5-2), GlaxoSmithKline (GSK) did not launch a non-prescription product in NZ, but a generic sumatriptan launched using a similar migraine questionnaire. Zolmitriptan reclassified in 2009[425] and rizatriptan in 2010.[435] The zolmitriptan application referred to the sumatriptan reclassification, the similar safety profiles, and that it would provide a questionnaire based on the sumatriptan one.[436]

The applicant receives the MCC minutes one day before publication, allowing generic competitors to launch even before the applicant.
“… the investment in time and money to then find someone else comes along and rides on your coat-tails is not really acceptable.” Industry participant

A couple of participants considered including health professionals in current practice was advantageous. However, the NZ Medical Association had difficulty finding nominees for this committee. I’d speculate low pay and low interest to doctors affected this. The Pharmaceutical Society had no difficulty finding committee members with post-graduate qualifications who were usually familiar and engaged with the process, presumably through greater pharmacist-interest.

“…you had to get the right GPs in the committee to make this happen, they had to be open-minded enough to say that there are lots of different ways of treating patients, and that doctors don’t have to be involved in every consultation…” Regulator participant

The small committee, the participant-described “lottery” involved in finding members, and the means of finding members are dictated by legislation. Only one participant expressed concern about the Chair representing Medsafe, and that was a representative of the regulator.

“…the MCC’s an accident of history, that’s how the legislation enacted it. It should have consumers on it and it doesn’t. It probably, it should have an independent chair that’s not a Ministry of Health employee, as well…” Regulator participant

With pharmacists and doctors making up the committee, patch protection could potentially arise which could affect decision making. Patch protection was mentioned in passing rather than as a strong effect in interviews. However, it came through overrides of MCC reclassification recommendations by the Minister’s delegate. Such overriding occurred or was threatened during 1999-2003, twice with NRT (Panel 4-2).

Panel 4-2 Case study: nicotine replacement therapy decision override

In 1991, the MCC suggested making NRT available through smoking cessation clinics, but the NZ Psychological Society were unsupportive, and the idea was abandoned.[403] In contrast, eight years later, the MCC did not support a Medsafe proposal to allow nicotine products to be available from smoking cessation clinics run by registered health professionals.[428] Minutes reported that “some members felt strongly that pharmacists should be involved in these programmes”. Subsequently, the Minister’s Delegate overrode this decision.

The following MCC meeting considered the reclassification of nicotine gum and patches to general sales. The committee was reminded to use the reclassification criteria, and warned that it could be overruled should it recommend against down-scheduling. “In the light of the current political trend and the nature of the bodies requesting reclassification…. Medsafe had reviewed the safety data and supported wider access,… [and] would be likely to submit parallel advice to the Minister once again should the Committee decide to recommend against wider access.”[418] The Cancer Society, Health Funding Authority and Smokefree Coalition had supported reclassification, but the recommendation from the MCC to reclassify these medicines required the Chair’s casting vote, showing some members disagreed.

Source: Medicines Classification Committee minutes.

MCC = Medicines Classification Committee; NRT = nicotine replacement therapy
In 2000 the minutes reported:

“One member queried the value of the Committee if its recommendations were able to be overridden. The Chairman said that this had happened only on two previous occasions one of which related to smoking cessation products. He said that it was up to the Committee to produce well-documented evidence. The advice should be based on key areas of safety rather than on the like or dislike of a proposal. The role of the Ministry was also to provide advice to the Minister. If Medsafe were able to make a stronger case, the Minister or his or her delegate would be likely to accept the more convincing recommendation.”

The Delegate’s last major override concerned the MCC recommendation against down-scheduling ibuprofen to general sales in 2003. The meeting minutes and ibuprofen papers suggest a conservative, patch-protective committee recommended against the reclassification, but without providing sufficient evidence for this decision. The effect of politics (NRT), and trans-Tasman and global influence (for ibuprofen) were evident in the overrides. An alternative possibility is that the regulator was heavy-handed, but given the ibuprofen reclassification followed the UK, US and Australia, this seems unlikely. For ibuprofen (2003), mystery shopping was cited by Medsafe against the MCC claim that access to professional advice is essential. Commissioned advice on ibuprofen by Dr GR Boyd, Public Health Medicine Specialist stated:

“The MCC came to a decision not to recommend general-sales status for ibuprofen with very little supporting evidence. The reasons given in the committee’s minutes do not represent a clear safety risk assessment and are, in part, outside the scope of the Medicines Act 1981....”

He suggested overriding the decision, or returning the matter to the MCC for reconsideration, noting however, that although three external members were changing, “they will still have been selected from amongst nominees from two professional organizations whose members have a vested interest in maintaining the status quo.”

While providing an “independent review”, Dr Boyd had been a long-standing employee of the Ministry of Health, and had previously chaired the MCC. His report was short, without references, and referred to Australian newspaper clippings presenting arguments for and against the change. While the decision for ibuprofen to down-schedule is not criticised, it seems surprising that an independent report was not more evidence-based (and more independent).

This suggestion of patch protection and lack of evidence appeared to be largely historical given that patch protection did not arise strongly in interviews, nor had major overrides occurred in recent years. I considered MCC members could sometimes be more consistently evidence-based. However, one long-time MCC member noted improvement:

“...the committee’s become more professional, more evidence-based, and... they’re moving into less sort of opinion of about how they see the medicine and more about the assessment, the true risks and benefits...” Regulator participant
Many other participants perceived the MCC to be generally evidence-based, although one industry participant considered two decisions “strange”. One participant reported that a medical specialist who was reluctantly persuaded onto the MCC was surprised at the importance, intellectual stimulation, rigour and evidence-base of the considerations. However, several people (and I) considered the decision quality depended on individuals (see 4.6.3).

“NZ seems to make really logical decisions and… I think it’s the make-up of the committee, you’ve had Stewart on there a very long time, you’ve had various other members of the committee, and yourself, very knowledgeable and think about how it’s going to affect the consumer...” Australian industry participant

The MCC was proactive. The committee suggested potential candidates for reclassification,[379, 437] were open to alternate mechanisms for reclassification, (exemption to prescription-supply), and drove the chloramphenicol reclassification. The MCC often suggested points to address for an application to be successful. Absolute rejections were rare.

Committee processes and considerations have evolved (see 4.4.1, 4.6.7). Recent initiatives (e.g. allowing applicants to observe meeting discussion) may enable reclassification.

Overseas reclassifications (particularly in the UK) frequently influenced classification considerations, e.g. omeprazole, sumatriptan, and simvastatin.

“Most members were now much happier about the efficacy of the 10 milligram dose [for simvastatin]. This was based on both better data than that contained in the last submission and on the UK confidence in the potency of the 10 milligram dose.... One of the members pointed out that the training program used in UK was extremely thorough and outlined the program to the Committee.” MCC minutes [379]

The MCC drove the chloramphenicol reclassification in the absence of sponsor interest. In doing this, they relied on information from the UK to assist the decision.

However, reclassification elsewhere did not guarantee approval or a smooth path in NZ. In 2012, the MCC rejected melatonin reclassification citing concerns about safety and self-treatment of insomnia despite melatonin being a supplement in Canada and the US.[427] Omeprazole followed a torturous route to reclassification. The sponsor contributed to the delay, attempting pharmacy-only (rather than the usual first step of pharmacist-only) in 2006, and attempting to reclassify higher strengths, and different indications to other countries.[426] Committee variation also apparently contributed, with reclassification not approved at one meeting[321] after the sponsor apparently met requirements outlined by the committee previously.[426]

Despite being pharmacy-only in the UK (but not Australia or the US), domperidone was not approved by the MCC in 2005 or 2006.[379, 438] The committee was unconvinced of domperidone’s benefits,[438] and the company did not reapply. This consideration occurred in June 2006 at a double
meeting that unusually started in the early afternoon\textsuperscript{19}, with two new members, and the Chair of the NDPSC attending (a gastroenterologist).\textsuperscript{[426, 438]} The meeting included an unusually high number of innovative reclassification considerations (oseltamivir, omeprazole, domperidone, sumatriptan and tranexamic acid), and other important considerations. Half of the agenda items were approved, with omeprazole also declined. I suspect the work volume in a compressed time, and meeting attendees may have influenced the outcome.

The MCC uses an old 1990 definition of suitability for non-prescription sale which requires that the medicine treats self-diagnosable self-limiting minor ailments. However, although referred to in 2012,\textsuperscript{[173]} the MCC is not fixed to this definition given the reclassifications of calcipotriol (for a chronic condition diagnosed by a doctor),\textsuperscript{[435]} influenza vaccination,\textsuperscript{[173]} and the willingness to consider simvastatin (a preventative treatment).\textsuperscript{[379]}

"… you can take a medicine, …[and] an indication and you can say 'is there a subset of the population in whom the use of this is really, really safe?' and if the answer's yes then … you can think about reclassifying it…" Regulator participant

Important local history was relevant for considerations of inhaled salbutamol and terbutaline under TTH. Overuse of a related medicine (fenoterol) was associated with down-regulation of receptors and death in NZ in the 1990s,\textsuperscript{[439]} which contributed to the MCC reluctance to reclassify these asthma relievers. Other local factors were also important, e.g. overuse of non-prescription sumatriptan was considered unlikely given the expected consumer cost (versus the low prescription charges).\textsuperscript{[426]}

4.7.3. Schedules and exemption to schedules

From my MCC membership experience, and from participant comments, one of NZ’s stronger enablers is the multiple tiered scheduling, particularly the pharmacist-only category. Participants from pharmacy, academia, industry and the regulator considered the scheduling enabled positive committee decisions, provided safety benefits for consumers, and professional reward for pharmacists. However, various participants expressed concern that pharmacists and pharmacy did not always meet required standards in supplying medicines.

Several participants (including a medical participant, and an industry participant) were concerned about medicines in supermarkets given a lack of advice and lack of ability for some consumers. In contrast, one participant considered supermarket availability a natural course:

"…the trickle down model says you start off as prescription medicines and then you gain experience, you reassess it, if it fits your criteria you let it come into pharmacy. But the corollary of trickle down is that eventually it trickles out of pharmacy and into supermarket…" Regulator participant

\textsuperscript{19} This meeting uniquely combined the 34\textsuperscript{th} and 35\textsuperscript{th} MCC meetings, as the 34\textsuperscript{th} had not been able to be scheduled six months prior. Single meetings usually ran from around 9.30am until around 3pm.
The exemption to a specified classification (usually prescription medicine) under certain criteria has increasingly enabled reclassifications. Typically used to allow supply from registered health professionals such as podiatrists and optometrists, this device has recently been used for pharmacist-supply. For oseltamivir, this mechanism addressed committee concerns: to reduce the risk of misdiagnosis; internet sales; and personal stockpiling. Exemption to prescription enables third-party reclassifications where labelling changes may not be possible.

4.7.4. Pharmaceutical companies

Sponsor activity in prescription to non-prescription reclassification in NZ varied over time (Table 4-5, Figure 4-2). In 2009-2011, only one sponsor application for an ‘innovative’ reclassification occurred, versus the decade’s peak of five sponsor applications in 2004-2006.

Multiple factors affect whether or not pharmaceutical companies pursue reclassification in NZ, divided into company, product, and country factors (Figure 4-3). Industry appreciates the low-cost environment for reclassifying. Financial return for reclassified medicines is limited by country factors such as the small population, low prescription copayment (4.7.6), lack of market exclusivity, and transparency of process (see 4.7.2). Post-reclassification OTC sumatriptan unit sales attained less than 5% of prescription sales. A product launch may be postponed until Australia has the same schedule for packaging reasons given the small NZ volumes.

Many pharmaceutical companies are multinationals, and therefore global effects usually outweigh NZ factors (particularly given the small market), both enabling and impeding reclassification. If a company globally does not pursue reclassification, reclassification in NZ may be limited. Alternatively, reclassification may be attempted early in NZ to help elsewhere, or a NZ reclassification may be in line with global strategy.

The population size and Pharmac policies have reduced local pharmaceutical industry; some has moved off-shore. Many companies concentrate on Pharmac’s sole supplies, a guaranteed market needing no promotion. Such companies usually lack interest and expertise in, and necessary infrastructure for, non-prescription medicines. Sole supply tendering results in low prices, frequent brand changes, and little market for many brands. Pharmacies may sell the low-priced competitor rather than the product from the company that drove the reclassification.

20 Noting, however, that the non-prescription sumatriptan was not the originator brand which did not launch post-reclassification
Company decides to submit reclassification application, or not

Is the reclassification financially viable?

Figure 4-3 Overview of factors affecting company decisions on reclassifications in NZ

* Cannot be displayed, for example chloramphenicol is refrigerated
Funding occasionally encourages reclassification attempts. Despite salbutamol internationally being in the GSK prescription stable, GSK supported the TTH-driven reclassification consideration of inhaled salbutamol in NZ when a generic salbutamol was expected to gain sole supply.[379] That reclassification was not approved, and the MCC suggested requirements to gain reclassification. The sole supply did not eventuate so the product threat was eased, which presumably was why GSK did not further pursue reclassification.

Regionally, Australia influences some decisions. Regulatory affairs and marketing may be managed from Australia, with resulting low knowledge of, or interest in NZ. With the MCC-driven chloramphenicol reclassification, regulatory staff in Australia were caught off-guard with the necessary labelling changes. Reclassifications in NZ were sometimes applied for around the same time (or from the mid 2000s just before) as in Australia with an expectation from industry around 2009-2010 that a NZ reclassification may help an Australian reclassification.

“Our advice consistently to our members they want to switch in Australia, is why don’t you try NZ first.” Australian industry participant

One of the biggest concerns for industry is the lack of market exclusivity in NZ, combined with a transparency of process and reclassifying the medicine and not the brand. Generics have launched even before the applicant’s product (according to a participant), and ‘me-too’ competitors have reclassified easily soon after an innovative reclassification. Transparency and lack of market exclusivity in medicines reclassification minimise return for the company developing materials (and in the case of sumatriptan, testing them thoroughly). These two factors prevent applications. The chloramphenicol sponsor did not submit applications to reclassify nor comment on reclassifications given sole supply changes were imminent and someone else would get the market.

4.7.5. Pharmacy

Pharmacy plays an important role in reclassification of medicines, particularly with the two pharmacy classifications, pharmacy-only and pharmacist-only, and, pharmacy-driven reclassifications since 2010. Participants see reclassification as an opportunity for the pharmacy profession to: help the patient; improve the profession itself; provide a business opportunity; assist with the fiscally limited over-burdened health system; and provide a responsible mechanism for medicines supply.

“Well, given the dynamic of what the country can afford, the dynamic of the workforce issues we’ve got confronting the country, the ageing, diseasing population and the fact that NZ pharmacists are highly trained in a good environment where they are in both institutions studying with the medical profession, we’re underutilised hugely.” Pharmacy participant

Barriers and enablers affect pharmacy’s role in reclassification, as outlined in Table 4-8, and expanded upon below.
Table 4-8 Pharmacy-related barriers and enablers for reclassification

<table>
<thead>
<tr>
<th>Barriers</th>
<th>Enablers</th>
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<tr>
<td><strong>Financial</strong></td>
<td>Pharmacy financially benefits from reclassification</td>
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<tr>
<td>Incentives in pharmacy to do many prescriptions (focus on dispensary)</td>
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<td>Low prescription co-payment drives consumers to the doctor</td>
<td>Bulk funding to GPs</td>
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<td>Incentives for GPs to have many consultations</td>
<td>Can reduce GP load*</td>
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<tr>
<td><strong>Behaviour/ professionalism</strong></td>
<td>Reprofessionalisation</td>
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<tr>
<td>Variable pharmacy practices</td>
<td>Good undergraduate education and continuing education (including diagnosis)</td>
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<td>Doctors and some pharmacists perceive that pharmacists can't diagnose</td>
<td>Improving relationships with doctors</td>
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<tr>
<td>Doctors lack understanding of pharmacists' role</td>
<td>Good performance with oseltamivir</td>
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<tr>
<td>Records not shared with doctors</td>
<td>Largely trusted by MCC</td>
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<tr>
<td><strong>Proactivity</strong></td>
<td>Pharmacy organisations responding to applications, helping with training</td>
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<tr>
<td>Pharmacy focus on dispensary over non-prescription</td>
<td>Many pharmacists positive about reclassification</td>
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<tr>
<td>Some pharmacists have high workload</td>
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<td>Negative pharmacy environment</td>
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*Mentioned but probably not currently viewed as an enabler by doctors

GP = General Practitioner; MCC = Medicines Classification Committee

4.7.5.1. Pharmacy behaviour

Participants were largely positive about the behaviour of pharmacy and pharmacists. Participants mentioned “reprofessionalisation” or “lifting the bar”, and confidence in younger pharmacists with strong undergraduate training and buy-in to continuing education. Various participants recognised the importance of health professional involvement in supply and appreciated the pharmacist-only and pharmacy-only categories. Several talked about change in pharmacy.

Many participants, particularly pharmacists, acknowledged the variable performance of pharmacy (for example in mystery shopping). Some noted the profession was let down by a minority of poor performers. Two pharmacist participants were concerned about pharmacists not maintaining their competence (although one noted that recent competence requirements should help this), and one was concerned about pharmacists being over-worked, affecting safety.

“Pharmacists need to do it properly and I think we need to take a long, hard look at ourselves in the mirror at times because we don’t, there’s been some Consumer surveys for example that have been a little bit disappointing, but I believe that in the main we do do a good job...”

Pharmacy participant

Reclassification in NZ is enabled by the committee and regulator’s reasonable level of trust in pharmacists, with the responsible provision of oseltamivir cited.
“...[oseltamivir] was a tangible demonstration of proof of the trust we put in pharmacy that could do this, and I said to various players involved that... this is an example of the profession behaving extremely professionally.” Regulatory participant

However, MCC’s trust in pharmacists has varied over time. The MCC in 2005 appeared more trusting of pharmacy and consumers in reclassifying moderate potency corticosteroids, than the committee in 2000.[379, 440] The MCC required pharmacist training and accreditation to supply the EHC,[416] in contrast to other countries. The committee was divided when considering chloramphenicol with concerns about pharmacy capability despite training material and an algorithm. While the MCC has often commented on training material submitted with applications, since 2010 the committee has typically required Medsafe sign-off on materials for innovative reclassifications.[423, 435]

The two medical participants expressed doubts about pharmacy assistants’ ability and training (but not that of pharmacists). However, most participants did not mention pharmacy assistants specifically, possibly because the interview focused on prescription to non-prescription reclassification, which typically occurs through pharmacist-only availability.

“...but that’s pharmacists and I think pharmacy assistants certainly don’t have that understanding. So I think that when you go into a pharmacy and you buy an over the counter thing, you most times just see your pharmacy assistant.” Medical participant

“Is there a real advantage in having pharmacy only medicines? We’re back to a trust question again.... purchasing a medicine in a pharmacy, from a pharmacy sales assistant, that person’s obviously got access to someone who’s got more information about this if the patient asks questions about it. They’ve also hopefully got access to training, they’re going to know more about that substance, or they’re in an environment where they can learn more about that medicine than a sales or checkout operator in a supermarket.” Regulatory assistant

Patch protection was raised by most participants (but not strongly). Doctors protecting their patch impaired pharmacy attempts to expand their role. Pharmacy patch protection was believed to occur with the MCC recommendations on NRT and ibuprofen (see 4.7.2). However, pharmacists on the committee during 1990-1996 and from 2004 appeared open to medicines going to general sales, e.g. ranitidine, phenylephrine and fexofenadine.

One medical representative volunteered that pharmacists were not trained in diagnosis, but the other medical representative did not raise this issue, and two participants who had worked in NZ pharmacy academia disagreed.

“[A] pharmacist’s ability to diagnose in the first instance [is] probably where the medical profession and the [medical organisation] has significant concerns. We don’t believe that pharmacy training is based on developing diagnoses. Some are obviously... the most important thing about prescribing medication is actually making a diagnosis, and that’s where we think doctors have the highest skills.” Medical participant
“The pharmacy students.... go through every single condition that could conceivably present to a pharmacy, they do papers in pathology, … physiology, … pharmacotherapy, etc…. if they can’t diagnose they shouldn’t be allowed to sell any non-prescription medicines. Because how on earth can you come to a decision about whether to sell a product, prescribe a product... unless you have some ability to make rational decisions about what’s in front of you.”
Academic participant

4.7.5.2. The role of pharmacy organisations

Pharmacy organisation representatives were positive about reclassification, seeing consumer benefits and pharmacy benefits (professionally and as a business).

The Pharmacy Guild (community pharmacy body) and the Pharmaceutical Society (professional organisation) proposed reclassifications in the early 1990s until the MCC required applications to provide specified information. Both organisations have submitted comments on reclassifications and developed resources such as training. PSNZ played a pivotal role during the chloramphenicol reclassification in the absence of an applicant. However, companies do not usually approach the Society pre-reclassification. Occasionally volunteered, but usually prompted, some participants believed pharmacy organisations should drive reclassification, but the Pharmaceutical Society and the Pharmacy Guild have not pursued this.

“…[we] don’t have the resources, don’t have the information, and anyway Medsafe’s got all that stuff in the registration of the product in the first place…” Pharmacy participant

“…despite a whole heap of encouragement for driving that process for change, the pharmacy profession have never really grabbed the nettle and said we want to drive some of these change agendas, and that’s probably because they’ve got the same issues as we have, and that’s how much resource is required to get an application up to a point where it can be considered.” Regulatory participant [2009]

However in 2010, Pharmacybrands started driving reclassifications (Table 4-5). Pharmacybrands is a pharmacy retail group, the marketing group for around a third of NZ pharmacies, with part-ownership of 68 pharmacies.[441] As at December 2012 Pharmacybrands had successfully driven four innovative reclassifications and one required a further submission.

4.7.6. Consumers

According to participants, reclassification decisions should focus on the consumer, the primary beneficiary of reclassification. The MCC largely trusts the consumer to do what is right.

“…there’s not a lot of post-change research happening, either in academic circles or in industry circles…. that kind of research… might do one of two or three things, it might confirm all our worst prejudices, like that the Australians are right, that we can’t trust consumers, and we can’t trust pharmacists either and this needs to be a prescription medicine. The other thing
is that it can demonstrate the opposite of that. The third is that I guess it can show that we’ve got it about right, that it’s not perfect but it’s never going to be perfect.” Regulator participant

Consumer use of non-prescription medicines is limited by the financial incentive to go to the doctor, and consumer expectations to pay little for medicines, reducing potential sales and reclassification attraction to companies.

“I don’t believe people are prepared to pay. The perception in NZ is I pay my taxes I should get my medicines for free…” Industry participant

“I spoke to a GP the other day and she said ‘I’m absolutely sick of mothers running in here and going ‘I need some paracetamol for my child immediately, could I have a prescription please?’ when they could go and buy it if they need it that urgently.’” Pharmacy participant

However, the low patient copayment was also enabling according to one doctor participant and my experience on the committee. The financial incentive to get many medicines from the GP reduced concern that people would have on-going non-prescription use rather than see the GP. This was a key point raised in the calcipotriol reclassification application.[442]

“…like ones like omeprazole if somebody was on it long-term I’d like to think that was controlled and reviewed by a GP and I think the way we’ve got it at the moment where you can buy small doses, but it would get very expensive to turn around and do 12 months worth OTC. So I’d like to think most people who are on that regularly would be getting it on a script…” Medical participant

Not all participants trusted consumers, three expressed doubt in some consumers’ abilities, and three expressed concern about supermarket availability.

“We are giving patients more benefit of the doubt, whether that’s a good thing or not I’m not 100% sure. Some of the patients no, we shouldn’t be, they need to be totally spoon-fed but you find most of those are uneducated and there’s a connection between being uneducated and their financial setup, so they’re less likely to be able to buy OTC medication…. So to me that takes some of the fear away, because it’s cheaper for them to come to me…” Medical participant

“I think the consumers need protection, consumers are not educated." Consumer participant

4.7.7. Medical profession

Although two nominees from the NZ Medical Association are members of the MCC, medical interest in this area is low. In my experience21, NZ doctors are uninformed about pharmacist-only and pharmacy-only categories, and recent reclassifications. Doctors’ organisations expect to be invited to make a submission (which does not usually happen) and usually make none.

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21 Talking to doctors over many years in various roles.
“I think we’re very reactive when it comes to that, which is not appropriate, but I would guess that we are much more reactive, of ‘oh my God they’re doing this to us’… rather than getting involved in and actually leading…”. Medical participant

Despite a looming workforce shortage, neither medical participant was particularly convinced of the merits of reduced workload, noting other patient benefits of the short consultation of opportunistic screening or building rapport during the consultation. One suggested training more doctors rather than role substitution with pharmacists.

“…as a GP we’d say [reclassification is] probably taking patients from our door going straight to the pharmacy, and sometimes that’s a good thing, particularly when we’re struggling, but other times how appropriate is that? So you’d have to say you’re suspicious it would be good for the pharmacists…” Medical participant

The doctor participants expressed concern about pharmacy’s ability to monitor ongoing usage. One suggested shared records, between pharmacies and between the pharmacy and the doctor, to help identify interactions, misuse and long-term use that may indicate need for investigation.

The distrust by GPs in pharmacists suggested with chloramphenicol was not reflected in the two GP interviews. However, one had concerns about pharmacists’ ability to diagnose (see section 4.7.5.1).

“I’ve always dealt with very good pharmacists, I don’t know if other people’s experiences are as good as mine. Being a younger, I call myself a younger GP, we’re used to interdisciplinary, we are used to using pharmacists to get advice, and I know a lot of the hospital doctors are used to pharmacists being involved in ward round and discussions. I think we’ve got a lot more confidence than the older doctors have.” Medical participant

4.7.8. Advertising

Advertising received little coverage. One participant raised advertising as an enabler, while the consumer representative preferred that advertising of pharmacist-only medicines be prohibited.

“You’re giving people expectations that subvert the very reason for the scheduling. The pharmacist-only should be recommended on the presentation of certain symptoms. But as soon as you advertise them you give people the false, well they start diagnosing their own issues. And the advertising people will always put a spin on it because they’re not interested in fixing problems, they’re interested in selling products.” Consumer participant

4.8. How could reclassification be enabled in NZ?

The key points arising from interviews that could enable reclassification are market exclusivity (a strong industry desire), pharmacy driving reclassification, and a desire for change in pharmacy and medical care of patients. The regulatory participant seemed prescient with the following statement in November 2009, prior to Pharmacybrands’ first reclassification application submitted in January 2010:
“...if we’ve got to sort of get back to the glory days of being in the first early adopters of change, or leaders of change, is actually for, a profession.... it could be NZ Nurses Organisation, it could be, the pharmacy profession, I don’t care where it comes from in there, as long as it is evidence-based, could run internally their own debate and agenda, for what they’d like to see reclassified…” Regulator participant

Several participants wanted to see funded minor ailment schemes, as in the UK, and a few discussed collaborative care and improving pharmacist (and pharmacy assistant) practice and knowledge. Changing dispensing funding was expected to change pharmacy practice and increase interest in alternatives to dispensing. Some participants thought that increased complexity of patients and increased burden of an ageing population would require pharmacy to step up, and make alternative models of care (such as non-prescription supply) more attractive to funders.

“... we’ve got a system that is directing resources to the wrong area. General practitioners want to be the centre of things, I have no problem with that, but in doing that they need to take a step up professionally. And allow nurses, pharmacists, optometrists, whoever, to give the appropriate level of treatment where it is most appropriately given." Academic participant

One participant wanted the government, industry and the regulator to align better and agree some key principles. Another participant suggested that the regulator review reclassifications, but the regulator participant noted resource limitations.

“...the regulators should be constantly looking at their medicines… To me there are so many products that have specific classifications that really need reviewing, it’s crazy.” Industry participant

Reclassifications driven by non-sponsors may create logistical difficulties and cost for companies, for example in labelling changes (particularly given short time-frames). Third-party reclassifications could have greater ramifications where companies avoid reclassification to protect other parts of their business. On the other hand, third-party reclassifications may benefit companies by saving them the cost and inconvenience of the reclassification.

4.9. Discussion

NZ appears surprisingly progressive, despite significant barriers including a small market, pharmaceutical funding factors, off-shore companies and immediate generic entry for many reclassifications. Thirteen innovative reclassifications occurred from 2003 to 2012, including four first-in-world innovative reclassifications (see macro chapter for a country comparison Chapter 11). NZ therefore presents an excellent model to study to ascertain the factors contributing to this activity.

While multiple factors emerged, I consider NZ’s progressiveness reduces down to four key factors: NZ’s ‘can-do’ culture, pharmacist-only availability, the ability to influence and be influenced by overseas markets, and individuals.
The small market size and NZ’s isolation has helped provide the culture of resourcefulness,[422, 443] allowing NZ to progress without creating complexities, legal challenges, or political pressure that might arise elsewhere. The ensuing generally flexible and pragmatic approach from the regulator and committee reduces reclassification barriers, and committee proactivity encourages reclassifications. The MCC could reverse (or modify) reclassifications if required, which I suspect enabled reclassifications. With two decades of reforms in NZ,[444] including health reforms,[396] stakeholders may expect and accept change more than elsewhere. Non-sponsor driven reclassifications (regulator, committee or pharmacy retailer-led) have widened consumer access to medicines, particularly during the 1990s, and since 2009. These applications epitomise the ‘can do’ attitude.

This attitude is also evident in the increasingly common exemption to prescription that is used to restrict supply and/or to avoid labelling changes (particularly for third-party reclassifications). Qualitative and quantitative research suggests that such restrictions appeared to prevent inappropriate supply,[80, 81] although consumer aspects were not explored. However, many barriers to supply existed, including lack of pharmacy proactivity, some arising from the strict criteria for supply.[279] Such effects on sales must reduce sponsor interest in such availability. NZ might also become less useful as a test market if non-prescription supply options differ from elsewhere.

WHO states that “adequate information on the appropriate use of medicinal products should always accompany the product”. [98] The exemption removed the consumer labelling back-stop, increasing reliance on appropriate pharmacist behaviour, which varies.[289, 294, 445] For trimethoprim, the need to successfully complete training and provide a consumer leaflet may provide sufficient safety. Further research is required to ascertain consumer benefits and risks with pharmacist-supplied medicines without non-prescription labelling. Labelling aside, exemption to prescription is similar to a pharmacist-only classification under the same criteria.

As suggested by Aronson,[79, 446] and Gilbert et al.,[31] I found that pharmacist-only availability strongly enables reclassification in NZ. Some reclassifications (e.g. oseltamivir, calcipotriol and trimethoprim) probably only reclassified because they were restricted to pharmacist-availability, and this was noted as a key difference between the NZ and UK trimethoprim attempts.[159]

The ability of NZ to influence other countries (particularly Australia), and be influenced by other countries has enabled reclassifications. While various countries have affected NZ reclassification, the UK and Australia have been strongest, reflecting their long influence on NZ generally,[387] and in pharmacy,[378] and TTH. Had the UK been less progressive in reclassification, NZ would probably have reclassified fewer medicines. The decline in reclassification approvals in Australia has not been replicated in NZ, and this is explored in the meso-level discussion (Chapter 6). However, some reclassifications in the UK have not occurred in NZ, i.e. simvastatin, domperidone, tranexamic acid, tamsulosin, mebeverine, or azithromycin.[116] The first two medicines were attempted, but companies did not resolve outstanding issues. Tranexamic acid had no sponsor interest, and the rest had not been submitted. While NZ appears progressive, a small market, no market exclusivity, and low prescription copayments are unlikely to make these attractive reclassification prospects.
This chapter has indicated that individuals can strongly influence reclassification. The Chair of the MCC (who heads Medsafe), individual MCC members, and my actions (alongside Pharmacybrands) have enabled reclassifications that would not otherwise have occurred. The effect of individuals is explored further at the meso-level (Chapter 6), and the macro-level (Chapter 11).

NZ varied from progressive to conservative then to progressive again over the last 23 years. The extra work sourcing and checking minutes and other documents back to 1990, has been rewarded with a view of change over time, and influence of individuals. Previous commentators have noted that the US has declined in progressiveness[112] and been overtaken by the UK,[34] but none have observed a change back again to progressiveness (although the recent oxybutynin reclassification in the US offers some hope of this).[118]

The middle conservative period may have arisen from several factors: the easier reclassifications had been done; new members were more conservative or more patch protective; TTH detracted from potential down-scheduling or caused a conservative shift; or fewer applications were submitted for reclassification. Supporting the theory of individuals causing the conservatism were: fewer innovative reclassification approvals, up-schedulings, no committee proactivity, and committee recommendation overrides during the period concerned. Additionally, a well-informed participant reported improved committee performance in recent years.

While Bowden in 1993 observed that pharmaceutical companies have the information and financial motivation to drive reclassification,[30] the latter appears less likely in NZ. With low generic prices and immediate generic entry, a retailer may potentially gain more than a sponsor. Market exclusivity is irrelevant for a retailer, and they are not limited to medicines in their pipeline or by global strategy (in many cases). While sole supply and low prescription prices can affect sponsor pricing for some non-prescription products in NZ, retailers can charge what the market will pay.

Pharmacy in NZ has long looked to retail, with insufficient business in early settlement years,[378, 390] and pressure on dispensing income even reported in the 1980s.[378] Movement from pharmacy to general sales (such as non-sedating antihistamines in 2009),[434] may increase pharmacy’s interest in new reclassifications. Given this environment, Pharmacybrands was amenable to driving reclassification when approached. However, tension exists between general practice and community pharmacy,[447] and pharmacists believe expanding their roles would be resisted by other health professionals.[448] Indeed, a medical organisation expressed concern about influenza vaccination in pharmacies[449] and trimethoprim reclassification.[450] Given many NZ pharmacies rely on dispensing income,[448] maintaining pharmacy-doctor relationships remains important. However, the two professions need to move forward more collaboratively given the health challenges ahead, as indicated by participants.

Other literature from NZ supports some of the findings in this chapter. Like the NZ part of my research, Lockhart’s qualitative research on drug development in NZ found ‘kiwi ingenuity’ and the influence of key individuals enabling, and the pharmaceutical funding system, a small industry, and
the population size hindering.[451] Similarly an OECD report found a high level of trust, transparency, and a self-sufficient, resourceful and entrepreneurial population enabled innovation in NZ.[444]

Concerns held by participants on pharmacy were borne out by NZ mystery shopping research. A large, well-designed study found inadequate behaviour on pharmacist-only medicine supplies in 1999.[289] Pharmacy behaviour may have improved since, given mandatory continuing education and highly-qualified pharmacy graduates replacing retiring pharmacists. Indeed, better performance occurred in 2003[365] over 1996[288] in a Consumer NZ (non-academic) mystery shop of pharmacy. Additionally, one newspaper-driven, small mystery shop (around 2006) found all pharmacies appropriately refused orlistat supply to a woman with a normal weight.[363] Qualitative research of the oseltamivir reclassification suggested that (self-reporting) pharmacists took their responsibilities seriously, and turned down inappropriate supplies.[80] Furthermore, prescription dispensing and pharmacist-supply records for oseltamivir showed few supplies occurred outside of the allowable period.[81] Trust in pharmacy was not misplaced for oseltamivir. In contrast, a small study using observers in pharmacies found 32% of pharmacist-only medicine supplies occurred without pharmacist involvement (although pharmacist observation of the supply was not mentioned).[294]

An important aspect of NZ reclassification has been trust in consumers, but this has been little studied. Few (3%) purchasers of diclofenac tablets exceeded the stated dose, but 40% took the tablets for longer than the recommended three days (although half consulted a doctor).[22] Despite being a pharmacist-only medicine and most reading the pack insert (87%),[239] nearly 7% of consumers had a possible contraindication to diclofenac (some were historical), resulting in significantly more adverse events. A study of transdermal nicotine found 28% of purchasers smoked while using the patch, but few reported side effects.[452] Surveying consumers at purchase, and a 13% pharmacy participation rate limited findings. Further research exploring consumer behaviour and outcomes with reclassified medicines is required, particularly with exemption to prescription medicines, and first-in-world reclassifications. Higher pharmacy participation rates are desirable.

Omeprazole took considerable effort to reclassify, despite being available in the US and elsewhere by 2006.[426] This appeared to be partly sponsor-related and partly committee-related, and perhaps reflects committee variation (including time pressure) or medicine-related factors (e.g. unusual dosing and delayed onset of effect). Along with domperidone and chloramphenicol, the omeprazole delays suggest that the MCC may vary in its openness to reclassifications.

While conservatism seems likely from 2000 to 2003, other factors possibly influenced the committee. Applications were few, and some rejections were repeated later despite MCC member changes, suggesting these reclassifications were not straight forward, e.g. omeprazole and salbutamol.

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22 Pharmacy participation rates were low (16%)
4.9.1. The way forward for NZ

Factors I believe would enable reclassification in NZ based on interviews, my experience and international findings are provided in Panel 4-3. Prescription subsidy effects may have other detrimental effects, therefore these enablers are included for completeness rather than because I recommend them. Some enablers already exist.

The MCC has encouraged reclassification and been unafraid to reclassify chronic medicines, to try new models, or reclassify medicines other developed countries have not. Continuation of this perspective depends on members, who need evidence-based decision-making skills, and to be open to different ideas. The MCC constitution could be reviewed to limit patch protection, provide a consumer voice, possibly a public health voice, and ensure expertise in evidence around non-prescription medicines, and minimise the risk of undue regulator influence (e.g. using an independent Chair). Pharmacists and GPs are important members, and coal-face experience is vital, providing appropriate other skills also exist and other members are added. Members would ideally have post-graduate qualifications, evidence-based decision making skills, and be open to reclassification. Members need to commit enough preparation time. Carefully selecting committee members rather than relying on nominees as required by legislation is preferable, but requires a Medicines Act change, and sufficient reimbursement. Training MCC members and providing feedback on performance may facilitate best practice. Some of these suggestions echo those of Brass and Hiatt for the US FDA advisory committees.[336]

Although industry-desired market exclusivity should enable some reclassifications, ‘me-toos’ can still reclassify soon after the innovative reclassification. Additionally, exclusivity would not resolve many fundamental difficulties that impede reclassification, including company factors, small population, low prices, and low patient copayments, so may not increase reclassification applications greatly.

Post-reclassification research is needed to inform further NZ reclassifications, make improvements post-reclassification, and assist in reclassifications elsewhere. Research into pharmacy and consumer behaviour may also assist reclassifications and inform development of relevant resources for both. Dissemination of this research will maximise desired outcomes.
## Panel 4-3 Potential enablers for prescription to non-prescription reclassification in NZ

### Process
- Ensure committee discussions are evidence-based (for example appropriately qualified members)
- Implement market exclusivity (for two to three years)
- Allow company to present at MCC meeting (or continue to observe the MCC discussion)
- Committee or regulator to continue to suggest potential candidates
- Allow a preliminary confidential meeting between the MCC and the applicant to discuss likely issues
- Update the definition of suitability for non-prescription sale used by the MCC
- Continue to innovate
- Consider changes to the committee constitution and encourage evidence-based decision-making

### Environment
- Put reclassification and pharmacy on the government agenda
- Research and disseminate evidence on benefits, risks and appropriate reclassification strategies
- Move from doctor-centred to patient-centred care
- Change the universal low prescription copayment (but this has other ramifications)
- Remove prescription subsidy on some OTC medicines (but has other ramifications)
- Electronic record sharing

### Companies
- Encourage use of NZ as a test market
- Ensure advertising is responsible and, for pharmacist-only medicines advises to consult with the pharmacist
- Work with other stakeholders, pharmacy groups, and the regulator
- Collect evidence of usage and safety
- Innovate

### Pharmacy
- Ensure pharmacists and pharmacy assistants keep up-to-date and meet appropriate standards
- Ensure staff have enough time for consumer consultation
- Encourage enthusiasm/improve proactivity on new reclassifications
- Continue to allow mandatory training of pharmacists in specific areas
- Communicate and work with doctors

### Consumers
- Inform consumers on what is available without prescription
- Educate consumers in responsible self-medication, including encouraging consumers to share relevant information with the pharmacist or pharmacy assistant and not to share medicines
- Empower and encourage to self-manage where appropriate

### Doctors
- Encourage consumer self-management
- Be open to patient-centred rather than doctor-centred models, including collaborative care models
- Communicate and work with pharmacists
Most post-2008 reclassifications arose from Pharmacybrands, including innovative areas for NZ (chronic care, vaccinations and antibiotics), using collaborative care models, and exemption to prescription. Sponsors may learn from the approach taken by Pharmacybrands, considering different reclassification mechanisms, and educational strategies to reduce investment, and working with pharmacy organisations before applying. For complex reclassifications such as the contraceptive pill or travel medicine, mandating pharmacist training (as with trimethoprim) may protect consumers and reassure the MCC.

Promoting NZ as a test market internationally may increase NZ reclassifications and enable research for reclassifications elsewhere. However, as noted above, different supply systems in NZ could limit the applicability of NZ as a test market.

**4.10. Summary**

NZ has been advanced in reclassification for much of the last 23 years. Given the many barriers, NZ’s progressiveness is remarkable and results from a variety of enablers. Given a recent slow-down in sponsor applications for innovative reclassifications, implementing some of the suggested initiatives could enable reclassification further. Research is required to ascertain consumer impact of the reclassifications, and ensure behaviour in pharmacy is reaching the necessary standard.
Chapter 5. Australia

5.1. Introduction

Australia has been both described as a ‘leading’ country in reclassification (in 2009)[26] and “extremely risk-averse” (in 2010).[453] It was the first country to reclassify orlistat,[454] but rejected sumatriptan for reclassification.[380] This contrast is explored at the micro-level of analysis in Chapter 5. Australia and NZ are then compared in the meso-level chapter (Chapter 6). Findings from this chapter contribute to the macro-level chapter to provide an overall picture of how countries differ in availability of medicines without prescription (Chapter 11).

5.2. Background

Australia is a vast, mostly sparsely-populated country first populated by aboriginal people about 40,000 years ago.[455] Following British settlement in 1788, Australia moved to self-governing individual colonies under British influence. Although becoming a federation in 1901, much power remains within the States and Territories.

Table 5-1 Demographic and health measures for Australia

<table>
<thead>
<tr>
<th>Variables</th>
<th>Australia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population (millions; 2011)[388]</td>
<td>22.6</td>
</tr>
<tr>
<td>Health system[372]</td>
<td>National health service</td>
</tr>
<tr>
<td>Life expectancy*[392]</td>
<td>81.8 years</td>
</tr>
<tr>
<td>Health Development Index Ranking[388]</td>
<td>2</td>
</tr>
<tr>
<td>Health spend as % of GDP total (2009)[392]</td>
<td>9.1%</td>
</tr>
<tr>
<td>Public proportion of health spend (2009)[392]</td>
<td>69.0%</td>
</tr>
<tr>
<td>Self-medication sales (2012)[219]</td>
<td>AUS$2.5 billion (US$2.6 billion)</td>
</tr>
<tr>
<td>Self-medication as % of total pharma (2012)[219]</td>
<td>23%</td>
</tr>
<tr>
<td>Growth in self-medication market</td>
<td>N/A</td>
</tr>
<tr>
<td>Pharmacist-only schedule?</td>
<td>Yes</td>
</tr>
<tr>
<td>Pharmacy-only schedule?</td>
<td>Yes</td>
</tr>
<tr>
<td>Drugstore schedule?</td>
<td>No</td>
</tr>
<tr>
<td>Physicians per 1000 persons[393]</td>
<td>3.1 (2009)</td>
</tr>
<tr>
<td>Number of doctor consultations per year per capita[393]</td>
<td>6.5 (2010)</td>
</tr>
<tr>
<td>Primary care doctor payment structure[14]</td>
<td>FFS</td>
</tr>
<tr>
<td>Number of pharmacists per 10,000 population[394]</td>
<td>~12</td>
</tr>
<tr>
<td>Pharmacies per 10,000 population[388, 456]</td>
<td>2.2</td>
</tr>
<tr>
<td>Percentage of pharmacists in community pharmacy[457]</td>
<td>70%</td>
</tr>
</tbody>
</table>
Demographic and health measures are presented in Table 5-1. The population is primarily of European ancestry,[458] with 2% Aboriginal and Torres Strait Islander,[459] and 4% Chinese ancestry.[458] Australia is relatively wealthy, with Gross National Income per capita well above NZ, similar to Japan and the UK, and below the US.[388]

Australia’s medicine distribution network and universal health care emulate other Commonwealth countries. GPs provide most primary health care, with prescriptions dispensed from community pharmacies. The government subsidises most prescribed medicines. In 2012, patients paid a copayment of AUS$5.80 (US$6; concession) or up to AUS$35.40 (US$36; non-concession).[460] Most doctors’ visits have no patient copayment, but some consumers pay a variable charge.[456] Community pharmacy is relatively protected, both in ownership and with restricted pharmacy numbers and location rules.[87, 456]

Three non-prescription medicines categories exist: Pharmacist Only Medicines23 (Schedule 3 or S3), Pharmacy Medicines (Schedule 2 or S2) and unscheduled medicines.[377] Pharmacist-only medicines legally require pharmacist involvement in the medicine supply. Pharmacy-only medicines are sold only from a pharmacy24. Unscheduled medicines can be supplied from any retail outlet (general sale).[461] Jurisdictions vary in requirements for pharmacy on the different schedules, e.g. product self-selection.[377] Pharmacist-only medicines can only be advertised to consumers if especially approved and listed in Appendix H of the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP). Such approval is unique among the countries studied.[453]

In 2000, Galbally reviewed costs and benefits of medicine controls and considered alternatives and mechanisms to improve efficiency.[84] Uncertain of the benefit of the pharmacist-only and pharmacy-only categories, Galbally recommended further review following independent research. The 2005 review considered that the research showed marginal benefit of both categories, but recommended further research and review given the newness of pharmacy initiatives.[462] The 2010 review led to continuation of the two pharmacy schedules.[83]

The pharmacy profession has introduced initiatives such as the Quality Care Pharmacy Programme (QCPP), using tools including mystery shopping to monitor and improve pharmacy staff behaviour,[463] and Project STOP to record real-time pseudoephedrine supplies to reduce diversion.[464]

Until 2010, the NDPSC decided medicine and poisons classifications. Any organisation or person could submit an application with no fee charged. The NDPSC included jurisdictional representatives (from six states, two territories and NZ) and appointees (including consumer, industry and pharmacy

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23 Pharmacist Only Medicines, Pharmacy Only Medicines and unscheduled medicines will be referred to by the generic terms pharmacist-only, pharmacy-only and general sales in line with other chapters
24 Minor exception/s will not be discussed here
Chapter 5

representatives), and was chaired by the Commonwealth (Therapeutic Goods Administration; TGA) member[465, 466]. Decisions required a majority vote from jurisdictional representatives.

As recommended by Galbally,[84] medicines and chemicals scheduling were split, and the ACMS was formed on 1 July 2010.[147, 467] The ACMS advises on reclassification, and on advertising decisions for pharmacist-only medicines, with the final decision made by the Secretary of the Department of Health and Ageing (or Delegate).[147, 468, 469] Committee members have expertise in specified fields and include nine nominated members (one from each State, two Territories and the Commonwealth) and up to six appointed members. Any organisation or person can submit an application. An evaluator typically provides a review of reclassification applications (as with the NDPSC) to the committee. The Therapeutic Goods Act outlines considerations for reclassification and Appendix H decisions.[468]

Both Gilbert et al. (in 2006),[31] and the USGAO (in 2009)[50] found Australia had more medicines available without prescription than most comparator countries. In 2005, Australia was described as “a laboratory for OTC switches”.[470] However, in 2010 and 2011 the industry organisation (Australian Self-Medication Industry; ASMI) described the reclassification environment as “extremely risk averse”.77, 453][p57]

5.3. Primary Data Sources

The primary data sources for Australian reclassification were interviews and documents. Eighteen key informants included 15 from Australia, two international industry participants with previous Australian reclassification involvement, and one person based in NZ who had participated in the NDPSC. Six participants had served on the NDPSC, and one participant served on the ACMS. Australian-based participants were from two pharmacy organisations (n=6), industry-related (n=3), academia (n=2), a consumer group (n=1), a medical organisation (n=1), and the regulatory authority (n=2).

Documents have been described earlier (3.2.11, 3.2.12). Given the heuristic approach, my relevant Australian experiences included observing at an NDPSC meeting in February 2007 (including orlistat and sumatriptan considerations), work experience25, and talking to Australian pharmacists about reclassification over many years.

5.4. Reclassifications in Australia 2000-2012

Some local and international participants considered Australia was progressive in reclassification relative to other countries during the early 2000s. Table 5-2 and Figure 5-1 support this perspective. Two reclassifications (dermal alclometasone and orlistat) were probably first-in-world reclassifications.

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25 I registered as a pharmacist in Victoria in 2005, “working” at two pharmacies over three days, under supervision, to understand differences between community pharmacy in Australia and NZ.
## Table 5-2 All prescription to non-prescription reclassification approvals in Australia* 2000-2012

<table>
<thead>
<tr>
<th>Year*</th>
<th>Innovative reclassification</th>
<th>Reclassification but not innovative</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>Tranexamic acid†</td>
<td>Flurbiprofen lozenges</td>
</tr>
<tr>
<td></td>
<td>Alclometasone dermal</td>
<td>Etofenamate dermal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Felbinac dermal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Triamcinolone nasal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fluticasone nasal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Azelastine nasal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Acetylcysteine oral</td>
</tr>
<tr>
<td>2001</td>
<td>Beclometasone nasal widened indications</td>
<td>Bifonazole scalp</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Desloratadine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nicotine lozenges</td>
</tr>
<tr>
<td>2002</td>
<td></td>
<td>Clobetasone dermal</td>
</tr>
<tr>
<td>2003</td>
<td>Levonorgestrel (EHC)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fluconazole oral</td>
<td></td>
</tr>
<tr>
<td>2004</td>
<td>Orlistat</td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>Pantoprazole‡</td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td></td>
<td>Ibuprofen (400 mg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ketotifen ocular</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Azelastine ocular</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mepyramine dermal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oxiconazole dermal and vaginal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clemastine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Paracetamol long-acting</td>
</tr>
<tr>
<td>2007</td>
<td></td>
<td>Butaconazole vaginal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Paracetamol plus caffeine</td>
</tr>
<tr>
<td>2008</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2009</td>
<td></td>
<td>Guiaphenesin slow release</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rabeprazole</td>
</tr>
<tr>
<td>2010</td>
<td>Chloramphenicol ocular</td>
<td>Omeprazole</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lansoprazole</td>
</tr>
<tr>
<td>2011</td>
<td>Famiciclovir oral</td>
<td></td>
</tr>
<tr>
<td>2012</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source: National Drugs and Poisons Schedule Committee meeting records and interim or final Delegate’s decisions

*Date of committee decision or recommendation to reclassify is provided

†Later up-scheduled (2007)[380]

‡Reclassification delayed while company prepared training material, finalised 2008[471]
Most participants considered Australia’s progressiveness had since declined, citing up-schedulings, age restrictions on cough-cold preparations for children\textsuperscript{26}, and rejected reclassifications. Two ‘innovative’ reclassifications occurred during 2006-2012 (Figure 5-1).

**Figure 5-1** ‘Innovative’ reclassifications in Australia from 2000-2012

![Innovative reclassifications in Australia from 2000-2012]

Source: National Drugs and Poisons Schedule Committee, and Advisory Committee on Medicines Scheduling meeting records

Compared to the early 2000s, 2006 onwards appears more risk averse, as demonstrated by advertising rejections (Figure 5-2), and comments in minutes (e.g. sumatriptan Panel 5-2 and advertising negativity). More innovative reclassification considerations were approved in the early 2000s than in the following periods (Figure 5-3).

**Figure 5-2** Appendix H advertising considerations for pharmacist-only medicines in Australia 2000-2011\textsuperscript{*}

![Appendix H advertising considerations for pharmacist-only medicines in Australia 2000-2011]

Source: National Drugs and Poisons Schedule Committee, and Advisory Committee on Medicines Scheduling meeting records

\*Many medicines or groups of medicines appear in multiple years, particularly proton pump inhibitors

Seven of nine innovative reclassifications occurred before 2006 (Figure 5-1). Positive NDPSC decisions for innovative reclassifications including tranexamic acid, topical alclometasone, and the

\textsuperscript{26} Part of an international trend
EHC demonstrated the dynamism of Australian reclassification (Table 5-3). Australia’s new millennium activity culminated in the first-in-world reclassification of orlistat for weight loss in 2004, but this flurry was not sustained. Most participants attributed this to committee member changes increasing conservatism.

**Figure 5-3 Innovative reclassification considerations in Australia 2000-2011***

Source: National Drugs and Poisons Schedule Committee, and Advisory Committee on Medicines Scheduling meeting records

*Tranexamic acid included in 2000 but reverted in 2007. Orlistat, neomycin-polymyxin-bacitracin, and different proton pump inhibitors appear in the first two periods, oseltamivir appears in the last two periods.

The meeting records confirm the increasing conservatism. From 2006 to mid 2012, only two ‘innovative’ reclassifications occurred: TTH-driven chloramphenicol, and sponsor-driven oral famciclovir.[472] Despite positive evaluations, oral famciclovir (for herpes labialis) took four considerations before reclassifying in 2011 (Table 5-3).[472]

**5.4.1. Failure of applications**

Although most innovative reclassification attempts in Australia failed from 2006 to 2012 (Table 5-3), sumatriptan was the only rejection of a medicine recently reclassified in multiple markets (the UK, NZ and Germany by 2007).[473-475] Thus, while rejections are common, Australia has not rejected multiple reclassifications that other countries have recently accepted, possibly signalling a reticence to try new reclassifications, or reflecting quality or appropriateness of applications (noting negative evaluations for some).
Table 5-3 Innovative reclassification attempts in Australia 2006-2012

<table>
<thead>
<tr>
<th>Medicine*</th>
<th>Meetings (number)</th>
<th>Source of change</th>
<th>Evaluator recommendation† and decision</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tranexamic acid (oral)</td>
<td>1</td>
<td>Application, TTH</td>
<td>Reclassified 2000 (then up-scheduled 2007)</td>
</tr>
<tr>
<td>Alclometasone (dermal)</td>
<td>1</td>
<td>Application</td>
<td>Reclassified 2000</td>
</tr>
<tr>
<td>Beclometasone (nasal, indication extension)</td>
<td>1</td>
<td>Application</td>
<td>Indication extended</td>
</tr>
<tr>
<td>Neomycin, polymyxin, bacitracin</td>
<td>2</td>
<td>Application</td>
<td>Evaluator negative, rejected 2001, 2004</td>
</tr>
<tr>
<td>Orlistat</td>
<td>4</td>
<td>Application</td>
<td>Negative evaluation Feb 2003, evaluation seemed positive, committee agreed Oct 2003, confirmed 2004</td>
</tr>
<tr>
<td>Silver sulfadiazine</td>
<td>2</td>
<td>TTH</td>
<td>Rejected 2005; resistance concerns</td>
</tr>
<tr>
<td>Lansoprazole</td>
<td>3</td>
<td>Application, TTH</td>
<td>Evaluator negative 2003. Reclassified 2010 (but no longer innovative by then)</td>
</tr>
<tr>
<td>Levonorgestrel (EHC)</td>
<td>2</td>
<td>Application</td>
<td>Evaluator positive, reclassified 2003</td>
</tr>
<tr>
<td>Fluconazole oral</td>
<td>1</td>
<td>Application</td>
<td>Evaluator unsupportive, reclassified</td>
</tr>
<tr>
<td>Oseltamivir</td>
<td>5</td>
<td>Application, TTH, application</td>
<td>Evaluator unsupportive, rejected 2004-2008</td>
</tr>
<tr>
<td>Sumatriptan</td>
<td>4</td>
<td>Application</td>
<td>Evaluator negative, rejected 2005-2007</td>
</tr>
<tr>
<td>Pantoprazole</td>
<td>1</td>
<td>Application</td>
<td>Evaluator positive, agreed to reclassify 2005 (but delayed until 2008)</td>
</tr>
<tr>
<td>Mometasone (dermal)</td>
<td>3</td>
<td>Application</td>
<td>Evaluator positive, agreed to reclassify, then overturned 2007.</td>
</tr>
<tr>
<td>Famiciclovir oral</td>
<td>4</td>
<td>Application, TTH, application</td>
<td>Evaluator positive 2009 but rejected, (benefits not outweighing risk, resistance, etc). Evaluator positive 2009 but rejected (resistance, renal impairment, etc). Evaluator supported 2011, approved</td>
</tr>
<tr>
<td>Vitamin D (increased dose 2009)</td>
<td>1</td>
<td>Application</td>
<td>Evaluator considered doctor intervention required, rejected 2009.</td>
</tr>
<tr>
<td>Montelukast</td>
<td>2</td>
<td>Application</td>
<td>Evaluator negative, rejected 2009, 2010</td>
</tr>
<tr>
<td>Zolmitriptan</td>
<td>1</td>
<td>TTH</td>
<td>Rejected 2009</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>2</td>
<td>TTH</td>
<td>Reclassified 2009, confirmed 2010</td>
</tr>
<tr>
<td>Orphenadrine + paracetamol</td>
<td>1</td>
<td>Application</td>
<td>Evaluator negative, rejected 2011 (toxicity, misuse potential, etc)</td>
</tr>
<tr>
<td>Vibrio cholera and enterotoxigenic escherichia coli vaccine</td>
<td>1</td>
<td>TTH</td>
<td>Rejected 2012</td>
</tr>
</tbody>
</table>

Source: NDPSC meeting records, interim and final Delegate’s decisions (excludes Nov 2012 meeting as results not released until 2013)

*Excludes line extensions (e.g. ibuprofen 400 mg), exemptions for cosmetic use and complementary remedies
† Unsupportive evaluator means appeared unsupportive but a negative recommendation was not apparent
5.5. Overriding themes

Participants perceived important barriers to reclassification, and few enablers. These barriers have prevented pharmaceutical companies submitting applications or caused reclassification attempts to fail. Repeated failures possibly discouraged some potential applications.

Seven main themes around reclassification emerged from the interviews. The most compelling theme was a sense of risk averseness or conservatism. Further important themes arising from the data (in no particular order) included financial motivation, effects of individuals, pharmacy, politics, global influences, non-evidence-based decision making, and TTH. Themes were commonly inter-linked.

These themes are discussed as an overview below (5.5.1-5.5.8), and then (to aid comparison with other countries) further detail is provided in the following sections, broken down by the different parties and factors involved (5.6) and demonstrating the interconnectivity of the different themes.

5.5.1. Risk averseness or conservatism

Participants often described the committee, the regulator, pharmacists, and/or individuals involved in the process as risk-averse and/or conservative, many considering this had increased recently. This theme came through in interviews with industry, pharmacy organisations, the regulator, academics and current and ex-committee members. Industry was not described as risk-averse or conservative.

“...conservatism on behalf of the committee and regulator comes into play quite often”

Pharmacy participant

The two participants who did not use “risk averse”, “conservative” or related words about the committee were from the doctors’ and consumers’ organisations. Although predominantly viewed negatively, such conservatism or risk-averseness was sometimes considered appropriate, usually by NDPSC or ACMS members (see 5.6.2).

“Now is it wrong to have resistance to change the down-scheduling? Probably not, and, you know, it’s better to actually, in this area of healthcare to tread warily.” Committee member

Minutes and interviews indicated that the risk-averseness partnered a distrust of pharmacy and consumers to behave correctly. Pharmacy organisations reportedly tended to take a conservative stance against advertising of most pharmacist-only medicines, opposed some prescription to pharmacist-only recclassifications, and opposed pharmacy-only to general sales reclassifications (see also 5.6.5). Pharmacist conservatism apparently reduced support for newly reclassified medicines, reducing financial viability of reclassifications.

The increasing conservatism may arise from increasing difficulty in reclassifications:

“I think some of the easier switches have been done and I think we’re now getting into the harder compounds to switch.” Industry participant
5.5.2. Financial motivation

Financial motivation swayed pharmaceutical companies in encouraging or (more commonly) discouraging applications for reclassification (5.6.4). However, local financial non-viability may be overlooked if an Australian reclassification could aid a reclassification in a larger market.

This financial motivation theme also permeated many other areas explored in the interviews, including patch protection for doctors (5.6.7) and pharmacists (5.6.5). Pharmacists were thought to focus on dispensing (as their main income), rather than being proactive with reclassified medicines. In contrast, some participants suggested some committee members and stakeholders (e.g. doctors) held concerns about the commercial motivation in pharmacy overriding pharmacists' professional and ethical obligations.

The financial theme includes concern that reclassification could disadvantage consumers if they have to pay more after reclassification, and an occasionally expressed desire for health funding savings from reclassification.

5.5.3. Individuals

As with the NZ MCC, turnover in individual committee members or individuals influencing committee members appeared to contribute to both the earlier progressive slant and later conservatism (5.6.2). This came through from a range of interviews as an important effect.

"...when those people dropped off and new people came on they became more conservative and the others just went with the flow." Industry participant

Individuals in companies and pharmacy organisations received a small mention.

"...the chairman of the company also threw his weight around a bit much and got up the nose of some of the people which didn’t help." Industry participant

5.5.4. Pharmacy

A ubiquitous theme was pharmacy (and pharmacists): their role; behaviour; influence on reclassification; capabilities; their representative bodies, and the pharmacy-only and pharmacist-only medicine schedules. Pharmacy both encourages and impedes Australian reclassification.

Participants believed pharmacy bodies influenced reclassifications through their submissions (both supporting and opposing). The Pharmaceutical Society’s training materials and Pharmacy Guild initiatives (Project STOP and QCPP) encouraged the NDPSC when reclassifying medicines, as primarily pharmacy participants recounted. Pharmacists and pharmacy assistant behaviour, as reported, experienced or perceived, significantly influences committee decisions (see 5.6.5). Participants disagreed about the effect of pharmacy with some believing pharmacy behaviour gave the committee confidence, and others reporting some distrust in pharmacy. Pharmacy behaviour (e.g.
substituting house brands) or potential backlash to down-scheduling from pharmacy-only to
unscheduled affects companies’ decisions whether or not to pursue reclassifications.

Australian participants supported current schedules, which were perceived to increase the likelihood
of a positive reclassification decision, and provide opportunity for health professional advice at time of
supply.

“…S3 is an enabler, but… it has its limitations because if you stuck everything in S3 it
wouldn’t work.” Regulator participant

The pharmacist-only category facilitated reclassification, although pharmacists sometimes lacked
confidence or proactivity, limiting this advantage. Pharmacist-only non-advertiseable was
acknowledged by industry and non-industry as a commercial graveyard (see 4.7.8).

5.5.5. Politics

Politics was another strong theme. Participants perceived politics affected the committee (see 5.6.2),
and medical and consumer organisations used it e.g. to highlight issues in pharmacy, or oppose
reclassifications and advertising (see Panel 5-1). Companies’ political desire to maintain relationships
with doctors or pharmacists reflects a financial motivation for all three parties – a reclassification could
reduce pharmacy or doctors’ finances, and their backlash on sponsors has financial consequences.

“[NRT was] S227 here and open sale in NZ, and we then harmonised, and … companies kept
supplying it through pharmacy, until the Minister asked the question, you’re on about
increasing access to medicines and wanting to make a difference, and public health interest,
etc, explain to me why you’re not in grocery… and the boss’s response to the Minister was:
‘Why don’t you ask the Guild why that is’. So one company went open sale and the other
maintained allegiances with the pharmacy chain.” Industry voice

Politics were evident in committee membership and voting.

“…the difficulty now for getting universal decisions is immense, and it’s not just in scheduling,
it’s in a wide range of areas. You only need one of the States to be particularly concerned
about something local to them, for them to mount almost like a State’s rights argument and it
then impedes getting a universal decision. So allowing the States to actually have a voice at
the table, you can’t do it without them…” Committee member

5.5.6. Global influences

Global influences emerged for companies (see 5.6.4), the regulator and the committee in particular,
and for pharmacy organisations to a lesser degree.

---

27 S2 Schedule 2 or pharmacy-only
“...the market’s relatively small for big companies.... I don’t think the Australian market will give you a return on investment per se, so you know you were actually doing it in Australia to be able to do it somewhere else ....” Academic participant

An increasing international trend for risk aversion came through from a few participants as influencing the Australian regulator and committee. Several participants acknowledged that reclassification elsewhere can influence the committee decision.

“...if there’s a lot of experience of a product that’s been safely used over the counter elsewhere then that would be very persuasive. OK? …it’s difficult for NZ to be persuasive because it’s so small.” Regulator participant

5.5.7. Non-evidence based decision making

The NDPSC was commonly criticised for not always being evidence-based, with examples provided (see 5.6), typically contributing to conservative decisions. Reversing the orlistat advertising approval was widely considered to be a media-related over-reaction. The potassium chloride up-scheduling was described as emotive. Participants described unexpected about-turns during meetings in which approval looked likely until a comment changed the committee “mood”. One participant suggested decisions could be affected by other agenda items.

5.5.8. Trans-Tasman harmonisation

The influence of TTH frequented many interviews (see the meso-level chapter, Chapter 6).

5.5.9. Summary of overriding themes

The most pervasive of the overriding themes was the risk-averseness or conservatism, seemingly partly driven by politics, non-evidence-based decision making and a move from progressive individuals on the committee to more conservative members. The findings will now be explained by stakeholder to allow comparison between countries.

5.6. Findings by stakeholder or factor

5.6.1. Government

Government influence was mainly seen at the States and Territories level, although one participant reported that parliament debated the EHC reclassification from a moral and ethical perspective. Most participants reported politics affected NDPSC decisions, and it possibly affected the potassium chloride up-scheduling highlighted in the meso chapter (Panel 6-3).

“[NDPSC members are] also State employees so they’ve got a direct line into the State government which means they’ve also got that downwards pressure, that they’re not there as experts, they’re there as representatives.” Committee member
“...there is a view that because of the nature of the committee structure of the NDPSC and the voting arrangements specifically, it is ultimately about a series of government or bureaucracy agendas, as to what will and won't happen versus a true evidence-based assessment.” Industry participant

Public pressure and media were discussed in several interviews (e.g. with orlistat, see Panel 5-1).

“... we live in a political climate, where people... do have a greater say. And I think where there’s safety issues people are more informed and they’re more likely to take those issues public. And governments I guess are a little bit concerned about that and the implications of that.... But I don’t necessarily see that as a bad thing. It’s good for democracy and good for good decision making.” De-identified quote

5.6.2. Regulator, committee and process

The regulator, the NDPSC and aspects of the process reportedly facilitated and hindered reclassification. Some reclassifications in the early 2000s occurred reasonably quickly (Table 5-1). In 2003, fluconazole (to pharmacist-only) and ibuprofen (from pharmacy-only to unscheduled) reclassified in just one meeting,[476] possibly aided by communication with progressive members.

“I think we did a reasonable job because we had [name removed] as chair of NDPSC at the time and there was also the [de-identified state] rep and the [de-identified state] rep were very on side at the time ... And that was a real struggle but we got it up first time much to my amazement.” Industry participant

In the early 2000s, industry often talked or perhaps lobbied with some committee members and the Chair prior to putting in an application which was enabling until being stopped in 2006.[477]

“...In the past you could... ask them were there any areas of concern, was there any more information they needed...” Industry participant

“...under the current framework there’s no-one for them to meet with. I’m not going to meet with them. I don’t think it’s appropriate. But once the decision’s being made in the TGA it’s a different ball game.” Regulator participant

Recent committee conservatism or risk-averseness provided the strongest hurdle to reclassification, and was thought to arise from turnover of individuals. Several progressive committee members were replaced by more conservative members, particularly including jurisdictional members and the Chair, although non-jurisdictional members were also mentioned. A previous NDPSC Chair was missed for “his experience and his ability to chair a meeting and just highlight the issues and get all the facts on the table...”. More recent Chairs were considered conservative, which participants suggested reflected increasing conservatism in the regulator.
“...if I have to ask for one thing to change on the committee, I would say the Chair ... the person is a regulator, it’s the Principal Medical Advisor of the TGA... it would be critical that the Chair would be completely objective and unbiased.” Industry voice

“So, it can constrain the argument or it can direct the argument in a particular way, ... the Chair can say well that’s really interesting but the Federal government’s position is that it will not support the over-the-counter sale of Tamiflu. And then, now let’s have a vote. So, ... you’re challenging the Federal government if you want to vote yes, never mind what the evidence is...” Committee member

Member changes other than the Chair and jurisdictional members were also cited in increasing risk aversion: the pharmacy representative was replaced with a non-community pharmacist; and a well-regarded and influential NZ member left the committee.

“...everyone sort of looked towards [the NZ member], and we relied very heavily on him to do what I think a Chair should be doing and what [former Chair] used to do.” Committee member

External factors contributing to committee conservatism included increasing risk averseness internationally (e.g. limiting cough-cold preparations in children, and up-scheduling codeine), and local events such as orlistat (see Panel 5-1) and a potassium chloride poisoning (discussed at the meso-level Panel 6-3).[478]

Most participants considered the NDPSC constitution contributed to the risk-averseness, particularly the jurisdictional representation. The consumer and medical participants did not discuss this factor, probably because they are somewhat removed from the process.

“...their life is to avoid risk. And I’m not saying that that’s a bad thing in their position, maybe… I’d think I want to make sure that we don’t make any mistakes, we don’t want any, any problems down the track. We’ve got to keep our Minister happy and all these other stakeholders, particularly the general public from coming and complaining.” Pharmacy participant

Two votes occurred for NDPSC decisions: all members, then the deciding vote using jurisdictional members. Several participants reported that representatives were sometimes directed how to vote from above, including a liberal chief pharmacist who instructed his committee member. Multiple participants mentioned two jurisdictional representatives whose progressive “quite lateral” thinking influenced other committee members until natural turnover replaced them with more conservative members. Several committee member participants described group behaviour in the committee:

“...the committee would, if you would allow it to have its own way, it would drift and there’s a very, very strong group thing, and they wait for one to take the lead – and there are a few leaders of the pack, and the rest would just rush in to support.” Committee member
Some participants who were or had been NDPSC members revealed the committee was sometimes emotively or “whim” driven, providing examples encompassing five different medicines. These participants considered that the committee could become more evidence-based and consistent.

“...it’s extraordinary that you get so close to it and then somebody can just come in and sort of very emphatically make a few statements, and the committee was ‘well yeah, better make sure that things don’t go wrong’.” Committee member

“[product de-identified] I think could have gone either way... you take one committee and they'll make one decision on one day and you bring them back two months later and they might come to a different decision on exactly the same... it just depends on who's most persuasive on the day.” Committee member

Political influence and risk-averseness mentioned above could perhaps stimulate inconsistent and emotively-driven behaviour. Using representatives of States and Territories rather than experts could reduce clinical knowledge or literature evaluation skills within the committee that may assist in evidence-based decision making. Participants also highlighted insufficient coalface expertise on the committee and excessive workload.

“... I felt that a lot of [committee members] were coming to the meeting to deal with an agenda item based on what they knew about a substance and their own opinion of where it was suitable for switch rather than necessarily being across all of that documentation because it was next to impossible to do.... And so I think that introduces variability...” Committee member

An evaluator’s report should facilitate an evidenced-based discussion. However, two participants volunteered that reclassifications with a negative report were always rejected, while the committee also sometimes rejected a reclassification or advertising approval despite a positive report. Meeting records support this contention, primarily for advertising approval since 2007, but during the early 2000s approval sometimes occurred despite a negative evaluation (Table 5-3).

“It’s easy to throw up barriers in any switch. So there’s very few things that have absolutely no risk, not going to cause any problems with misuse, that are efficacious and better than anything else on the market for those particular problems, I mean those don’t tend to exist, and by and large, my view’s always been that providing you can put the adequate training back-up to it, you should be able to get quite a reasonable result out of pharmacy for those who want to go down that path...” Pharmacy participant

Many participants believed that Australia was part of increasing risk-averseness in regulators internationally. However, local events may have increased the committee’s or regulator’s risk-aversion e.g. an extensive recall of products manufactured by Pan Pharmaceuticals. Half of the Australian participants discussed orlistat, most of whom raised the topic (Panel 5-1). This advertising reversal had long-lasting effects according to participants, and supported by the advertising consideration
outcomes (Figure 5-2). With orlistat, the NDPSC was under political pressure. While meeting records provided surprisingly little mention of pharmacy performance (blame focusing on the company’s advertising transgression), trust in pharmacy may have been damaged (see 5.6.5).

Panel 5-1 Orlistat case study

Concerns about the advertising of the pharmacist-only orlistat during a TV programme targeting teenagers were reported in Australian media in October 2006. Following a consumer organisation complaint, the company (Roche) was found to have breached the advertising code. A de-identified source requested the NDPSC reconsider the scheduling and Appendix H listing. In October 2006, the NDPSC duly added orlistat advertising to the next meeting’s agenda. The NDPSC Chair later added reconsideration of orlistat scheduling with a view to potentially up-schedule the medicine.

The Australian Consumer Association then conducted a mystery shop, and found 80% of 30 pharmacies inappropriately sold orlistat to a young woman with a BMI lower than that allowed. The mystery shopping was reported in the media just prior to the February 2007 NDPSC meeting.

“Methods are shockingly bad but you can see why they do those types of surveys to try and catch the profession out, and create a few headlines…” Academic participant

The February 2007 NDPSC meeting records reported a consumer email campaign directing consumers to the NDPSC Secretariat requesting that orlistat be removed from Appendix H and up-scheduled to prescription, with 36 emails received. Conversely, many submissions supported the pharmacist-only status of orlistat. However, one organisation took the opportunity to raise concern about the NDPSC's decision making process over the last three years noting the lack of practicing medical practitioners on the committee was a “contributory factor in the increasing down-scheduling of substances with serious adverse effects.” The NDPSC considered advertising increased pressure on pharmacists, potentially resulting in inappropriate orlistat supplies, so withdrew the right to consumer-advertise the medicine, but retained the pharmacist-only scheduling.

“…the consumer people jumped on them from a great height and it became a political thing rather than, than, you know anything that was based on evidence…” Pharmacy participant

“I guess the court case round [orlistat] really shook the NDPSC in terms of how they had made the original decision…. I don’t think they had inappropriately made a decision back then, but because the trigger for this ad incident was such a huge drama that, that they potentially felt they had to go and reverse that because otherwise they would have ongoing flack around it…” Pharmacy participant

Roche legally challenged the NDPSC decision, but the Federal Court upheld the advertising ban. One pharmacy participant suggested withdrawing advertising of orlistat while allowing “shonky products” to advertise was incongruous. A committee member reported on-going effects:

“…the experience of Roche when they got their weight loss medication down-scheduled and allowed to be advertised and they advertised in a way that really was, I think, recognised by the courts as an abuse of their allowance. It has further impeded a likelihood of a liberalisation of advertising.”

Source: National Drugs and Poisons Schedule Committee meeting records

NDPSC = National Drugs and Poisons Schedule Committee; BMI = Body Mass Index

Various participants disagreed with the sumatriptan rejection, and one reported that the sponsor would address the committee’s issues and then new ones would arise, as supported by meeting record analysis (Panel 5-2). Another participant noted the rarity of concerns the committee raised.

“…when you read the sumatriptan record of reasons here they’re just nonsensical and then I think the company just gives up” Industry participant

“I thought sumatriptan was the classic risk-averse decision making…. it’s not like you’re supplying hundreds of tablets, you know, it’s something that’s beneficial, used quickly and it’s only for a stat dose scenario, and it’s a bit strange.” Pharmacy participant

28 Complementary remedies with a lower level of proof of efficacy
Panel 5-2 Sumatriptan case study: timeline and meeting record analysis

June 2005[479]
First NDPSC sumatriptan consideration with a negative evaluation report
Recategorisation denied citing clinical diagnosis needed, no validated diagnostic tool, safety profile (including high prevalence of cardiovascular disease), and need for medical supervision of therapy

June 2006[477]
Reapplication with updated safety data, updated validated Migraine Questionnaire, and revised education program developed with professional pharmacy bodies. Negative evaluation report
Decision deferred requesting expert advice on: appropriateness of pharmacist-only triptans, potential to mask meningitis or subarachnoid haemorrhage, and the proposed Migraine Questionnaire

October 2006[104]
Sponsor confirmed consultation with local experts on the switch program and questionnaire, and provided expert panel meeting minutes, and updated tools. No further NDPSC evaluation report
Two independent experts were unconcerned about sumatriptan masking subarachnoid haemorrhage and meningitis, but noted cardiovascular risks, and medication overuse headache
Decision deferred pending information on serotonin syndrome if used with serotonergic antidepressants

February 2007[380]
No cases of triptan-associated serotonin syndrome reported to Adverse Drug Reactions Advisory committee
Some negative submissions (e.g. criticism of pharmacists)
Reclassification rejected. The NDPSC considered the medical management and safety profile concerns were not insurmountable, but emergency supply provisions meant there was no public health need to reclassify

The meeting records show that while the committee criticised the questionnaire for not reflecting current guidelines, the meeting discussion itself diverged significantly from National Prescribing Service (NPS) guidelines,[480] in wanting the questionnaire to include non-pharmacological treatment first-line, and considering that prophylaxis might be warranted for someone suffering one or two migraines per month. Despite expert panel reports, experts involved in developing the Migraine Questionnaire and Protocol, and information from independent experts, none of whom highlighted serious serotonin syndrome, the committee sought advice about serious serotonin syndrome. Another time the committee expressed a “much greater concern” about potential for pain relief from sumatriptan in subarachnoid haemorrhage or meningitis than about the overuse of sumatriptan,[477] a well-established issue later raised by experts as meriting consideration.[104]

A participant who was at the meeting reported:

“[The committee] took the view that people with severe headache would go to the pharmacy and would buy sumatriptan, or pharmacists would want to sell them sumatriptan, so we’re in a trust question... and pharmacy were, they were probably a bit equivocal around that issue of how willing were they as a profession to take on that risk, I suspect... and then, a complete lack of trust in the Australian consumer behaving reasonably.”

Source: National Drugs and Poisons Schedule Committee meeting records
NDPSC = National Drugs and Poisons Committee

At the final meeting considering sumatriptan (February 2007), the NDPSC also reversed a mometasone reclassification decision, reversed advertising approval for orlistat, and dermal moderate potency corticosteroids, and seriously considered returning orlistat to prescription.[380] This unusual cluster of negative decisions supports industry’s contention that the NDPSC was becoming

29 The NPS guidelines do not recommend non-pharmacological therapy first-line, and suggest considering prophylaxis for three or more severe migraines per month
increasingly risk averse. Inappropriate advertising of orlistat and poor pharmacy performance in orlistat mystery shopping discussed at this meeting probably affected the NDPSC’s risk tolerance.

One participant suggested the phenacetin example in the 1970s[^30] contributed to risk aversion. While a committee member and an academic were unaware of this affecting reclassification decisions, it arose in 2003 when the NDPSC considered combination analgesics.[481]

Committees’ perceptions of pharmacist behaviour were an important consideration (see 5.6.5). Some committee participants believed that the NDPSC’s 20 plus membership was too large. The medical participant considered “the more medical input [in the committee] the better”, expressing disappointment with outcomes such as chloramphenicol. This was echoed in the orlistat meeting records (Panel 5-1).

Some participants distrusted industry. Three participants suggested conflict between the NDPSC and industry, feeling that industry push caused a pushback from the committee (some thought this pushback was appropriate). One participant speculated the conflict may lead to the industry voice being disregarded in NDPSC meetings (suggesting a further difficulty with representative members).

Participants appeared to divide into three groups: those who particularly criticised the committee’s ‘risk averseness’ (generally industry participants); those who considered the committee too risk-averse at least sometimes (some pharmacy participants and some committee members); and those who articulated their own conservatism around reclassification or that the committee needed to avoid risk. The latter group included some committee members, regulators, a consumer participant and a medical participant.

“… it’s better..., in this area of healthcare, to tread warily. And in fact the resistance of those State jurisdictions to that change is almost the counterbalance to the arguments made by the sponsors for the change… to move into a more liberal environment.” Committee member

“...my own sense is if something is a prescription medicine it’s a prescription-only medicine for a reason.” Committee member

The second quotation is surprising. Medicines are almost always classified as prescription when first registered because there is little experience with them. Over time a medicine may simply remain prescription because reclassification has not been applied for.

Several industry and pharmacy organisation participants expressed frustration at pre-meeting gazette notices which excluded the nature of the reclassification proposed, making submissions difficult.

Interviews and meeting records suggested committee and regulator rigidity. For example, meeting records frequently mentioned Section 52E of the Therapeutic Goods Act, which outlines

[^30]: Combination analgesics containing phenacetin caused kidney damage, particularly in Queensland women owing to a culture of frequent usage.
considerations in scheduling and advertising decisions for pharmacist-only medicines\(^\text{31}\). Section 52E does not mention pharmacists’ training or cost, limiting the consideration.

“… it’s not a consideration of the committee because cost is not one of the categories under section 52E…” Committee participant

Further rigidity occurred with oseltamivir, when the committee decided Australia and NZ were harmonised because oseltamivir was a prescription medicine in both.[104] This saved the committee considering a medicine they appeared not to want to reclassify.

5.6.3. Schedules

Participants agreed that the scheduling system enabled reclassification. Some participants noted that the pharmacist-only category could be professionally satisfying:

“I think the more proactive amongst the profession would embrace that and see it as our category…. the more we get in our pharmacist-only category… that’s better for the profession to demonstrate our expertise and drug knowledge…” Academic participant

Despite this enthusiasm, the schedules reportedly work imperfectly. Participants reported that some pharmacists do not want the responsibility, and worried about achieving best practice in a busy pharmacy. For industry, pharmacist-only medicines often cannot be advertised, and pharmacists can be conservative with them or can switch consumers to-house brands, and advertising is often not allowed (see 5.6.8). Although work on improving pharmacist performance has occurred, participants agreed some need to improve further (5.6.5). Lack of consumer understanding of schedules and the pharmacists’ role with those schedules adds to the difficulties.

Two pharmacy and one industry participant mentioned a proposed class of pharmacist-only medicines, S3 notifiable, for which the purchase would be recorded on an accessible national database (as for Project STOP). They suggested this sub-schedule could enable reclassifications with strict supply criteria, such as statins, addressing a concern that pharmacovigilance and data on usage are lost post-reclassification.

5.6.4. Pharmaceutical companies

Pharmaceutical companies’ interest in submitting applications strongly influences Australian reclassification. Companies consider many factors in contemplating potential reclassifications (Figure 5-4), some of which are interlinked (not shown). Negative factors (red oval) overshadow positive

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\(^{31}\) Section 52E requires consideration of: risks and benefits; indications and extent of use; toxicity; dosage, formulation, labelling, packaging and presentation; abuse potential; any other matters that the Secretary considers necessary to protect public health. (Therapeutic Goods Act 1989, Australia, updated 28 Mar 2012)
characteristics (green oval), and factors working either way (orange oval). Companies consider financial viability and other factors (e.g. do they have OTC infrastructure).

“...a lot of companies don’t have an OTC arm. So, it costs a lot of money to market an OTC product properly, very different from an Rx product, you have to have almost a separate field force, you have to have your advertising, promotion...” Industry participant

Even with OTC infrastructure a company may not reclassify a particular medicine, because of potential doctor backlash, global strategy, or safety concerns. One participant could not interest sponsors in reclassifying oral contraceptives. Chloramphenicol was not pursued by a multi-national (with an OTC arm) that marketed it on prescription: “it was all too hard at that time I think”.

Financial viability includes effects on prescription and global business (see 5.5.6), and likelihood of success which reflected concerns about the committee and process (see 5.6.2).

“... [companies will consider] which permutation of the prescription or Rx to consumer or a combination of both, gives the best return.... [and] other strategic considerations... and ... other things like competency to deliver switch products...” Industry participant

Frustrations around the committee and process, lack of market exclusivity, advertising restrictions and small market arose strongly from industry participants.

“I don’t necessarily mind a high hurdle for regulatory approval, as long as I know it’s consistent and I know the process is transparent... I think when you get a process which is opaque, and would seem to be altered by whatever reason, political reason or whatever else, that’s when it does become a bit dispiriting to companies...” Industry participant

Industry believes market exclusivity would enable reclassifications because of the time and costs taken to establish a reclassified medicine, but has not gained traction. Without exclusivity, transparency and inability to advertise cause applicants difficulty. Published meeting records provide insight into decisions, but also inform competitors, enabling generic entry, or “me-too” applications.

“...if you’ve got a product that is off patent, in effect the company can do all the hard yards of advertising the product and the pharmacist then has the ability to switch them to a house-brand... in store to all the patients who present.” Industry participant

Sponsor applications received some criticism. One participant reported excessively large applications, and an application that omitted important safety information. Some participants (and minutes) reported that companies did not always demonstrate public benefit in their application (Panel 5-2).
Figure 5-4 Factors affecting company decisions to reclassify medicines from prescription to non-prescription in Australia
Pharmacy factors help and hinder companies. Industry participants considered pharmacy practice was good and supported the current scheduling, but pharmacy staff supplying house-brands and not supporting newly reclassified products affected viability and future reclassifications (see 5.6.5). Industry participants reported that early feedback from pharmacy groups provided benefit. However, stakeholders were not working together on reclassification. Industry most desired this, and pharmacy organisations are interested, but the regulator seems uninterested, and the medical representative could not think of reclassifications their organisation had been supportive of.

“There’s no sense of stakeholder collaboration by any of the pharmacy bodies, the medical bodies, … the department, in setting any medicines access agenda.” Industry participant

During the early 2000s, enablers for companies included: the pharmacist-only category; progressive committee members; the ability to meet committee members to get feedback; and that advertising was often approved. The latter three of these four factors have changed.

5.6.5. Pharmacy

This section considers participants’ views of pharmacy, pharmacists and pharmacy organisations’ influences on Australian reclassification.

Pharmacy benefits of reclassification received little commentary. Several participants observed that reclassification benefits include reducing reliance on dispensing, and increasing professionalism (but concern by some that the medicines will move out into general sales).

“I’m not too sure that there’s a great extra benefit for the pharmacist or the pharmacy… I think it’s just a public benefit, that’s all. In some cases it is more beneficial for the pharmacist to have more products available to recommend, and ultimately financial benefit…” Pharmacy participant

Pharmacy was a ubiquitous factor in interviews, both aiding and hindering reclassification (Figure 5-5 and Figure 5-6). Comments about insufficient care in selling medicines, and excessive conservatism in supplying reclassified medicines were reported, sometimes by the same participants. A very conservative approach by pharmacy may give committee members confidence in reclassification, but, reduces financial viability for sponsors (Figure 5-5), particularly without advertising.

“…if you don’t prepare the profession, the profession clinically is very, very conservative, they’re scared, so they’re not going to touch anything like that.” Academic participant

"...certainly the older brigade within the profession is very conservative about their role there. Many of them still see themselves primarily on the supply side rather than the prescribing side.” Pharmacy participant
Figure 5-5 Effects of pharmacy behaviour on reclassification (coding red for barrier and green for enabler) in Australia
Chapter 5

108

Lack of confidence with new products
Companies focused on sell-in not behaviour change
Busy pharmacies
New discount model created price competition
Prescriptions biggest focus
One man pharmacies
Lack of privacy
Traditional model of pharmacy
Can’t diagnose, do pathologies
Supplying medicine too cheap -> inadequate time allocated
Pharmacy assistants not trained
No records of most OTC supplies
Patient can visit multiple pharmacies
Multiple pharmacists in one pharmacy (lack continuity)
Pharmacy organisations not focusing on behaviour change

Supply house brands
Reclassification not viable
Low support of newly reclassified S3 medicines
Advertising causing inappropriate demand
Companies do/don’t submit applications for reclassifications
Negative Appendix H decisions
Positive Appendix H decisions
Negative reclassification decisions
Positive reclassification decisions

Pharmacist behaviour

Negative effects
Companies focused on sell-in not behaviour change
Lack of confidence with new products
Pharmacy organisations not focusing on behaviour change
New discount model created price competition
Supplying medicine too cheap -> inadequate time allocated
Traditional model of pharmacy
One man pharmacies
Prescriptions biggest focus
Can’t diagnose, do pathologies
Pharmacy assistants not trained
Lack of privacy
No records of most OTC supplies
Busy pharmacies
Patient can visit multiple pharmacies
Multiple pharmacists in one pharmacy (lack continuity)

Positive effects
Monitoring system
Pharmacists cautious
4 year university degree
Continuing education
Protocols
Quality programme
Increasing professionalism
Mystery shopper programme
Remuneration of cognitive services
Pharmacy organisations proactive with materials
More pharmacies with privacy

Case reports
Mystery shopping
Other research
Anecdote/personal experience
Perception

Committee

Media and politics

Figure 5-6 Factors contributing to pharmacist behaviour in Australia and effects of that behaviour on reclassification
Many (particularly pharmacy) participants were positive about pharmacy overall, considering that pharmacy was becoming more professionally focussed, and that the committee’s faith in pharmacy enabled reclassifications. Several participants (including a non-pharmacy committee member) highlighted the QCPP programme, which improves questions asked, and Project STOP.

“I think there’s lots of enablers in Australia, despite the view that we don’t practise well, I think there’s a view that we can change the profession. It’s relatively small, …we’ve got a good monitoring system, pseudo patient system, … the profession wants it, the universities have all incorporated really good OTC courses in there…” Academic participant

“We know that people go to [pharmacists] and they seek advice and they trust them… and we pay them for it. So as far as I’m concerned that’s got to be a good thing for the quality of the medicines. So I think that we should absolutely value that and make sure it works properly.” Consumer participant

“…Australia, by and large, is one of the more advanced countries in the world for practice of pharmacy.” Industry participant

Participants reported that protocols and education for reclassified pharmacist-only medicines are commonly used, receive strong pharmacist support and enable reclassifications. However, many participants reported the committee’s conservative stance arose partly from under-confidence that pharmacists (and pharmacy staff) would consistently ask appropriate questions and refuse inappropriate requests for non-prescription medicines.

“… there’s quite a level of control in pharmacy in Australia that doesn’t really exist elsewhere, and yet with some of these NDPSC decisions are seemingly almost a lack of confidence in pharmacy being able to appropriately discharge their responsibility…” Industry participant

“…their perception of the commitment of the pharmacy profession to… the management of schedule 3 and schedule 2, has a huge bearing on decisions of further rescheduling.” Committee member

“Unfortunately, in reality, it’s not always the pharmacist that you get to speak to, it’s often the 16 year old pharmacy assistant and that really annoys me.” Committee member

Perceived poor pharmacy behaviour reportedly may encourage the committee to approve pharmacy-only to general sales down-scheduling. Some committee members worried discounting affected the pharmacist’s consultation time, others reportedly seemed to believe that the retail model encourages pharmacists to “just sort of go for the dollar”.

Committee members’ perceptions were reportedly influenced by personal experiences in pharmacies, by the jurisdictional members’ awareness (through their work) of inappropriate pharmacist behaviour, by mystery shopping, and by media and political pressure. However, the fast reclassification of
chloramphenicol and retaining pharmacist-only scheduling of inhaled salbutamol and terbutaline shows confidence in pharmacy, suggesting committee perceptions can vary.

A key pharmacy participant was unaware of complaints against pharmacists or pharmacies regarding negligence in supplying non-prescription medicines. Moreover, most participants (including those who worried about pharmacy behaviour) considered that a pharmacist-only category was enabling, suggesting some confidence in the pharmacist's role. Participants considered changing practices, particularly pharmacists moving out from behind the dispensary enabled reclassification. One relatively conservative committee member believed down-scheduling would increase if the committee saw pharmacy being serious about reclassified medicines, but change is difficult:

“…practice change is quite a complex process…. I don't think the profession has ever been prepared well enough to deal with S3... most people’s views were OK, we can actually give them education and magically they’re going to go back to their pharmacy tomorrow and apply the legislation.” Academic participant

Stakeholders’ perceptions of pharmacy behaviour affect their reclassification submissions. Pharmacists’ behaviour was most criticised by the medical representative who espoused that pharmacists cannot examine a patient, take a history, order pathologies or diagnose; pharmacies lacked privacy; and unrecorded supplies affect pharmacovigilance. This participant referred to a pharmacist survey reporting pharmacists believed that they were not trained to diagnose, and expressed concern about insufficient pharmacists’ advice around contraception and sexually transmitted infections with the EHC, and adverse events.

“I'm just not sure the pharmacist says by the way you know you’ve got a one in a million chance of having acute fulminant liver failure from [fluconazole].” Medical participant

While noting that training pharmacists would help, he still considered that chloramphenicol should not have reclassified, and that vaginal antifungals and the EHC should be prescription. Somewhat contrarily, he volunteered that community pharmacists were generally “quite conservative” and that he often received referrals from pharmacists who considered a problem outside their capabilities.

Pharmacy organisations featured prominently in interviews, but were not proactive in reclassification. Pharmacy organisations could influence committee decisions by supporting or opposing reclassification, and (commonly) opposing advertising approval. The Pharmacy Guild and PSA were reportedly strongly opposed to pharmacy-only to unscheduled down-scheduling, and the Pharmacy Guild reportedly affected company distribution decisions (e.g. NRT see 5.5.5).

“… when we switched Nurofen into grocery…. The plethora of documentation we got back from many pharmacists with rude comments on and all sorts … ‘we’re never stocking your products again’, etc.... because they were going to lose money .... [Pharmacy Guild person]... said ‘I will die in a ditch before Nurofen ever finishes up in a supermarket. We will fight it tooth and nail.’ He said that many times in public.” Industry participant
5.6.6. Consumers

Consumer access (savings, convenience and efficiency) was typically the main benefit espoused by participants. Many participants believed without consumer benefit, reclassification should not happen. Participants diverged in views about doctor access for consumers (5.6.7).

“Well, there is also the interest of the patient in all of that too. Just in terms of forcing them to go back to the doctors for medication when it may not be necessary to go through that process. I mean, that’s a cost to somebody in the scheme of things.” Pharmacy participant

The consumer participant considered consumer input important, including through the NDPSC consumer representative. Few others commented on the consumer representative’s role, possibly because it was not considered an important barrier or enabler, the main thrust of the interview. However, many were aware of the orlistat advertising complaint driven by Choice (a consumer group), and some reported a strong government influence from the Consumer’s Association.

Post-reclassification cost arose, including the medical participant and a committee member worrying about post-reclassification loss of prescription funding, incorrectly believing this typically occurred.

“…I do worry that a lot of things if they’re pushed over the counter, people can’t afford them. And the other thing is… you may actually transfer prescribing to more expensive things…” Committee member

The high non-concessional prescription copayment received surprisingly little mention as an enabler. Participants noted that some people may pay for the convenience of OTC, but others may not, e.g. pensioners with time for doctor consultations and a low copayment, and others “want it to count towards their safety net.”

Three pharmacy participants observed that consumers lacked understanding of scheduling and the pharmacist’s role.

“They see something advertised or have something recommended to them… and they say can I have some of that, and then they get the third degree from the pharmacist as to whether it’s appropriate or not. They have no understanding that this is the way it should happen, and they should only get it if in the view of the pharmacist it is the best, most appropriate drug…” Pharmacy participant

A minority of participants worried about consumers’ ability to self-manage, but others considered many consumers could manage minor ailments or medicines. The medical participant worried about misdiagnosis but conceded: “we expect parents to take on their role – we don’t want to see every single minor condition, so there is certainly a level of medical knowledge that everyone carries…” The meeting records suggest under-confidence in consumers.
“…60% of people in this country don’t have good health literacy for instance…. certainly there are sections of the community who can self-medicate, but that doesn’t apply to everybody.” Consumer participant

“I worry about people diagnosing things for themselves, not seeking medical attention when they should, or… not necessarily being in the best position to know when they should or shouldn’t be taking something.” Committee member

5.6.7. Medical profession

Participants revealed that the medical profession opposed many reclassifications, with suggestions that fee for service funding could fuel negativity. Although the medical participant supported the two pharmacy schedules and believed in the main there’s a fairly high level of confidence in the pharmacist…”, he raised multiple concerns about pharmacy (see 5.6.5).

“…diagnosis is something that is in the lap of the doctors – pharmacists are not trained in diagnosis…” Medical participant

Participants disagreed on doctor access. A pharmacy participant reported significant access difficulties, and an academic participant considered that people with an eye infection would not want to wait a day and a half to see the doctor. However, the medical participant, while acknowledging a doctor-shortage and long waits for regular appointments in some places, considered doctors were accessible for urgent conditions the same day or the next day, and suggested access concerns be managed by increasing medical school output and using nurses collaborating with doctors.

“…the emergency contraception is available pharmacy-only32 in Australia and the AMA was dead against that as well. The argument at the time was that people simply can’t get to a doctor to be prescribed the product and I disagree with that entirely… there’s almost no State or place in Australia you can’t get access to a doctor seven days a week.” Medical participant

One participant observed industry wanted to keep doctors onside, citing this reason for companies not pursuing oral contraceptive reclassifications.

5.6.8. Advertising

Advertising to consumers commonly arose in interviews. Most participants acknowledged consumers needed awareness of reclassifications, but two conflicting viewpoints emerged: that advertising should be permitted for more pharmacist-only medicines; and that such advertising should be minimised. Pharmacy participants fell into both camps. Industry wanted more advertising to inform consumers and ensure financial viability. Some committee members articulated concerns about inappropriate pressure on pharmacists causing overuse, and distrusted industry to advertise

32 The EHC is pharmacist-only in Australia
responsibly (particularly given orlistat, Panel 5-1), a fact shared by the medical participant. The consumer participant had no view on advertising when asked.

“Having down-scheduled the medicine to offer that therapeutic option but not telling the public that it’s available does seem to be a stupid outcome.” Committee member

Pharmacy organisations reportedly typically opposed advertising. However, one pharmacy participant who advocated advertising noted: “if the pharmacist fulfils their full professional responsibility in its sale then there shouldn’t be a problem.” Pharmacy participants supporting advertising wanted informative advertising, advising to “ask your pharmacist about it”. Other participants, including committee members, preferred an educational rather than sensationalist approach.

The committee was considered to have become more conservative in advertising considerations, as supported by minutes. No pharmacist-only has been approved for Appendix H since the orlistat reversal (Figure 5-2, Panel 5-1).

Industry participants expressed frustration, and one considered an inability to advertise was not evidence-based. They considered pharmacist-only not advertiseable a “commercial graveyard”, particularly without market exclusivity, (4.7.4), and with pharmacy conservatism, (4.7.5), and house brand recommendations. Rejected Appendix H requests probably hindered further reclassification.

“Boots never sold any Nurofen until we got it advertiseable as a S3.” Industry participant

“I know that’s where industry’s coming from…. coming from the professional side, we don’t really consider the graveyard issue to be an issue.” Pharmacy participant

5.7. How could reclassification be enabled in Australia?

Participants suggested many enablers. The key enablers from industry were: government and/or regulator support for reclassification; lower risk-averseness from the committee and regulator (including advertising approvals); stakeholder communication and working together; and market exclusivity (preferably for three years).

“… if there could be some true discussion and debate amongst the various stakeholder groups, that’s medical, that’s pharmacy, that’s consumer groups, on what is appropriate access to medicines, and that if government… can drive that sort of regulatory change then that would be tremendous.” Industry participant

Industry wanted regulator or evaluator meetings.

“…it’s not a common thing to be able to meet with the evaluator. We would certainly welcome that, and even at the stage of pre-submission or almost pre-development sort of planning or whatever as well.” Industry participant
Several participants talked about improving pharmacist availability for supplying non-prescription medicines. The consumer’s understanding of the role of pharmacy could improve, and the pharmacy organisations saw they could help with that.

The key change desired by some (particularly industry) participants is “a different committee with relevant expertise”. The committee needs to be evidence-based, and less political.

“...there is a lot of hope pinned on the committee splitting and it becoming an expert committee that we will get better outcomes...” Industry participant

“But my sense is that the Chair would make a huge difference.... If you have someone who is flexible and open, but inclusive as well, that can make a huge difference.” Industry participant

An academic participant wanted industry and pharmacy organisations to work on practice change to help overcome pharmacist conservatism (and potentially overcome the need for advertising).

5.8. Discussion

Australian reclassification was progressive from 2000 to about 2005, then conservative since 2006. Multiple reasons appear to be behind the change. The biggest effects seem to be increasing risk averseness from the committee and regulator, partly because of changes in individuals involved, events, and politics. This risk aversion sits alongside an apparent (and probably related) committee distrust of pharmacy, industry and consumers. While pharmacy has been lifting its standards, further change may help pharmacy embrace the professional opportunity of reclassified medicines.

ASMI recently opined that Australia is extremely risk averse in reclassification,[77, 453] but others found Australia had as many (in 2007)[50] or more (in 2003)[31] medicines available without prescription than the UK (considered the world leader).[24, 333] This difference probably reflects both timing and methods. The ASMI opinion was likely based on current events, while WSMI table research is historical, with limitations (see 2.3.2.12). I found risk aversion, but it did not seem extreme compared with other countries (see Chapter 11). Australia is still reclassifying some medicines, with rejections typically medicines not widely reclassified elsewhere. Sumatriptan was the only rejection that had recently reclassified in several countries.[123]

The view of ‘extreme’ risk aversion may arise from advertising decisions, up-scheduling decisions, or some apparently ‘emotive’ decisions, or be relative to earlier progressiveness. Rejection of (according to some participants) reasonable reclassifications or advertising, or reasons provided for rejections may have contributed to the view. The committee negativity to advertising apparently arises from a single campaign and stakeholder concerns. Perhaps the committee and stakeholders are correct, that advertising causes problematic behaviour, but many recently reclassified medicines have low sales elsewhere despite advertising, e.g. sumatriptan in NZ,[436] and simvastatin,[115] and omeprazole in the UK.[96] Harm from orlistat advertising seems unlikely (see meso-level, 6.5.2.1). Advertising
changes may be needed to regain committee (and stakeholder) confidence. Confidence in pharmacy and consumers probably also affect perceptions about advertising causing inappropriate behaviour.

Ideally a second interview would further explore the medical viewpoint, but the study breadth precluded this. The Australian Medical Association has publicly opposed many reclassifications, and stated that pharmacists are not trained to diagnose, and that general practice nurses should treat minor ailments instead.[482] Thus the medical participant reflected a typical view for an Australian medical organisation. Duckett recently opined that Australia had doctor-centred care with a paternalistic focus,[456] and medical practitioner-pharmacy tension was reported recently in Australia.[301] Some medical concerns about Australian pharmacy were not raised by others. Given these concerns came from one participant with a possible bias, are these concerns valid for Australian pharmacies in the 21st century? An EHC mystery shopping study in Sydney found inadequate privacy in about 10% of pharmacies,[307] and some pharmacists reported privacy difficulties for counselling.[464] Emmerton found 0.8% of observed pharmacy purchases had privacy breaches.[483] Thus, some privacy issues remain, but are far from widespread.

The medical participant reported pharmacists believed they were untrained in diagnosis, probably based on an Australian survey about pharmacist prescribing,[484] not non-prescription supplies. Other participants disagreed and Australian research showed high patient satisfaction with community pharmacists diagnosing minor skin conditions.[485] However, pharmacist research using vignettes found concerning under-referral in one scenario,[293] suggesting room for improvement exists.

The committee’s distrust of pharmacy, consumers and industry appeared to develop over time (for comparison see meso- and macro-level chapters 6.5, Chapter 11). Research shows variable pharmacy adherence to medicine supply protocols, in mystery shopping and observation in Australia.[76, 230, 285, 294, 297, 307, 486-488] Mystery shopping of (pharmacist-only) salbutamol inhaler requests found sub-one minute visits, often apparently without pharmacist involvement.[285] However, many pharmacy staff members provide good care, e.g. researchers rated over a third of pharmacies excellent and over 40% satisfactory by the third QCPP mystery shopping visit and feedback.[489] An insomnia mystery shop showed 42% of pharmacists asked about sleep hygiene factors, 67% looked for insomnia causes, and 24% gave sleep hygiene advice.[487] This compares favourably with Australian research that found GPs prescribed medicines (usually hypnotics) in 95% of insomnia consultations, providing advice in under 20%.[367] An EHC mystery shop found 97% of pharmacists provided advice,[307] whereas a GP self-report study found 48% of their EHC consultations included counselling, advice or education.[490] Possibly the studies differed in what construed advice, and neither study provides the quality or extent of advice. However, half of the GP consultations included an STI test, versus STI counselling in only 9% of pharmacy EHC supplies. These comparisons, albeit with different methods, lend weight to participants’ observations that GPs do not provide perfect care either. Research does not support concerns about consultation quality in busy pharmacies.[285, 487]
Pharmacist-only supplies require both pharmacist and consumer responsibilities. Pharmacists may judge that the well-versed person mystery shopping them does not need much help, and provide different care to someone who seems more uncertain or fits a different risk profile. Schneider, et al. found one mystery shopper had different results to others, supporting this idea. Little Australian research examines consumer outcomes following non-prescription versus prescription supply. Douglass, et al. found that asthma outcomes were not worse with non-prescription versus prescription supply. Further research on consumer outcomes for reclassified medicines is merited.

QCPP may advance pharmacy, but surprisingly, as QCPP has improved behaviour the committee has seemingly distrusted pharmacy more, supporting the idea of committee member changes causing conservatism not poor pharmacy performance. The orlistat mystery shopping in 2007 may have outweighed the QCPP gains. Alternatively, perhaps the multiple mystery shopping studies and reviews following the Galbally report highlighted variability to committee members. The committee’s conservative shift may be appropriate, given pharmacy variability. However, no innovative reclassifications from the progressive 2000-2006 period were reversed, suggesting risk has not been excessive from these reclassifications. Even with orlistat, public harm from advertising and variable pharmacy behaviour seems unlikely (see 6.5.2.1).

Like pharmacy participants, research showed community pharmacists worried about advertising, but supported educative advertising. These pharmacists also raised concerns around discounting and resulting service levels. Banning advertising of pharmacist-only medicines deflects from concern about inadequate pharmacist performance. Advertising probably causes direct product (product name) requests, which reduce pharmacy questioning. However, direct product requests come from various sources (including previous usage or word of mouth). Hence, improving the pharmacy consultation, in pharmacist behaviour and consumers volunteering information and asking about medicine suitability may help; appropriate advertising may assist this.

Companies have not sought Australian reclassification in the period studied for some medicines reclassified in the UK e.g. simvastatin, mebeverine, domperidone, azithromycin, and chloramphenicol, suggesting low commercial opportunity. Market exclusivity and advertising of pharmacist-only medicines may help, but other important barriers exist. Despite advertising permission and no generic competitors, tranexamic acid was never launched (possibly because of a company merger) and dermal clobetasone took years to be marketed.

5.8.1. The way forward for Australia

Many possible enablers for reclassification exist (Panel 5-3). Changing to the ACMS has partly addressed many concerns participants voiced. The ACMS Chair (in 2012) is independent of the regulator and jurisdictions. The committee is smaller, includes medical member(s), and workload should have reduced, with chemicals managed separately. All votes count, but jurisdictional members with an open-ended term remain, and the ACMS Chair may not necessarily be independent, so some concerning aspects remain. Additionally, the advisory committee’s decisions may be
override. Further research is warranted to ascertain outcomes of the changes. So far decisions do not suggest risk tolerance has altered, particularly in advertising (Figure 5-2, Figure 5-3).

Panel 5-3 Potential enablers for Australia

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<th>Process</th>
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<tr>
<td>Implement market exclusivity (for 2-3 years)</td>
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<td>Allow company to meet with relevant regulatory staff prior to application submission</td>
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<td>Allow company to attend discussion at ACMS meeting, and possibly present to the meeting</td>
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<td>Collect data on consumer outcomes and advertising to inform the committee</td>
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<td>Improve advertising to regain confidence</td>
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<td>Ensure discussion is evidence-based (and committee members have evidence-based decision skills)</td>
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<td>Move to a pragmatic, flexible approach, possibly including techniques such as the S3 notifiable</td>
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<td>Reduce influence of politics</td>
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<td>Encourage non-industry reclassifications</td>
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<td>Add reclassification to the government agenda</td>
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<td>Educate consumers about non-prescription medicines (including scheduling)</td>
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<td>Move from doctor-centred to patient-centred care</td>
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<td>Research benefits, risks and appropriate management strategies</td>
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<td>Continue with pharmacist-only and pharmacy-only schedules</td>
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<td>Improve pharmacist and pharmacy assistant behaviour further</td>
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<td>Encourage pharmacy enthusiasm for reclassifications</td>
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<th>Companies</th>
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<tr>
<td>More informative and responsible advertising</td>
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<td>Work with other stakeholders, pharmacy groups, consumer groups, regulator</td>
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<td>Collect and distribute evidence of usage and safety</td>
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<td>Consider supporting behaviour change in pharmacy</td>
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</table>

5.9. Summary

Australia has many positive features, a pharmacist-only schedule, highly skilled pharmacists, mandated training for pharmacy assistants, industry attempting to drive reclassification, independent evaluation, and interested pharmacy organisations. While these are currently outweighed by negative factors, the new ACMS may help address these. Other barriers may be addressed by increasing government interest in patient-centred care, stakeholders working together, and further pharmacy improvements (and evidence of these improvements).
Chapter 6. Meso-level: NZ compared with Australia

6.1. Introduction

NZ and Australia have been harmonising medicines schedules for over a decade. No other countries are known to be doing this. The two countries have similar histories, societies, economies, health systems and medicines schedules, and they have both appeared conservative and progressive in reclassification over the period studied. This chapter compares how and why NZ and Australia have varied in their experience of reclassification since 2000 for reasons including committee variation and regional influences, and considers the effect of TTH.

6.2. Background

Australia has a larger population and land mass, and higher standard of living and economic growth than NZ.[376] However both countries have ageing populations, mostly of European ancestry (and a minority of indigenous people),[389, 458], well-developed welfare systems,[376] and are in the top five countries of the Human Development Index (2011).[388] Universal health coverage occurs in both countries, patients usually enrol with a GP,[14] and three non-prescription categories exist.[400, 461] Community pharmacies typically include dispensing and retail, and must be supervised by a pharmacist.[400] Pharmacist training and the ratio of community pharmacies to population are similar.

Panel 6-1 Trans-Tasman Harmonisation principles

1. For both countries there should be:
   - equivalent scheduling for drugs and poisons
   - equivalent general exemptions from scheduling
   - a common set of definitions and scheduling criteria and guidelines (not yet occurred)
   - consistent interpretation of scheduling criteria
   - common nomenclature for drugs and poisons
   - within the schedules, common descriptions for generic drug and poison classes etc.
   - harmonisation of labelling and packaging
   - harmonisation of safety directions, warning statements and first-aid instructions

2. Where differences in scheduling of a drug or poison currently exist between NZ and Australia, the following principles should apply:
   - the classification should be reassessed using the common set of definitions and scheduling criteria with a view to achieving a common outcome
   - the underlying principle is to harmonise on the less restrictive schedule while giving due consideration to public health and safety issues and/or specific jurisdictional needs.

3. The process of harmonisation of drug and poisons scheduling should recognise the wider regulatory requirements of other agencies and any complexities should not be exacerbated by harmonisation of schedules.

Source: Medsafe website, accessed 28 May 2012
TTH started in the mid-1990s with both countries attempting to harmonise medicines scheduling to the lowest schedule while considering public health, safety and/or jurisdictional needs (Panel 6-1).[136, 375, 408] A joint medicines regulatory agency is expected effective from 2016.[137]

Table 6-1 compares the committees used for reclassification in Australia and NZ. Both now use advisory committees.

<table>
<thead>
<tr>
<th>Factor</th>
<th>NZ</th>
<th>Australia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advisory or decision-making?</td>
<td>MCC: advisory committee [401]</td>
<td>NDPSC: decision committee - jurisdictional majority vote decides ACMS: advisory committee [147]</td>
</tr>
<tr>
<td>Committee constitution</td>
<td>Two nominees from Pharmaceutical Society, two from the NZ Medical Association, and two from the Ministry of Health[400]</td>
<td>NDPSC: jurisdictional members represented each State, two territories, and NZ[465, 466] Expert members(^{33}) and representative members included a regulator nominee, and industry, pharmacy and consumer representatives. ACMS:[469] Nominated members (one from each State and from two Territories) and up to six appointed members. Members need expertise in specified fields(^{34}).</td>
</tr>
<tr>
<td>Chair</td>
<td>Ministry of Health member[400]</td>
<td>NDPSC: Commonwealth officer[466] (normally regulator member) ACMS: Appointed from the Committee by the Minister of Health[469]</td>
</tr>
<tr>
<td>Independent evaluation?</td>
<td>Rare since 2000. Available on Medsafe website with agenda</td>
<td>Independent evaluation of company applications provided to committee and applicant. Applicant can respond before the meeting. Summarised in the meeting records</td>
</tr>
</tbody>
</table>

MCC = Medicines Classification Committee  
NDPSC = National Drugs and Poisons Scheduling Committee  
ACMS = Advisory Committee on Medicines Scheduling

### 6.3. Data Sources

The data sources for this chapter were qualitative interviews and document analysis (3.2.9, 3.2.11). Participants were located in NZ (n=10), Australia (n=15), and overseas (n=4, including two with Australian experience). Several knew both markets well: two industry participants; an academic; and a participant with experience of the NDPSC and MCC.

### 6.4. Reclassifications in NZ and Australia 2000-2012

Most participants considered that the two countries differ little in current scheduling, but some considered the attitude to scheduling varies, with Australia progressive in the early 2000s but becoming increasingly risk averse and NZ seemingly conservative then progressive.

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\(^{33}\) The Minister may appoint experts: a medical practitioner expert in clinical pharmacology; an expert in veterinary medicine or pathology; an expert in toxicology; and/or an expert in occupational health

\(^{34}\) Appointed members need to have expertise in at least one of: regulation of scheduled medicines in Australia; toxicology or pharmacology; clinical pharmacology; pharmacy practice; medical practice; consumer health issues relating to the regulation of therapeutic goods; industry issues relating to the regulation of therapeutic goods. Membership should come from the widest possible range of fields.
Both countries varied in their progressiveness (Table 6-2, Figure 6-1, Figure 6-2). First Australia seemed more progressive (including two first-in-world reclassifications). Then from 2006 to 2012, NZ had more ‘innovative’ reclassifications than Australia, and four first-in-world reclassifications. This divergence arose because more applications were submitted in NZ than Australia, and NZ approved reclassifications that Australia rejected. Consideration solely under TTH resulted in one innovative reclassification approval in each country over the period studied (Table 6-2).

### Table 6-2 Innovative reclassifications in NZ and Australia 2000-2012

<table>
<thead>
<tr>
<th>Year of committee decision/recommendation</th>
<th>NZ</th>
<th>Australia</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td></td>
<td>Tranexamic acid (reversed 2007)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dermal alclometasone</td>
</tr>
<tr>
<td>2001</td>
<td>EHC</td>
<td>Nasal corticosteroid expansion of indications</td>
</tr>
<tr>
<td>2002</td>
<td>Nasal corticosteroid expansion of indications (TTH consideration)</td>
<td></td>
</tr>
<tr>
<td>2003</td>
<td></td>
<td>EHC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oral fluconazole</td>
</tr>
<tr>
<td>2004</td>
<td>Oral fluconazole</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Orlistat</td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>Dermal alclometasone</td>
<td>Pantoprazole (delayed implementation)</td>
</tr>
<tr>
<td>2006</td>
<td>Sumatriptan</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Oseltamivir</td>
<td></td>
</tr>
<tr>
<td>2007</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2008</td>
<td>Omeprazole</td>
<td></td>
</tr>
<tr>
<td>2009</td>
<td>Oral famciclovir</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ocular chloramphenicol</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nasal zolmitriptan</td>
<td></td>
</tr>
<tr>
<td>2010</td>
<td>Calcipotriol</td>
<td></td>
</tr>
<tr>
<td>2011</td>
<td>Vibrio cholera and enterotoxigenic Escherichia coli vaccine</td>
<td>Famciclovir single dose</td>
</tr>
<tr>
<td>2012</td>
<td>Influenza vaccination</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Trimethoprim</td>
<td></td>
</tr>
</tbody>
</table>

Source: Medicines Classification Meeting minutes and Therapeutic Goods Authority records

TTH = Trans-Tasman harmonisation; EHC = emergency hormonal contraceptive
Innovative reclassification approval rates trended upwards in NZ and downwards in Australia (Figure 6-2). The number of considerations varied in NZ. Committee proactivity, positive NZ decisions, and/or potential influence on Australia reportedly encouraged NZ applications in the middle period. Sponsor interest in NZ then dropped more than the figure suggests, with only three sponsor-driven innovative applications. The NZ market remained unchanged, and reclassification approvals and committee proactivity should have encouraged further applications. However, reclassifying in NZ to help Australia seemed to stop: Australia seemed little influenced by NZ for sumatriptan, oseltamivir and famciclovir, and no sponsors applied for innovative reclassifications in both countries in 2010-2012.

**Figure 6-2 Innovative reclassification considerations in NZ and Australia 2000-2011**

Source: Medicines Classification Meeting minutes and Therapeutic Goods Authority records

*Medicines were counted once per period, regardless of the numbers of considerations for each medicine.

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35 Famciclovir reclassified in Australia two years after NZ, suggesting little NZ influence
6.5. Reasons for trans-Tasman variation and similarities

This section explores the key reasons for trans-Tasman variation arising from interviews (Figure 6-3). More key barriers than enablers arose for Australia, while NZ was the reverse. I examine the TTH effect; the differing attitudes, individuals and politics; financial motivations; perceptions of pharmacy and culture. I also consider why applications differed in each country. The attitudes, individuals and politics arose strongly, and I therefore explore that most in the context of literature around decision-making, and triangulating participants’ views with meeting records.

6.5.1. Trans-Tasman Harmonisation

TTH arose often. One committee member considered that NZ’s influence made Australia less risk averse (particularly in early harmonisation) and more data-focused. Two others concurred that Australia seemed to be following NZ, particularly in down-scheduling to general sales. This caused angst in pharmacy organisations who considered NZ was excessively influential, and made it clear politically. A participant involved in TTH reported that NZ up-scheduled many fewer products than Australia down-scheduled in order to harmonise.

“I think by and large Trans-Tasman harmonisation is good. I think there have been some specific issues that have probably been difficult for Australia to rationalise, because in many cases it was felt that the tail, if you’ll excuse the expression, was wagging the dog a bit. … for some time it was felt well there were a few things where the schedule was lower in NZ and therefore that automatically applied.” Pharmacy participant

In 1994, the two countries had 200 scheduling differences; NZ was more restrictive in only 17 of these.[415] With the TTH intent to harmonise to the lowest schedule, it is unsurprising that NZ appeared to have fewer changes, although some medicines up-scheduled in NZ to prescription without evidence of harm (e.g. colestyramine, oxybutynin, insulin and nitrates). A lone voice wondered if Australia had recently pushed back against NZ decisions. However TTH-driven innovative reclassifications were too few to verify this possibility.

“I think a lot of those where there’s a divergence, it’s the result of fairly robust discussion, and certainly there’s no intention to diverge, and they try to harmonise where they can. But if they feel strongly enough about it then they don’t.” Australian committee member

From my view as a committee member (2004-2009), we were very conscious of Australian decisions when considering a reclassification, attempting to harmonise where possible, but able to diverge.

“…there are legitimate differences in medical practice, difference in disease severity, difference in models of care between the two countries…” NZ regulatory participant

TTH allows harmonised products, saving small production runs for NZ alone, benefiting industry.
Figure 6-3 Key reasons for trans-Tasman variation

Green represents factors generally considered enablers, and red represents factors generally considered barriers. Combined colours indicate variable influence; individuals in the early 2000s were considered enabling, then more recently hindering in Australia, while the opposite occurred in NZ. Many of these factors are inter-related, which is discussed in the text and not depicted in the diagram.
TTH has affected many medicines’ classifications. Australia would not have pharmacist-only chloramphenicol without TTH (given no sponsors had applied for it), and some medicines in NZ were up-scheduled to prescription because of TTH in the late 1990s and early 2000s (see 4.4.2). However, little direct effect on innovative reclassifications was evident over the 13 years studied, with one of 15 innovative reclassifications in NZ and one of nine innovative reclassifications in Australia exclusively arising from TTH (Table 6-2). Australian industry participants reported strategically attempting reclassification in NZ slightly before Australia to help the Australian reclassification. Thus, TTH stimulated some NZ reclassifications. Initially a sub-committee of four (including a NZ representative) aided harmonisation in Australia, considering the reclassifications first, then persuading the rest of the NDPSC to make the changes.

Most harmonising occurred at least five years before the interviews. Thus, apart from two people particularly involved with harmonisation, others said little about it. Had the interviews occurred five years earlier, TTH probably would have arisen more.

Based on interviews and meeting records, NZ and Australia differ in many factors, including: in committees; and in politics and lobbying; and in attitude. The two committees sometimes differed in approach, e.g. sumatriptan (Panel 6-2), and oseltamivir (6.5.2.1) considerations, and the Australian potassium chloride up-scheduling (Panel 6-3).

In summary, both countries have been considerably influenced by TTH, such that they are almost completely harmonised. However, from 2000 to 2012, TTH has generally affected reclassifications other than the innovative ones on which this research primarily focuses.

Table 6-3 Trans-Tasman differences and similarities in reclassification

<table>
<thead>
<tr>
<th></th>
<th>NZ</th>
<th>Australia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Committee</td>
<td>Small, pragmatic and evidence-based. Potential for patch protection.</td>
<td>Large NDPSC, little medical representation, but medical evaluation typical</td>
</tr>
<tr>
<td>Individual (committee</td>
<td>“Expert” committee</td>
<td>Jurisdictional representatives (politics)</td>
</tr>
<tr>
<td>and other)</td>
<td>“Can do”, flexible, pragmatic approach</td>
<td>“Risk-averse” or “cautious”, rigid approach</td>
</tr>
<tr>
<td>Schedules</td>
<td>Selected individuals enabling. Individual committee members may affect progressiveness or conservatism</td>
<td>Selected individuals enabling in early 2000s Replaced by individuals considered to hinder reclassification</td>
</tr>
<tr>
<td>Politics</td>
<td>Little mention</td>
<td>Important. TGA, jurisdictional representatives, pharmacy, consumer, medical groups</td>
</tr>
<tr>
<td>Legislative system</td>
<td>Relatively easy to get legislative change</td>
<td>Complicated by States and Territories and federal system, making change difficult</td>
</tr>
<tr>
<td>Government</td>
<td>Rarely involved</td>
<td>Negative effect owing to politics and media</td>
</tr>
<tr>
<td>Exclusivity</td>
<td>No market exclusivity</td>
<td>No market exclusivity</td>
</tr>
</tbody>
</table>

Table continued below
<table>
<thead>
<tr>
<th></th>
<th>NZ</th>
<th>Australia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advertising</td>
<td>Can advertise pharmacist-only (enabling)</td>
<td>Denial of advertising approvals for pharmacist-only hinders reclassifications</td>
</tr>
<tr>
<td>International</td>
<td>NZ might influence Australian decisions – encouraged industry</td>
<td>Reclassification in Australia may help reclassification elsewhere</td>
</tr>
<tr>
<td>motivation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Population size</td>
<td>Very small market hinders company-driven reclassification</td>
<td>Small market limits reclassification attraction</td>
</tr>
<tr>
<td>Pharmacy</td>
<td>Variability mentioned, but committee seem to have reasonable faith in pharmacy. Pharmacists conservative, busy, and sometimes dispensary-focused. Dispensary income limitations cause pharmacy to look further</td>
<td>Variability mentioned, committee faith in pharmacy differs. Pharmacists conservative, switch consumers to &quot;house-brands&quot;. Pharmacists busy and often dispensary-focused, but retail still important. Good dispensing income at time of interviews</td>
</tr>
<tr>
<td>Pharmacy organisations</td>
<td>Pharmacy organisations positive about reclassification, but not proactive until Pharmacybrands started driving in 2010. Industry rarely works with pharmacy organisations pre-reclassification Pharmacy organisations limited resource and lobbying power</td>
<td>Pharmacy organisations conservative about advertising and some reclassifications. Proactive with QCPP and Project STOP. Industry sometimes works with pharmacy organisations pre-reclassification Pharmacy organisations powerful lobbyists</td>
</tr>
<tr>
<td>Regulator</td>
<td>Enables reclassification, pragmatic. Meets industry regarding reclassification</td>
<td>Considered risk-averse. NDPSC Chair would not meet industry regarding reclassification</td>
</tr>
<tr>
<td>Patch protection</td>
<td>Some patch protection (doctors, pharmacy, and potential for patch protection on MCC), but not significant in interviews</td>
<td>Significant patch protection with doctors and pharmacists.</td>
</tr>
<tr>
<td>Subsidies</td>
<td>Low patient prescription copayment limits potential post-reclassification market, but copayment for the doctor</td>
<td>High patient prescription copayment may help post-reclassification market – but many doctor visits are free</td>
</tr>
<tr>
<td>Company environment</td>
<td>Negative environment. Limited awareness of NZ process and interest in reclassification</td>
<td>Australia somewhat protective of industry</td>
</tr>
<tr>
<td>Agenda</td>
<td>Agenda published with link to applications. Generic launch, ‘me-too’ reclassification helped by seeing application</td>
<td>Minimal information provided in agenda. Competitors can prepare to launch generic, or prepare a ‘me-too’ reclassification application</td>
</tr>
<tr>
<td>Meeting records</td>
<td>Detailed minutes published on website</td>
<td>Meeting record on website, variable detail</td>
</tr>
<tr>
<td>Cost</td>
<td>No fee for reclassification. Special studies not usually required</td>
<td>No fee for reclassification (but expected). Special studies not usually required</td>
</tr>
<tr>
<td>Industry role in</td>
<td>Closed committee meeting. Applicants can observe part of the discussion on their application as a pilot</td>
<td>Closed committee meeting. Industry representative on NDPSC assisted industry with insight and a voice in the meeting.</td>
</tr>
<tr>
<td>committee meetings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Historical effects</td>
<td>Overuse of reliever inhalers associated with death contributed to a cautious approach to reclassifying these agents</td>
<td>Overuse of phenacetin causing renal damage caused caution with combination analgesics. Orlistat controversy affects advertising</td>
</tr>
</tbody>
</table>

MCC = Medicines Classification Committee; NDPSC = National Drugs and Poisons Schedule Committee; QCPP = Quality Care Pharmacy Program
6.5.2. Attitude, individuals and politics

In interviews, NZ's 'can do', risk-tolerant attitude contrasted with the "risk-averse" or "conservative" Australian attitude.

“... whereas Australia is risk-averse, NZ takes a risk management view, and that I see is the key difference between NZ and Australia – throughout the whole regulatory regime, not just reclassification." NZ industry participant

“...the general sense is that the philosophy of regulation in NZ has been more that people should have access to medicines, unless there is a reason for that to be restricted. In comparison the philosophy in Australia is, certainly the sense that many have is that everything should be restricted unless it's proven safe." Australian industry participant

Individuals on the NDPSC, the MCC and at the regulator, and the constitution and voting of the MCC versus the NDPSC were thought to contribute to this difference. Politics and media apparently had little effect in NZ, but contributed to risk-averseness in Australia.

“...the NZ committee’s an expert committee; it's not a representative committee. The Australian committee is representative, so it's there to represent the interests of the individual State and Commonwealth, so that potentially allows the political element of decision making to move into consideration of reclassification." NZ Pharmacy participant

The committees were thought to echo the regulator perspective somewhat. With an independent Chair, the TGA may influence ACMS less than the NDPSC, but the Delegate to the Department Secretary can now override decisions. Although Medsafe could influence NZ reclassification (through the MCC Chair and advising the Minister of Health’s Delegate on overriding the committee), the MCC has appeared both conservative and progressive under the same MCC Chair since 1997 (Figure 6-2), suggesting that such influence has not been heavy-handed. However, interviews suggested the MCC Chair was a primary reason for the progressiveness in NZ, and I support this contention.

Australia seems rigid while NZ seems relatively flexible. The NDPSC attempted to consider only legislated criteria for reclassification, while the MCC seemed less curtailed. The NDPSC’s inability to ensure training would be provided affected reclassification decisions,[494] but algorithms and training enabled NZ reclassifications. NZ’s flexibility allowed unusual approaches (e.g. prescription exemptions and mandatory training) and proactivity that were not evident in Australia.

Several people suggested the federal system in Australia slowed change and created complexity, while others opined that change was possibly too easy in NZ under the political system. An Australian regulator participant considered identifying and fixing a problem would be easier in NZ as a smaller country. Other comparative research has reported that the political system allowed faster and more extensive change in NZ than Australia in the 1980s reforms.[495, 496]

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36 Most interviews occurred before ACMS was enacted
37 Chair does not have to be independent, however
Panel 6-2 Sumatriptan Case Study

**Australia (see also Panel 5-2) – reclassification rejected after four considerations as follows:**

2005: negative evaluation, reclassification denied on diagnosis and safety (particularly cardiovascular) requiring medical oversight

2006: negative evaluation. Committee sought expert advice on appropriateness of triptans as pharmacist-only, potential masking of meningitis or subarachnoid haemorrhage symptoms and the diagnosis questionnaire. Advice received for the next meeting (later 2006) suggested masking symptoms was not problematic, but the two advisors were split on reclassification, one concerned about cardiovascular risks if reclassified, and both noted potential medication overuse. Decision deferred to seek advice on serotonin syndrome.

2007: Serotonin syndrome question resolved, and committee considered issues were not insurmountable, but reclassification rejected as the NDPSC considered no real public health need existed for increased access to sumatriptan given emergency supply was available.

**New Zealand – reclassification approved after one consideration:**

2005: MCC proactively sought the reclassification application

2006: Sumatriptan reclassified at first application. The MCC took confidence from the UK reclassification, noting their favourable safety consideration. The MCC considered that a two-tablet pack, the product cost, the pharmacist’s involvement and the Migraine Treatment Questionnaire would limit misuse of the medicine (including excessive use), and ensure proper diagnosis and referral. The MCC widened the indication for use from that sought, considering previous doctor diagnosis of migraine unnecessary.

**Differences between the countries (based on interviews and meeting records)**

NZ was proactive, welcomed the reclassification, did not appear to have negative submissions, and was encouraged by the UK reclassification. The NDPSC appeared to be uninfluenced by the reclassifications in the UK, Germany and NZ. Australia took a risk-averse approach, perhaps influenced by initial hesitation from pharmacy organisations, doctor negativity, and the fact that funding on prescription is limited to second-line use in people on or who have failed prophylaxis. This was discussed in the meeting and by two participants, despite being largely irrelevant to reclassification. NZ had no funding restrictions, so medical practice and perspectives on sumatriptan probably varied in each country. Many Australian participants disagreed with the sumatriptan rejection.

“[NZ considered] that this was giving migraineurs access to an effective treatment. [Australia] took the view... that people with severe headache would go to the pharmacy and would buy sumatriptan or pharmacists would want to sell them sumatriptan, so we’re in a trust question again.... [Australia] had a strong medical argument that said no you shouldn’t reclassify, and equivocal or weak pharmacy argument as to how prepared are they to accept managing these patients, and then, a complete lack of trust in the Australian consumer behaving reasonably.” Committee member

Some concerns seem surprising (to some participants, and me). Masking a serious non-migraine headache seems more likely with other analgesics. Serotonin syndrome is rare and other self-medications (dextromethorphan and St John’s Wort) have this potential.[497] Finally, pharmacist-only supply might not be less safe than emergency supply – the pharmacist would use a questionnaire to screen for appropriateness of use, most pharmacists would receive training on sumatriptan, and the product packaging provides advice. For a person with an infrequent classic migraine, pharmacist-supply may be reasonable and emergency supply might not be, given that Australian emergency supply requires the patient is “...under medical treatment with the poison and continuation of medication is essential”.[461]

Source: National Drugs and Poisons Schedule Committee meeting records, Medicines Classification Committee minutes, and interviews.
The NDPSC appeared to distrust pharmacy, consumers and companies. One non-industry participant considered the MCC starts with: “what harm can come to a reasonable NZ consumer if they buy a pack of this medicine from a pharmacy or a supermarket, and they read the label?” However, the NDPSC started with “could the consumer get into harm if we lock them in the room with a bucketful of this medicine in the dark?”

The Australian meeting records stated that consumers would demand medicines inappropriately (particularly if advertised) unduly pressuring pharmacists to supply. Meeting records and interviews show the committee protecting consumers from very rare risks in Australia, (e.g. sumatriptan Panel 6-2, and potassium chloride, Panel 6-3).

### Panel 6-3 Potassium chloride up-scheduling case study

**An accidental fatal poisoning**

A two year old child in Australia took 30 slow-release potassium chloride tablets; the parents thought it was safe, so did not act until the child became unwell, but the child died.[498] The tablets had been used by the parents for themselves and their children (including the two year old), despite the pack instructions providing an adult dose only. Multiple pharmacies over five years of purchasing reportedly provided no information when supplying the medicine which was available for self-selection. The coroner criticised pharmacy and recommended up-scheduling and label warnings.

**Australia**

The NDPSC initially chose to up-schedule potassium from unscheduled to prescription (for over 100 mg per dosage unit, with exceptions) in Australia in 2006.[478] Labelling changes and child resistant closures were also discussed. Following concerns about inadvertently up-scheduling glucosamine products containing potassium, the committee instead up-scheduled potassium to prescription (for ≥600 mg per dosage unit, with certain exemptions).[104]

One committee member reported that potassium became an emotive issue with little regard for science, describing it as “the most astonishing decision that I’ve ever seen.”

**NZ**

The MCC considered the classification under TTH, concluded it was a one-off event, problems were not evident in NZ, and “…controls in pharmacies were such that no change was required.”[321] This product was only available in large dispensary packs in NZ (versus the front-of-shop availability in Australia described in the coroner’s report). NZ retained the pharmacy-only classification.

**Commentary**

The coroner had addressed her recommendations on scheduling not only to the NDPSC but also to the TGA and the Minister of Health in New South Wales to ensure urgent consideration at “all the appropriate levels.”[498] thus political pressure (or the possibility of political pressure) may have influenced the outcome. Additionally the hot climate in Australia but not NZ may increase the use of such medicines.

This childhood poisoning was highly unusual. Adults administered a medicine not normally used in children to a very young child (despite no child’s dose on the pack), and help was not sought initially when the child consumed an overdose. The large tablet would normally preclude use in children. Labelling stating not to use in children, and to seek help immediately in case of overdose, and using a child-resistant closure should prevent a recurrence. Up-scheduling to pharmacist-only (rather than prescription as chosen) would have allowed genuine access but prevented self-selection up-scheduling have been considered necessary.

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Source: NDPSC records; MCC minutes

TGA = Therapeutic Goods Agency; NDPSC = National Drugs and Poisons Schedule Committee; TTH= Trans-Tasman Harmonisation; MCC = Medicines Classification Committee
Yet sometimes the positions are reversed. Stimulant laxatives remain unscheduled in Australia and pharmacy-only in NZ, with both committees unwilling to change.[103, 379, 432, 440, 499] Inhaled beta-agonists remain pharmacist-only in Australia and prescription only in NZ despite multiple considerations in both countries.[379, 416, 440, 499-501] Chloramphenicol was an easier, faster reclassification in Australia than NZ (Panel 6-4).\footnote{The more restrictive availability of pseudoephedrine in NZ to Australia is unmentioned as it relates to NZ Misuse of Drugs legislation not reclassification} Thus, risk averseness and progressiveness can vary, perhaps reflecting the different committee constitution, or different individuals.

**Panel 6-4 Chloramphenicol consideration NZ and Australia**

**NZ**

An MCC member raised ocular chloramphenicol in 2005 as a potential reclassification candidate. Medsafe approached sponsors, but no application ensued. Instead, the MCC considered chloramphenicol without sponsor support during four MCC meetings using some information from the UK reclassification. The Pharmaceutical Society agreed with the reclassification but would not commit to providing materials.

Misdiagnosis was raised throughout the considerations, and ultimately the committee was divided with the two GP members against the reclassification given misdiagnosis concerns. The MCC recommended reclassification in 2009 providing the Pharmaceutical Society developed pharmacist training, a protocol for supply, and a consumer information sheet, and delaying reclassification until these were in place.

**Australia**

In Australia, the NDPSC considered chloramphenicol under TTH shortly in 2009. Information used appeared to be MCC minutes and submissions to the NDPSC, including one seemingly thorough submission probably from a pharmacy organisation including information on safety, risks and benefits, place in treatment and guidelines for pharmacist supply. The NDPSC discussed potential misdiagnosis, but committee members agreed that neither pharmacies nor GPs have routine access to a slit lamp for accurate diagnosis, and that pharmacists were already treating bacterial conjunctivitis with less effective products.

The reclassification was approved at a single meeting and confirmed in 2010. The NDPSC did not require training, algorithms or consumer information in place.

**Commentary**

Both countries had sulfacetamide eye drops available without prescription before this consideration. Lack of an external driver of the reclassification provided a major barrier in NZ, but not in Australia where the submissions perhaps filled some of that gap. The NDPSC had greater confidence in pharmacy than the MCC. In NZ concerns about misdiagnosis (and lack of labelling) were resolved by requiring the Pharmaceutical Society to develop pharmacist and consumer materials. In Australia, pharmacist materials were already in place for eye infections. The constitution of the committee or committee individuals appeared to cause the concerns in NZ, which differ from the UK medical acceptance of chloramphenicol reclassifying.[302, 502]

The lack of sponsor interest in both Australia and NZ contrasts with the UK where two sponsors attempted reclassification.[503] This sponsor interest may arise from the reclassification by product in the UK allowing some market exclusivity (albeit that unusually two companies applied at the same time).

Source: Medicines Classification Committee and the National Drugs and Poisons Schedule Committee meeting records, interviews and my involvement on the MCC

MCC = Medicines Classification Committee; NDPSC = National Drugs and Poisons Schedule Committee; TTH = Trans-Tasman Harmonisation

One participant suggested the agenda could influence a consideration; another observed: “it just depends on who’s most persuasive on the day”. One participant suggested that some members were insufficiently prepared. These comments came from Australia, but I consider they could apply in NZ.
too. Some MCC meetings had many agenda items, which might affect preparation and consideration by members, affecting the outcomes (see 4.7.2). Conversely, an ex-committee member suggested a light agenda could cause nit-picking on an item that should have passed easily. From my experience, on a big day possibly some committee members chose their battles, rather than conflicting on multiple agenda items. These factors suggest the process could become more evidence-based and thorough. The busy peak TTH consideration period may have affected workload, which should have since reduced, particularly with ACMS restricted to medicines.

6.5.2.1. Defining moments in reclassification: orlistat and oseltamivir

I consider that two defining moments in reclassification widened the distance between the committees: orlistat in Australia; and oseltamivir in NZ. While the NDPSC appeared increasingly conservative following the orlistat contretemps, the MCC appeared to gain confidence from oseltamivir. These two first-in-world reclassifications are briefly summarised below.

The NDPSC finally approved advertising of orlistat in 2006, but regretted the decision when Roche advertised it inappropriately, and media magnified concerns about advertising and pharmacists’ poor performance in a mystery shop (Panel 5-1). This event appeared to confirm the NDPSC’s worst fears: that companies and pharmacy were not trustworthy, and the consumer needed more protection. Risk-avoidance subsequently increased, with the committee reversing orlistat advertising, the dermal mometasone reclassification decision and dermal moderate potency corticosteroids advertising at the same meeting.[380] No advertising requests have been approved since. Industry and pharmacy participants believed the NDPSC had over-reacted on orlistat, but a committee member participant supported the NDPSC’s decision.

The MCC reclassified oseltamivir in 2006,[438] using strict criteria to minimise potential risks (Table 6-4). Pharmacists could supply oseltamivir between May and September to consumers 12 years or over presenting in a pharmacy with early symptoms of seasonal influenza.[504] The NZ regulator participant believed pharmacists behaved very responsibly in supplying this medicine. Consequently, the criteria for supply were relaxed, particularly during the pandemic.[505, 506]

The negative experience with orlistat reinforced the NDPSC conservatism, making them careful to avoid the same situation again (regret avoidance bias[507]). In contrast, the positive oseltamivir experience for the MCC seemed to encourage further ground-breaking decisions.

The MCC and NDPSC apparently held similar concerns about oseltamivir (Table 6-4), but handled them differently. The MCC created tight criteria for supply, and trusted pharmacy to work within those criteria. The NDPSC considered that an exemption to prescription, as in NZ, was not possible,[104] perhaps influenced by their complex State and Territory system. The NDPSC rejection arose from potential for increased resistance, lowered influenza vaccination rates, and misdiagnosis.[103]
Table 6-4 Oseltamivir considerations compared for NZ and Australia

<table>
<thead>
<tr>
<th>NZ</th>
<th>Australia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diagnostic algorithms</strong></td>
<td>Helped reclassification</td>
</tr>
<tr>
<td><strong>Diagnosis</strong></td>
<td>Delay in treatment for serious illness already exists for cold or influenza products. Pharmacist intervention and high price would prevent use for colds.</td>
</tr>
<tr>
<td><strong>Pharmacists</strong></td>
<td>Trusted to get it right</td>
</tr>
<tr>
<td><strong>Resistance</strong></td>
<td>Experts advised resistance was low despite substantial use. Roche would monitor resistance. Could reverse decision if new evidence of concern emerged</td>
</tr>
<tr>
<td><strong>Immunisation</strong></td>
<td>Possibility of reducing influenza immunisation rates</td>
</tr>
<tr>
<td><strong>Usage</strong></td>
<td>Some members thought that most people recover from seasonal influenza so keep it aside to be effective in a pandemic</td>
</tr>
<tr>
<td><strong>Pandemic supplies</strong></td>
<td>No impact on national pandemic supplies, and reclassification could increase stocks in the country in case of pandemic. Non-prescription supplies could be shut down in a pandemic.</td>
</tr>
<tr>
<td><strong>Epidemiological data</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Benefits</strong></td>
<td>Considerable consumer benefit. Timely therapy initiation. Public good given potential transmission in doctors’ waiting rooms, and reduced sick days</td>
</tr>
<tr>
<td><strong>Internet sales</strong></td>
<td>Concern about uncontrolled internet sales</td>
</tr>
<tr>
<td><strong>Drug safety</strong></td>
<td>Few concerns around product safety</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>Two virologists supported the reclassification</td>
</tr>
</tbody>
</table>

Source: Medicine Classification Committee, National Drugs and Poisons Schedule Committee meeting records

With no similar reclassification elsewhere to inform the committees and indeterminate resistance, the differing committee responses are understandable. I consider that neither committee was wrong, given the circumstances and information available. Post-reclassification qualitative research showed NZ pharmacists took the reclassification seriously and consumer pressure was largely manageable.[80] A quantitative study found low pharmacist-supply, minimal resistance, and influenza
vaccination uptake did not decline.[81] This study used sentinel data rather than collecting data specifically for the research, and potentially findings could be affected by Roche funding, and an ex-MCC member as a researcher. However, the five years of data (including pandemic usage) and high participation rate strengthened the findings. These studies and participant comments suggest the MCC did not err in reclassifying oseltamivir. The strict criteria for supply probably helped. Had Australia reclassified oseltamivir simply to pharmacist-only, different outcomes may have occurred. In uncertainty no single ‘right’ answer exists, but a committee and regulator willing and able to be flexible (and able to reverse the process) may assist a reclassification. Post-reclassification research can usefully ascertain if concerns eventuated.

6.5.2.2. Why have the committees varied?

One likely reason the committees vary is uncertainty. Even with evidence-based decision making, committees should naturally differ sometimes if uncertainty exists. A health task force showed that values and beliefs played a greater role in decision-making under uncertainty.[508]

Initially NZ was seemingly conservative (following a progressive period) and Australia was seemingly progressive. In the second six years this was reversed. The instrumental difference appears to be risk attitude; the post-2006 NDPSC appeared largely risk-averse while the post-2004 MCC appeared largely risk-tolerant. Interviews in the early 2000s earlier should have led to different findings.

The committees appeared to differ on risk mainly owing to: individuals on the committee or to whom committee members reported; committee constitution and voting; events; politics; and media. Distrust and risk aversion appeared to increase together on the post-2006 NDPSC, not surprisingly given distrust increases both perceptions of risk and unacceptability of risk.[509]

Given that committee decisions should be evidence-based, the effect of individuals may seem surprising. However, the literature shows effects of individuals in groups,[508, 510, 511] e.g. individuals’ personalities or position influenced discussion on a health-related task force.[508] Experience affects decision making,[511, 512] as alluded to by participants, e.g. jurisdictional representatives possibly jaundiced by awareness of inappropriate pharmacist practices, or in considering that coal-face experience was beneficial. Individuals’ experience of a previous successful (e.g. oseltamivir) or problematic (e.g. orlistat) reclassification could colour future considerations. An additional individual’s effect has been my influence in approaching Pharmacybrands. This action stimulated four innovative reclassifications in NZ not mirrored in Australia, and represents nearly a third of innovative reclassifications and half of the first-in-world reclassifications. I did not expect to contribute to the divergence between the countries to this degree.

“Groupthink” can affect judgement and prevent individuals from challenging others, sacrificing quality decision-making to avoid conflict and achieve consensus.[510] Where a directive leader states his/her preference early in the discussion, the group tends to have less dissent, adopt the leader’s preference, and “adopt an illusion of morality”.[509][p150] When a bias commonly occurs in members, groups can heighten such effects,[513] possibly causing heightened risk-aversion in the NDPSC.
Participants discussed group effects within the NDPSC, which may impact on decision quality. While a group effect was unmentioned for the MCC, I suggested that a committee member might pick their battles (4.7.2), and thus conflict avoidance or desire to reach consensus might affect decision-making. Polarisation can occur in groups, with an ‘in-group’ norm, and others effectively an ‘out-group’. [509] which might cause a push-back on industry suggested for the NDPSC.

Concerns arose about the NDPSC size, and members’ preparation. Concerns about committee size, insufficient preparation and reliance on anecdote rather than evidence were raised about FDA advisory committees. [336] Individuals tend to contribute less effort as the group size increases. [509]

Suggestions that jurisdictional members’ organisations affected their risk attitudes are unsurprising. Organisational culture and managers’ suggestions can distort risk perceptions. [514] Organisational culture’s effects likely differed in NZ, as two-thirds of the MCC were not representing an organisation as such (although their professions could affect risk perceptions). [515] With two MCC members regulatory employees, the regulator’s “open” perspective probably diffused into meetings, e.g. in flexibility and proactivity seen or encouraged.

National norms and expectations can influence risk attitudes. [511, 516] Attitudes to risk may be similar between NZ and Australia, [515, 517] but NZ is more open and liberal economically than Australia. [495] As both committees varied over the period, a strong national influence seems unlikely.

Reclassification, pharmacy and Medsafe have received little media criticism in NZ in recent years, and the Minister of Health in 2012 desired innovation and flexibility in health and encouraged further reclassification. [518] In contrast in Australia, media covered the TGA Pan Pharmaceuticals difficulty and pay-out, [519] and highlighted advertising and pharmacy problems with orlistat. [228, 230]

A risk event or a public interest group can amplify risk, as can media coverage, social discourse or other communication. [516, 520] Heightened risk perceptions seem likely from the potassium chloride poisoning, particularly given the coroner’s communications to State institutions and a politician. [498] A public interest group, then media appeared to augment orlistat concerns. The real risk of teenagers inappropriately using orlistat is probably extremely low given the high cost, embarrassing side effects and modest efficacy. [521] However, orlistat was nearly up-scheduled and had advertising approval removed (Feb 2007), suggesting exaggerated perceived risk. In contrast, four months later, the NDPSC rejected up-scheduling laxatives to pharmacy-only with TTH. [102] Although research showed laxative misuse in Australia, [522] an eating disorders group considered that up-scheduling would make little difference. [102] Perhaps the NDPSC lacked confidence that pharmacy staff would screen laxative purchases appropriately, given the orlistat mystery shopping, or lack of media attention (and non-concern from a public interest group) reduced the perception of threat compared to orlistat. Conversely, in NZ the MCC believed stimulant laxatives should remain pharmacy-only but accepted orlistat as a pharmacist-only medicine. The experience of MCC members in refusing pharmacy sales to people suspected to be misusing stimulant laxatives (as minuted) and an eating disorders organisation’s opposition to down-scheduling [432] may have heightened their risk perceptions. The
MCC seemed more attuned to stimulant laxative abuse, while the NDPSC seemed more attuned to potential for orlistat misuse, illustrating the effects of media, a public interest group, pharmacy behaviour and members’ experiences in committees.

Both countries had historical events that heightened concern around a particular topic: phenacetin in Australia[380] and inhaled beta-agonists in NZ.[439] These events probably contributed to unharmonised classifications for combination analgesics and inhaled short-acting beta-agonists. Other research has found historical events may change risk perceptions.[515, 516]

A further bias seen in the NDPSC (and perhaps the MCC) is a status quo preference, possibly because of conservatism, fear, inertia, convenience or rationalisation.[507] Pressures or expectations (e.g. suggested TGA conservatism) can strengthen this bias, as can uncertainty. Losses typically weigh heavier than gains in decisions,[507] making the status quo attractive. With the NDPSC concentrating heavily on risks (e.g. sumatriptan and oseltamivir) and minimising potential gains (e.g. sumatriptan, oseltamivir and advertising), rejections seem inevitable, even with highly unlikely risks (Panel 5-2). ‘Regret avoidance’ in which people avoid risk they may later regret (e.g. orlistat and the NDPSC), can also contribute to a status quo bias. The MCC, at least since 2004, has not shown the status quo bias to the same degree as the NDPSC, though it possibly occurred with domperidone, omeprazole, and stimulant laxatives. A preferential bias in which members’ initial preferences bias their discussion and evaluation of information[523] seemed possible in the NDPSC, with jurisdictional members thought to arrive with their minds made up.

Bias is also positive, being ‘fundamental to reasoning’.[524] Without appropriate experience, committee members would struggle with the decisions, and not know what information need to be focused on. Coalface experience was acknowledged as important in both countries to help recategorisation decisions. A diversity of experts (not representatives) with strong evidence-based skills may maximise the benefit of bias and dilute its deficiencies. The change to the ACMS should improve decision-making, but a fully expert committee may be even better.

Exceptions to the NZ risk-tolerant, Australia risk-averse view exist, e.g. stimulant laxatives and beta-agonists, mentioned earlier. Chloramphenicol reclassified quickly in Australia, but was nearly rejected in NZ seemingly reflecting different committee constituency and individuals. Omeprazole took five meetings to reclassify in NZ versus one meeting for pantoprazole in Australia[39]. Partly reflecting the application, the MCC also seemed uncertain about the need.

Possibly suggesting the NDPSC was not evidence-based may have reflected industry’s dissatisfaction at the rejections. However, the sumatriptan, orlistat and potassium chloride case studies seem to support the criticisms of the NDPSC. Requiring evidence-based decision making skills in all members of reclassification committees should benefit decision-making.

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39 Omeprazole and pantoprazole were the first proton pump inhibitors to reclassify in NZ and Australia, respectively
Rather than Australia being too risk averse, NZ could be excessively liberal, and the MCC’s ‘evidence-based’ moniker may have arisen because industry liked the outcomes. However, participants did not suggest NZ was too liberal, and no recent reclassifications have been reversed. MCC rejections and multiple deliberations (Table 4-5), including of medicines reclassified elsewhere, suggest the committee is not excessively pro-reclassification. NZ’s sumatriptan reclassification echoed decisions elsewhere.[473-475] Research suggests the NZ oseltamivir reclassification was reasonable.[80, 81] Both industry and non-industry participants considered NZ evidence-based and Australia risk-averse, or questioned Australian decisions, supporting the notion that Australia has become more risk averse rather than NZ has become excessively liberal.

“…philosophically the MCC is probably these days closer to MHRA in terms of switch philosophy than it would be to NDPSC.” Industry participant

The MCC was often specific about training, consumer information and algorithms for supply, and sometimes used strict supply criteria to reduce potential risks, suggesting high awareness of risks. Perhaps these activities and flexibility helped because they were perceived to control risks that the NDPSC considered they could not control in the same way.40 I suspect they also reflect a ‘can do’ MCC attitude while the NDPSC seemed to prefer to reject reclassifications where uncertainty existed.

Some committee findings have been echoed in a 2013 criticism of Australia’s committee on medicines reimbursement for having representative members and excessive political influence.[525]

6.5.3. Financial motivation

Similarities and differences exist between the countries in financial motivation for companies, pharmacists, doctors and consumers. Reclassification market opportunity is limited by relatively small markets, transparency and no market exclusivity. In NZ, a very small population and low generic prices prevent reclassification applications. Advertising limitations, exacerbated by house-brand sales, affect Australia. Reclassification in both countries may benefit from zero fees, but reclassifying a medicine, providing training and establishing an OTC product incurs costs with potentially low sales, e.g. with sumatriptan[436] and oseltamivir[80, 81] in NZ. Allowing more advertising in Australia and market exclusivity in both countries would probably stimulate sponsors to apply. If NZ no longer helps reclassification in the bigger Australian market (6.5.1), commercial imperative for NZ reclassification is limited, except for harmonised packaging, or being a test market.

Pharmacy motivation and support for reclassification appears higher in NZ than Australia, possibly reflecting the dispensary funding environments (when interviews were conducted). However, given pharmacy negativity about down-scheduling to general sales emerged more strongly in Australia than NZ, retail must be important in Australia. This negativity might also reflect the political power and resource of pharmacy organisations in Australia versus NZ.

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40 The NDPSC stated that they could not ensure training materials and protocols were used
Medical organisations’ and medical participants’ negativity to reclassification appeared higher in Australia than NZ, a factor attributed to different payment models. Although unmentioned by participants, NZ GP funding increases[526] may also have reduced concern, and/or medical organisations in NZ may be less resourced than in Australia. However, subsidised healthcare would ensure many consumers still sourced their medicine through the doctor in both countries even if reclassified. NZ doctors’ organisations provided little opposition to medicines reclassification between 2000 and 2011. However, the two NZ medical participants worried about losing opportunistic screening. While the GP MCC members opposed chloramphenicol, other reclassification approvals suggest this was not patch protection. Media reported doctors’ concerns about fragmenting with vaccinations in pharmacy[449] and trimethoprim through pharmacists.[450]

6.5.4. View of pharmacy

The differing committee views of pharmacy, with the MCC seemingly having higher faith than the NDPSC, are surprising given similarities in pharmacy (according to participants and myself).

“...the practice of pharmacy in New Zealand I wouldn’t regard as too dissimilar from Australia...” Industry participant

Participants believed Australian pharmacy qualifications and training standards were as high as elsewhere, and pharmacy education in both countries is accredited by the Australian Pharmacy Council. Indeed, Australian pharmacy has been proactive around improving pharmacy supply of non-prescription medicines since about 2000 through QCPP.[489, 527-529] Initial implementation of the standards used repeated audit visits, and mystery shopping, with feedback to improve performance in pharmacy supply of non-prescription medicines.[527] They still have an annual visit. The QCPP aims to achieve quality professional service in community pharmacies, with 92% of Australian pharmacies accredited,[463] and may enable reclassification. NZ pharmacies have standard operating procedures and are audited, but have not used mystery shopping and feedback. Variability in pharmacist performance was raised as a concern in both countries, particularly from pharmacy participants. Simulated patient studies[285, 307, 487, 488] and a 2007 observational study[294] still show variation despite the quality program in Australia.

Little research compares community pharmacy practice in the two countries, with the only study limited by a small sample size (15 Queensland pharmacies and six NZ pharmacies) and comparing two related studies.[294] Although differences were observed, both countries disappointing had no pharmacist involved in around a third of pharmacist-only medicine supplies. Simulated patient studies in both countries suggest room for improvement,[285, 289, 307, 487, 488] but cannot be directly compared. Even where the same medicine was mystery shopped in both countries, small sample sizes and design flaws (e.g. pharmacy selection limitations) limit conclusions. In Australia, Choice (a consumer organisation) found 24 of 30 pharmacies in Sydney supplied orlistat to a person outside the permitted Body Mass Index (BMI).[290] A NZ newspaper found six of six pharmacies declined orlistat requests by a person outside the BMI range.[363]
The view of pharmacy may have changed in Australia with increasing risk-averseness. In 2004 the NDPSC expressed confidence in pharmacy when retaining inhaled beta-agonists scheduling:[530]

“The NDPSC members endorsed the view expressed by the XXXXXXXXXX Member that pharmacists had demonstrated that they played an important role in asthma management.”

I suspect that the committee view, not pharmacy practice, currently varies between the two countries, at least partly because of members’ experience and awareness of variable pharmacy performance (6.5.2.2). The NDPSC had orlistat mystery shopping,[290] the coroner’s criticism of pharmacy,[498] and the Galbally report and subsequent review[84, 85, 462] which questioned pharmacy’s role. In NZ, the last academic mystery shop of a pharmacist-only medicine was published in 2002, while in Australia, multiple recent publications demonstrated pharmacist variability.[285, 307, 487, 488] The most recent consumer organisation-led mystery shop in Australia (orlistat, 2007) found poor performance.[290] Disciplinary action occurred against pharmacists in NZ in 1997[531] and 2002[532] following failures in consumer-organisation mystery shopping. This may have provided confidence to the MCC that action was taken, particularly when the next consumer organisation-led mystery shop in NZ (vaginal antifungals, 2003) was more positive.[365] No NZ mystery shopping of pharmacist-only medicines has been reported since 2003, to my knowledge. Thus, although participants in both countries (particularly pharmacists) considered some pharmacies could improve, the MCC’s awareness of inappropriate behaviour may be less top-of-mind than the NDPSC’s.

6.5.5. Other pharmacy aspects

Australian pharmacy organisations seemed possibly more conservative with some reclassifications than NZ pharmacy organisations (based on interviews). Pharmacy conservatism with recently reclassified medicines came through more in Australia than NZ. Neither of these differences seemed strong, and they may not reflect reality. There is no comparison of pharmacist opinions of reclassification in NZ versus Australia, and pharmacy organisations submissions to the committees were not published at the time of the interviews to confirm or deny the feeling. Possibly this arose in part because Australian pharmacy organisation/s reportedly often opposed advertising applications while advertising was not considered in NZ. Alternatively, without advertising for some reclassified medicines in Australia, pharmacy conservatism may be more important in achieving post-reclassification sales. Pharmacy participants in Australia generally disagreed with the sumatriptan rejection and some criticised the NDPSC’s reversal of orlistat’s advertising approval. In 2007, most interviewed NZ pharmacists welcomed the oseltamivir reclassification and prepared themselves for it, but were not proactive in supply.[81] In 1993, Bowden found negativity towards reclassification in Australian pharmacists.[30] This may have since changed, and research comparing views between Australia and NZ would answer this question.

Pharmacy organisations emerged from various interviews as more political than in NZ. The strong political power of the Pharmacy Guild of Australia has been publicly criticised.[87, 533] This may reflect the environment, politics generally came through more strongly for Australia than NZ, and may
reflect a likely larger size and resource of Australian organisations compared to NZ, and the different political structure of each country (as participants suggested).

“The lobbying power of the professions is also hugely different in the two countries. …the medical profession and the Pharmacy Guild and Society [in NZ]… they’re moderately effective lobby groups to government. In Australia, the AMA and the Pharmacy Guild are very effective lobby groups at State and Federal jurisdictions…” De-identified participant

6.5.6. Other factors

Culture has permeated this chapter, e.g. in the ‘can do’ attitude in NZ, and a ‘risk-averse’ or ‘conservative’ culture from the committee, regulator, and (to an extent) pharmacy organisations and pharmacists in Australia (6.5.2.2, 6.5.5). Reasons behind this include committee members, committee experiences (6.5.2.2), politics (6.5.2), and financial motivators (6.5.3). Consumer culture did not arise from interviews as different in either country.

“Having lived in both countries I think they are quite similar in terms of people’s behaviours. Obviously you’ve got different economic healthcare funding situations. …. it’s a similar kind of set-up with self-care, with promotion of consumers to take care of their own health. There could be an ethnic difference…..” Academic participant

Australia and NZ received different reclassification applications. Australian applications not submitted in NZ include dermal mometasone, an orphenadrine-paracetamol combination, a topical antibiotic, rabeprazole, and montelukast. NZ’s applications not submitted to Australia include simvastatin, domperidone, zolmitriptan, rizatriptan, fusidic acid, calcipotriol, the travellers’ diarrhoea and cholera vaccine, trimethoprim, melatonin, influenza vaccination, and tetanus, diphtheria and pertussis vaccination. Zolmitriptan and the travellers’ diarrhoea/cholera vaccine were considered under TTH in Australia.

Differences in applications arose partly from differing previous committee decisions, available products, and company activity. The NZ sumatriptan approval encouraged further triptan applications. Neither rabeprazole nor orphenadrine-paracetamol are marketed in NZ.[534] Pharmacybrands, which submitted five innovative reclassifications in NZ has no Australian presence.[441] To date, no Australian pharmacy organisation or retail group has driven reclassification. This may reflect different financial environments (6.5.3), or that the idea had not been seriously considered (as participants signified). Given Pharmacybrands has now submitted five reclassification applications, and the closeness of Australasian pharmacy, it will be interesting to see if Australia follows NZ. It is unknown why other reclassification applications were submitted in only one country; contributing factors might include likely sales, different company presence or interest, or lack of approval in one country.

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41 Rabeprazole, rizatriptan and the paracetamol-morphine combination were not deemed innovative reclassifications so do not appear on the tables, but show differences between the countries.

42 Where an exemption from prescription was used in NZ, Australia did not automatically consider it.
With the joint Trans-Tasman regulatory agency a joint committee considering medicines classification is expected. While my interviews have not explored the ideal constituency of a committee considering reclassification, feedback suggests an expert committee rather than representative committee is desirable to minimise politics and maximise evidence-based decision making. Based on interviews and my experience, I submit that members should include coal-face experience from NZ and Australia, both pharmacists and GPs, one or more experts in non-prescription medicines, appropriate medical knowledge with a bigger picture (e.g. a public health physician), an independent Chair, a regulatory member from each country, and consumer representation. Committee members should be open to patient-centred care rather than entrenched in current models. Clear up-to-date criteria for committee considerations would be useful. Limited terms may help allow new blood. Flexibility by committee and regulator may help enable future reclassifications while maximising safety.

6.6. Summary

Across all non-prescription medicines, scheduling in NZ and Australia differs on very few. However, recent activity in innovative reclassification decisions since 2005 shows important divergence. Australia appeared more progressive in the early 2000s at a time when NZ seemed more conservative; and this pattern then reversed.

Three primary reasons appear to cause divergence: increased conservatism in Australia versus NZ; the MCC’s flexibility enabling reclassifications; and non-sponsor driven reclassifications in NZ. The varying committee risk attitudes probably arise from the influence of individuals, committee constituency, and politics. Changes in the committee constitution (as expected with ANZTPA), changes in individual members, changes in government support, availability of evidence on recent reclassifications (in Australasia or elsewhere), or a risk event may change reclassification attitudes and therefore decisions, and may cause the countries to converge or to further diverge. Third party interest in either country, like Pharmacybrands, may have a similar effect. A new joint committee should converge the countries, but the committee attitude and recommendations will depend on the many different factors highlighted in causing divergence.

It is unrealistic to expect total harmonisation. NZ and Australia are similar, but not identical, so divergence is unsurprising. The countries have diverged in other areas, e.g. foreign policy and industrial relations,[495, 496] sometimes converging then diverging again.

For further international comparison see the macro-level (Chapter 11).
Chapter 7. The United Kingdom

7.1. Introduction

This chapter aims to understand the reclassification environment in the UK, the acknowledged European and world leader in reclassification.[24, 333] Although the UK now publicly consults on most reclassifications, meeting minutes and information about reclassification attempts that have not reached consultation stage are not publicly available. Low transparency and the project scope limit the research primarily to interviews with supplementary document analysis for reclassification process and consultations. I examine the UK as an outsider who interviewed key informants, as in other countries. This approach allows me to elucidate factors that well-versed participants considered most likely to affect reclassification in the UK, and to compare multiple countries.

7.2. Background

The UK has had long-standing government health policy to encourage consumer self-management and better manage minor ailments, including through medicines reclassification.[17] Stakeholders developed a list of prescription to non-prescription reclassification candidates in 2001.[24, 106] Candidates included medicines for chronic conditions, preventative therapy, minor illnesses, and several antibiotics. Initial doctor consultation and professional practice guidance were recommended. First-in-world reclassifications ensued, including simvastatin and azithromycin,[116] and the government desire to continue ground-breaking reclassifications was reiterated in 2011.[28]

Reclassification in the UK receives media and academic attention, commonly opinions or reports of upcoming or recent reclassifications, such as simvastatin,[29, 124, 535-540] sumatriptan,[281, 541, 542] or tamsulosin.[28, 114, 122, 543, 544] Applications for trimethoprim and nitrofurantoin reclassifications were abandoned following medical attention focusing on resistance concerns.[127, 545] The British Medical Association commissioned a report on non-prescription medicines emphasising reclassification.[24]

Key aspects of the UK market are presented in Table 7-1. The UK OTC market provides 10% of the European market, with minimal growth and sales primarily through pharmacies or drugstores (55%) and supermarkets or hypermarkets (31%) according to MarketLine.[546] IMS Health shows mass market is growing while pharmacy is declining.[218]

The UK National Health Service (NHS) provides universal health care, funded and provided by the state.[372] Consumers register with one general practice and GP visits and most hospital visits and hospital treatments incur no patient charge.[547] In England, prescriptions are free (90%) or incur a patient copayment (£7.65 (US$11.72)/item).[548] Exemptions include people on income support, with a chronic condition, or aged over 59 or under 16 years.[549] Wales, Northern Ireland and Scotland stopped patient copayments.[548]
### Table 7-1 Key aspects of the UK market

<table>
<thead>
<tr>
<th>Variable</th>
<th>UK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population (millions; 2011)</td>
<td>62.4</td>
</tr>
<tr>
<td>Health system[372]</td>
<td>National health service</td>
</tr>
<tr>
<td>Life expectancy*[392]</td>
<td>80.6 years</td>
</tr>
<tr>
<td>Health Development Index Ranking[388]</td>
<td>28</td>
</tr>
<tr>
<td>Health spend as % of GDP total (2009)[392]</td>
<td>9.8%</td>
</tr>
<tr>
<td>Public proportion of health spend (2009)</td>
<td>84.1%[550]</td>
</tr>
<tr>
<td>Self-medication sales[77]</td>
<td>€ 2.7bn (US$3.52bn) (2010)</td>
</tr>
<tr>
<td>Self-medication as % of total Pharma [77]</td>
<td>12.5% (2010)</td>
</tr>
<tr>
<td>Growth in self-medication market [77]</td>
<td>-0.9% (2010)</td>
</tr>
<tr>
<td>Pharmacist-only schedule?</td>
<td>No</td>
</tr>
<tr>
<td>Pharmacy-only schedule?</td>
<td>Yes</td>
</tr>
<tr>
<td>Drugstore schedule (licensed person)?</td>
<td>No</td>
</tr>
<tr>
<td>Physicians per 1000 persons[393]</td>
<td>2.7 (2010)</td>
</tr>
<tr>
<td>Number of doctor consultations per year per capita[393]</td>
<td>5.0 (2009)</td>
</tr>
<tr>
<td>Primary care doctor payment structure[14]</td>
<td>Mix capitation &amp; incentives</td>
</tr>
<tr>
<td>Number of pharmacists per 10,000 population[394]</td>
<td>~8 (Great Britain)</td>
</tr>
<tr>
<td>Pharmacies per 10,000 population [394]</td>
<td>~2 (Great Britain)</td>
</tr>
<tr>
<td>Percentage of pharmacists in community pharmacy[457]</td>
<td>44%</td>
</tr>
</tbody>
</table>

Two non-prescription categories exist: pharmacy medicines (available from a pharmacy, under pharmacist supervision); and general sales (available from any retailer).[551] Pharmacy medicines cannot be self-selectable, although that is expected to change from October 2013.[552] Prescription to non-prescription reclassification is commonly known as “POM-to-P” or “POM-to-P switch”.[43]

While government support[17, 28] has encouraged reclassifications, reports suggest government targets have been undershot,[117] and some reclassifications have failed commercially.[115, 553] Kelly in 2013 reported Europe was slowing the UK down.[100]

#### 7.3. Primary data sources

Eight interviews included UK-based participants from pharmacy organisations (n=2), industry (n=3), the regulator (n=2), a consumer organisation (n=1) and academia (n=1). One participant had been a member of the committee considering reclassifications. Two European participants and three industry or industry-related participants provided views. One doctor-stakeholder in reclassification withdrew as the interview began. To include medical views I instead reviewed consultation responses from medical organisations for omeprazole, chloramphenicol, and tamsulosin, on the MHRA website.

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[43] POM is Prescription Only Medicine and P is Pharmacy medicine.
7.4. UK prescription to non-prescription reclassifications 2003-2012

Table 7-2 illustrates the UK’s strong activity in prescription to non-prescription reclassifications. Twelve ‘innovative’ reclassifications (see 3.2.14) occurred from 2003 to 2012. Seven of these innovative reclassifications appeared in the 2002 candidate list published (italicised in Table 7-2).

Table 7-2 Key UK prescription to non-prescription reclassifications 2003-2012

<table>
<thead>
<tr>
<th>Medicine*</th>
<th>Year approved</th>
<th>Innovative reclassification?</th>
<th>Comments, including factors considered in deciding if the reclassification was innovative or not</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omeprazole</td>
<td>2003 - Yes</td>
<td></td>
<td>More effective than H₂ antagonists[332]</td>
</tr>
<tr>
<td>Hyoscine transdermal</td>
<td>2004 – Yes</td>
<td></td>
<td>One patch lasts 3 days, rather than dosing 2-3 times a day</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>2004 – Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chloramphenicol eye drops</td>
<td>2005 – Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alclometasone dipropionate (dermal)</td>
<td>2005 – No</td>
<td></td>
<td>Clobetasone butyrate previously reclassified</td>
</tr>
<tr>
<td>Trimethoprim (oral)</td>
<td>Withdrawn</td>
<td></td>
<td>Application withdrawn in 2010 [127] so no final determination</td>
</tr>
<tr>
<td>Amorolfin nail lacquer</td>
<td>2006 – Yes</td>
<td></td>
<td>Low efficacy,[332] but no other nail antifungals OTC[116, 554]</td>
</tr>
<tr>
<td>Sumatriptan, zolmitriptan</td>
<td>2006 – Yes (sumatriptan)</td>
<td></td>
<td>Triptans used in migraines non-responsive to simple analgesics.[332] Zolmitriptan stopped by sponsor[117]</td>
</tr>
<tr>
<td>Penciclovir (topical)</td>
<td>2006 – No</td>
<td></td>
<td>Aciclovir previously reclassified</td>
</tr>
<tr>
<td>Naproxen (oral)</td>
<td>2008 - Yes</td>
<td></td>
<td>Maximum daily dose 750mg,[116] Longer acting and higher relative dosing (to prescription) compared with ibuprofen [332]</td>
</tr>
<tr>
<td>Azithromycin (oral)</td>
<td>2008 – Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diclofenac (oral)</td>
<td>2008 – No</td>
<td></td>
<td>Maximum daily dose 75mg,[116] similar relative dosing (to prescription) compared with ibuprofen [332]</td>
</tr>
<tr>
<td>Nitrofurantoin (oral)</td>
<td>Withdrawn</td>
<td></td>
<td>Application withdrawn in 2010 [127] so no final determination</td>
</tr>
<tr>
<td>Tamsulosin (oral)</td>
<td>2009 - Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pantoprazole (oral)</td>
<td>2009 - No</td>
<td></td>
<td>Central European reclassification. Omeprazole reclassified</td>
</tr>
<tr>
<td>Orlistat (oral)</td>
<td>2009 - Yes</td>
<td></td>
<td>Central European reclassification</td>
</tr>
<tr>
<td>Tranexamic acid (oral)</td>
<td>2010 - Yes</td>
<td></td>
<td>No previous treatment for menorrhagia</td>
</tr>
<tr>
<td>Domperidone (oral)</td>
<td>2010 - Yes</td>
<td></td>
<td>No previous nausea and vomiting treatment (except migraine)</td>
</tr>
<tr>
<td>Diclofenac (patch)</td>
<td>2011 - No</td>
<td></td>
<td>The patch (for local pain) unlikely to have substantially greater benefit than existing non-prescription oral and topical NSAIDs</td>
</tr>
<tr>
<td>Ibuprofen (dermal)</td>
<td>2012 - No</td>
<td></td>
<td>For sunburn. Other OTC sunburn products are available.[555]</td>
</tr>
<tr>
<td>Rabeprazole (oral)</td>
<td>2012 - No</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source: Application to Reclassify Medicines (ARM) consultations on Medicines and Healthcare products Regulatory Agency. Approval dates from the Pharmaceutical Journal or the Proprietary Association of Great Britain NSAID = Non-steroidal anti-inflammatory drug; OTC = over-the-counter (used to mean non-prescription)

*Italicised medicines were identified in the Potential Candidates for Reclassification from POM to P (2002)[121]
Three medicines that achieved a public consultation did not reclassify: trimethoprim; nitrofurantoin; and zolmitriptan (see Table 7-2). Pharmacy-medicines to general sales were consulted on more frequently than prescription to non-prescription reclassifications.

Four first-in-world reclassifications occurred: simvastatin; sumatriptan; azithromycin; and tamsulosin. Three of these vary in different ways from treating self-diagnosable minor ailments.[116] Simvastatin is for long-term preventative therapy in asymptomatic patients. Also for asymptomatic patients, azithromycin is unique both as an oral antibacterial and requiring a positive urine result before supply. Tamsulosin treats a long-term condition, and requires doctor review soon after therapy initiation.

UK participants regarded the UK as the most advanced or among the most advanced countries in reclassification, yet some participants felt that barriers prevented potential reclassifications. Table 7-2 supports this idea, showing that innovative reclassifications have recently slowed.

7.5. Broad themes

Six broad themes arose from the interviews. The government policy of widening access to medicines, of patient empowerment and of health reforms seemed most important, stimulating a facilitative regulatory approach. Cooperation alongside proactivity, financial motivation, pharmacy involvement and pharmacy scheduling, lack of transparency, and culture were the other interlinking themes.

7.5.1. Government Policy and Politics

All UK-based participants acknowledged the role of government policy, particularly the desire to widen access to medicines from the current medical-centric model, causing other effects that helped reclassification.

“I think the thing that made the single biggest difference was government policy as a key driver in the 2000 onwards.” Academic participant

Such policies reportedly helped the MHRA move from a conservative organisation restricting reclassification to become more facilitative, providing useful direction to applicants regarding potential and proposed reclassifications (see 7.6.1). The MHRA was given reclassification targets, and gathered stakeholders to advance reclassification (see 7.5.2, and 7.6.1). However, potential improvements were highlighted. The requirement for medicines registered centrally to go through centralised reclassification, affected by ‘conservative’ European influence worried three UK-based participants.

“Switches ... from here on in are mostly going to be dealt with by Europeans because they were products that were licensed centrally.... and trying to get them all to agree will be a complete nightmare.” Industry participant
Government policy also stimulated proactivity from pharmacy organisations, and the industry organisation, Proprietary Association of Great Britain (PAGB). The resulting positive environment stimulated reclassification applications and some use of the UK as a test market.

PGDs, another initiative arising from policy to expand access to medicines, seemed to enable reclassification by reassuring doctors, the CHM and assessors about the role of pharmacy.

The only mention of politics adversely affecting reclassification was for antibacterials to treat urinary tract infections, although confidentiality limited details.

“I haven’t got a huge amount of information about why trimethoprim failed, but I think probably, I think there’s a lot of politics that goes into POM to P switching as well.” Pharmacy participant

7.5.2. Cooperation and proactivity

The MHRA brought together stakeholders to progress reclassification, and proactively tried to improve processes or encourage reclassifications (see 7.6.1 and 7.6.5).

“I think that was a huge amount of hard work and co-operation really between all parties, MHRA, CHM, the marketing authorisation holder, and the community pharmacy community made [a recent reclassification] happen.” Pharmacy participant

Participants’ comments suggested a largely cooperative environment between industry and the MHRA. Pharmacy organisations worked with industry to develop safe systems and relevant training for each reclassification. The collaboratively developed 2002 candidate list stimulated some reclassifications. A pharmacy organisation approached industry regarding a potential reclassification raised by a user group.

“…normally the MHRA would encourage companies to contact the [Pharmaceutical] Society in the very early stages of an application… and companies would want to engage as well because they would be looking for us to produce professional guidance which would be independent…” Pharmacy participant

Medical support seemed mixed, for example with greater support for minor ailment treatments than reclassifications of antibiotics or for chronic conditions (7.6.7).

7.5.3. Financial motivation

Financial motivation arising from interviews primarily involved companies, doctors and the government, and surprisingly little emerged for pharmacy. Companies’ concerns about return on investment, and time and resources required limited applications for prescription to non-prescription reclassifications (see 7.6.4).
“POM to Ps are grindingly slow to become profitable, whereas P to GSLs are very, very successful. We still haven’t cracked the POM to P model in the UK.” Industry participant

However, reclassification by product (brand) not medicine, retaining prescription funding, advertising and ability to use the same brand as the prescription medicines post-reclassification provided financial advantage (see 7.6.1 and 7.6.4). One company developed a niche reclassification model capitalising on features of the UK market to maximise return (see Panel 7-1).

Reclassifications, particularly complex ones, can be costly. Additionally, perceived lack of market for many products prevented applications and caused market failure of some reclassifications (such as simvastatin). Prescription funding of most medicines apparently reduced consumers’ willingness to pay for some non-prescription medicines, limiting market potential. Medicines retailing below the prescription copayment are less affected by prescription funding.

“…the most important thing to [companies] is: ‘are people likely to buy it?’…. If … pharmacists have been asking for it and there’s an unmet clinical need – no brainer. But… for long-term use for a chronic disease, in this country everybody’s [got] free access to the doctor from the NHS…. why on earth would you start buying something for yourself?” Industry participant

Many participants considered doctor funding contributed to medical groups’ willingness for many minor ailment treatments to reclassify. GPs are paid per capita and incentivised on long-term conditions, so reclassification should reduce workload without reducing income. However, no medical representative was interviewed. Commercial conflict for pharmacy was unmentioned in interviews, but highlighted in submissions on reclassifications from a medical organisation (see 7.6.7).

Financial motivation contributed to the government policy favouring reclassification.

“… the Wanless report … was the economic analysis of what will happen to healthcare in the UK in the next 20 or 30 years depending on how much responsibility people take for their own health.” Academic participant

7.5.4. Pharmacy medicines and the role of pharmacy

Pharmacy came through strongly in interviews. The pharmacy schedule strongly enabled reclassification (see 7.6.1). Pharmacy organisations’ proactivity and involvement helped also (see 7.5.2), as did tools for supply. However, variable performance in community pharmacies, lack of pharmacist proactivity with reclassified medicines and frustrations with complex protocols and questionnaires created barriers (see 7.6.5).

The consumer participant wanted pharmacy to improve, and medical organisations sometimes expressed concerns about aspects of pharmacy supply (see 7.6.7).
7.5.5. Lack of transparency

The reclassification process was secretive, with minutes and committee members’ names not publicly available, and confidentiality before public consultation. Reclassifications that have failed remain confidential and little emerged from interviews.

The lack of transparency enabled and hindered reclassifications. It delays generic entry which helpfully gives applicants effective market exclusivity (Panel 7-1), but potentially wastes effort. Several participants raised unclear process, applications seemingly entering a “black hole” for a period, and applications that took years.

“…the lack of transparency encourages me to submit… It does lead to a duplication of effort and wasted resources because, on occasion, there have been more than one company that’s submitted the same application…. I knew [trimethoprim] was never going to happen because I’d tried [Drug X] 10 years ago and that should have gone OTC because that’s all it’s used for, single dose,… it was perfect… my application never saw the light of day, so the poor people who were trying to push trimethoprim through, I knew it was going to end in a train wreck…”

Industry participant

7.5.6. Culture

Consumer culture arose in most interviews. Consumers were considered to be used to buying medicines from the pharmacy and supermarket, thus creating a potential non-prescription market. However, note the omeprazole quote (7.6.4), which indicated that consumer culture of self-selection negatively affected the market potential for omeprazole as a pharmacy medicine.

The MHRA was described as bureaucratic, but also appeared to be open to change (see 7.6.1).

Pharmacists were used to providing self-medication and advice, but were sometimes described as conservative and “scared” with reclassified medicines (7.6.5). An American participant observed (from visiting) that UK consumers and pharmacists were used to discussing medicines in a pharmacy, unlike the US. However, free doctor visits and copayments influenced consumer culture, limiting non-prescription sales of long-term and higher-priced medicines (see 7.6.6).

7.5.7. Summary of broad themes

Government policy appears to be the most important enabler, helping to drive the proactivity and cooperation seen within the MHRA and from stakeholders. Many stakeholders (and the government) have a financial interest in reclassification, although many reclassifications have limited industry gains. The pharmacy schedule, pharmacy itself and the culture both help and hinder reclassification.
7.6. Findings by stakeholder or factor

I now move from the broad themes that emerged, to more specific aspects of reclassification in the UK, in the same order as other micro-level chapters. Like the broad themes, these are often linked.

7.6.1. Government

The government policy was the primary enabler in the UK. Respondents mentioned government papers such as the Wanless report, and White papers which highlighted self-care. Some mentioned NHS reforms during the 2000s. Several noted the NHS expense and potential to save money, whereas others explained how reclassification allowed doctors more time for long-term conditions (as per government policy).

“…government has given a very clear direction in response to patient expectation… where it is safe, give wider access to medicines…. Having said all that, the applications are assessed, the Commission gives its advice in the best interests of the UK.” Regulator participant

Government interest in reclassification saw an enabling legal change to reclassification by product (rather than medicine) in the early 2000s. This delayed competitor entry, providing effective market exclusivity (albeit for a short time) a fact Galpharm used innovatively (see Panel 7-1).

7.6.2. Regulator, committees and process

The regulator appeared to both enable and limit reclassification.

“…they’re being pushed by the government and the Health Minister to say we need to cut more off the NHS bill, we need to do more switches. You know, but at the same time we don’t want any safety to be compromised.” Industry participant

Depending on the reclassification’s complexity, the MHRA encourages an early preliminary scientific advice meeting (for a fee), and further scientific advice meeting(s) as the application develops.[61] The 2012 reclassification guideline recommends innovative reclassifications receive input from key opinion leaders and various other groups (as appropriate).[61] The applicant prepares a risk management plan framework outlining mechanisms for managing possible risks, e.g. using labelling, and pharmacy education and materials. After submission, the MHRA assesses the application. Major reclassifications may use a stakeholder group (comprising pharmacy, therapeutic expertise and patient/lay perspective), and/or an Expert Advisory Group (an existing MHRA group). The CHM advises on significant reclassifications.

The MHRA reportedly proactively encourages reclassifications, contacting companies to suggest submission or resubmission of a reclassification application, and drawing stakeholders together to progress reclassification generally, or a particular candidate. The MHRA’s Reclassification Strategy Group included stakeholders such as doctors’ and pharmacy organisations gathered to progress reclassification. A Women’s Health Group and a Men’s Health Group were convened to consider
potential reclassifications. These groups commonly included patient organisations, and the MHRA considered consumer/patient input into decision making, and user-testing of pack inserts, important advances. The MHRA’s reclassification guidelines provided benefit.

“…our switch guideline, which was one of the first ones,… it was very well written, it’s very pragmatic…. The only problem we’ve got is the interpretation by the bureaucrats, but that’s the case for everybody.” Industry participant

One participant noted that face-to-face meetings at the MHRA helped build relationships, promote understanding of problems, resolve misunderstandings, and find solutions: “…it’s so much a facilitator”. Applicants appreciated being able to present to the CHM expert advisory meetings which pharmacy organisations were also sometimes invited to.

“Once you submitted it and [the assessors are] happy with it, you’ve answered their questions it’s then their reclassification and they have to justify it in their assessment report to the CHM.” Industry participant

Aspects of the process, such as reclassification by product not medicine, provided financial benefit to companies on reclassification (see 7.5.3, 7.6.4), but a one-year market exclusivity was reportedly difficult to achieve and insufficient.

While industry found the MHRA somewhat rigid, preferring to follow previously used approaches, with a regulatory system “designed for prescription products”, two non-industry participants (and the first-in-world reclassifications) suggested the MHRA was open to innovation.

“Azithromycin… is going to be indicated for women and men who are 16 years and over for Chlamydia without any symptoms. And it is the first oral antibiotic that is going to become available from pharmacies, and … it is going to be directly linked to an accredited diagnostic test…. it is a first for community pharmacies – you are only going to be able to primarily supply this product if you have undertaken appropriate training.” Pharmacy participant

Industry concerns focused primarily on bureaucracy (including time taken and multiple committees); a lack of transparency (although this could also be enabling, see 7.5.5); and misperceptions by regulator assessors and committee members.

“…they have a whole pile of committees now…. it’s not clear to us who’s on these committees because they are not published, and they are very ad hoc and their decision making is not recorded in any way." Industry participant

“…the assessors, because they’re all coming from high-end, they come to this switch application thinking the minute you take it OTC everybody is going to go, is going to turn into mindless consumers and take as much as [they] can.” Industry participant
MHRA conservatism was raised by one participant, who thought conservatism had improved, but still hindered reclassification.

More complex reclassifications typically took around two years, and occasionally up to five years. Industry discussed undertaking studies or doing work (incurring cost and delays) that did not then progress the reclassification. One participant worried about post-marketing surveillance (PMS) studies, noting that while the MHRA delayed generic entry during the study, this may not withstand legal challenge.

“[PMS studies] are hugely expensive and they are definitely a deterrent for even putting an application for switching because you get no data protection.... Are these studies really necessary, or are they being done to address maybe the concerns that health professionals have about the process being too easy, or not sufficiently robust in the first place? I would rather we get it right then when it is switched, rely on the yellow cards rather than have to go through formal post marketing surveillance, which probably isn't going to show us anything.”

Industry voice

Industry thought the MHRA did not understand the commercial reality of reclassification, for example in requiring multiple studies, and expecting reclassifications automatically generate high sales. However, the regulator representatives were aware industry wanted longer market exclusivity.

7.6.2.1. Committees

The committee was primarily raised by industry. One industry participant considered the biggest barrier to reclassification in the UK was the CHM being too high-powered, with no members working at the coal-face. A second participant agreed that the medical consultants on the committee typically see more difficult presentations of conditions: “...GP input on these committees is so important”.

“None of them have got the slightest idea about the dynamics probably of general practice for physicians, let alone community practice for pharmacists, and they just see spooks everywhere...” Industry participant

However, a previous member of the committee saw no overall benefit in moving to a committee specifically for reclassification or an OTC medicines expert group. This participant considered a pharmacy member needed a big picture perspective.

“I always felt that my [pharmacy] input was actively sought in that group, and I think that the group ...paid attention to the expertise that had relevance to the issue being addressed.”

Academic participant

“... do we need to have a pharmacist on those committees? Yes we do. But it's also that person is critical and their preparation, leadership skills, influencing skills, ultimately in my view are actually more important than is this a community pharmacist.” Academic participant
Committee members were sometimes criticised for being opinion-based, e.g.:

“…doctors are great at remembering all the anecdotal stuff…. So you have got a picture of the molecule, thousands and millions of doses used safely… against: ‘I have had one patient who had this dreadful adverse reaction’, and that gets dealt into.” Industry participant

Two industry participants believed one individual had negatively affected the reclassification of naproxen. Although naproxen had reclassified elsewhere and would only be used for dysmenorrhoea, ensuring short-term usage in a low-risk population, it took five years, special studies and an appeal before reclassifying with a maximum pack size of three days’ supply.

Most participants considered protocols and training material enabled reclassification, but several noted protocols and questionnaires had become excessive (see 7.6.5) because “the last thing they want to do is make a mistake”. Likewise, while PGDs appeared to enable reclassifications, but could also promote excessive restrictions.

“…some of the evidence for the switches includes an account of how it’s worked in a PGD scenario, that it safely and effectively delivered supplies. And … there seems to be a view towards CHM that, well, that’s what we need to do to make it safe… I don’t think that’s what a pharmacy medicine supply should be… you’re actually taking away the clinical discretion.” Pharmacy participant

“…emergency contraception PGD … preceded the POM to P switch, and I think the experience of pharmacists’ supply on PGD for emergency contraception actually demonstrated some principles that were very relevant to the P medicine situation… and some of the concerns that might have been raised had actually been addressed through the PGD.” Academic participant

When asked, participants thought information from reclassifications in countries similar to the UK could help, but naproxen suffered an arduous process despite being reclassified elsewhere.

Several participants viewed the multiple committees used in complex reclassifications helped, providing input relevant to the therapeutic area, but some industry participants found them time-consuming and arcane.

7.6.3. Medicines schedules

The pharmacy-only category strongly enabled reclassification, reassuring assessors and committee members that the consumer would have health professional assistance. However, companies found the pharmacy-only category limited sales. Sales increased considerably on down-scheduling to general sales, owing to consumer self-selection culture in pharmacy and supermarket. Pharmacy generally opposed such down-scheduling, reportedly for commercial reasons.
“…I think there is a view… that actually one of the functions of the P category should be to enable the public to learn about medicines, and that at some point in the future it might then become more widely available through GSL…” Academic participant

7.6.4. Pharmaceutical companies

Reclassification in the UK depends on company applications.

“…we were regularly asked… ‘why has [salbutamol] not been reclassified here?’ … we have not received a reclassification application.” Regulator participant

Many UK-specific factors affect companies’ desire to seek reclassification (Figure 7-1), including many enablers and many barriers. Fewer product-specific or company-specific factors emerged, although one company developed a unique reclassification model for the UK (Panel 7-1).

Half of the participants reported that companies consider prescription to non-prescription reclassification commercially unattractive. Undertaking special studies, using experts, compiling information and developing and providing resources such as training material and protocols take time and money, discouraging reclassifications (alongside poor sales of recent reclassifications). Industry wanted market exclusivity for three years rather than just one year.

“It’s the NHS being willing to pay for everything. So you have a population which is not used to doing anything for themselves, and it’s the lack of incentive to the company to make the switch. No data protection, increased data requirements, length of time it takes, post marketing surveillance, layer upon layer which is the thing we are trying now to dismantle.” Industry participant

“Why has it slowed down? Because a lot of the easy ones have been done. It is getting more expensive and more time-consuming …” Industry participant

Global strategy could help, with the UK used as a test market, or hinder reclassification. One participant speculated that Schering Plough possibly chose not to reclassify its pharmacy-only non-sedating antihistamine (loratadine) to general sales in the UK, in order to protect the larger US market where it was fighting against reclassification.
Figure 7-1 Company considerations for reclassification in the UK

*PGDs = patient group directions; Rx = prescription; OTC = over-the-counter; ROI = return on investment; PMS = post-marketing surveillance studies
Panel 7-1 Case study: Galpharm

Galpharm, the company that has done more reclassifications than any other is, unusually, a local generics company that has specialised in this area. Galpharm has since been sold to Perrigo, but the reclassifications continue, both prescription to pharmacy-only and pharmacy-only to general sales. Reclassifying a medicine using their own marketing authorisation, they can then 'sell' an exclusive period to a company involved in the same non-prescription therapeutic area and later bring out house-brands. Having generics in the UK, and licenses for importing products from Europe into the UK, means the company is not limited to a single pipeline (as multinational innovator companies can be). Additionally, being smaller than traditional multinationals helped drive reclassifications faster than with the big companies which could be slower to start and stop projects, and may need to work within a global strategy. Return on investment is potentially greater than for typical brand-driven multinationals because of the sales to a company for a branded product, and then supply of house brands. The key person involved in these reclassifications, Richard Eggleston, was named in several interviews as having a significant role in UK reclassifications.

“Galpharm… have done quite a lot of switches. In part it’s because they happen to have developed an expertise in that area, but it is also quite efficient for the companies [they sell the exclusive period to] because most of our companies work on very lean manpower, and the switch can take a huge amount of time, take a whole team away from other work…” Industry voice

Examples of prescription to non-prescription reclassifications driven by Galpharm include chloramphenicol, omeprazole, and naproxen. Pharmacy-only to general sales examples include loratadine and cetirizine. This model, ‘selling’ an exclusive period to a company then launching own-brands, is only workable where reclassification is attached to a marketing authorisation (product licence) rather than including all medicines. Thus a local company has maximised an opportunity in their own country that may not exist elsewhere.

Product factors affect a reclassification (Figure 7-1) from the perspective of market potential, including the place of the product in treatment, pricing, and other products already available off-prescription.

“Azithromycin, I don’t see how they are going to make a penny out of that, it’s ridiculously expensive OTC, and again it’s this ridiculously cumbersome protocol… young people either… will be getting themselves checked up regularly at what we used to call STD clinics and azithromycin is cheap there… or they’re totally ignorant and they won’t be doing anything about it…. Omeprazole, that was never a great success… upper GI [gastro-intestinal] the category here in the UK is [general sales], people in the UK, unlike the rest of Europe, are so used to walking in and grabbing a pack of calcium carbonate to buy, they’re not used to, and they’re not prepared to stand around in front of a chemist counter waiting for the pharmacist… Chloramphenicol – this has been a great success…. There was a treatment before but really it wasn’t appropriate… but people are used to going to pharmacy to get drops for treating pink eye…” Industry participant

“… [simvastatin] hasn’t been that successful, possibly because the dosage is 10mg rather than the higher dosage which you can get on prescription.” Pharmacy participant

Product factors also affect the likelihood of reclassification, e.g. antibiotics and chronic medicines receiving medical negativity (7.6.7).
For companies, ability to use the existing prescription brand name helps create the non-prescription market, and advertising the OTC product may increase prescription sales. Reclassification by product rather than medicine provides the applicant up to one year market advantage over generic competitors. Allowing advertising of non-prescription medicines was enabling, albeit expensive, and therefore requiring sufficient non-prescription pricing to ensure an appropriate return.

“...pharmacists in the UK... have actually been quite critical of advertising of P medicines... and the companies have said 'well, actually we need to advertise, otherwise we're not sure that you would actively promote them'”. Academic participant

The industry organisation has pushed reclassification, including lobbying the regulator for 25 years, and collating industry experiences to suggest improvements.

7.6.5. Pharmacy

Reclassification appears important to UK pharmacy for many reasons. Two participants considered that a new community pharmacy contract enabled pharmacy progression, e.g. providing consultation areas which would help reclassifications.

“... with the new community pharmacy contract, we are seeing a move from that traditional dispensing role, to utilising all those skills that you learn at university level.... I think [reclassification] is absolutely fundamental if you are in a community pharmacy setting... it is using your clinical skills, it is helping customers more, being part of the wider health care team. You are able to sign-post, and also commercially as well it would be of benefit.” Pharmacy participant

Two pharmacy organisations, the Pharmaceutical Society (professional body) and the National Pharmacy Association (community pharmacy body), provided early input on potential reclassifications, and input into meetings to progress reclassification. The Pharmaceutical Society often provided independent practice guidance for supplying reclassified medicines.

Pharmacy seemed to want reclassification, but industry participants reported that pharmacists often lacked proactivity, behaved conservatively, and sometimes switched people to a cheaper product or lifestyle measures.

“...if a pharmacist was as proactive as they say they are, you would expect that if you went in to buy say Solpadeine for period pain, ... if you gave some clues to the fact that you were buying this for period pain, you might expect the pharmacist to say 'actually there is something new you might want to try.' They never do that, they never do that. They are extremely cautious, almost scared about the things that switch.” Industry participant

“...one wonders if it seems to take a while for pharmacies to get the hang of it.” Consumer participant
Various participants considered excessive protocols discouraged pharmacists. One participant suggested protocols “…suck the will to live out of [the pharmacist], out of the patient/customer, and treat them like an idiot. That’s why Zocor didn’t work, it was just so complicated.”

While pharmacy-only medicines are not restricted to pharmacists, one participant reported the Pharmaceutical Society unusually specified in its simvastatin guidance that the pharmacist should make the first supply, and “subsequent sales can be delegated to appropriately trained staff”. Pharmacy technicians are registered, and medicines counter assistants must be trained.

One participant considered insufficient evidence of pharmacy practice aided reclassifying medicines into general sales. Several participants reported that stakeholders held some concerns about pharmacy availability (particularly for systemic antibacterials), and an industry participant thought that pharmacy’s role was overstated. The consumer voice reported their organisation did not support further reclassifications given pharmacy underperformance in mystery shopping.

“Sometimes the pharmacist would give the nod which the mystery shopper would record, but they didn’t seem to be involved or anywhere near really.” Consumer participant

One medical organisation expressed concern when submitting on tamsulosin and omeprazole reclassifications that pharmacists’ commercial conflict may bias their advice. Other medical responses and participants did not raise this concern. Conversely, an industry participant observed that pharmacy can “be a little bit North Country Protestant and polish our halo if we can send one of our customers off saying inhale steam it will do you just as much good and won’t cost you any money…”

### 7.6.6. Consumers

Consumer culture has been reported earlier (7.5.6). Consumers reportedly balance their familiarity and benefit of buying medicines from the pharmacy and supermarket against free doctors’ visits and subsidised prescriptions.

“…if people can get things free on prescription I think it will have a big impact because they wouldn’t want to pay for [simvastatin] over-the-counter.” Pharmacy participant

Consumers influenced reclassification in other ways, including as the object of the government policy (consumer access to medicines and empowered in health). Consumer representatives and patient groups were involved MHRA-run meetings, and the MHRA required user-testing of labels and inserts.

The consumer participant reported that consumers think that supermarket medicines are very safe, and that pharmacy-only medicines are quite safe, and suggested that consumers may be reluctant to request advice. This participant wanted pharmacy staff to ask more questions and offer more advice.

### 7.6.7. Doctors

Doctors significantly influenced reclassification, as stakeholders commenting on proposals and as committee members who decided on reclassifications (see 7.5.7).
Doctors supported some reclassifications for minor ailments, but were reportedly largely negative about reclassifying oral antibacterials and medicines for long-term conditions. Responses for selected MHRA consultations confirm the chronic condition concern. More medical organisations supported the chloramphenicol reclassification than opposed it.[502] Medical groups supported chloramphenicol more than omeprazole, and tamsulosin received little support. The Royal College of General Practitioners, opposed omeprazole and tamsulosin, but supported chloramphenicol. Seven doctors’ organisations opposed tamsulosin reclassifying,[556] citing no patient examination, insufficient privacy, delay to doctor’s consultation, and unnecessary treatment. Most responding medical organisations did not oppose omeprazole reclassifying, although some suggested improvements, particularly shortening the treatment time. Some medical submitters on tamsulosin and omeprazole worried about NHS cost increases if people initiate (sometimes unnecessary) treatment in a pharmacy then switch to prescription use.

Various participants attributed the increasingly positive medical view to minor ailments funding (see 7.5.3), workload pressure, and confidence from the pharmacists using PGDs for minor ailments.

“…there’s certainly been, as everywhere, huge workload pressure on GPs, and there has been quite a big debate about whether people should go to see the GP for, if you like ‘minor ailments.’” Academic participant

The 2004 General Medical Services contract change reportedly focused GPs more on long-term conditions, with reclassification enabling that. However, two participants considered that doctors, including some committee members, were “…reluctant to let go” of treatments to other health professionals. Two participants reported doctor-pharmacy turf battles, and an industry participant believed GPs have an unrealistic view of their role versus self-management.

7.6.8. Reclassification ahead

I consider that the reclassification process is better in the UK than elsewhere, with government policy, and lobbying by the pharmaceutical industry group having shaped the proceedings. However, although participants were not asked what improvements they would like to see, some participants volunteered possible improvements, particularly in the process.

“…my feeling about the future and POM to P switches, is that we have to be creative about using different models to generate some evidence that can then be used to support POM to P proposals.” Academic participant

Given that doctors apparently gained confidence from PGD supplies, perhaps if a chronic care/collaborative care type pharmacy model was shown to work, they may support reclassification for long-term conditions.
Panel 7-2 Potential improvements for increased reclassification from interviews

Ideas for improving reclassification in the UK:

- Extend market exclusivity to three years
- Increase transparency to reduce potential for double-up of applications, and provide feedback to companies
- Consider sharing information on rejected reclassifications
- Consider mechanisms to shorten reclassification time (e.g. fewer committees)
- Consider mechanisms to reduce reclassification cost
- Try to make protocols manageable or do without
- Consider widening of shared records, or try to demonstrate they are unnecessary
- Consider formal data protection for PMS studies
- MHRA assessors and CHM committees to become more flexible
- Have open dialogue on what is needed and why
- Collect evidence of pharmacy performance
- Improve pharmacy behaviour

7.7. Discussion

The 12 innovative reclassifications (2003-2012), including four world firsts and moves into chronic care stand out internationally, but the pace has slowed. Enablers helped to achieve these world-firsts, particularly government policy, which has positively influenced the regulator, stakeholders, and process. However, I found industry enthusiasm for prescription to non-prescription reclassification has waned with inadequate returns, and costly, time-consuming, and onerous reclassifications.

Others have reported government policy and associated regulator reclassification targets encouraged reclassification.\[24, 34, 115\] Law changes and improved processes\[155\] have created “a positive environment in which to discuss new and possibly radical proposals for self care.”\[115\] The MHRA considered omeprazole and simvastatin reclassifications delivered on its aim “to change the switching culture from acute, short-term, self-limiting conditions to new areas of chronic or recurrent disease”.\[155\] Moreover, the 2002 move to reclassify by product rather than by medicine stimulated reclassifications.

Flexibility, innovation and proactivity in reclassification appear important in the UK’s progressiveness, although further improvements may be possible. Azithromycin, tamsulosin and simvastatin\[116\] used unusual models of non-prescription supply, including collaborative care for tamsulosin and a secure web portal for azithromycin\[557\]. The cooperative, proactive regulator stance has been reported elsewhere, e.g. with simvastatin,\[115\] and the EHC.\[259\] Perhaps industry criticisms are unfair – industry will probably always want improvements and cheaper and faster reclassifications. However, innovative reclassifications have slowed, suggesting that change is required to regain momentum. MHRA initiatives may address bureaucracy concerns. In 2011, reclassification became a priority.
MHRA initiative,[558] and new guidelines for reclassification were released in 2012.[61] However, significant barriers remain, particularly the short market exclusivity, and the centralised European reclassification requirement for centrally registered products.

Despite the positive environment, in 2006 reclassifications reportedly had “fallen considerably short of the Government’s target and other people’s expectations”.[117] However, the government target of 10 reclassifications per year[117] included prescription to pharmacy-only and pharmacy-only to general sales. Reclassifications in 2002, 2003 and 2004 were close to the target, but most were pharmacy-only to general sales,[24] and some were not ‘innovative’ (see Table 7-2) reducing potential benefits to consumers. Perhaps the 2002 list of candidates developed created high expectations, but few have been reclassified (Table 7-2), probably because industry would find them too hard, approval too uncertain, and/or likely sales too low. Despite reasonable medical support overall, doctor negativity with chronic conditions may reduce chances of approval, or success post-reclassification. Other medicines require central reclassification, noted by Kelly to limit UK reclassification.[100] Six innovative reclassifications (2003-2012), (e.g. tamsulosin and azithromycin), were absent from the 2002 list, suggesting reclassification options change with time, or some candidates were overlooked.

Others have suggested industry reticence in driving reclassification.[117] ‘Me-too’ drugs have not followed ground-breaking reclassifications, despite the relative ease for followers, and the zolmitriptan and lansoprazole reclassifications were withdrawn.[117] I found multiple reasons behind the low market potential, some of which have been suggested by others. Two of Mann’s reasons for low simvastatin supplies[115] mirrored participants’ comments (complex pharmacy protocols and dosing concerns). Vamvakopoulos, et al. found 87% of pharmacists reported difficulty with simvastatin guidelines, mainly owing to lack of time, but would check the medical and drug history and most would encourage the consumer to inform their GP of their treatment.[165] Medical criticism of the reclassification[115] probably contributed to concerns about dose and efficacy raised in my research. A limited study (in three pharmacies and published as a letter) found that most people who would consider buying simvastatin would first ask their GP,[329] and other research found low awareness and low support for the availability amongst consumers.[165] While Mann’s case study discussed consumer behaviour, reluctance to pay was unmentioned,[115] despite being raised in my research. Research suggests cost hindered supply for sumatriptan,[559], orlistat,[299] and omeprazole and simvastatin.[247] UK consumer culture to self-treat only for four to seven days,[560] which could limit sales of medicines for long-term conditions.

While UK commentators have suggested a patent effect,[115, 117] UK participants did not mention it (although market exclusivity was raised). However, Galpharm, a generics company, drove many innovative reclassifications, possibly obscuring any life cycle effect.

Some contradictory findings occurred. One industry person considered lack of transparency enabled reclassification, but another from industry considered it a barrier, suggesting specific areas that should be more transparent. The UK’s lack of transparency in registering new drugs is considered to benefit industry.[343] Pharmacy both helped (proactive organisations, and health professional
supervision of supply), and hindered reclassification (not embracing new reclassifications and the pharmacy-only category preventing self-selection).

Others have found UK pharmacy slow to embrace reclassifications,[247, 261, 304] but chloramphenicol sales increased considerably soon after reclassification.[203] I suspect the medicine, condition, price and current consumer and pharmacist behaviour for that condition affect pharmacist buy-in. Reinforcing this concept, Stewart et al. found pharmacists more supportive of the omeprazole than simvastatin reclassification.[247] Omeprazole is for a commonly self-treated condition, while simvastatin non-prescription supply is perhaps perceived outside of usual pharmacy work. While aspirin is also a medicine sold for heart health, perhaps pharmacists view simvastatin differently because of dosing and cholesterol measurement questions. A pharmacist survey following the tamsulosin reclassification (despite a low response and sampling deficiencies) provides further evidence of pharmacists discomfort outside of their usual recommendation field.[304] Only 44% of pharmacists agreed with the reclassification. Despite satisfaction with training materials (as with omeprazole and simvastatin),[247] pharmacists preferred to refer patients than provide tamsulosin, owing to misdiagnosis concerns.

With chloramphenicol, pharmacists were already managing this condition, but wanted greater efficacy. Eye infections are acute and infrequent for consumers, and the product retails under £5 (US$7.75), reducing the incentive for having it prescribed. However, while sumatriptan also treats a common self-medicated condition, pharmacists perceived high cost and low consumer demand limited non-prescription supply.[559] Migraineurs usually have repeated migraines, which other non-prescription medicines can treat, so they may use another non-prescription medicine or get a large quantity of triptans doctor-prescribed with a low copayment, and therefore not need non-prescription sumatriptan.

Little consumer-level research on post-reclassification usage has been published, so consumer outcomes remain largely unknown. One study of ibuprofen purchasers found some contraindicated use: 8% taking more than the maximum daily dose; and a third of people using it for seven days, despite purchase from a pharmacy.[182] One paper reported most non-prescription simvastatin use was inappropriate.[561] but these findings were probably inaccurate. In a large health study 0.7% of participants reported taking non-prescription simvastatin; most were already taking prescription statins and on low incomes. The question about OTC statins was long and included the words doctor and prescription, so was probably misunderstood by some prescribed statin users. People eligible for free prescriptions or accessing the doctor for prescription medicines tend not to buy non-prescription medicines.[562] The largely US-based authors did not appear to consider they may have erred.

With a recent affirmation of the government’s support of reclassification,[28] and the regulator continuing to listen to industry and other stakeholders, I anticipate that further evolution will keep the UK innovating in reclassification. Attracting further reclassifications could be easier if consumers further embraced self-medication, market exclusivity lengthened for ground-breaking reclassifications, and/or pharmacy support post-reclassification increased. The proposed self-selection of pharmacy-
only medicines in pharmacies has been contentious.\[563\] Should it occur, post-reclassification sales potential should increase, but the committee may worry about consumer safety if it believes pharmacy’s role will change.

7.8. Summary

The UK has been progressive in reclassifications, particularly with first-in-world innovative reclassifications moving into new therapeutic areas. The UK’s innovation has primarily been driven by long-standing government policy, proactivity from the regulator and stakeholders, and often with medical support. However, barriers to reclassification remain, particularly the lack of viability of many ground-breaking reclassifications, and European centralised reclassification, which may be contributing to the recent reclassification slowdown observed.
Chapter 8. United States of America

8.1. Introduction

The US was selected as a core country, being the biggest OTC market in the world, and with a
different distribution model and different health system to other countries.

Reclassification in the US receives attention from media and academia, including many papers
published in a wide range of medical journals, law journals, and business literature.[220, 334, 567-569] Commentaries,[130, 160, 566, 570, 571] reviews,[112, 233, 572] and research[573-575] including case studies[19, 21, 51, 565, 576] are all seen. Key reclassification considerations such as the EHC (Plan B) refusal then acceptance for reclassification, statins, nicotine replacement, and non-sedating antihistamines stimulate a new round of papers. The FDA website provides transcripts of public hearings on reclassifications, analysis of which is available in multiple published case studies and commentaries, particularly of loratadine,[149, 150, 233, 574-576] and the EHC.[19, 51, 129, 130, 249, 250, 564, 565, 570, 577-583]

This research makes no attempt to provide a comprehensive overview of US reclassification. Instead, I look as an outsider into the US using the same semi-structured, conversational interviews with key informants as undertaken elsewhere. This approach allows me to elucidate factors that key informants considered most likely to affect reclassification in the US, and to compare the US experience with other selected countries in reclassification.

8.2. Background

The US is the single most important OTC pharmaceutical market in the world, with MarketLine
reporting sales of $28 billion, including non-prescription medicines, vitamins and minerals and
bandages.[584] These sales are mostly through pharmacies or drugstores (59%) and supermarkets
or hypermarkets (36%). Key aspects are reported in Table 8-1.

The US is unusual in its scheduling, with a single unrestricted non-prescription category. The US
health system is also unusual. Many people have private insurance, while others are uninsured
(around 50 million in 2007),[585] and some receive state funding. Medicare funds healthcare for
people aged over 65 years, Medicaid funds healthcare for those under 65 years with low income or
meeting other criteria,[585] and children’s health is covered above the Medicaid threshold to a specific
income. Costs for underinsured or uninsured people may reduce access to health care.[586] The US
has a shortage of primary care physicians, which is expected to worsen.[5]
### Table 8-1 Key aspects of the US market

<table>
<thead>
<tr>
<th>Key aspects</th>
<th>US market</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population (millions; 2011)</td>
<td>313.1</td>
</tr>
<tr>
<td>Health system</td>
<td>Private insurance</td>
</tr>
<tr>
<td>Life expectancy*</td>
<td>78.7 years</td>
</tr>
<tr>
<td>Health Development Index Ranking</td>
<td>4</td>
</tr>
<tr>
<td>Health spend as % of GDP total (2009)</td>
<td>17.7%</td>
</tr>
<tr>
<td>Public proportion of health spend (2009)</td>
<td>49.0% [392]</td>
</tr>
<tr>
<td>Self-medication sales (IMS)</td>
<td>US$22 billion (2010)[587]</td>
</tr>
<tr>
<td>Self-medication as % of total Pharma (IMS)</td>
<td>7.1% (2010)[587]</td>
</tr>
<tr>
<td>Growth in self-medication market (IMS)</td>
<td>2.2% (2010)[587]</td>
</tr>
<tr>
<td>Pharmacist-only schedule?</td>
<td>No</td>
</tr>
<tr>
<td>Pharmacy-only schedule?</td>
<td>No</td>
</tr>
<tr>
<td>Drugstore schedule (licensed person)?</td>
<td>No</td>
</tr>
<tr>
<td>Physicians per 1000 persons [393]</td>
<td>2.4 (2010)</td>
</tr>
<tr>
<td>Number of doctor consultations per year per capita [393]</td>
<td>3.9 (2008)</td>
</tr>
<tr>
<td>Primary care doctor payment structure [14]</td>
<td>Fee for service</td>
</tr>
<tr>
<td>Number of pharmacists per 10,000 population [394]</td>
<td>~9</td>
</tr>
<tr>
<td>Pharmacies per 10,000 population [394]</td>
<td>~2 (2000)[588]</td>
</tr>
<tr>
<td>Percentage of pharmacists in community pharmacy</td>
<td>Not available</td>
</tr>
</tbody>
</table>

Reclassification has slowed recently, with no considerations by NDAC between 2007 and 2012, and statins rejected.[112] This slowdown has been partly attributed to the lack of BTC category.[33, 566] However, despite multiple considerations of implementing a BTC category, including USGAO reports in 1995[49] and 2009,[50] and an FDA hearing in 2012,[94, 589] commitment to BTC is not apparent.

The USGAO reported on the BTC category in February 2009,[50] It stated that proponents had suggested that increased availability of medicines and greater utilisation of pharmacists would improve public health, and costs could reduce through fewer physician visits and lower drug prices following reclassification. The USGAO noted that opponents were concerned that all new reclassifications would move into BTC as default, which would reduce access compared to open availability; that pharmacists’ service may be inadequate; and that the cost to consumers could rise if health funding did not cover BTC medicines; and that it would further fragment the health system. The cost of BTC needs consideration according to the USGAO. Consumer privacy needs protection and BTC counselling by pharmacists should be assured. The USGAO previously (1995) found "little evidence supports the establishment of a pharmacy or pharmacist class of drugs in the United States at this time".[49][p3]
8.3. Primary data sources

Twelve interviews (10 face-to-face, two Skype) occurred in 2011 with 15 people with US work experience. Participants were from the regulator (the FDA), industry, pharmacy organisations, academia (health economics) and health insurers. Requests to the American Medical Association, Public Citizen’s Health Research Group (a consumer and health lobbying group), and a pharmacy academic member of the NDAC failed to yield interviews. A further two participants with global expertise also provided information about the US. Thus, 17 participants contributed to this chapter.

8.4. Prescription to non-prescription reclassifications 2003-2012

Most participants thought that the US was less progressive than the UK, but views differed.

“... if you look at the whole set of non-prescription products country to country, category to category, it’s really the same.” Industry participant

One industry voice noted that the US was ahead of continental Europe, usually ahead of Canada, and always ahead of Japan. A few discussed increased medicines access through mechanisms other than reclassification. Examples included physician assistant prescribing, and collaborative practice agreements in which pharmacists supply or administer specified medicines under a written doctors’ agreement (e.g. vaccinations and statins).

<table>
<thead>
<tr>
<th>Medicine*</th>
<th>Indication</th>
<th>Year</th>
<th>Innovative?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omeprazole</td>
<td>Heartburn</td>
<td>2003</td>
<td>Yes, first proton pump inhibitor</td>
</tr>
<tr>
<td>Loratadine</td>
<td>Hives relief</td>
<td>2003</td>
<td>Yes, first non-sedating antihistamine for hives</td>
</tr>
<tr>
<td>Ecamusle</td>
<td>Sunscreen</td>
<td>2006</td>
<td>No, previous sunscreens</td>
</tr>
<tr>
<td>Levonorgestrel (EHC)</td>
<td>Emergency contraception</td>
<td>2006</td>
<td>Yes</td>
</tr>
<tr>
<td>Terbinafine</td>
<td>Dermal antifungal</td>
<td>2006</td>
<td>No</td>
</tr>
<tr>
<td>Ketotifen eye drops</td>
<td>Topical antihistamine/mast cell stabiliser</td>
<td>2006</td>
<td>No</td>
</tr>
<tr>
<td>Polyethylene glycol 3350</td>
<td>Laxative</td>
<td>2006</td>
<td>No – other laxatives available</td>
</tr>
<tr>
<td>Orlistat</td>
<td>Weight loss</td>
<td>2007</td>
<td>Yes</td>
</tr>
<tr>
<td>Cetirizine</td>
<td>Antihistamine and hives relief</td>
<td>2007</td>
<td>No</td>
</tr>
<tr>
<td>Lansoprazole</td>
<td>Heartburn</td>
<td>2009</td>
<td>No</td>
</tr>
<tr>
<td>Fexofenadine</td>
<td>Antihistamine</td>
<td>2011</td>
<td>No</td>
</tr>
</tbody>
</table>

*Excludes combination medicines

Source: Consumer Healthcare Products Association Website

Only four ‘innovative’ reclassifications occurred from 2003-2012 (Table 8-2), fewer than other countries studied. However, two industry participants considered that most categories had effective
over-the-counter (OTC) coverage in the US, reflecting a focus on significant market opportunities rather than reclassification candidates.

8.5. Overriding themes

Six over-riding themes emerged strongly: scheduling; financial, cultural, and political and legal influences; and evidence-based decision-making.

8.5.1. Scheduling

The biggest barrier, but also a significant enabler to reclassification was scheduling because there is no category restricted to pharmacy-only or pharmacist-only (see 8.6.3). Without a BTC category, complex reclassifications were difficult, expensive and time-consuming. However, easy access provided high reward, maximising the market potential for reclassification. Scheduling affected culture (and was affected by it in turn).

“… regulators are less comfortable about switching something straight from prescription to a drug store situation, so it’s no surprise, if you look at the number of ingredients in the US that have been switched is lower than the UK for example, and other markets.” International industry participant

8.5.2. Financial influences

Multiple, sometimes conflicting, financial factors significantly influence reclassification in the US. Pharmaceutical companies want to maximise profits (8.6.4), first with the lucrative prescription market, then at patent expiry considering reclassification. US reclassification is a high cost exercise with potentially very high returns. To this end, US reclassification can influence the rest of the world.

“… the other main reason for doing the [UK triptan] switch, I’m convinced, is to do it on the safety profile to support the FDA application in the US, because that’s where all the money is made.” International industry participant

Further influencing reclassification are consumers wanting to save money (8.6.6), and physicians wanting to retain income (8.6.7). Pharmacy would like BTC (providing they can work out payment aspects), but that would probably limit post-reclassification sales for companies and could cost consumers more (8.6.3). A BTC category might help retailers’ businesses.

Health insurers have tried driving reclassification, apparently for cost reasons. Government pressure from rising health costs was considered likely to make them more interested in enabling reclassification (and BTC) in the future.

“The US in contrast [to the UK], has no government interest in, at least from an economic point of view right now, in alleviating themselves of a burden which they say continues to grow in their Medicare payments and stuff. We think eventually, you know, that dam has got
to break; you know, there’s got to be someone in the government who thinks that maybe, you know, responsible switch is a way to alleviate cost, but it hasn’t happened to date.” Industry participant

8.5.3. Cultural effects

Cultural aspects came through in many interviews from the US. OTC medicines have open access and can be purchased anywhere, at any time without questions: “Americans love convenience”. A health insurer participant talked about consumer self-efficacy – e.g. only going to the doctor when necessary. Several participants expressed concern about people who “don’t have access to a physician.” Consumer rights came through because of the triumph of individual autonomy in the US.

“…people say [reclassification] is part of people controlling their own health care.” Regulatory participant

Pharmacies or drugstores differ in the US to elsewhere (especially Europe), with large retail-focused drugstores. Consumers do not expect to be asked questions, and pharmacists usually are not proactive in discussing OTC medicines.

“…in the US the pharmacy system is so different. I mean it’s like supermarket shopping…. The intervention level seems to be, the opportunity at least for intervention, seems to be a lot less in the US. And that really is driven on self selection and self diagnosis, and self management.” International industry participant

The mindset change for consumers and pharmacists appears to be an important hurdle to BTC occurring.

8.5.4. Politico-legal environment

Political and legal issues came through interviews in several regards. Most important was the requirement for Congress to change the system (e.g. to implement BTC), which was reportedly burdensome and slow.

“The government is a little bit equivocal, it’s not getting a lead from industry so it’s not taking it anywhere.” International industry participant

One global participant considered reclassification depends on the White House, and on lobbying: “…everything is by lobbying in the US”. Several participants noted that the pharmaceutical industry and health insurers had considerable lobbying might. Consumers were considered to have a strong voice. A participant spoke about the reclassification of vaginal antifungals in the 1990s:

“…there was actually so much consternation within the community itself. You know, I mean women saying ‘come on’, it was almost kind of a women’s rights, women’s health.” Regulatory participant
The political influence for the EHC was noted or criticised in most interviews, but seemed an anomaly, given various sources commented that reclassification was about the data or science rather than politics. However, because of the importance of the US market, consumer pressure there even affected company decisions elsewhere. A manufacturer was quoted on why they chose not to reclassify the oral contraceptive in other countries “…because the backlash in the US from the religious right would be enormous”. Political pressure had also affected the FDA’s advisory committees and the FDA and industry relationship.

“…in the last five years or so there’s been so much public, media and political attention paid to that relationship between FDA and the industry, the FDA’s become a lot more distant from industry, intentionally.” Industry participant

Legal issues including litigation arose in almost all interviews, largely as a barrier to reclassification. Participants used the words legal, process, procedure, litigation, tort, liability, courts or lawyer, sometimes frequently. With interview recording declined by some, and a witness present in an interview, legal concerns seemed rife. The FDA was thought to be avoiding legal action in not forcing a reclassification for non-sedating antihistamines, although a regulatory participant expected legal action as a regular occurrence.

“…we’ve sort of come to a bit of a dead end with the FDA, we’ve almost decided to sort of try and force it with a legal discussion.” Industry participant

The system lacked flexibility, for example with several mentions of the FDA avoiding a practice that occurs elsewhere because the FDA considered they did not have the legal right.

“It’s amazing to me, things we don’t even think about because we’re not allowed to take economics into our decision-making.” Regulatory voice

8.5.5. Evidence-based decision making

Evidence-based decision making emerged strongly from interviews, with stakeholders respecting the FDA process. The FDA requires considerably more data (including consumer behaviour) for an innovative reclassification consideration than other countries, partly because there is no BTC category. However, the market size and possible market exclusivity can provide sufficient return to justify the cost. Such research enables evidence-based decision making, as agreed by several participants, but the effort prevents some reclassifications progressing (see 8.6.2).

“…it’s always easier when you’ve got data to help you. Because then the judgement is much better informed.” Industry participant

“…I think for the most part you’re, anything that’s going through the Rx to OTC switch process in the US at least, will have a sufficient and over-abundant amount of data to back that product up. So… if it were to go over the counter… of course there could still be risks that
would be unexpected, but it would be highly, highly unlikely for that to occur.” Academic participant

8.5.6. Summary of over-riding themes

The often intertwining themes throughout these interviews echoed some other countries. The financial theme seemed magnified in the US, primarily because of the market size and the cost of reclassifying. Culture came through strongly also, particularly the culture of consumerism, and the culture of the drugstore with a fast-moving consumer goods (FMCG) type environment and the typical lack of participation by the pharmacist in the OTC supply of medicines. Legal impediments and politics arose, including the lack of federal government support for the BTC category. However, ultimately decisions are based on the volumes of data usually required for innovative reclassifications.

8.6. Findings by stakeholder or factor

This section reflects on specific aspects of reclassification in a similar way to other countries to aid comparison.

8.6.1. Government

The government is not currently driving the reclassification agenda, nor the BTC change. A couple of participants expected that the federal government would become more interested in reclassification and politics would drive change, but without government interest, BTC would not happen.

“The government in the US is not taking a proactive stance, and really engaging in this area. And when they do, I think you’ll see a dramatic change in switch activity…. And when Congress takes an interest in alleviating their own healthcare cost burden, they will change the system. I think that’s usually the way it works here.” Industry participant

The health reforms were likely to increase pressure on doctors which could increase interest in reclassification.

8.6.2. The regulator, committee and process

Most reclassifications in a new class require research on consumer label comprehension, self-selection, and actual use. A new indication for the OTC environment requires new evidence, as for omeprazole with a frequent heartburn indication. Extensive safety data across multiple markets are usually required. Where the medicine has become generic or different companies held the licence for different countries, safety data across multiple manufacturers or distributors are needed, with databases providing the data (at a cost). The resulting high cost (US$30 million or more), long process, and uncertainty of success (for some medicines) prevent many applications. On the other hand, by doing further clinical research, market exclusivity should apply, allowing three years without generic threat (for both prescription and OTC supplies).
Some medicines are straight-forward, requiring few studies and no public meeting because of their safety. Examples included the non-sedating antihistamines (safer than OTC sedating antihistamines); and a product for poison ivy which went directly to OTC.

“…it’s still the same principles of: is it self-diagnosable, is the safety profile one that you think you don’t need any special monitoring? I mean, can a consumer actually use this rationally without having to have some kind of intermediary? And we had one that was called Ivy Block which made all the sense in the world, it was something to keep poison ivy and stuff away, you just put it on, there was no absorption.” Regulatory participant

Considerable background work occurs before submitting a New Drug Application (NDA) for a reclassification. Company representatives usually meet with the FDA to help the company ascertain likely requirements for a reclassification (including studies) and to comment on collected data. Initially the company submits background information and development programme ideas, and the FDA outlines what the company needs to show. A Phase II meeting considers what has been done and what the FDA thinks is still needed. A pre-NDA meeting provides a final discussion before submitting the NDA. These free, confidential meetings help inform decisions about whether to continue with an application, and plan the studies required.

“…switches can be so unique, and you want to understand FDA’s biggest concerns up front.” Industry participant

Companies communicate with the FDA between meetings. Later meetings help align the FDA and the companies, so on submitting a protocol for the next study “they don’t reject it or throw up a lot of questions that you weren’t ready for.” The FDA usually provides written pre-meeting comments, allowing the meeting to concentrate on critical points. When studies are completed, companies formally apply to reclassify, paying the FDA US$1.6 million.

The FDA combines two committees in a public meeting to consider a reclassification: the NDAC and the relevant therapeutic committee. Organisations and individuals can present, and there are no other agenda items. A regulatory participant considered the variety of perspectives in the committee (including consumers) provided a strength. Two industry participants with international experience endorsed the transparency of the meeting and ability for sponsors and others to present.

There is no clear acceptable ‘pass mark’ for consumer studies to meet, as this varies for different reclassifications. Without an exact figure to work towards, industry can be frustrated. However, one industry participant accepted this, noting (enthusiastically) that reclassification was more of an art than a science. A regulatory participant reported that even with this research, judgement was still required.

Participants largely respected the process and the committee decision, but raised small concerns regarding committee members. One industry member suggested conflict of interest requirements caused vacancies, reduced the pool of eligible committee members, and thus affected the discussion.
quality. Additionally, the unfamiliarity of the therapeutic committee with reclassification provided difficulties.

“…in some of the FDA committees in the US there are very pro-OTC people and very anti-OTC people. And some categories find it easier to get approvals than others, and that’s because they’re all humans, and some of the professionals really do have a bee in their bonnet about not seeing more products in the OTC sector.” Industry participant

A lack of flexibility filtered through the interviews, with a very formal process, and an inability to do things differently, e.g. cost should not be considered by the committees.

“FDA have indicated on a couple of occasions at least where they feel they cannot be referring to other company data. They don’t have the legal right to do so. But I think that’s peculiar to that country in the way that the legislation and the way that the FDA processes work. Plus there’s a much more legalistic environment for everything…” International industry participant

“…it’s hard to have a lot of informal dialogue and talk about the FDA’s policy around switch. And there are a lot of policy implications to how we switch things here …” Industry participant

A further aspect of the market, considered enabling in a couple of interviews, was that a medicine is OTC by default.

“…there’s an assumption in the US which is almost unique… a medicine is automatically OTC unless it’s proven it needs to be in the prescription market for reasons of safety. So there’s a presumption that all medicines except the really high end opiates or whatever, will at some stage go over-the-counter.” International industry participant

8.6.3. Behind-the-Counter Category

The lack of BTC category emerged as the primary reason why the US was less progressive than the UK in reclassification. Many compared the US to the UK in this, particularly noting the statin example.

Participants concurred that BTC would enable reclassification and nearly all were generally positive about such a category, considering it would enable complex reclassifications, help relieve pressure from the primary physician shortage, help pharmacy given pressure on dispensing income, and save consumers and funders money if more medicines reclassify. The industry organisation representative preferred using technology (e.g. a talking label on a product) to advance reclassification, rather than BTC. However, a pharmacy organisation representative embraced the idea of pharmacists recommending medicines such as triptans.

“…professionally it’d be very interesting to me to develop a behind the counter class…” Pharmacy participant
Many factors were considered to have contributed to the lack of an official BTC category (Figure 8-1). Most importantly, Congress would need to action a change, but government interest is low. Consumer associations reportedly supported BTC: “they think anything that drives down the cost is good.” However, the culture of medicine purchase including lack of pharmacist involvement is not conducive to a BTC category.

“I think there will be a lot of Americans who feel like, ‘well I go to my doctor, which they do, and I have my check up and I’m told what to do by this person and that person. And I don’t want another person to tell me what to do.” Academic participant

While seeing benefits in BTC, pharmacy organisations want logistical concerns resolved to fully support BTC (Figure 8-1). With strong retailer price competition, some participants want payment for the pharmacist’s time to ensure viability, adequate staffing and uniform process. One retailer participant considered US pharmacy was very advanced internationally, being “well beyond dispensing” with influenza vaccinations, medication management, and collaborative practice agreements in many allowing the pharmacist to add medication such as aspirin, or statins, or change doses. This perhaps reduced pharmacists’ interest in reclassification and BTC. Others also noted these advances, but one considered BTC may resolve issues with the collaborative care model, including physician support, and differences between States.

“I think one of the things that we may ask for first is well just to be able to give immunisations without having to have the protocol order with a partnering doctor. And … there’s a lot of pushback from, like, nurse groups and, and medical, and the doctors saying, you know, that’s our turf.” Pharmacy participant

Although industry as a group opposed BTC, many individuals in industry were apparently privately positive about it. Industry could benefit if complex reclassifications were enabled, and BTC may see more supplies through independent pharmacies, improving profit margins for industry over drugstore chains. However, industry knows that most reclassifications fail commercially elsewhere, so worries about losing the open access model. Industry worried that a BTC category could see up-scheduling, but another participant considered the legal process and burden of up-scheduling would make this unlikely.

“The pharmacists want it, the body that represents retail pharmacy wants it. The government is a little bit equivocal, it’s not getting a lead from industry, so it’s not taking it anywhere. And I think one committee took a look at it recently and said there was no overwhelming case for it because there was no submission from the industry, but that could change in the next five years. You couldn’t even get the issue discussed 10 years ago, now it’s being raised an awful lot when I go around privately and talk… That gives you a chance to get some pretty amazing products over the counter.” International industry participant
Concern products will up-schedule from open to BTC
Concern all new reclassifications will go to BTC
Sales volume high with open access
Multiple State Pharmacy Acts to change
Congressional change required
Fragmented care
No evidence that BTC better than OTC
Physician negativity
Pharmacists perceived as dispensers not health advisors
Physician negativity
Pharmacists do not usually initiate OTC discussions
Copayments for physicians and prescriptions
Self-efficacy culture
Convenience mentality
Personal rights
Want payment model in place first
Documentation/communication
No need - doing collaborative care
Focus on other clinical opportunities
Liability/insurance concerns
New technology instead
Concern medicines will stay in BTC
Industry somewhat negative
Government not pushing
Pharmacy organisations not pushing
Culture
Figure 8-1 Key barriers to behind-the-counter availability in the US
Although insulin, pseudoephedrine, and the EHC, are effectively behind the counter, participants considered these anomalies, rather than forerunners for BTC. Pseudoephedrine is controlled by a different government agency because of its manufacture into methamphetamine. The EHC (to verify the purchaser’s age) was politically motivated and apparently stated not to be setting a precedent.

8.6.4. Pharmaceutical company factors

The dollars dictate reclassifications sought in the US. Prescription earnings rule the decision first and foremost as health insurer funding usually stops after reclassifying. Then considerations include likely post-reclassification sales, likely cost of reclassification, likelihood of approval, and payback compared with other opportunities (Figure 8-2). However, with a large easy-access market, reclassification in the US can be very successful. Figure 8-2 shows more enablers than barriers, yet innovative reclassifications can be few, illustrating the strength of the main barriers in the US.

The company nature, size and focus can encourage or discourage reclassification. A regulatory participant reported that companies often abandoned reclassification ideas after discovering the complexities involved. While lack of OTC infrastructure can prevent reclassifications elsewhere, this need not hinder US reclassification, given the market size. Sanofi-Aventis reportedly bought a US company with an OTC infrastructure when reclassifying their non-sedating antihistamine, fexofenadine. While small or local companies occasionally submit reclassifications (usually simple reclassifications without exclusivity), mostly multinationals drive them, particularly those with previous reclassification experience. A dossier for reclassification from overseas may be adapted for the US.

Prescription prices and sales benefit from the two key participants in the prescribing (the doctor and the patient) usually being unaware of prices. In contrast, for OTC medicines, consumer expectations and retailer competition apparently force prices down. The prescription market is therefore more attractive for a medicine within patent, but reportedly drops 80% on patent expiry. Thus the OTC market becomes attractive when patent expiry looms, particularly if a three-year market exclusivity appears likely allowing high prices to be retained longer.
Chapter 8

Company factors

- Mergers/changes
- Other better opportunities
- Insufficient resource
- Prescription focus only
- OTC focus not on reclassification
- Short-term focus

Negative factors

Can be positive or negative

- Prescription-OTC divide

Positive factors

- Previous reclassification experience
- OTC infrastructure

Product factors

- Off patent
- Long patent life
- Complex reclassification
- Consumer backlash
- Wrong price point
- Sales potential
- New indication needed
- Nearing patent expiry
- Likely to reclassify
- Minor, self-diagnosable condition

US factors

- No BTC
- Legal requirements
- High prescription prices
- Long, time-consuming, costly process
- Politics
- Advertising (Rx and OTC)
- Self-efficacy culture
- Self-selection
- Confidential meetings with regulator
- Patient payment for healthcare
- Open regulator
- Large population
- Evidence-based decisions
- 3 year market exclusivity

Is the reclassification financially viable?

Company decides to submit reclassification application, or not

Figure 8-2 Company factors in the US market
Interviews with industry in the US and international experts suggest that the perfect alignment of factors for a company in pursuing a US reclassification would be as follows:

A multi-national company with other OTC products,

previous US reclassification experience,

and sufficient resource (financial and personnel),

which has a medicine with a strong brand name (in the US),

about to come off patent,

which requires special studies to reclassify (so should get market exclusivity),

and is for a common, self-diagnosable condition,

with a good safety profile,

a unique selling proposition,

the right price point,

and that can be used by a consumer without help from a learned intermediary

“But in the last five to 10 years, the industry really has been scratching their heads about what’s left that they can propose that’s going to be available anywhere.” Industry participant

The main reasons for non-submission are that the company has a prescription focus (including generic companies), expected return is insufficient for the predicted cost, reclassification approval seems unlikely, or there are better opportunities elsewhere.

“So it’s the studies, it’s the safety review, and then of course the resource, the man hours … you’re really talking about easily a five-year timeline to get it developed and approved. And so there are few and far between that will really be funded, because it has to be a very nice sized payoff to be able to justify that long in the development path here.” Industry participant

Usually candidates are considered from the company pipeline (favouring large multinationals), but licensing to a consumer company can occur, as AstraZeneca did with omeprazole. The product needs to suit non-prescription use without a learned intermediary, be appropriately priced for OTC, have a compelling reason to buy above competitors, and preferably have a strong brand name. Although ideal, market exclusivity is not essential for success. Straight-forward reclassifications have no exclusivity, but cost less, are faster, and may work well sometimes, including for niche products. Niche products probably would not warrant the cost and effort of multiple studies even with exclusivity. Market exclusivity for three years clearly enabled some reclassifications, but was considered insufficient by one participant.

8.6.5. Health system and pharmacy

The consumer cost of accessing healthcare; and the OTC medicine supply model strongly affect reclassification, helping achieve commercial success. However, the open access supply model also hinders complex reclassifications (e.g. statins).
The funding model can favour self-treatment owing to the consumer cost of doctor visits and prescriptions. Uninsured and underinsured people reportedly rely on OTC medicines because of the cost of seeing the doctor (although an industry participant said they were not a target market). Other people have copayments on doctors’ visits and prescriptions making OTCs usually cheaper for consumers, as well as time-saving. Participants variously reported copayments for doctor visits of $10-25 and $30-50.

“...the way the market is set up in the US is particularly favourable to switch in that ... pretty well everyone pays to see a doctor.” International participant

The high cost of health care is paid by health insurers, the government (through funded care and tax breaks for insurance premiums), and consumers (as copayments, in premiums, or full-cost for the uninsured). Health insurers are exploring ways to reduce costs, e.g. funding influenza vaccination by pharmacists, funding some minor ailment treatments in pharmacy clinics (using nurses and pharmacists under standing orders), and encouraging self-treatment, e.g. with a cold and flu pack for members. Health insurers are positive about reclassification, BTC, and pharmacists doing more. Insurers save the doctor and prescription cost if the consumer self-medicates, and usually stop funding a medicine (or occasionally increase the patient copayment) when it reclassifies. Delisting on reclassification sometimes increases consumer costs, frustrating consumers, and potentially limiting OTC sales. For pharmaceutical companies, losing prescription funding is a further incentive to reclassify only when the prescription market is about to be largely lost with patent expiry.

“...once things go over the counter, the price goes down, however, patients are no longer sharing that cost with their insurance company, so they ‘hey it's down but I may be responsible for the whole price of the product rather than my $10 copay.” Pharmacy participant

The OTC medicine supply model means almost all OTC medicines are available from retailers without pharmacist-presence. Competition lowers the OTC medicine prices, assisted by low staffing. Large retailers pressure suppliers on pricing, affecting supplier profitability. However, extended-hour liberal access to medicines through multiple outlets maximises sales. This retail-focused model probably discourages pharmacist involvement in OTC supply, through consumers expecting to self-select. Although pharmacists were in over-supply, many were still very busy.

“... many of the chain pharmacies here see that they've hired a pharmacist to dispense X number of prescriptions per hour.... If you don't meet that... then your job may be less secure.” Pharmacy participant

“... the pharmacy system is so different ... it's like supermarket shopping.... the opportunity at least for intervention, seems to be a lot less in the US...” International industry participant

A culture of consumers self-selecting and expecting no questions, and the culture for many pharmacists of not being proactive in OTC supplies, affect how pharmacists are perceived (by
consumers and stakeholders), impeding the creation of a BTC category (Figure 8-1). One participant reported independent pharmacies had higher pharmacist involvement in OTC, although prescription business remains their main income, and independent pharmacies are declining in number. One participant said the biggest question is “can pharmacists triage?” However, federal agencies reportedly recognised pharmacy more after their vaccinating role in the influenza pandemic (2009-2010). The move to the pharmacy doctorate course was considered to help pharmacists embrace new clinical roles, but also increased variability between pharmacists in ability and attitude.

Pharmacy has been evolving, with increased clinical work, and it seemed that pharmacy was perhaps more focused on that than opportunities with reclassification and BTC. Pharmacy has driven immunisations by pharmacists, and is providing other clinical services including supplying certain medicines under specific conditions in a collaborative care model.

8.6.6. Consumers

Consumer impact on reclassification included effect on sales, use of consumer studies to show whether a medicine could go OTC, and the culture of consumer expectations in purchasing medicines. This culture of expecting to purchase products without question, means consumer education will be necessary should a BTC category arise. A couple noted the lack of privacy in pharmacies and that American consumers would not like to be questioned in front of other people.

Concerns were held about the potential to self-treat instead of seeing the doctor, especially for the uninsured and underinsured, but the very poor have state health care. One participant suggested health literacy was lower than desired, but also lamented that the system assumes “that people need a physician to manage their health”, noting that many consumers could probably manage better than what they’re given credit for.

“... many more people in this country than one might expect don’t have a personal physician. Whether it’s by choice or because they can’t afford it. And so OTCs for that class are more enabling ... it gives them an option that they otherwise wouldn’t have. Because they can’t get a prescription because they can’t pay for the doctor visit.... You can enable that class, but will they be able to pay for the OTC?” Industry voice

Consumers were considered to have power politically and in the media. Politics arose with the EHC with a couple of participants noting the influence from the “puritanical past” or “religious right” that differed from elsewhere.

8.6.7. Doctors

The medical perspective was unable to be discussed first-hand without a medical participant, limiting findings from this section. Impressions from the participants were that medical negativity occurred, including concerns about fragmented care. Several participants (from different stakeholder groups) considered medical views may be motivated by potential loss of consultations. Allergists had opposed
the reclassification of non-sedating antihistamines. Physicians were reportedly reluctant to allow changes of scopes of practice for other health professionals that would encroach on their own area.

“What they don’t like are front-line products that they can use almost as a scatter-gun approach to come out of the prescription area, ‘cos then they lose the consulting fee… they fought bitterly to prevent hydrocortisone 1% going over the counter, because any patient going to the doctor with skin rashes gets treated with 1% hydrocortisone … For reflux… for a lot of the [gastro-intestinal] specialists it was so easy, you just bang this out. Try this, come back and see me if it doesn’t work, and here’s my bill for $100, and they hate this, anything associated with switch, or an enabling mechanism like the third class, they don’t like at all…”

International industry participant

“…the medical societies will come and speak in the open public forum, and in many cases will speak to their concerns about what happens in that switch. And people aren’t ready, you know, and the consumers that they see or the patients that they see, could never manage it on their own, whatever it might be. A lot of times you get a fairly biased point of view and you have to look through that to see whether there’s anything real in there from a public health point of view that is cause for concern.” Industry participant

Committee members involved in reclassification are “overwhelmingly doctors”, so the medical voice is definitely heard. However, medical negativity seemed less important than other factors in preventing reclassification. Some participants mentioned physicians were over-burdened, with low numbers per capita, and expressed concerns about future doctor shortages.

One participant recommended talking to medical associations and community before a reclassification to get them on-side afterwards as doctors can influence their patient’s use of the OTC product.

8.6.8. Advertising

Advertising received little mention in most interviews. However, an industry participant noted that pre-reclassification advertising was a big advantage. Advertising prescription medicines built a brand name and a heritage that helped the business case for reclassification. After reclassifying, advertising oversight moved from FDA to the Federal Trade Commission. The FDA was stricter in balance, requiring an equal risk and benefit to be presented, while the Trade Commission did not. Thus the disclosure of risk was different, using statements such as “use as directed” rather than outlining specific risks (an advantage for industry), and relying on consumers to read packaging. Although the industry participant reported concern from some healthcare professionals, it did not arise in the interviews with pharmacists.

8.6.9. Reclassification ahead

Sponsors remain interested in reclassification, but recognise new thinking is needed for complex reclassifications. Other stakeholders recognise changes are needed to reverse the trend of declining
reclassifications and address increasing healthcare costs and a primary physician shortage. Some participants expect Congress will be stimulated to change by rising healthcare costs.

“[Congress has] the ability to get all the players to the table, and start to make the change… there’s an investment involved, just in pharmacy systems, just electronic systems. To be able to make that all work, so, you know, the US system is so far down the road, developed to manage the current environment…. So, that’s why I think no one has tackled it, it’s such a big issue, and… the payout isn’t great enough to anyone to really start pushing everyone in that direction yet.” Industry participant

Reclassifications of chronic medicines and more complex categories could be enabled using BTC (which some apparently considered will come eventually), or technology with or without BTC. An FDA participant and industry participants suggested that labelling is currently narrowly defined, and a desire to allow labelling to encompass new technology exists.

“…in the next five to 10 years I really expect there to be technology available so people can manage a condition chronically OTC if they’re using, you know, diagnostics. They’re using communication devices, all of which can link back to the doctor’s office. So their doctor is getting real time data, even if they’re not going to the office, and they can monitor them that way and maybe only see them on a yearly basis. All of that has to be proven out.” Industry participant

A couple of participants considered that pharmacist and doctor sharing of electronic records will help manage fragmented care and enable complex reclassifications. However, other mechanisms to increase access to medicines already exist. A collaborative care model may provide greater opportunity than reclassification for pharmacists to work clinically and improve consumer access, but patch protection with physicians can still limit this. Reclassification relies on sponsors to drive it, takes a long time, typically causes loss of funding of the medicine, and is limited to one medicine at a time (rather than a therapeutic group).

Participants did not expect a repeat of Wellpoint’s third-party reclassification attempt with non-sedating antihistamines, owing to legal challenges, time taken, and the cost of studies (which may be required). The FDA seems unlikely to drive reclassification themselves, and this probably goes against the FDA’s desire to minimise legal action, and require pre-reclassification studies.

8.6.10. Discussion

The large US market, easy accessibility of non-prescription medicines, consumer culture and cost of accessing prescription medicines aids reclassification in the US. However, reclassification is limited, apparently resulting from scheduling, perverse incentives to remain prescription-only until the last minute, and the cost, effort and time required for reclassification.

A BTC category should enable reclassification but has been discussed for years without success.[49, 50] Pharmacy has perhaps sidelined reclassification, preferring to advance consumer access using
other mechanisms, rather than waiting for manufacturers to reclassify one painful step at a time. A BTC category would require changes in consumer and pharmacy culture. High cost and resource would probably still limit reclassification if the same or more pre-reclassification studies are required as suggested in the FDA’s 2012 public hearing on increasing access to medicines.[94, 589] However, if BTC were implemented, these requirements may change over time, enabling niche product reclassifications that cannot be justified in the current high-cost environment.

Achanta, et al. also found key informants believed BTC or similar would be beneficial, but believed political hurdles were insurmountable.[341] My finding that a range of participants supported BTC, including some from industry, suggests that industry opposition reported by Achanta is dissipating, that dichotomy exists in industry on this matter (as suggested in my interviews), or may reflect small numbers of participants in both studies. Divided views in industry are understandable given the concern that BTC availability will impede sales off-sets the desire for new reclassifications. Reclassifications have slowed since Achanta’s work,[112] which may help industry reconsider the BTC option to advance reclassification. However, this was not evident in the 2009 USGAO report[50] or at the 2012 FDA hearing.[94]

BTC and/or new technology may be limited for further reclassifications. The cost of reclassification is already high. Developing new technologies and then testing them, and potentially having kiosks, talking product labels or similar will add significant cost.[94, 589] While facilitating reclassifications of blockbusters like the statins, for small products sufficient return is unlikely. Some industry presenters suggested market exclusivity would need to be extended beyond three years. In 1999, Kraushaar believed three years’ exclusivity was insufficient, noting study requirements have increased since it was exclusivity was devised in 1984, e.g. an actual use study using 75 000 participants.[590] The anticipated need for studies also suggests inadequate confidence in pharmacists as health professionals to manage this well in a BTC environment (echoing the USGAO).[50]

Studies from outside the US examining pharmacy benefit are few, but several report some pharmacy interventions identifying non-prescription drug-related problems.[82, 312, 591] Others support seemingly responsible pharmacist-supply of oseltamivir.[80, 81] Mystery shopping studies suggest variability but suggest that some consumers at least do get good care elsewhere.[285, 297] Studies showing consumer outcomes, e.g. with NSAIDs[180, 181, 592] do not show the effect of pharmacy on these outcomes, and, given cultural differences, may not predict US effects. However, the US BTC consideration could take heart from US pharmacists’ role in vaccinations, which has increased access[593-595] and been endorsed by the Centers for Disease Control and Prevention,[596] and medical bodies.[597] US pharmacists receive up to six years of training and should be able to fulfill an expanded role with supplying selected medicines. A small US consumer survey (n=168) found high support for BTC availability.[15]

The FDA meeting in March 2012 on innovative technologies, BTC, and other potential enablers for reclassification[94, 589] found some similar issues to those arising from my research around BTC. Industry was interested in innovative technologies but not BTC because availability would be limited
Chapter 8

to 60,000 pharmacies nationwide, instead of 500,000-750,000 retailers currently selling their products. Technology proponents often perceived that technology would preclude the need for pharmacist involvement, although some suggested combining it with pharmacist expertise.

As in my research, pharmacy organisations at the FDA hearing were keen on BTC, considering pharmacists were well-trained, but noting the need to work out documentation and payment. However, at least one pharmacy organisation suggested payment could be worked out during the change, noting that payers would pay if they saw benefit. Ried, et al. considered payment would be the critical factor in success of BTC, with funding of pharmacists necessary for optimal uptake and consumer outcomes.[598] Pharmacy has moved forward with collaborative care, supplying immunisations and other medicines according to specific criteria, yet the BTC category is not trusted. Even if the BTC category is implemented (by no means certain), the FDA hearing suggested multiple studies will still be needed to ensure safety.[94] There seems to be a double-standard: collaborative care appears reasonable, but BTC either should not happen or if it did would need advance studies. Perhaps this reflects an excessive protection of the public by the FDA, or maybe collaborative care supplies are taken more seriously than a retail product that is advertised to go and buy, given that US pharmacists apparently often do not proactively ask questions about OTC medicines.

As suggested by my participants, the American Medical Association opposed BTC at the FDA hearing, believing that it would lead to poorer care, threaten patient safety, and may increase consumer costs, and that if pharmacists wanted to move into this area they needed a medical degree. However, sometimes medical support occurs for reclassification, e.g. multiple medical voices supported the EHC reclassification,[599] and recent calls for reclassification of the oral contraceptive have arisen from the American College of Obstetricians and Gynecologists.[315]

After reading the FDA hearing transcripts, I felt, as I had after completing my interviews in the US, that the US may have moved past a straight-forward pharmacist-only supply model. While BTC discussion has been reignited,[33, 94, 598, 600] implementation seems unlikely when industry worry about following the UK path of limited sales. For example, omeprazole in the US has been hailed a commercial success with US$40 million per year in sales,[23] while sales in the UK are negligible.[96]

Advertising received surprisingly little mention given the importance Direct to Consumer Advertising (DTCA) for prescription products has on creating a consumer-known brand.[119] However, Soller suggested that DTCA could also delay reclassifications because the prescription marketers can already communicate with the consumer, so this mixed effect might dampen the positive side.[63] Probably other important barriers and enablers were top-of-mind. With no ‘innovative’ reclassifications for a few years at the time of interview, barriers seemed to be the biggest discussion area.

The legal and political environment I found is reflected in the literature, e.g. in a legal discussion about BTC[566] and the Wellpoint attempt to reclassify non-sedating antihistamines.[150] The EHC provides an interesting mix of politics and law that differs from other countries.[19] Francesco spoke of the UK moving ahead of the US because of policy that slowed US reclassifications versus positive
government policy in the UK. [34] I found respect for the process, and that the FDA was available to assist companies to work out the requirements for reclassifications, but the long time and expense of reclassification discouraged reclassifications. Like others, [34, 51, 336] I found some concerns about the committee, despite no committee meetings for four years at the time of the interviews.

My finding of the difficulties for US companies to find candidates for reclassification that fit the current model, including providing sufficient return on investment, has not previously been identified in research, to my knowledge. This difficulty limits consumer access to medicines in the US.

8.7. Summary

The US reclassification environment is both helped and hindered by its size, health funding system, culture and non-prescription supply model. Reclassifications can have immense commercial success. There is a desire to change systems (including allowing new technologies) to cater for more complex reclassifications including for chronic conditions, but this may increase the cost of reclassifying and limit opportunities. At this stage it is unclear if sufficient will exists to make such changes. In the meantime, pharmacy (and others) appears to have moved on with increasing consumer access to medicines using collaborative care models. Such models may resolve payment, documentation and use of algorithms, without a huge cost attached or reliance on the manufacturer to drive it for the small number of medicines for which the likely return outweighs the cost.
Chapter 9. Japan

9.1. Introduction

Japan adds diversity in culture and scheduling to the research. As a large developed country, Japan should have a significant non-prescription market and therefore be attractive for reclassification for pharmaceutical companies. However, the EHC, proton pump inhibitors and orlistat, which have reclassified in the other four core countries, have not reclassified in Japan.[77] Thus, barriers may exist that differ from the other core countries.

Reclassification in Japan has received minimal coverage in academic literature in English[44], suggesting that Japan is not standing out in this area, or that research (if any) is not being published in English. Japanese pharmacy is also rarely seen in English-language literature[45]. However, Achanta included Japan when he described varied scheduling of medicines across selected countries despite similar processes and scientific principles.[32] He neither provided examples of differences in medicine scheduling (as I have here), nor compared Japan to other countries in medicines reclassified.

The Japan chapter of the AESGP’s Economic and Legal Framework for Non-prescription medicines reports a changing environment for reclassification in Japan, including an expectation that the recent change in medicines categories will widen the scope of OTC medicines to prevent “lifestyle diseases” such as metabolic syndrome.[77] This chapter of the AESGP book does not compare reclassification in Japan to that in other countries, and nor does it comment on the general non-prescription environment. Owing to the size of the project academic literature or website information in Japanese was seldom accessed or translated.

As with the UK and the US environments, I look at Japan from the perspective of an outsider who conducted semi-structured interviews with key informants. This approach allows me to elucidate factors that key informants (including people driving or implementing reclassifications) considered most likely to affect reclassification in Japan. Japanese findings would then be compared with those from key informants in other selected countries at the macro-level. Language difficulties and use of translators for some interviews is unlikely to affect major findings, but may impact finer points.

Seventeen people were interviewed in nine face-to-face interviews. Participants came from academia, community pharmacy, industry, government roles (including the Ministry of Health, Labour and Welfare, MHLW), and pharmacy and medical organisations. Three participants were currently or previously members of the committee deciding on reclassification. Participants have been identified by their perspective (e.g. pharmacy voice), unless in J1 interview, which used an interpreter and

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[44] Japanese literature has not been accessed owing to the project scope

[45] For example, a search of International Pharmaceutical Abstracts from 1995-2012 (on 20 Nov 2012) found four papers regarding community pharmacy in Japan in English-language publications
included an academic, a government employee, a previous committee member and a pharmacy group head, all reported simply as J1.

9.2. Background

MarketLine reports that the Japanese OTC pharmaceutical market earned revenue of US$13 billion in 2010, including non-prescription medicines, vitamins and minerals and bandages, based on retail value. [601] Traditional (Chinese) medicines comprised about a third of this value. Sales are mostly through pharmacies or drugstores (67%), with supermarkets or hypermarkets having little market (11%) according to MarketLine. The Japan Self-Medication Industries provides ex-manufacturer figures from the MHLW of 645 billion yen (US$6.6 billion) per year in 2009. [77] Table 9-1 presents key aspects of the Japanese market.

Table 9-1 Key aspects of the Japanese market

<table>
<thead>
<tr>
<th>Key aspects</th>
<th>Japan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population (millions; 2011) [388]</td>
<td>126.5</td>
</tr>
<tr>
<td>Health system [372]</td>
<td>Social insurance</td>
</tr>
<tr>
<td>Life expectancy at birth* [392]</td>
<td>83 years</td>
</tr>
<tr>
<td>Health Development Index Ranking [388]</td>
<td>12</td>
</tr>
<tr>
<td>Health spend as % of GDP total (2009) [392]</td>
<td>8.3%</td>
</tr>
<tr>
<td>Public proportion of health spend [392]</td>
<td>80.2%</td>
</tr>
<tr>
<td>Self-medication sales (2009) [77]</td>
<td>645 billion yen (US$6.6 billion)</td>
</tr>
<tr>
<td>Self-medication as % of total Pharma (2009) [77]</td>
<td>9.5%</td>
</tr>
<tr>
<td>Pharmacist-only schedule?</td>
<td>Yes</td>
</tr>
<tr>
<td>Pharmacy-only schedule?</td>
<td>No</td>
</tr>
<tr>
<td>Drugstore schedule (licensed person)?</td>
<td>Yes</td>
</tr>
<tr>
<td>Physicians per 1000 persons [392]</td>
<td>2.23 (2010)</td>
</tr>
<tr>
<td>Primary care doctor payment structure [2]</td>
<td>Fee for service</td>
</tr>
<tr>
<td>Number of pharmacists per 10,000 population [394]</td>
<td>~22</td>
</tr>
<tr>
<td>Pharmacies per 10,000 population [394]</td>
<td>~4</td>
</tr>
<tr>
<td>Percentage of pharmacists in community pharmacy [457]</td>
<td>46%</td>
</tr>
</tbody>
</table>

Chinese medicines were traditionally provided by doctors until rapid westernisation in the Meiji period from 1868, which included shifting to Western medicine. [602] Pharmacy was a late developer, with dispensing authority only provided to a ‘drug seller’ (now pharmacist) from 1874. Doctors’ primary income in the early 20th century was dispensing, [2] with pharmacy dispensing little medicine. Government policy gradually moved most dispensing to community pharmacies. [603] Pharmacy

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46 Pharmacies and drugstores differ as discussed in 9.5.5
dispensed only 11% of all prescriptions in 1989, but by 2009 it was dispensing 61% of all prescriptions. Pharmacy numbers increased by 73% over this period.[604]

Other recent changes have also affected pharmacy.[605] Community pharmacists were incentivised to provide verbal information with dispensed medicines in the 1990s.[606] Pharmacy education changed from a hard science focused four year course to six years including clinical components and externships in community and hospital pharmacy.[254, 605, 607] In 2009, medicine categories were revised to provide three categories (Table 9-2).[77, 605, 608]

The concept of the registered person was enabled along with the change in categories in 2009.[605] A one-year training period (on-the-job) and passing an examination allows a person to register to sell category two medicines. This person cannot dispense prescription medicines or supply category one medicines. Some drugstores have a registered person and supply category two medicines or lower.

Japan’s low birth-rate, ageing population and associated concerns about rising health care costs, and decreasing economic growth have stimulated health reform.[2, 254] Self-medication is likely to be important in the need to manage health independently in the future.[609]

### Table 9-2 Categories of medicines in Japan from 2009[77, 605, 608]

| Category 1: Higher risk medicines available only from a pharmacist who must supply verbal and written information with the product. Reclassified medicines typically move into category 1. They can be sold from pharmacies and drugstores with a pharmacist, and cannot be available for self-selection. |
| Category 2: Moderate risk medicines available only from a pharmacist or registered sales person who must endeavour to provide information necessary for proper use. These medicines can only be sold from pharmacies or drugstores with a pharmacist or registered person. |
| Category 3: Low risk medicines which only require information provided if requested by the consumer. Non-qualified staff can supply these medicines, but the store must be licensed47. |
| Quasidrugs are available outside of drugstores and pharmacies, and include vitamins and minerals and some medicines.[77] |

Japan’s low birth-rate, ageing population and associated concerns about rising health care costs, and decreasing economic growth have stimulated health reform.[2, 254]

### 9.3. Reclassifications 2003-2012

Reclassification in Japan is moving ahead since the mid-2000s after apparent inactivity in 2003 and 2004 (Table 9-3). Eleven innovative reclassifications occurred in the decade to 2012. No first-in-world innovative reclassifications occurred. Many therapeutic groups that have reclassified in all or some of the other key markets are missing, such as triptans, proton pump inhibitors, emergency contraceptive,

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47 A licensed store is different from a drugstore or a pharmacy.
and orlistat. Japan has lagged behind the other core countries on some other reclassifications, e.g. dermal aciclovir, vaginal antifungals and nasal corticosteroids.

The medicines in the table reflect differences in Japan compared with other countries. For example, some of the medicines are only available in Japan, such as tiquizium, and troxipide, and others are uncommon outside of Japan, such as loxoprofen and lanoconazole.[332] The dosages of the medicines reclassified are not readily available. Indications can also vary from elsewhere, for example oral tranexamic acid was reclassified for use in “liver spots” not menorrhagia.[77, 610-613]

Few participants were asked about, or provided opinions on where Japan was positioned internationally in reclassification. An international participant with good knowledge of Japanese reclassification considered Japan “very conservative”. A local industry participant reported that reclassification activity had increased following a quiet period in 2003-2004, and that Japan was not far behind other countries in numbers of reclassifications, although statins had not reclassified in Japan. This was confirmed by Table 9-3, but many recent reclassifications are delayed compared with many other countries. The omission of the EHC, proton pump inhibitors, triptans, oral fluconazole, and domperidone suggests that Japan remains somewhat conservative.
### Table 9-3 Key reclassifications in Japan 2003-2012

<table>
<thead>
<tr>
<th>Year</th>
<th>Medicine</th>
<th>Indication or class</th>
<th>Innovative?</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>Ketotifen nasal</td>
<td>Allergic rhinitis</td>
<td>No</td>
<td>Sodium cromoglycate previously reclassified[612]</td>
</tr>
<tr>
<td>2004</td>
<td>Roxatidine</td>
<td>H2 antagonist</td>
<td>No</td>
<td>Famotidine previously reclassified[612]</td>
</tr>
<tr>
<td>2004</td>
<td>Nizatidine</td>
<td>H2 antagonist</td>
<td>No</td>
<td>Famotidine previously reclassified[612]</td>
</tr>
<tr>
<td>2004</td>
<td>Minoxidil topical</td>
<td>Women’s hair loss</td>
<td>Yes</td>
<td>Minoxidil only for men previously</td>
</tr>
<tr>
<td>2005</td>
<td>Azelastine oral</td>
<td>Antihistamine/mast cell stabiliser</td>
<td>No</td>
<td>Non-sedating antihistamine available previously,[612]</td>
</tr>
<tr>
<td>2006</td>
<td>Ketotifen oral</td>
<td>Antihistamine/mast cell stabiliser</td>
<td>No</td>
<td>Sodium cromoglycate previously reclassified[612]</td>
</tr>
<tr>
<td>2006</td>
<td>Tiquizium bromide</td>
<td>Stomach cramps</td>
<td>No</td>
<td>Scopolamine already reclassified for stomach cramps in 1987,[612]</td>
</tr>
<tr>
<td>2006</td>
<td>Lanoconazole topical</td>
<td>Athlete’s foot</td>
<td>No</td>
<td>Other similar medicines previously reclassified[612]</td>
</tr>
<tr>
<td>2006</td>
<td>Triamcinolone topical</td>
<td>Mouth ulcers</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2007</td>
<td>Aciclovir topical</td>
<td>Herpes labials</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2007</td>
<td>Ketotifen eye</td>
<td>Antihistamine/mast cell stabiliser</td>
<td>No</td>
<td>Sodium cromoglycate previously reclassified[612]</td>
</tr>
<tr>
<td>2007</td>
<td>Ambroxol combination</td>
<td>Cold remedy</td>
<td>No</td>
<td>Bromhexine long-standing OTC in Japan[610]</td>
</tr>
<tr>
<td>2007</td>
<td>Flavoxate oral</td>
<td>Urinary incontinence</td>
<td>Yes</td>
<td>No previous reclassifications found for this indication[610]</td>
</tr>
<tr>
<td>2007</td>
<td>Tranexamic acid oral</td>
<td>Liver spots</td>
<td>Yes</td>
<td>Maximum 750mg/day, combined with vitamins</td>
</tr>
<tr>
<td>2007</td>
<td>Isoconazole vaginal</td>
<td>Vaginal candidiasis</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2008</td>
<td>Miconazole vaginal</td>
<td>Vaginal candidiasis</td>
<td>No</td>
<td>See isoconazole</td>
</tr>
<tr>
<td>2008</td>
<td>Nicotine patch</td>
<td>Smoking cessation</td>
<td>Yes</td>
<td>Gum OTC,[612] patch provides even nicotine levels and is not addictive[452]</td>
</tr>
<tr>
<td>2008</td>
<td>Emedastine oral</td>
<td>Antihistamine</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>2008</td>
<td>Minoxidil (5 x strength)</td>
<td>Hair loss</td>
<td>Yes</td>
<td>Stronger than previous product</td>
</tr>
<tr>
<td>2009</td>
<td>Diclofenac topical</td>
<td>Anti-inflammatory</td>
<td>No</td>
<td>Topical NSAIDs previously reclassified in 1985[612]</td>
</tr>
<tr>
<td>2009</td>
<td>Vidarabine topical</td>
<td>Herpes labials</td>
<td>No</td>
<td>Aciclovir already reclassified</td>
</tr>
</tbody>
</table>

Table continued below
<table>
<thead>
<tr>
<th>Year</th>
<th>Medicine</th>
<th>Indication or class</th>
<th>Innovative?</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>Troxipide ( Combination)</td>
<td>Gastritis and peptic ulcer</td>
<td>No</td>
<td>Teprenone previously reclassified[612]</td>
</tr>
<tr>
<td>2009</td>
<td>Epinastine oral</td>
<td>Anti histamine/ mast cell stabiliser</td>
<td>No</td>
<td>See azelastine (above)</td>
</tr>
<tr>
<td>2009</td>
<td>Loxoprofen oral</td>
<td>Anti-inflammatory with range of indications</td>
<td>Yes*</td>
<td>Non-prescription dose same as prescription dose.[332, 614] Oral ibuprofen previously reclassified but in lower dose than prescription [612, 613, 615]</td>
</tr>
<tr>
<td>2010</td>
<td>Clotrimazole</td>
<td>Vaginal candidiasis</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>2010</td>
<td>Oxyconazole nitrate</td>
<td>Vaginal candidiasis</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>2010</td>
<td>Beclometasone nasal</td>
<td>Nasal corticosteroid</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2010</td>
<td>Oxymetazoline nasal</td>
<td>Vasoconstrictor for rhinitis</td>
<td>No</td>
<td>Phenylephrine nasal spray already available[610]</td>
</tr>
<tr>
<td>2011</td>
<td>Acitazanolast eye [611]</td>
<td>Allergic conjunctivitis</td>
<td>No</td>
<td>Leukotriene inhibitor but no evidence of improvement over alternatives†</td>
</tr>
<tr>
<td>2011</td>
<td>Pemirolast oral [611]</td>
<td>Allergy</td>
<td>No</td>
<td>Similar to ketotifen[332]</td>
</tr>
<tr>
<td>2011</td>
<td>Ibuprofen + butylscopolamine[613]</td>
<td>Dysmenorrhoea with soft stool</td>
<td>No</td>
<td>New combination, previously available separately.</td>
</tr>
<tr>
<td>2011</td>
<td>Mequitazine oral [613]</td>
<td>Allergy</td>
<td>No</td>
<td>Increased dose; others non-prescription have comparable dosing</td>
</tr>
<tr>
<td>2012</td>
<td>Ibuprofen oral[613]</td>
<td>Anti-inflammatory for pain</td>
<td>No</td>
<td>Increased dose Loxoprofen already available at same as prescription dose</td>
</tr>
<tr>
<td>2012</td>
<td>Fexofenadine[613]</td>
<td>Allergy</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>2012</td>
<td>Ketotifen + naphazoline nasal [613]</td>
<td>Allergic rhinitis</td>
<td>No</td>
<td>These ingredients or similar already available separately</td>
</tr>
<tr>
<td>2012</td>
<td>Eicosapentaenoic acid</td>
<td>Hypertriglyceridaemia</td>
<td>Yes</td>
<td>This appears to be the first reclassification with this indication</td>
</tr>
<tr>
<td>2012</td>
<td>Cetirizine hydrochloride</td>
<td>Non-sedating antihistamine</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>

Sources include: PMDA website [http://www.info.pmda.go.jp/ippan](http://www.info.pmda.go.jp/ippan), with assistance from Prof Kurosawa and Mizuho Yamamoto. Quasi drugs and nutritionals excluded
* As loxoprofen non-prescription is available at prescription strength it has been deemed innovative. It is unknown if prescription dosing for ibuprofen and loxoprofen are equivalent. No head-to-head studies in humans arose from a Medline search (12 Nov 2012). †Acitazanolast has little information in English, topical leukotriene inhibitors unmentioned on allergic conjunctivitis in Martindale,[332] or in Medline indexing.
9.4. Broad themes

The broad themes emerging from the Japanese interviews comprise doctor influence, financial motivation, culture/history, politics, pharmacy factors, global influences and a conservative approach. As with other countries, these themes are inter-linked.

9.4.1. Doctor influence

The doctors' voice provides the greatest barrier to reclassification, most strongly through a direct action, vetoing potential reclassification candidates, effectively preventing reclassifications being considered (see 9.5.2). Doctor members influence the committee deciding reclassifications. Pharmaceutical companies sometimes do not reclassify medicines because of doctors (see 9.5.4), and pharmacy does not want to upset the doctors. Consumers consult the doctor rather than self-medicating (see 9.5.6).

Established prescribing patterns also can influence reclassification, with ocular chloramphenicol believed to be an unlikely candidate for reclassification, as it is not typically prescribed in Japan.

9.4.2. Financial motivation

Financial motivation encompasses many barriers, and some enablers for reclassification.

The government interest in reclassification was cited by many as an enabler. The ageing population and increasing health costs are raising concerns and the government considers one mechanism to address this is to reclassify medicines and encourage self-care. Almost all participants considered concern about loss of income caused medical negativity (9.5.7).

Multiple financial motivators affect the pharmaceutical industry (9.5.4). The most important one is the uncertain and potentially low sales for reclassified medicines, while the prescription market provides higher, certain income. Financial effects on others, including pharmacy, drugstores and consumers, influence these low sales (see 9.5.5, and 9.5.6, respectively). Because most pharmaceutical companies' primary business is the prescription market, reclassification is sometimes not pursued to avoid harming relationships with doctors, reflecting the financial motivation of the company and the doctors. The costs of reclassification, including post-reclassification advertising, discourage companies, or cause a higher OTC than prescription price. A potential financial enabler for the companies is the market exclusivity of three years that can occur where post-market surveillance is conducted (see 9.5.4).

9.4.3. Culture, history and beliefs

Japanese people have a culture of consulting a doctor, even for minor conditions. This seems to be encouraged by doctors (see 9.5.7), and may also arise from their accessibility. One participant suggested this practice arose from the history of going to the doctor for Chinese medicines, and because medicines used to be given out by the doctor rather than the pharmacy, so the pharmacy
was little-visited. It may also be because pharmacy seems to be valued less in Japan than some other countries (suggested by two participants). Possibly pharmacy is not entirely trusted by consumers. Historically, pharmacists have had little power compared with doctors, and this remains true today. One participant compared the individual’s right to decide in the US to the belief in oriental cultures such as Japan, that the government will decide what is right.

“…for a long time Japanese historical background or cultural background is the medicine you get from the doctor directly… so not used to [using] an OTC medicine…” Pharmacy voice

Historically, pharmacists have largely been uninterested in OTC medicines, primarily because they have not been trained in that area. Until very recently, pharmacy schools have had little focus on training pharmacists to work in the community, with many graduates working in the pharmaceutical industry and research.

“In the past, in Japan, the pharmacist could not touch the patient, could not make decisions.” Pharmacy academic

Reclassified medicines have often been lower strength than prescription medicines, e.g. minoxidil, first reclassified in a very weak strength. This shapes pharmacists’ and consumers’ beliefs and encourages consumers to visit the doctor when they want an effective treatment.

One aspect of the Japanese culture that emerged from a couple of interviews was the desire to avoid clashing, e.g. with other organisations. Consequently, companies are less willing to reclassify and the route to reclassification is circuitous, slow and easily halted.

“…the Japanese Doctors’ Association, they have a very, very strong presence in many ways, so they can’t do it, so they have to somehow go around and do it another way.” J1 (interpreter)

“…the Pharmaceutical Association would avoid at any cost to have this type of clash.” J1 (interpreter)

9.4.4. Politics

Two very strong opposing political influences came through most interviews. The governmental desire for self-medication and reclassification, stimulating recent reclassification activity (see 9.5.2), and the doctors’ organisations inhibiting reclassification (see 9.5.7).

“The JMA [Japan Medical Association] and medical conventions represent major influences because of their political power.” Industry voice

An international participant considered industry lobbying had stimulated the government interest in reclassification, but no local participants suggested this. However, industry’s initiative for three years’ market exclusivity was adopted and was considered enabling (see 9.5.4).
The relatively low power of pharmacy organisations may prevent them effectively pushing for reclassification. However, government support has stimulated interest from the pharmaceutical industry and pharmacy organisations, and inspired regulator proactivity. It also may be diluting the doctors’ effect, with the Pharmaceutical Society in 2011 having further input after the medical organisation had commented on reclassifications (see 9.5.2), and in 2012, a medicine was reclassified despite a medical member of the committee opposing the reclassification (see 9.5.2). A participant reported that, in a Japanese first, the incoming political party in late 2012 included “promotion of responsible self-medication” [translated] and “expansion of Rx-to-OTC switches” [translated] on their work list. This confirms government support for reclassification will continue.

9.4.5. Pharmacy factors

Given most reclassifications move into pharmacist-only availability, the role of the pharmacist is important in companies achieving sales post-reclassification. Pharmacy has many factors against it in this respect, e.g. the unusual pharmacy/drugstore model (9.5.5), non-interest by pharmacists in non-prescription medicines, a lack of consumer trust and use of the pharmacist (see 9.5.5), and lack of political power (see 9.4.4). Poor performance in mystery shopping may hinder further reclassifications, and pharmacies do not always stock reclassified medicines.

“Switch is an ideal thing, it’s a good thing to have but in practice it’s not really happening, not really, because it’s too much of a hassle and not much profit, so therefore 60% of pharmacies are not stocking up the category one medications.” J1 [interpreter]

Enablers around pharmacy exist, including a government desire to raise the position of pharmacy, and proactivity in reclassification from pharmacy organisations (which contrasts with reported low pharmacist interest). A pharmacy chain normally focused on dispensing was becoming interested in non-prescription medicines and tonics.

9.4.6. Global effects

Japan in some ways is very local, e.g. with a large local industry (including medicines unique to Japan), but Japan has looked internationally for examples of reclassification, and in shaping the new medicines scheduling system. Openness to ideas from abroad came also from related areas, such as education and managing internet supplies. One participant discussed the desire to introduce label comprehension testing and actual use testing as used in the US.

“…every year we look at the [reclassification] candidate of the [UK and USA]” Pharmacy academic


Many discussions led to comparisons with other countries, such as doctor access which doctor and pharmacy participants compared positively with the UK. Japan was also compared favourably against
the UK on the lower death rate from the influenza pandemic (2009), according to the medical participant, when suggesting consulting doctors about minor ailments was important.

“In UK, people think OTC is very important for them because they don’t have a good access to a doctor. They need to do self-medication. But it is opposite in Japan.” Medical participant (translation)

“In a personal opinion… I think that UK is very inconvenient for the patient, but Japan is very convenient for the patient, it is easy to access a medical doctor and [specialist] but UK is not easy… sometimes the GP waiting time is two days, maybe… so the UK government decided some medicines have to move to OTC on the advice of the pharmacist.” Pharmacy participant

9.4.7. Conservative approach

Several participants expressed concern about safety, e.g. when sumatriptan, fluconazole and oseltamivir were mentioned as having reclassified elsewhere. There were concerns about diagnosis, particularly from the doctors, but also from some pharmacy voices. The committee was noted to be conservative, although this conservatism had (according to one group of participants) lessened since the government started supporting reclassification.

Three participants mentioned consumer concern about side effects. The cautious approach was part of the reason for doctors wanting to see minor ailments, in case it was a more serious condition.

 “…omeprazole… it hides a symptom or rare disease… fluconazole internal use medicine has several kinds of side effects and interactions, so not easy to use… chloramphenicol is already second class ointment or eye drop…” Pharmacy participant

 “…medicines always have adverse effect. So that medicines should be dealt with caution and professional’s advice for safe management.” Medical participant [translated]

Companies were conservative with reclassifications (9.5.4).

9.4.8. Summary of over-riding effects

The strong influence of the doctors (direct and indirect) and multiple pharmacy factors cross political, financial, and historical and cultural themes. Politics is influential, particularly the medical voice, but also the government in encouraging reclassification, which is a strong enabler. Companies, as everywhere, have financial motivations. The impacts of these effects are that reclassification is continuing to progress, but without breaking new ground. Some potential reclassifications (including ground-breaking ones) raised by stakeholders are not reaching the committee as yet.
9.5. Results by stakeholder or factor

Many negative factors hinder reclassification in Japan, across all the stakeholder groups (government, regulator, industry, pharmacy, consumers, doctors), but there are a few important enablers also, as outlined below.

9.5.1. Government

Government interest was the strongest enabler coming through, and was recently reiterated when a change of government occurred. Government interest prompted the MHLW to become more proactive in reclassification. The government also funded a working group to promote reclassification and was working with the industry association to develop an improved environment for reclassification.

“…the government are very keen to have OTC they want to control the expenditure of the medicine… Also they bring up the position of the chemist if you like, the social standing of the chemist if you like” J1 [interpreter]

“It’s not only a financial side but it’s availability for their people, the easy access… that’s the sort of the government direction, ministry…” J1 [interpreter]

9.5.2. Regulator, committee and process

Japan has an extraordinary system of reclassification as described by participants and represented by Figure 9-1. The process has recently been unusually initiated by the MHLW, through inviting stakeholders (including “public sector, private sector”) to suggest candidates. The Pharmaceutical Society develops these candidates suggesting training needs and requirements around supply, which medical groups then review. The MHLW will contact sponsor companies to invite an application for candidates that pass this preliminary process. An application is evaluated before going to the committee.

The two most important barriers within this process, according to participants, are the doctors’ organisations frequent veto of candidates, and the pharmaceutical company not putting forward an application for a medicine on the agreed list.

“…the government requested the Society, and the Society answered to the government and then the government asked the medical societies and they get the comments to the report from the medical societies. And if the medical societies have an opposite opinion we discuss why, how we improve the system, and that type of discussion. And we fix the list of the candidates for the switch to OTC…. Used to be that we couldn’t get the information from the medical societies, but from this year we can have opinions from medical societies before the decision by the government. So we can have a meeting with the member of medical societies and we discuss can we change the report or not, something like that.” Pharmacy voice
Regulator asks stakeholders including sponsors for candidates

Pharmaceutical Society creates candidate list

MHLW

Exchange of opinions about rejected candidates between Pharmaceutical Society and JMA

MHLW

Final list created based on opinion of Pharmaceutical Society and JMA

PAFSC considers the candidates

Companies do not pursue reclassification

MHLW decides the candidates and encourages the pharmaceutical companies to develop application

Companies develop applications including conducting clinical trials

Company applies to PMDA, which evaluates application

Company submits application and PMDA assessment report to MHLW

PAFSC consideration

Reject reclassification

Reclassify

Figure 9-1 Process of reclassification in Japan

PAFSC = Committee on Non-prescription Drugs, Pharmaceutical Affairs and Food Sanitation Council
MHLW = Ministry of Health, Labour and Welfare
PMDA = Pharmaceutical and Medical Devices Agency
From 2011, the Pharmaceutical Society could discuss with the doctors’ groups the rationale behind the veto, to try to resolve concerns (previously no discussion was held). However, the medical representative interviewed remains reluctant to see chronic medicines reclassified, believing doctor management to be necessary.

“The Ministry of Health has a final say but basically the Japanese Doctors’ Association is a very, very, very strong group so they have to go along with that.” J1 (interpreter)

“There are many medications such as omeprazole, [raised as] a candidate, but first they ask the opinion from the Pharmaceutical Society of Japan, and then if it passes then it goes to Medical Society of Japan and there are 110 subgroups under the Medical Society, so they ask the opinion from all these groups and if there is no opposition toward that ingredient then it will mean a candidate ingredient, however, sometimes they may encounter opposition because of very strong adverse drug reaction or possibility of masking serious disease..... if physician and pharmacist agree on certain ingredients to be considered, then the Ministry of Health can ask pharmaceutical company to [apply to] make them OTC product.” Government employee (interpreter)

Companies apply for the reclassification following an elaborate process identifying suitable candidates for consideration (Figure 9-1). Clinical studies are carried out in at least five facilities with 150 cases. Companies may consult with the medicines regulator to assist with developing the reclassification. A reclassification application costs 1,291,600 yen (US$13,150).

Reclassifications are decided by the Committee on Non-prescription Drugs, Pharmaceutical Affairs and Food Sanitation Council (PAFSC). The committee members include medical and pharmacy academics, pharmacy managers, a representative of the Japan Medical Association, a representative of the Japan Pharmaceutical Association and various medical specialists, currently a dermatologist, paediatrician, obstetrician, cardiologist and urologist. Temporary members may be included according to the treatment/s considered. The decision is by majority vote. This committee first decides if the ingredients raised by the Pharmaceutical Society and reviewed by the Medical Association are appropriate for consideration. Then it considers them and makes a decision following the company application. Examples of medicines that were on the list from the Pharmaceutical Society and have been considered as possible candidates by the PAFSC are clobetasone butyrate (2009), fluticasone nasal spray (2008) and domperidone (2010). None of these medicines have had company application and formal consideration as at December 2012. Two participants seem to have differing explanations, (highlighting the difficulties of translation and communication in English as a second language). Either the PAFSC postponed the decision to list as reclassification candidates on their first consideration (not the company application), or the PAFSC agreed they could be candidates and the companies have not applied. The outcome remains that the medicines have not been reclassified in Japan despite being highlighted as candidates.
The meeting is closed, and, while the agenda is publicly available on a website two weeks before the meeting, public submissions are not accepted. However, minutes (in Japanese) are available later. One participant noted that the medical voice carried a lot of weight. Two participants noted the difficulty of reclassifying medicines through the committee.

However, a long-term use medicine, eicosapentaenoic acid (EPA), was reclassified for hypertriglyceridaemia in 2012. A fish oil constituent took multiple committee meetings, and unusually was approved without the customary unanimous committee decision. The single dissent was from the medical association representative who cited concerns about poor mystery shopping performance in pharmacy. A checklist to be used in pharmacy, company-provided training and intention to conduct two post-marketing surveillance studies helped convince other committee members. Previously the committee has sometimes required companies to provide pharmacy training, for example with H₂-antagonists and vaginal antifungals.

9.5.3. Schedules

The schedules changed in 2009 from a legal requirement for non-prescription medicines to be provided by the pharmacist to three risk-based categories. Three participants reported this change occurred because sales had previously occurred illegally with no pharmacist on-site, when a pharmacist was required for all supplies. A further participant suggested mail order and internet supplies influenced the change. Thus the scheduling changed to risk categories, with medium risk managed by a licensed person (a new initiative), allowing the pharmacist to concentrate on the “OTC switch drugs which require more advanced judgement”.

“…before the system everything else sold by the pharmacist, you have only one or two pharmacists within the organisation, it’s just too much workload, so therefore the people without any qualification they were selling those OTC medications, right. So this is not really the ideal situation, it’s not safe for the patients concerned, the customers concerned, it’s not a good idea so therefore they changed the system.” J1 [interpreter]

Three participants noted that the pharmacist-only category should help reclassification, by providing more information on higher-risk medicines. One participant noted pharmaceutical companies liked having category one to help reclassification. However, the pharmacist-only category hindered reclassification too, primarily because many drugstores and pharmacies do not stock these medicines (see 9.5.5). This may be influenced by the relatively few medicines in category one and the low sales of some of these medicines. One participant reported that on implementation of the amendment, 20-30% fewer outlets sold category one medicines.

9.5.4. Pharmaceutical companies

Pharmaceutical company interest in reclassification is affected by multiple factors (Figure 9-2). Companies can be reluctant to reclassify for various reasons, particularly doctor influence (see 9.4.1), and because the model of supply is harder and less financially rewarding than the prescription model
they are used to. Potential sales for reclassifications are limited by pharmacy and drugstore factors (see 9.5.5) and consumer behaviour (see 9.5.6). Low sales reduce company interest in reclassification. One participant talked about non-prescription products sometimes being withdrawn after just one season of sales.

Multiple participants in one interview reported that medicine prices do not drastically drop when the patent expires, as in some other markets. Consequently, the product lifecycle effect on reclassification is diminished or non-existent in Japan, with the prescription market still important after patent expiry.

“First, yes, the medical doctors association won’t like you if you do a switch. Prescription drugs is a kind of a stable income.” J1 [interpreter]

“Pharmaceutical companies [don’t] need to switch OTC. Other countries they need to switch because they cannot get money after expiry of patent.” Industry voice

A further barrier to reclassification was the inadequacy of company applications for reclassification, according to one participant.

“There was some concern that pharmaceutical companies are not doing their due diligence, … not enough to convince everyone, so that’s the common criticism actually used.” De-identified quote

The process is not as simple as a company applying for a reclassification (see Figure 9-1).

“There is no actual formula for the Japanese pharmaceutical company to solicit things to the Japanese Ministry of Health.” J1 [interpreter]

An industry initiative adopted in Japan is three-year market exclusivity contingent on post-marketing surveillance in 3,000 patients over three years. In reality closer to four years’ exclusivity is achieved after the data are reported to, and considered by, the Ministry. Such research may also provide data for further down-scheduling. This exclusivity enables reclassification and collection of data, although the data are rarely published. Other companies can reclassify before the exclusivity, but need to put in a full application and data as was required for the first applicant. Additionally, companies do not lose prescription funding for a product once reclassified; the idea arises from time-to-time but so far has not happened. The OTC product is not reimbursed, but the ethical product remains funded.

Companies have increasingly been providing training on reclassifications, and sometimes tools for pharmacist-supply (such as flow-charts) are mandated, as for vaginal antifungals.

“…there was enormous opposition whether the H2 blockers shouldn’t be OTC. But it was approved on condition that pharmacists would go and learn how to provide appropriate information, so it has been a tradition for the pharmaceutical company to provide the product meeting for the pharmacists.” Government employee (interpreter)
Chapter 9

Company factors

- Low patent expiry effect on Rx pricing
- Rx better payback
- Do not want to upset doctors
- Companies conservative
- Costs and effort of OTC promotion

Product factors

- Chronic care not accepted
- OTC usually low strength
- Need local trials for product registration
- Medicine not available in Japan long
- Me-too products in the market
- OTC sales potential
- Place in current practice
- Will it need POC testing?

Japan factors

- Pharmacists not proactive
- Doctors against
- Doctors accessible
- Rx cheaper for consumers than OTC
- Most pharmacies have little focus on OTC
- OTCs perceived as weak
- Pharmacists lack knowledge
- Culture to go to doctor
- Pharmacists cannot diagnose

Can be positive or negative

OTC infrastructure/experience?

Positive factors

- JSMI can help
- Previous reclassification experience

Negative factors

- No generic competition
- OTC in other countries

Company decides to submit reclassification application, or not

Is the reclassification financially viable?

Figure 9-2 Factors affecting pharmaceutical company reclassification decisions in Japan
A variety of products were discussed as suitable or not for OTC. If a medicine is “mild”, has “hardly any side effects” and is for a condition already self-medicated, it is more likely to be seen as a reasonable candidate by all. One participant commented that a candidate that is a “money making one for the doctors” will not reclassify easily.

Companies may avoid reclassifications or change indications, doses and pack sizes for the reclassified medicine to avoid affecting the doctor’s business.

“[companies] are so worried about the reaction of the doctors’ association. They have to, the doctors’ association’s just so powerful, so influential, so they don’t want to have a clash” J1 [interpreter]

Some unusual features occur in Japan compared to Western countries, including the need for local studies before a new medicine can be registered, and the fact that some medicines are unique to Japan or uncommon in the rest of the world. This causes a different array of products to be available on the Japanese market compared with elsewhere. Working through the list of medicines in Table 9-3 was difficult because many products were unique, or reclassifications reflected different practices to elsewhere (e.g. tranexamic acid for liver spots not menorrhagia, ocular leukotriene antagonists and low ibuprofen dosing). Additionally, there was little information in the English literature about appropriate doses or comparison of effects to understand whether a new reclassification provided an advantage over previous reclassifications.

“At the OTC meeting they always compare the information whether the ingredient had been released for OTC in other countries.... Some of the ingredients are not available in foreign countries, they are unique to Japan...” Government employee voice (interpreter)

One participant speculated that the EHC remains prescription-only in Japan because it is a recent arrival to the Japanese market. Ocular chloramphenicol was reportedly not typically used in Japan, and therefore illogical to reclassify.

9.5.5. Pharmacy and drugstore models

Retailer and pharmacist factors impacting on reclassification are multifaceted (Table 9-4, Figure 9-3). Three strong influences are: minimal undergraduate education on non-prescription medicines and ailments (until recently), the fact that most sales go through drugstores rather than pharmacies, and that dispensing provides better income than selling non-prescription medicines. However, many other influences also exist causing many pharmacists to lack experience, knowledge and interest in non-prescription medicines.

Retailers supplying medicines were described as fitting into three groups: dispensing-focused pharmacies; American-style drugstores; and “Mom and Pop” pharmacies.

Large dispensing-focused pharmacies concentrate on dispensing. This financially-driven perspective has a flow-on effect to pharmacist interest, encouraging a prescription focus. One participant
suggested that pharmacists often prefer these pharmacies over working in drugstores. Such pharmacies often are located near and have a special relationship with a nearby hospital, and are not located for foot traffic, so demand for non-prescription medicines may be low. Such pharmacies limit their stocks of non-prescription medicines, and may not stock some category one medicines.

“At the moment… category one is not making any profit, it’s not really viable… however, for the social responsibility and for the long-term business plan we want people to come to us before they go to the doctor, so we stock up this category one medications.” J1[interpreter]

The second retailer group is American-style discount drugstores in high foot traffic areas (which may or may not dispense prescriptions). These are the largest suppliers of OTC medicines and are open long hours, supplying various goods which may include food. Because drugstores supply most OTCs, that may further reduce potential market and interest from the dispensing-focused pharmacies. These drugstores can only supply prescriptions and category one medicines if a pharmacist is on-site. Given the relatively few category one medicines, and the high cost of pharmacists, drugstores often have a registered person rather than a pharmacist, or have a pharmacist only for limited hours. This affects potential supplies of category one medicines (Figure 9-3).

The final group of retailers are owner-operated “Mom and Pop” pharmacies. The owner, often a pharmacist, sometimes owns two or three pharmacies. These small pharmacies see both OTC and prescriptions as important, and are often attached to a small medical clinic.

Pharmacy and drugstore ownership is not limited to pharmacists or a maximum number of stores. Consequently, chains are common, with store focus directed by head office. One participant in a large chain of dispensing-focused pharmacies spoke of prescriptions being most important, but that head office was becoming more interested in non-prescription opportunities, including training their pharmacists for non-prescription medicine supplies.

The limited availability of category one medicines for the public impairs the sales potential for most reclassifications (see Figure 9-3).

“…category one medicine is very small item, estimate 40 items.” Pharmacy voice

The pharmacy workforce may also have affected supplies of non-prescription medicines in both availability and education. The 2009 change in schedules coincided with the change in pharmacist education from a four year course to a six year course, which resulted in no graduates for two years, reducing the number of pharmacists available at a time when more were needed.

Undergraduate pharmacy courses have only focused on clinical skills and included minor ailments and OTC medicines in all pharmacy schools in recent years. Such education is expected to encourage pharmacists in supplying non-prescription medicines, and improve professional capabilities and recognition. The doctors’ representative also noted a need for improving clinical skills to help the doctor more. However, there is no good OTC textbook in Japanese, and one participant suggested that OTC teaching was still limited at some universities.
Chapter 9

Pharmacist required for category 1 medicines, but high wages

Category 1 medicines often not available in stores

Consumers buy an alternative category 2 or 3 product instead

Low sales of category 1 medicines

Companies avoid reclassification

Drugstore

Some drugstores employ no pharmacists or employ pharmacists for limited hours

Few category 1 medicines

Drugstores mainly supply category 2, category 3 or non-medicinal products

Pharmacist required for category 1 medicines, but high wages

Few category 1 medicines

Figure 9-3 Influence of drugstores and pharmacies on category one medicines
One participant observed that OTC continuing education for pharmacists is minimal, including in trade journals. He considered that if continuing education were mandated, it would improve pharmacists’ knowledge and their advice to consumers who would then consult them more about self-medication. The inability of pharmacists to diagnose (by law, only doctors can diagnose) limits pharmacists, and is apparently used by doctors to pressure the pharmacists and reduce reclassifications.

Some disparity occurred with respect to how pharmacists reportedly perceive non-prescription medicines. While some participants noted that these medicines are unimportant to many pharmacists, others highlighted the intrinsic reward of using professional knowledge. All participants indicated that more training is necessary to help manage OTC medicines, at undergraduate level and for qualified pharmacists. Some considered this would increase reclassification. Two participants suggested that for some medicines, such as sumatriptan, some pharmacists would worry about missing warning signs of an important cause such as stroke. One participant said, “I don’t know why you want to sell OTC anyway, we dispense so many sumatriptan anyway.” This participant was also concerned that non-prescription supplies were not documented.

“Not all [pharmacists are keen] but on the whole the Japanese pharmacists are very keen if they can help people prescribing or recommending medication to the people… [but] they have to have experience and knowledge.” J1(interpreter)

“Over-the-counter kind of lower-grade pharmacist job [perception of some pharmacists].” Pharmacist participant

The pharmacy organisations are proactive in supporting reclassification or suggesting reclassifications, although they have limited power. The Pharmaceutical Society suggests training needs for reclassification candidates when developing the candidate list.

“JPA [Japan Pharmaceutical Association] policy is to strongly support [reclassification]… but what kind of medicine to switch is a very difficult question.” Pharmacy voice

Several participants noted that pharmacists were not always “trusted” or perceived well by the public, and that their status is low. One participant considered the government supported reclassification to help raise the pharmacists’ standing. Poor performance in mystery shopping was considered damaging for the profession (and industry and reclassification). Pharmacists have not always been on-site when they should be.

“I tell them ‘you’d better do good job’, a better job, because OTC is such a privilege to the pharmacist.” Pharmacist
Table 9-4 Pharmacy or drugstore factors impinging on reclassification

<table>
<thead>
<tr>
<th>Barriers</th>
<th>Enablers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Consumer-related</strong></td>
<td><strong>Consumer-related</strong></td>
</tr>
<tr>
<td>Consumers often go to the doctor for minor ailments</td>
<td>Some people may find it easier to speak to the pharmacist than the doctor (an authority figure)</td>
</tr>
<tr>
<td>Copayment on doctor’s visit and prescription is often cheaper than OTC</td>
<td>Training is provided by companies, and recommended by the Pharmaceutical Society when a reclassification is considered to increase confidence</td>
</tr>
<tr>
<td>Consumers perceive OTC medicines lack potency</td>
<td><strong>Pharmacist-related</strong></td>
</tr>
<tr>
<td>Consumers are wary that the pharmacist or store owner will try to sell them more than is necessary</td>
<td>Pharmacists now get OTC training at university, sometimes including learning to take vital signs</td>
</tr>
<tr>
<td>Consumer perceive that pharmacists just dispense</td>
<td>Some pharmacists gain professional interest from supplying OTCs</td>
</tr>
<tr>
<td>Consumers do not regard pharmacists highly</td>
<td>Pharmacy organisations and some pharmacists working at a high level are proactive about reclassification</td>
</tr>
<tr>
<td><strong>Pharmacist-related</strong></td>
<td>Consultation tools such as flowcharts are being supplied for some reclassifications</td>
</tr>
<tr>
<td>Pharmacists have not had OTC training at university and so have low confidence and ability with OTCs</td>
<td><strong>Business-related</strong></td>
</tr>
<tr>
<td>Pharmacists think OTC medicines are less important than prescriptions (and weak)</td>
<td>Some pharmacies offer the range of OTCs as a service to their customers (even if low sales)</td>
</tr>
<tr>
<td>Pharmacists are busy. Technicians can only input prescriptions into the computer, increasing workload for pharmacists with simple tasks</td>
<td>Drugstores are usually located near high foot-traffic areas</td>
</tr>
<tr>
<td>Pharmacists prefer dispensing-focused pharmacies to drugstores</td>
<td>Pharmacies have to have a “consultation corner”</td>
</tr>
<tr>
<td>Pharmacists are not taught clinical skills, and did not give clinical advice, until recently</td>
<td>Extra payment to give advice with prescriptions, encouraging more patient contact</td>
</tr>
<tr>
<td>Pharmacists are not allowed to diagnose</td>
<td></td>
</tr>
<tr>
<td>Historically better pharmacy graduates worked for pharmaceutical companies rather than in pharmacies</td>
<td></td>
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<tr>
<td><strong>Business-related</strong></td>
<td></td>
</tr>
<tr>
<td>Prescriptions are financially better than OTC for pharmacies</td>
<td></td>
</tr>
<tr>
<td>Some pharmacies are located near hospitals for prescriptions rather than high foot-traffic areas</td>
<td></td>
</tr>
<tr>
<td>Pharmacist wages are high, so many drugstores do not employ a pharmacist or only employ a pharmacist for limited hours. Thus category 1 products are not stocked in many drugstores, or not always available</td>
<td></td>
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<tr>
<td>Some pharmacies perceive category 1 medicines as a hassle with low margin and so do not stock them</td>
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<tr>
<td><strong>Other</strong></td>
<td></td>
</tr>
<tr>
<td>Doubts about pharmacy performance exist, and mystery shopping results not always good</td>
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</tbody>
</table>

9.5.6. Consumers

Consumers tend to consult the doctor even for minor conditions, because of cost, culture, history and probably doctor encouragement. In contrast, one community pharmacist participant, considered that sometimes people can talk to a pharmacist instead, because they feel “really scared” to talk to the doctor because of the doctor’s esteem.
“Basically the Japanese people like doctors.” Pharmacy voice

Many participants reported that high subsidy of prescriptions and low-cost doctor visits financially motivate patients to consult the doctor rather than self-medicate. Concessional patients (e.g. elderly) contribute 10%, towards the cost of the doctor and the prescription and children contribute 20% and non-concessional patients contribute 30%. A monthly maximum exists. A typical charge for a first doctor visit would be 1000-2000 yen (US$10-20). Manufacturers charge more for OTC-marketed medicines than the same ingredient on prescription (see 9.4.2).

“…for the patient it’s cheaper and more convenient to go to see the doctor.” Government employee (interpreter)

Historically consumers have consulted the doctor rather than presented at the pharmacy. Doctors think it is appropriate to go for minor conditions. One participant suggested that with a two to three hour wait at the doctors, some consumers will find it easier and time-saving to visit the pharmacy. Another participant suggested that consumers shop at a drugstore (which may have no pharmacist present) for convenience, and are not used to obtaining OTCs or advice at pharmacies.

While some consumers perceive that OTC medicines are weak, two participants also mentioned concerns from consumers not wanting to take OTCs because of important side effects.

“Many Japanese people think about OTC medicine that it is weaker than ethical [prescription] medicine…. better way go to doctor.” Pharmacy voice

A couple of participants mentioned concerns from consumers who have had important side effects from drugs and have applied “very strong pressure to the government”, suggesting a political effect. A further participant speculated that consumer pressure might affect reclassification because consumer groups have a “very strong voice”.

9.5.7. Doctors

Most participants considered doctors are the key barrier to reclassification, primarily through vetoing potential reclassification candidates (see 9.5.2), and their committee role. One participant noted that some doctors are more positive than others. Given the multiple recent reclassifications (see 9.3), despite the opportunity to veto candidates and influence the committee, doctors must be agreeing to at least some reclassifications.

“… the company can send an application to [reclassify] however they don’t want to do that without having agreement with the Japan Medical Association…. Because the company does not want physicians to have a bad image of pharmaceutical companies since they have been using their prescription medicine.” Government employee (interpreter)

Participants generally agreed that doctor access was easy, with most stating it was easier and more convenient than in other countries such as the UK. High doctor access caused concerns about rising
health costs from an ageing population. Typically the patient can turn up and wait “six hours” or “two to three hours average”. People can visit different doctors, including specialists when they choose to, with the cost the same across all doctors. Doctors' clinics are often conveniently located, e.g. in office blocks for workers. The medical representative considered that, while the UK needed reclassification, the need in Japan is lower because the doctors are accessible. He also believed this accessibility was a key part of Japan’s good health and longevity.

“… it is very convenient to access to doctors and hospitalisation, and it gets an excellent result for our health. Japanese medical system is very high quality and cost is low and allows easy access to doctors” Medical participant (translated)

The doctors’ opposition to reclassification was almost universally considered to be income-related. Doctors are paid a low rate per patient consultation and therefore “doctors need to see patients as much as they can” [translated]. However, the medical representative noted that easy access facilitates screening for something serious, e.g., “only medical professionals can tell differences between a cold and influenza”, particularly given use of point-of-care tests and diagnostic equipment within clinics. He reported that medical organisations promote to consumers not to go to the hospital for minor ailments, instead go to a doctor’s clinic. A few participants reported that switch for “lifestyle diseases” was discouraged by doctors who considered that they should be doctor managed.

“…medical practitioners are very concerned about losing their tools or their customers to the pharmacist.” Industry participant

Both pharmaceutical companies and the local pharmacies prefer to avoid upsetting doctors. Pharmacies may therefore not promote non-prescription medicines.

9.5.8. Advertising

Advertising received little mention. A couple of participants (including non-industry) noted the need for (and cost of) advertising, which one participant considered meant the price needed to be increased (versus prescription) in order to gain sufficient return on investment.

9.5.9. Potential enablers of reclassification in Japan

Several ideas emerged from the interviews, which appeared likely to help reclassification in the future.

Proactivity from various stakeholders has stimulated reclassification in recent years, and is likely to continue to do so. Participants all believed that the new pharmacy undergraduate education would help with OTC supplies and/or clinical skills, and may raise the pharmacist’s standing. Pharmaceutical companies, or pharmacy organisations are training pharmacists for reclassified medicines. One participant suggested that mandating continuing education for pharmacists would help build skills.

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48 The term “lifestyle diseases” was used by some participants to describe diseases that arose from lifestyle such as diabetes and hypertension
Interesting medicines have been proposed for reclassification, including a diabetes medicine, and an antihypertensive. Talk of diagnostic testing in pharmacy, including influenza testing, and blood pressure monitoring, suggests future opportunities may lie beyond the standard reclassifications. EPA reclassified in 2012 despite medical negativity (9.5.2), suggesting that the doctor’s voice on the committee may be losing power. Some doctors are more accepting of reclassification than others, and in time this may evolve, particularly as pharmacists’ clinical skills improve.

“...in the new education system for the pharmacists we can teach about the assessment of the patients or consumers. Some schools teach about how to assess the vital signs. So maybe in the future the pharmacists can do, not diagnose, but triage. That will be very effective to sell the new type of OTC I think. Like anti-hypertensive drugs or anti-cholesterol drug or something like that.” Academic participant

Two participants considered under-treatment of conditions like diabetes, hypertension and hypercholesterolaemia could enable reclassification. One participant suggested that pharmacy could improve access for the “latent patient”, with a mild condition and currently untreated, referring those with moderate conditions.

One participant suggested that increased government spend on prescriptions was not what was expected when separating dispensing from prescribing. Should dispensing income become curtailed, reclassification may appear more attractive for pharmacy owners and therefore pharmacists.

9.6. Discussion

Stimulated by government support and proactivity from stakeholders, Japan has become active in reclassification, and started to catch up to more progressive countries. Although Japanese stakeholders look internationally for ideas on reclassification, they have even considered areas untouched by reclassification in developed countries, such as diabetes and hypertension. This promise is tempered by the many and often considerable impediments to reclassification.

Doctors apparently provided the strongest barrier to reclassification. Increasing numbers of doctors for a declining population (albeit an ageing one),[616] may cause high doctor competition.[77] However, international data (2010) suggests the number of doctors per capita is not dissimilar from other countries.[393] Doctors’ fees per visit are low[2], which may encourage short, easy visits as for minor ailments. Short visits are likely given that Japanese people visit a doctor more than twice as frequently as in other countries studied.[2, 393] Further encouragement for frequent short visits arose from doctor dispensing, with a maximum of 14 days’ treatment supplied before 2002.[2] The medical participant’s belief that frequent, easy medical access contributed to good population health and longevity suggests that further reclassification may negatively influence Japanese health, but other commentators attribute high Japanese longevity to other factors.[602, 617]
Multiple reclassifications in the last decade suggests some medical acceptance of certain reclassifications. The reported veto of proton pump inhibitors and difficulty with EPA suggests that doctors are not yet prepared to go as far as reclassification elsewhere.

Consumers prefer to consult a doctor than self-manage. Ohkusa, et al. (2005) opined that visiting doctors for minor ailments is partly driven by financial incentives and easy access, noting that “Japanese consumers are relatively reluctant to take an active role in decision making regarding their own health care.” Aoyama, et al. confirmed the disempowerment, finding many consumers would see a doctor for themselves (66%) or their child (90%) for a high fever because they think they should not make their own judgements on health. Consumers reported reasons other than saving money motivated the doctor’s visit, but 43% of consumers reported difficulty affording OTC medicines (versus 21% for prescriptions). Consumers doubted the efficacy of non-prescription medicines, but considered the pharmacist a good source of advice regarding minor ailments (unlike my findings), suggesting promise for the future of self-medication, but also suggesting education on newer, more effective non-prescription medicines was required.

Interviews in Japan suggested pharmacist and pharmacy owners had low interest in OTC medicines, but that pharmacy organisations were supportive and proactive (as confirmed by JPA annual reports). Others have also found that although pharmacy is evolving, continuing education is inadequate, and pharmacies are not all stocking OTC medicines (e.g. 66% of pharmacies and drugstores stocked category one medicines). Yamamura, et al. reported that dispensing provides 94% of community pharmacy income. Watanabe, et al. considered that the new six-year pharmacy course would address their concern that the “…the role and education of Japanese pharmacists has lagged behind those in the Western world…”, with little clinical focus and performing simple technical tasks. The change in undergraduate education may only gradually help as most of the workforce received the four-year education. Pharmacist culture, concentrating on prescriptions and doing simple ‘technician’ tasks, may take time to change. The discount drugstore model (and registered person) with a retail focus accounts for much of the non-prescription medicine market, also probably limiting opportunities for pharmacy to supply these medicines. However, faith in the drugstore model may have been shaken by a drugstore chain fabricating records allowing over 200 ineligible employees to become ‘registered persons’. Mystery shopping shows deficiencies with category one medicines also, with 9-16% of sales by non-pharmacists, non-provision of written information, and incorrect display of these medicines.

Consumer behaviour and pharmacy factors may continue to limit non-prescription sales of medicines. Consumer, pharmacy and medical changes seem necessary to maximise the government desire to increase self-management of minor ailments, and prompt companies to drive reclassification. However, the three year market exclusivity provides a sponsor incentive. Consumer and pharmacy attitudes may change as reclassified medicines become more effective, and as increasing numbers of pharmacists have the necessary clinical skills (and hopefully a desire to use them). Changes in funding may increase interest by stakeholders in reclassification, e.g. dispensing income pressure, greater cost containment on prescription medicines (for industry), and changed doctor fee structures.
Several likely enablers or barriers were not raised in interviews. The large population and high value of the OTC market,[601] albeit in decline,[77] should enable reclassification. A further potential barrier to reclassification is the common use of complementary and alternative medicine in Japan (by 76% of people, more than in Australia, the US and the UK).[623]

9.7. Summary

I found that Japan has considerable long-standing barriers to progressing reclassification, causing conservatism in reclassification. A recent initiative, the registered person at a drugstore, has not helped. However, proactivity by the government, regulator, pharmacy groups, and industry body has provided progress since 2005. While some conservatism remains, the incoming government statements in December 2012 show this proactivity is likely to continue.

Reclassification in Japan has been barely mentioned in English language academic literature, despite the market size and recent reclassification activity. Not only does this chapter help to address this gap, but these findings also show how the role of government can stimulate reclassification, and how strongly doctors and negative pharmacy factors and culture can inhibit it. I compare findings from Japan with other countries in the macro-level chapter (Chapter 11).
Chapter 10. Europe and remaining countries

10.1. Introduction

This chapter provides findings for Europe (particularly the Netherlands and Denmark). Given space constraints\(^49\), reporting of Canada and Singapore is summarised into two tables, but the findings from these countries were incorporated into the macro-level chapter. Brief consideration of these markets provides a valuable insight into whether or not themes in the core five countries extend to other jurisdictions. Additionally, Denmark, Netherlands, and further European interviews provide a second example (after Australasia) showing regional effects on reclassification.

10.2. Background

Western Europe provides 23\% of the worldwide sales of OTC medicines, more than any other region including North America. The 27 EU member states, including Denmark and the Netherlands, form a market of half a billion people. European centralised procedure is used for registering new medicines and can be used for reclassification, providing sponsors with the world’s biggest market following a single application.\(^{[77]}\) The key aspects of Denmark and the Netherlands are presented in Table 10-1.

Denmark was highly progressive in reclassification during the 1980s, with multiple government-driven prescription to non-prescription reclassifications including ibuprofen, non-sedating antihistamines, paracetamol, hydrocortisone 1\%, and H\(_2\)-antagonists.\(^{[20]}\) The primary reason behind these reclassifications was cost-savings. However in 1991, Juul suggested that the effect of European Economic Community membership was likely to limit further Danish endeavours.

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\(^{49}\) A strict word count is enforced
Table 10-1 Key aspects of the Netherlands and Denmark

<table>
<thead>
<tr>
<th></th>
<th>Netherlands</th>
<th>Denmark</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population (millions; 2011)</td>
<td>16.7</td>
<td>5.6</td>
</tr>
<tr>
<td>Health system[372]</td>
<td>Social insurance</td>
<td>National health service</td>
</tr>
<tr>
<td>Life expectancy at birth</td>
<td>80.8 years (2010) [392]</td>
<td>79.3 years (2010) [392]</td>
</tr>
<tr>
<td>Health Development Index Ranking[388]</td>
<td>3</td>
<td>16</td>
</tr>
<tr>
<td>Health spend as % of GDP total (2009)[392]</td>
<td>11.9%</td>
<td>11.5%</td>
</tr>
<tr>
<td>Public proportion of health spend (2009)</td>
<td>85.4% [392]</td>
<td>84.5% [392]</td>
</tr>
<tr>
<td>Self-medication sales</td>
<td>€ 678m (US$885m) (2010) [77]</td>
<td>€170m (US$222m) (2010)[77]</td>
</tr>
<tr>
<td>Self-medication as % of total pharma</td>
<td>N/A</td>
<td>14.5% (2010) [77]</td>
</tr>
<tr>
<td>Growth in self-medication market</td>
<td>+1.3% (2010) [77]</td>
<td>+2.9% (2010) [77]</td>
</tr>
<tr>
<td>Pharmacist-only schedule?</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Pharmacy-only schedule?</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Drugstore schedule (licensed person)?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Physicians per 1000 persons[392]</td>
<td>2.9 (2009)</td>
<td>3.5 (2009)</td>
</tr>
<tr>
<td>Number of doctor consultations per year per capita[393]</td>
<td>5.7 (2009)</td>
<td>4.6 (2010)</td>
</tr>
<tr>
<td>Primary care doctor payment structure</td>
<td>Mix FFS/capitation[14]</td>
<td>Unknown[14]</td>
</tr>
<tr>
<td>Number of pharmacists per 10,000 population[394]</td>
<td>~3.5</td>
<td>~7</td>
</tr>
<tr>
<td>Pharmacies per 10,000 population</td>
<td>~1[394]</td>
<td>~0.5[394]</td>
</tr>
<tr>
<td>Percentage of pharmacists in community pharmacy</td>
<td>Not available</td>
<td>18%[457]</td>
</tr>
</tbody>
</table>

10.3. Sources of information

Email correspondence, my involvement as an expert in a centralised European reclassification, and my leading of a workshop for Dutch pharmacists on reclassification supplemented these 17 interviews. As these remaining countries are not the key countries for this research, background information is minimal, recent reclassifications are not listed, and few documents have been analysed.

Table 10-2 outlines by country the numbers of interviews and the number and background of participants in the interviews. One participant was a member of the CHMP, the committee that considers marketing authorisations and centralised reclassifications for Europe.[36]
### Table 10-2 Interviews used for Europe, Singapore and Canada

<table>
<thead>
<tr>
<th>Country</th>
<th>Number of interviews</th>
<th>Number of participants</th>
<th>Background of participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Denmark</td>
<td>2</td>
<td>3</td>
<td>Two different pharmacy organisations and the regulator</td>
</tr>
<tr>
<td>Netherlands</td>
<td>2</td>
<td>3</td>
<td>One pharmacy organisation and the regulator</td>
</tr>
<tr>
<td>Pan-European</td>
<td>2</td>
<td>2</td>
<td>One pharmacy organisation, one industry organisation</td>
</tr>
<tr>
<td>Singapore</td>
<td>2</td>
<td>4</td>
<td>One pharmacy organisation, and the regulator</td>
</tr>
<tr>
<td>Canada</td>
<td>2</td>
<td>2</td>
<td>One pharmacy organisation, one academic</td>
</tr>
<tr>
<td>International</td>
<td>4</td>
<td>4</td>
<td>Two working in industry, and two working for industry-related organisations</td>
</tr>
<tr>
<td>Other countries</td>
<td>3</td>
<td>3</td>
<td>A US participant who had lived in the Netherlands</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>An industry participant with an Asia-Pacific role</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>A UK industry participant with European experience</td>
</tr>
</tbody>
</table>

I now present the results, firstly for Europe including Denmark and the Netherlands, then very briefly for Singapore and Canada.

### 10.4. Europe (including Denmark and the Netherlands)

Although not a core country, Europe receives more attention than Singapore or Canada because the market is very important internationally, and has previously been compared by commentators to the UK and US.[95] With centralised reclassification, sponsors can potentially reclassify a medicine for a market of half a billion people in one application. However, only two sponsors have successfully achieved this to date. Denmark and the Netherlands were chosen for having similar sizes to NZ and Australia, respectively, i.e. one small country and one a bit bigger. Additionally, the Netherlands has had a drugstore category since 1921,[218] which is highly unusual.

For this section I concentrate on key stakeholders or factors that emerged from interviews, following similar headings as for the chapters for the core countries.

#### 10.4.1. Government, regulator, committee, process and scheduling

Participants reported that the ability to reclassify a medicine in single application for market of half a billion people stimulated reclassification. However, the short market exclusivity of one year considerably limited the attraction, as did the cost and difficulty of succeeding, and compromises needed for success, as illustrated in the quote below.

“...you're actually often switching a product that has different strengths in different countries and different dosage amounts and different indications, it's very hard, so often it comes down to a lowest common denominator. So you end up with a lower strength than you really want because Spain would only accept that.” Industry participant
Pantoprazole and orlistat reclassified through the centralised process, but other candidates failed to reclassify. The diversity across the member states (as described below), and aspects of the CHMP arose as key barriers. The CHMP approves new medicines as well as reclassifications, and was criticised for considering reclassifications in a similar way to new medicine approvals. The evidence required caused high regulatory burden and cost which one participant found excessive for well-defined medicines.

Two allocated CHMP members (the rapporteur and co-rapporteur) and assessors do background work on the application and give their opinion which is sent to the applicant for comment. Further work occurs, then the rapporteur and co-rapporteur’s comments and opinions and the applicants’ documents are circulated to other members. The application is discussed by all members at a large CHMP meeting as one item on a busy agenda. The applicant presents at the meeting and is available for questioning.

One participant believed that the committee made subjective or intuitive decisions rather than following structured decision-making. Multiple participants considered CHMP members were particularly conservative. One participant stated that only medicines that would be considered safe enough for general sales supply could successfully reclassify through the central process. Two participants reported a reclassification application for ibuprofen-diphenhydramine withdrew because the CHMP wanted more data, despite the long-time non-prescription availability of the active ingredients in many countries.

“…there’s such a level of conservatism, and these assessors are so frightened of making a mistake that’s why they’re pulling back so far from the edge, you know they’re miles away from the edge they’re so conservative.” Industry participant

CHMP members are representatives of each member state, usually regulatory employees, and five co-opted experts who remain the same regardless of topic considered. Participants reported that the committee consists mainly of doctors, with little understanding of pharmacy and, according to one participant (and my experience), a distrust of pharmacists or pharmacy.

“…a lot of the assessors, non-UK and also the European competent authority and also CHMP…. None of them have got the slightest idea about the dynamics probably of general practice for physicians, let alone community practice for pharmacists. And they just see spooks everywhere.” Industry voice

Although members bring their country’s perspective, they reportedly decide reclassifications based on the countries with the least consumer protection (e.g. those without a pharmacy-only category). Three participants considered that this fact provides a major road-block for centralised reclassification.

“I think we at CHMP have the obligation to try to understand what is going on in other member states, and put safety first. And even though you could argue that you think it would be safe to put on every market except Spain and Italy, say it would then put the patients in these two
countries at risk, and is that risk reasonable to run in these two countries as compared to the rest of Europe.” CHMP member

“One of the main arguments [the company] were using [for the orlistat centralised switch] is the pharmacist. Saying that the pharmacist is actually a safeguard for the safe use of this medicine. However, there are countries where … it goes out of the reach of the pharmacist.” European pharmacy participant

The CHMP decides whether a medicine is reclassified or not; the regulator cannot overrule the committee. Member states must comply with centralised reclassification approvals, but choose which non-prescription classification is used (in countries with a choice). Local labelling and advertising issues may need resolving. Two participants commented that getting the centralised approval was only part of the job.

“…yeah we’ve got Brussels signed off but we have now got to still go to each of the countries and get our local approval on the details.” International industry participant

A guideline requires that medicines first registered under the central process are reclassified centrally. Given the barriers to attaining a central reclassification, member states that are progressive and innovative in reclassification, such as the UK, will miss out on medicines that would probably be approved if considered nationally, but not if considered centrally. Thus centralised reclassification is perversely more a barrier to reclassification than an enabler. Some frustration at this limitation was expressed in the UK.

Industry participants appreciated being able to present to the CHMP, the ability to work with people at the European Medicines Agency (EMA) during the reclassification process, and confidentiality during the central process. However, pharmacy voices criticised the confidentiality and lack of consultation of stakeholders about reclassifications being considered, particularly without community pharmacy or consumer representation on the CHMP.

Not all reclassifications are considered centrally, many are considered at the national level instead. Like the CHMP, reclassification processes at the Danish national level were criticised for lack of transparency and consultation. National regulatory authorities typically do not report rejected reclassifications. National committees (including the Danish one) which were advisory could be overruled, and an example arose of calcipotriol in Germany which the committee recommended to reclassify, but was overturned by the Minister of Health for confidential reasons.

Like the CHMP, neither Danish, nor Dutch committees included community pharmacy representatives and both committees considered new medicines and other matters in addition to reclassification. Although the Danish pharmacy organisation had suggested candidates with pharmacy background for the committee, none had been appointed at the time of the interview. When a European regulator participant was asked if anyone on the committee had community pharmacy experience, the response was “not really but the hospital pharmacist, let’s say they’re the most highest educated
pharmacists in [this country], so they know exactly what is happening in the normal pharmacies..."

This comment demonstrates misunderstanding of the differences between sectors of the profession, and appears not to appreciate the relevance of community pharmacy experience. Lack of community pharmacy knowledge on the Dutch committee may have led to an unusual situation whereby St John’s Wort when registered as a medicine was scheduled pharmacist-only, but if not registered can be purchased anywhere. Consultation about reclassification did not appear to occur in the Netherlands.

Most European participants considered that member state diversity strongly hindered central reclassifications. Such diversity includes scheduling (as discussed above), pharmacy model, pharmacy behaviour, pharmacy continuing education, and consumer behaviour. Pharmacy undergraduate education was noted by some to differ between countries, but one disagreed:

“Pharmacy is one of few professions that have harmonized educational and training requirements in EU, including a minimum list of subjects that need to be taught and period of undergraduate training.” Pharmacy participant

The regulator perspective, and possibly the country in general, may differ in reclassification attitudes. For example, one industry participant believed that the UK and Belgium were “liberal” while others such as the Netherlands, Sweden and France were “conservative” or “very conservative” with reclassification.

“We have a European Union and they’re trying to create a single market and all of that. But ... pharmacists’ system and health system ... are still quite different, and therefore the industries or the medicine agencies locally, they have different concepts and different models of working.” European pharmacy participant

The CHMP struggled with this diversity, particularly scheduling, pharmacy practice and educational requirements. CHMP members reportedly worried that pharmacy in some countries could not decline inappropriate supplies, but one participant said that was “untrue”. However, another participant noted that in Denmark a sale could be declined in suspected misuse, but it was tricky to do so. One participant reported the CHMP lacked faith in pharmacy, and commonly believed that pharmacies would give out anything for money. The variation in pharmacy created difficulties in achieving a consensus across countries at the European pharmacy body, as well as difficulties for the CHMP.

“...in UK and Spain pharmacies are very different. They are not that restrictive, the employees are maybe not as educated as in other countries, and in UK you have the possibility to become, as I understand it, specialised as a pharmacist. So you can have post-graduate education specialising in some kind of areas. And of course, if you have this kind of pharmacy it might be more safe to put a drug in OTC there.... specially educated pharmacists ...can do the assessment of these patients and screen for co-morbidities and then the OTC will be safely used. Whereas... maybe in other countries where pharmacy is very liberal and very
much less regulated it will be unsafe because this screening in OTC will not take place.”

CHMP member

The Danish regulator has proactively up-scheduled and down-scheduled medicines. The Danish regulator reclassified some medicines from prescription to non-prescription without application in the late 1980s (including H$_2$-antagonists, see below). This exercise remains unrepeated, perhaps because it did not achieve the desired health savings.

“The [Danish] government said ‘let’s have [H$_2$-antagonists] available over the counter and see what happens.’ Nothing happened, the customer didn’t want to buy it, the pharmacist didn’t want to sell it and I think it was abandoned after about a year. And there’s never been much action for switch since then.” International industry participant

However, Danish regulator proactivity remains, with reclassifications of ‘me-too’ compounds suggested following the omeprazole reclassification, and pharmacy-only to general sales candidates suggested following political pressure. The resulting increase in general sales medicines was said to rival the UK list. Possibly this political pressure occurred because pharmacies are relatively scarce in Denmark (Table 10-1), but this was not raised by participants. Further political pressure stimulated up-scheduling of dextromethorphan following misuse causing death. Although the pharmacy organisation had suggested such an up-scheduling to the regulator, action only occurred following a journalist’s investigation and media pressure.

Government interest in reclassification (for cost and access reasons) described in both Dutch interviews, has not obviously increased reclassifications. Indeed, up-scheduling had been at least as common around the time of interviews, with domperidone and dextromethorphan up-scheduling from pharmacy and drugstore to pharmacy-only. Sweden has also not repeated their government-driven reclassification of omeprazole.

“…[Sweden] was the very first market where omeprazole was over the counter. But it never took more than 5% of the antacids market, even with the market leader driving it. There’s just no interest really when you can go to a doctor and get the thing free of charge anyway.”

International industry participant

One regulator participant believed that non-prescription medicines are “for acute episodes, not chronic diseases”. Others (regulators, committee members and some pharmacy members) probably hold similar views, limiting reclassification opportunities in these European countries.

Regional influence was reported in Denmark which looked to other Scandinavian countries and sometimes the Netherlands when considering reclassifications, because of similarities between the countries including their health care systems. The UK was considered less relevant in Denmark because of a different pharmacy model. Several participants (regulatory and pharmacy) dismissed the UK reclassification of simvastatin as inappropriate for their own country or for Europe, citing efficacy concerns with 10 mg and inability to self-diagnose. However, the Netherlands appeared to look to the
UK, for example with government discussion about considering sumatriptan and simvastatin like the UK, although a manufacturer application is required.

One participant described distrust from governments and the committee in pharmaceutical companies (partly arising from data with-holding scandals), in pharmacy, and in consumers.

10.4.2. Pharmaceutical companies

The pharmaceutical industry drives down-scheduling in Europe, and their interest depends largely on the post-reclassification market potential. For example, with small populations (and probably conservatism), Denmark and the Netherlands provide little reclassification interest to multinational companies. In some European countries, advertising limitations and an inability to use the prescription brand name in the OTC environment can reduce market potential post-reclassification. In contrast, a “comfortable” reimbursed prescription environment in some countries, such as France, reduced interest in reclassification, according to one participant.

De-reimbursement, a loss of prescription funding on reclassification, hinders reclassification in the Netherlands. The likely loss in the funded prescription market deters companies from reclassifying. Lagging behind many other developed countries, the Netherlands was late in reclassifying vaginal antifungals, with the first, clotrimazole, only reclassifying from prescription to pharmacy-only and drugstore in limited strengths in 2011. Unusually, hydrocortisone 1% remains prescription-only.

“…for example in antihistamines in hay fever, patients don’t want to pay for their medicines. So the doctor prescribes a different hay fever medicine that is prescription only. And that is often even more expensive for the community. Then the patient is happy because he gets it funded.” Netherlands pharmacy participant

Two participants considered that ingredients that are available without prescription should not be reimbursed. Reimbursement of “semi-ethicals”, medicines available as self-medication and prescription-funded, was believed to hinder non-prescription sales. However, the example of the Netherlands suggests that de-reimbursement dissuades companies from reclassification, and can cause doctors to shift patients to other medicines.

Consumer culture (10.4.4) and pharmacy interest in reclassification in different countries (10.4.3) are likely to affect sales potential for companies.

10.4.3. Pharmacy (and druggists)

Several participants described variation between pharmacy models in different countries. One participant noted some countries did not have pharmacy chains owing to ownership restrictions, and believed that pharmacy was more powerful as a lobby group in parts of Europe than the UK. For example, the monopoly-type pharmacy set-up in Denmark includes a government claw-back based on dispensing and retail supplies, de-incentivising growth of the non-prescription business. Two participants reported Danish pharmacies to be few in number compared to other countries, with only
322 pharmacies or branch pharmacies. With one pharmacy per 10,000 or more people (Table 10-1), these are very large pharmacies compared with the rest of continental Europe. This pharmacy model may have influenced the interest in increasing the general sales supplies (see 10.4.1) and may be partly why pharmacy in Denmark did not appear to be proactively seeking prescription to non-prescription reclassification.

“If you don’t have a monopoly for pharmacies, you might also get a broader interest in selling drugs.” Danish regulator

In addition to trained pharmacists, Denmark also has ‘prescriptionists’, who have had three years’ university training, can run a branch pharmacy or pharmacy outlet and dispense prescriptions.

The unusual Dutch schedules, with pharmacy-only, pharmacy and drugstore only (with a licensed person in the drugstore) and general sales, led to most non-prescription medicines selling from drugstores not pharmacies. Consumer perceptions of pharmacies being expensive reportedly also contribute to higher drugstore sales. Low non-prescription medicine sales may contribute to a focus in pharmacies on prescription rather than non-prescription medicines. An international participant reported little interest from pharmacists in the Netherlands in reclassification, and attributed it to the ownership model (as for much of Europe), and their businesses providing a comfortable living.

An expected enabler of future reclassification in the Netherlands was the national prescription information. As pharmacies record sales of pharmacy-only medicines, using national records was expected to help reclassification.

Two pharmacy participants noted disappointing mystery shopping results for pharmacy in two continental European countries. Mystery shopping was also noted to indicate variable and often suboptimal behaviour for druggists. Druggists have one year of training, but “only one druggist has the training”, the rest are just “sales ladies”, and the medicines are often available for self-selection with some druggists stocking mainly non-medicinal goods.

In the Netherlands and Denmark, the pharmacy organisations were not involved in prescription to non-prescription reclassifications (sometimes only learning after approval), and were not proactive about down-scheduling, but wanted increased involvement. One Danish pharmacy organisation had been proactive in both recommending an up-scheduling and suggesting a community pharmacy member for the committee considering reclassifications.

Pharmacy behaviour was believed to differ across Europe, affecting the perceptions of the regulators and CHMP (10.4.1). Some related it to education, others to practice. One non-pharmacy participant noted that protocol use was unknown in Denmark, and seemed unsure that it would work there. Another participant reported that German pharmacists found protocols insulting given they were health professionals. One pharmacy participant noted that some pharmacists think a medicine is given OTC status when it is safe “so there’s not much attention needed by the pharmacists.” Low
pharmacy interest in reclassification and/or non-prescription medicines in some countries would affect market potential and reclassification approvals.

“…there is a different culture amongst pharmacists across Europe in terms of how important [supplying non-prescription medicines] is.” Pharmacy participant

10.4.4. Cultural differences, and consumers

Most participants discussed cultural differences as an influence on reclassification. This included consumer behaviour, culture in pharmacy, and conservatism or risk-aversion (in the regulator, committee, and government). Two participants discussed differing UK and French cultures, with self-efficacy in the UK, and paternalism in France.

“I think the culture is quite different and the notion of risk is quite different in the two countries. The healthcare system may also be a bit different… I think people are so much more empowered to more take care of themselves [in the UK]. I would say the French system is a lot more paternalistic.” European industry participant

Consumer buying behaviour was also noted to vary across Europe.

“…upper GI the category here in the UK is GSL, people in the UK, unlike the rest of Europe, are so used to walking in and grabbing a pack of calcium carbonate to buy, they’re not used to and they’re not prepared to stand around in front of a chemist counter waiting for the pharmacist to get that.” UK industry voice

“…my experiences between the UK and the other EU countries, there’s definitely a different culture of pharmacy services and what people expect to get from their pharmacy and what they expect to get from their doctor. And so self-medication or self-care in itself is developed to varying degrees in all these different countries…” Pharmacy participant

Cultural differences between Northern and Southern Europe were frequently identified. One participant contrasted the Southern European tendency to use speciality shops (including pharmacies) with supermarket use for many goods in the UK and some other countries. A second participant considered that Southern European was paternalistic and conservative, and the UK, Germany and Scandinavia were more progressive in reclassification. However, another participant noted Spain to be very conservative, like Denmark, and the Netherlands which is less suggestive of a North-South divide. Two participants reported that “if you go to the Southern part of Europe they use a lot more medicinal products, antibiotics and so on” in contrast to a “very low usage of medicinal products” in Denmark. Participants reported that Denmark and the Netherlands have lower medicine consumption than other countries. One US participant who had lived in the Netherlands commented that a conservative perspective of medicine use permeated society citing multiple examples including a pharmacist recommending against using a medicine available OTC in the US (that was prescription in the Netherlands). These sometimes conflicting statements suggested variability between European countries.
Consumer culture also contributed to market opportunities, with consumers in some countries (e.g. the Netherlands, France and Denmark) preferring funded prescribed medicines over self-purchase. A simvastatin reclassification in France would reportedly provide an unworkable return on investment. In some countries consumers commonly use alternative remedies, e.g. herbal remedies in Germany, Switzerland and Austria. Presumably such practices could limit the sales potential for reclassified medicines.

10.4.5. Doctors

Doctors greatly influence European reclassification, including through their role on the CHMP and national committees, and as assessors. A European regulator reported using external medical specialists (but not pharmacists) to advise on reclassifications. Participants reported that reclassification affected doctors’ control, status and/or income. Four participants observed that where doctors receive payment for service (rather than capitation funding) they are less keen on reclassification. One participant commented that governments were less desirous of reclassification where doctors are not keen on the concept. However, two participants suggested that a doctor shortage encourages reclassification.

“...I guess there is also a barrier to that change from the physician’s side, because the general practitioner will say they are stealing our patients, they don’t understand, they have no knowledge about diseases, why should they do that? But at the moment GPs are getting more and more overloaded... so I guess that might also change the cut-off level for what they would like to see, and 'well that can be taken care of by the pharmacist.'” Regulator voice

The doctors’ payment system was considered to affect acceptance of pharmacy taking a greater role in supplying medicines.

“...you have to have a vision of the remuneration system of the doctors, not only about the pharmacists. Because if you look at the UK, the doctors are very happy of pharmacists doing services and providing counselling... [whereas] Austria [is] remunerated for visit, so I want the patient to come for paracetamol because I'm going to be paid for that.” Pharmacy voice

10.4.6. Discussion

I found that Europe is considerably affected by member state diversity and conservatism, hindering reclassification and consequently limiting consumer access. My concern about the current environment limiting consumer access is borne out by the fact that only five medicines are non-prescription across all EU member states.[624] Probably unsurprisingly, the President of the Pharmaceutical Group of the EU (PGEU) in 2012 wanted an effective reclassification model to fill gaps in effective medicines for problems presenting in pharmacy.

Some reclassification barriers I found have been discussed elsewhere, e.g. member state diversity.[218, 624, 625] Diversity includes pharmacy ownership, medicines display in
pharmacies,[625] and availability of consultation areas.[47] While concerns were voiced about variable teaching of pharmacy practice skills, as supported by commentators,[624] the PGEU reported some harmonisation of pharmacy training across Europe, and that clinical pharmacy is typically part of the curriculum, although communication skills are sometimes taught in the internship period rather than earlier.[626] Previous commentators have attributed diversity in medical support of self-medication,[110] or pharmacist role extensions[627] in part to medical labour supply[627] or funding.[110]

Concerns about Southern Europe versus Northern Europe are illustrated by (or may arise from) research showing that antibiotic self-medication is higher in Eastern and Southern Europe than Northern and Western Europe, with Netherlands and Denmark very low.[628] Antibiotic use varies three-fold across Europe, with low use in the Netherlands and Denmark.[629] These studies support participants’ comments about culture of medicine taking. Differences in consumer perception of pharmacy might be suggested by variation from consumers in different European countries in having a range of medicines ‘prescribed’ by community pharmacists.[627]

Pharmacy mystery shopping results have sometimes disappointed, e.g. orlistat was supplied inappropriately in many pharmacies in Vienna, Spain and Italy.[624] Pharmacies have supplied antibiotics without a prescription in Spain.[630, 631] A European Consumer Organisation representative recommended better undergraduate education, mandatory continuing education and quality control mechanisms for pharmacy to help address these problems.[624]

The interviews and involvement in a centralised reclassification left me feeling that European centralised reclassification is nearly impossible for all but the very straight-forward medicines. The promise of centralised reclassification[218] has not been realised. Progressive EU member states, particularly the UK, could find reclassification curtailed as increasingly potential candidates will have been centrally registered, as recently highlighted by the UK industry body.[100] The ageing population, health funding challenges,[624] and current economic environment of ‘austerity’[632] require changes to health. Considerable (35%) growth in medical consultations for minor ailments in the Netherlands, to a cost of €100 million (US$130 million) in 2009 for such consultations adds to funding challenges.[633] Having pharmacists step up and consumers self-medicate where possible could provide health system savings and free doctors’ time.

Mechanisms to overcome difficulties of the centralised reclassification may need legislation or guidance changes. Permitting medicines registered centrally to be reclassified in individual member states would allow data collection to inform other member states’ decisions. A pharmacy-only or pharmacist-only schedule in all member states (or a European-wide pharmacy-only category as previously suggested)[35] would help resolve the current inability to approve medicines needing pharmacist or pharmacy assistance. A third solution might be using exemptions allowing pharmacist-supply, possibly with mandatory training where necessary, as in NZ (see 4.7.2), although this might be impossible across 27 member states.
If pharmacist-only supply became possible across Europe, more centralised reclassifications may ensue. However, the workforce needs the necessary skills and willingness to manage more complex reclassifications. This may require education of qualified pharmacists, undergraduate education improvements, and mandated continuing education for all EU pharmacists. Research showing whether or not pharmacists can manage complex reclassifications and protocols (in some cases after training) would provide evidence for reclassification decisions, and Kelly suggested using the UK for this.[100] The governments may need to encourage consumer self-management of health where appropriate.

Industry apparently wanted three-year market exclusivity for Europe, and would probably be more prepared to endure the cost and difficulty of reclassification if this occurred. While this enabler may be easier to enact than mechanisms suggested above, it may not increase the chances of an application succeeding, which is probably the primary barrier.

For both the centralised reclassification and for national reclassifications, the doctor-centric process appears to hinder reclassification. The addition of one or more pharmacists with knowledge of community pharmacy and relevant literature may provide a useful perspective that identifies and addresses possible misconceptions on the committee.

10.5. Singapore

Despite the small population, Singapore appears active in reclassification but without first-in-world reclassifications. However, some reclassifications such as orlistat (2005), and naproxen (2003) seemed early compared with other major markets [634-636]. Some reclassifications (such as domperidone in 2000)[636] have occurred as exemptions to prescription, avoiding the need for unique country packs,[634, 635] similar to NZ.

Singapore has been reasonably progressive for some years. Vaginal antifungals reclassified in 1995, and aciclovir, nasal beclometasone, and domperidone reclassified in 2000.[636] Some medicines reclassified elsewhere remain prescription-only, e.g. EHC, triptans, and chloramphenicol. From the interviews, enablers appeared to outweigh barriers (Table 10-3), noting the limitations of a small number of interviews. Proactivity, pharmacy support and confidence in pharmacy emerged.

“…one of the main concerns that we had about [orlistat was]… being used by a person that might not really necessarily require the medicine. But then after launching it as a pharmacy medicine in Singapore, based on the information that we have been given so far, or the feedback … actually the pharmacists here are very compliant. They actually measure the patient’s BMI before they decide whether to give Xenical or not.”
Table 10-3 Enablers and barriers for reclassification in Singapore

<table>
<thead>
<tr>
<th>Enablers</th>
<th>Barriers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proactive, flexible regulator</td>
<td>Small country</td>
</tr>
<tr>
<td>Regulator works with the company in advance of committee meeting</td>
<td>Doctor dispensing (companies will not want to get them off-side)</td>
</tr>
<tr>
<td>Regulator faith in pharmacy (responsible approach to orlistat)</td>
<td>Consumers view pharmacists as storekeepers rather than health professionals (because of strongly retail focus)</td>
</tr>
<tr>
<td>Confidential process</td>
<td>Expectation of reclassification for minor ailments rather than chronic disease</td>
</tr>
<tr>
<td>Fast reclassifications (six months)</td>
<td>Potential reclassifications limited to those that have happened in “the big agencies” first</td>
</tr>
<tr>
<td>Reclassification by product (for market advantage)</td>
<td>Accessible doctors (open seven days)</td>
</tr>
<tr>
<td>Can reclassify generics using exemption to prescription[637] (a leaflet is provided)</td>
<td>Relatively few pharmacies (300) versus GP clinics (1600)</td>
</tr>
<tr>
<td>Proactive pharmacy professional body (suggesting reclassification candidates, providing training and consumer leaflets)</td>
<td>Consumer culture to consult the doctor</td>
</tr>
<tr>
<td>Pharmacists enthusiastic about reclassification and keen on training</td>
<td>Traditional Chinese medicines used</td>
</tr>
<tr>
<td>Pharmacy strongly retail because of doctor-dispensing</td>
<td>Cultural values may limit interest in EHC (and low teenage pregnancy, so less need)</td>
</tr>
<tr>
<td>Government –led reclassifications</td>
<td></td>
</tr>
<tr>
<td>Mandatory recording of pharmacy-only and exemption to prescription medicines</td>
<td></td>
</tr>
<tr>
<td>Reclassifications have happened elsewhere first, making them easier</td>
<td></td>
</tr>
<tr>
<td>Strict pharmacy supply requirements (pharmacist involved)</td>
<td></td>
</tr>
<tr>
<td>Pharmacists not busy with dispensing</td>
<td></td>
</tr>
</tbody>
</table>

10.6. Canada

The Canadian interviews were the most limited, comprising two participants and no industry or regulator voice. However, interesting aspects emerged that echoed findings elsewhere. The enabling effects of the multiple schedules seemed outweighed by de-reimbursement, and a low potential market because of advertising limitations and house-brands, and low pharmacy interest (Table 10-4).
<table>
<thead>
<tr>
<th>Enablers</th>
<th>Barriers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Politics helped reclassification with vaginal antifungals and EHC</td>
<td>Pharmacy did not seem interested in reclassification</td>
</tr>
<tr>
<td>Three schedules provide a good step-down approach for reclassification</td>
<td>Other models of supply, e.g. pharmacist prescribing, minor ailment schemes</td>
</tr>
<tr>
<td>At least one pharmacy organisation supports reclassifications generally</td>
<td>Pharmacy made more money on prescription than OTC</td>
</tr>
<tr>
<td>Pharmacists probably appreciate using their professional skills (but not top-of-mind)</td>
<td>Risk of further down-scheduling out of pharmacy</td>
</tr>
<tr>
<td></td>
<td>Insufficient evidence for committee decisions (need more research)</td>
</tr>
<tr>
<td></td>
<td>Committee concern about pharmacy performance</td>
</tr>
<tr>
<td></td>
<td>Variability in committee member performance</td>
</tr>
<tr>
<td></td>
<td>De-reimbursement on reclassification</td>
</tr>
<tr>
<td></td>
<td>House-brands and inability to advertising pharmacist-only medicines barrier to sales</td>
</tr>
<tr>
<td></td>
<td>Media pressure from inadequate mystery shopping performance</td>
</tr>
<tr>
<td></td>
<td>Consumer caution may reduce on supermarket availability</td>
</tr>
<tr>
<td></td>
<td>Fee charged for reclassification</td>
</tr>
<tr>
<td></td>
<td>Medicine reclassified by ingredient not product</td>
</tr>
</tbody>
</table>

### 10.7. Summary of the chapter

Europe’s disparities and conservatism hinder centralised reclassification. Lack of pharmacy-only or pharmacist-only schedules in some countries, lack of trust in consumers and pharmacies, and committee make-up contributed to the fact that only two medicines had reclassified centrally since this process started in 2005. Failures of some centralised reclassification attempts, and concerns about limited sales post-reclassification probably discouraged companies from embarking on costly and time-consuming centralised reclassifications.

Singapore is a small, proactive country, providing an interesting comparison to NZ and Denmark. Canada’s environment appears somewhat negative towards reclassification with a variety of barriers emerging.

Similarities and differences can be seen compared to the other countries, and these will be drawn together in the next chapter, the macro-level results.
Chapter 11. Macro-level Discussion

11.1. Introduction

This chapter provides a big picture view, effectively answering the question “why do different developed countries have different medicines available without prescription?” I integrate information from the micro- and meso-levels, and look at company and product factors affecting decisions to pursue reclassification or not.

Reclassification of medicines may increase consumer access and autonomy, save costs for funders (and sometimes consumers), better utilise pharmacy, and reduce pressure on doctors.[24, 638] It may help relieve the pressure to meet growing healthcare demands in the context of ageing populations and increasing health costs in most countries. Without reclassifications that have occurred to date, health funding and workforce pressures would be even greater than currently.

Reclassification risks include inappropriate use in pregnancy,[639] misdiagnosis or delayed diagnosis, adverse effects, drug interactions, unnecessary use, and suboptimal therapy.[24, 157, 160] Patients may not act responsibly at times, and their views may differ from those of health professionals.[640] Continuity of care and opportunistic interventions in general practice[641] may be lost. However, the reclassification process carefully considers risks, as safety always remains important.

My thesis describes practices and initiatives in developed countries that cause variation in reclassification. The innovative reclassifications documented, although largely objective, necessarily contain a degree of judgement.

Countries differ in reclassification in two ways: whether or not reclassifications are being driven in their country; and whether or not reclassifications that are submitted are approved or rejected. I integrate the preceding chapters and further analyse 17 pharmaceutical industry interviews to examine how pharmaceutical company decisions to apply to reclassify (or not) reflect company factors, product factors, and market factors (Figure 11-1). Under market factors I compare the core countries in reclassification using multiple tools. The chapter finishes by developing illustrated ‘Principles of Reclassification’.
11.2. Company factors

As pharmaceutical companies are the main drivers of reclassification, whether or not they decide to pursue reclassification in different markets contributes significantly to international variation in reclassification. Pharmaceutical companies make decisions based on financial return. Companies typically consider global and local factors, and sometimes regional factors, in deciding whether to apply in a particular country to reclassify a medicine. Often they initially seek to reclassify in progressive countries and/or larger markets. Some factors arose in earlier chapters, but here I integrate all the company interviews.

Given the financial focus, the prescription business generally comes first. Should reclassification potentially reduce prescription sales through consumer or doctor backlash, losing prescription reimbursement, or facilitating generic market entry, reclassification is unlikely. Conversely, a reclassification might be considered to help prescription sales (e.g. through advertising).

“… you look at sales volumes and profitability it’s 80% Rx and 20% OTC, at best. So,…. who’s on top in companies, it’s always the Rx person.” Industry participant

Prescription divisions sometimes transfer reclassification candidates to the consumer health division as patent expiry approaches, but may be reluctant to lose the sales. Products may remain with the prescription division, e.g. salbutamol, which has not been considered for UK reclassification (7.6.4),
and only briefly pursued in NZ (4.7.4). Absence of OTC infrastructure may reduce company interest in reclassification. Use of different distributors or licensees internationally may also hinder reclassification, as could a company sale or merger.

Sponsors may reclassify a medicine in one country to help reclassification in a larger market. Reclassification in smaller markets that risk the company’s sales in a larger market will be avoided (e.g. oral contraceptives with US backlash).

Many generic companies are prescription-oriented, without reclassification experience, prescription brand-names to leverage off, or OTC marketing strengths. While multi-national innovator companies know key opinion leaders to support their reclassification, generic companies usually have no such relationship. However, local generic companies are not limited to a company pipeline or potential effects on other markets, and may move faster. Galpharm in the UK exemplifies how a generic company can specialise in this area in the right environment. Given some reclassification candidates are off patent, if generic companies do not drive them they may not be reclassified.

While prescription to non-prescription reclassification has been important for consumer health companies or divisions, most “low hanging fruit” has been picked (according to industry and regulatory participants). The cost and time taken, slow pay-back and uncertain returns may cause consumer health companies, given their typically short-term focus, to pursue other priorities. Some consumer health companies have no interest in reclassification.

“…most switches fail outside of the US, and the ones that succeed – it’s a very painful journey…. Many of them don’t pay back. If they do pay back it takes a long time, and there’s a lot of upfront investment.” Industry participant

Discussing an uncertain reclassification with considerable doctor and pharmacist negativity and certain backlash, one participant suggested companies needed courage.

“… switch is more or less the lifeblood of the OTC industry, and self-medication is really important in terms of reducing the impact on the health budget, but there are a lot of barriers, and so the companies tend to wax and wane.” Industry participant

The triptans illustrate differing strategy between companies and within a company. GSK Consumer Healthcare attempted to reclassify sumatriptan in the UK and Australia,50 naratriptan in Germany around the same time, and sumatriptan in NZ soon after (see Panel 5-2, Panel 6-2). All but the Australian application succeeded. That GSK applied for naratriptan in Germany suggests local factors modified the global strategy. The non-launch by GSK in NZ post-reclassification suggests non-viability without Australia, and a desire to help the Australian application. Post-patent expiry, Galpharm (a generic company) unsuccessfully attempted a central European reclassification of sumatriptan in 2011.[642] In most countries sumatriptan remains prescription-only,[123] possibly suggesting GSK might have changed strategy given reportedly low UK non-prescription sales. Although a participant

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50 In 2005 Australia was considered progressive
speculated the UK sumatriptan reclassification was to help a US attempt, the US statin reclassification failures may have lowered expectations for that market. Two other multinational companies with triptans have been less active. AstraZeneca (which has no consumer health arm) withdrew their UK zolmitriptan reclassification before approval for market reasons[117] but reclassified it in NZ, where Merck Sharp and Dohme also reclassified rizatriptan. These medicines appear prescription-only elsewhere,[123] suggesting an affect of local factors such as subsidy arrangements, and ease of reclassification following sumatriptan.

Other commentators have highlighted the need for companies to maximise their earnings,[217, 220, 221] and the long timeframe of reclassifications.[643] Stibel and Kapoor reported that the prescription-OTC conflict in companies, and the higher profitability of prescription products affected reclassification.[119] Furler, et al. reported that prescription H2-antagonists outsold non-prescription H2-antagonists by eight times in the US and 10 times in the UK, soon after reclassification.[97] Many of my findings echo Haverkost (1985) who reported company sensitivity to doctors’ views (given the larger prescription business), the importance of post-reclassification saleability, use of products from the company pipeline, and company fit (effectively considering OTC structure).[217] He reported the need to consider cost and requirements for the reclassification. However, Haverkost suggested using reclassifications to fund future research and development, while my research found difficult returns (primarily outside of the US). This difference may reflect changes 30 years on, reclassification costs (particularly in the US) have risen, and few if any big-earning reclassifications remain in most countries. However in 2002, US-based Stibel and Kapoor believed OTC blockbusters lay ahead (starting with omeprazole and loratadine).[119]

11.3. Product factors

Panel 11-1 summarizes product influences on which medicines to reclassify.

“…there are two parts of it and they are: can you switch it; but then can you sell it… in some instances it is easier to get it approved than it is to get it accepted by the consumer.” Industry participant

Within and between countries, some reclassifications are unpredictable, in both approval and success post-reclassification. One participant expressed surprise that non-prescription triptans in Germany amount to five times the UK sales. One participant suggested high-end reclassifications in the UK occurred:

“…to test the water, to see if by some magic we got it right, ‘cos there’s a lot of chance in these things, like Voltaren Emulgel was a great surprise at how successful it was; now why would that of all products be successful? It’s a nice product but the brand name was very old … but sometimes something just hits the public.” Industry voice
Panel 11-1 Product influences on company decisions to pursue reclassification, and committee likelihood of approval*

**Is the medicine likely to be approved? (and at what effort/cost?)**
- Does it have manageable safety concerns, e.g. side effects, interactions, contraindications?
- Does it have no or low potential for misuse/abuse?
- Is the benefit-risk equation favourable?
- Is the medicine used in current practice/best practice?
- Is self-diagnosis straight-forward, or relatively straight-forward with help of a pharmacist (in some markets)?
- Is delayed diagnosis unlikely, unimportant or no worse than currently?
- Is the condition already treated with non-prescription medicines? (facilitates reclassification)
- Does it treat minor, self-limiting conditions? If not, the reclassification may be harder, less certain, and cost more
- Is data for reclassification current and relevant? An old product may need considerable work (and cost) to reclassify in some markets

**Is the post-reclassification return likely to sufficiently reward a company?**
- What is the potential market size (e.g. niche product versus mass market)?
- Is brand name leverage possible?
- Will the consumer see an advantage over what is already in the market (e.g. does the medicine work *noticeably* faster, better, have *noticeably* fewer side effects)? Is there an unmet need?
- Is generic competition likely – now or soon?
- Is the consumer price-point workable?
- Is the product easy to use?
- Is backlash by consumers likely, e.g. oral contraception?
- Are doctors likely to be vocal against it, e.g. low dose simvastatin?
- Will pharmacy support it? (already working in the space, happy with efficacy and safety, see a need)
- What promotion will be needed to establish the product?
- Is supply reasonably straight-forward (e.g. algorithms are unnecessary / tools are simple)?
- Are there likely to be extensive exclusions of potential purchasers?

*Product factors provided are general, other product factors may arise in specific markets (see country chapters). These factors are based on interviews and my own views.

Companies may reclassify just before patent expiry to maximise sales ahead when prescription sales will decline. This effect appears to vary across markets, e.g. being strong in the US where three years of market exclusivity is attractive.

“…you’ve really drawn all blood out of it and you hand it over to the OTC mob and say ok it’s your turn. That may be a bit harsh but I think there’s probably some element of truth in that.”

*Industry participant*

However, company, market and product factors need considering together (Figure 11-1), as other factors may overtake patent expiry. Such factors include a company prescription focus, a large
market, or difficulty in manufacture (e.g. for nicotine products) hindering generic entry, and therefore “the story will be different in every case”.

“If you’ve got a good strong brand and you think you can extend that brand equity into the OTC then you are more likely to be willing to invest in the cost of [reclassification].” Industry participant

Reclassification costs vary according to the market and the medicine.

“If it’s a heavily genericised molecule, and … the judgement is that it’s going to be too expensive, you’re not going to recoup your costs, then it won’t happen.” Industry participant

Product complexity (e.g. confusing dosing, uncertainty about usage, extensive questionnaires) can impair sales. Pharmacists and other staff may not recommend it or advise against use of a complex product. A committee may require controls that potentially prevent reasonable supplies, or seem excessive to pharmacists, pharmacy staff and consumers.

An international participant noted that in developed countries the prescriber and consumer typically do not consider a prescribed medicine’s price which a third-party is largely paying. However, non-prescription supply requires consumers to have product awareness, and willingness to pay. A small therapeutic advantage in a clinical trial might influence a prescriber’s behaviour, but remain unnoticed by the consumer who, for example, rejects the relatively expensive proton pump inhibitor behind the counter, for the faster-acting, lower-cost, self-selection antacid.

Other commentators and researchers support my findings on product factors, particularly return on investment,[217] patent expiry,[220, 568, 643-646] and saleability[217] (including brand name strength,[26, 221, 643] and consumer benefit over other products).[217, 221] Multiple issues including safety and usage, and lack of patent were considered to hinder sponsor interest in reclassifying naloxone, a niche product, in the US.[647] Fruchter and Mantrala reported that optimising timing of partial reclassifications51 in the US depended on various product factors.[220] Four to five-fold higher margins from prescription versus OTC supply and three year market exclusivity often led to companies reclassifying in the US just before patent expiry.

11.4. Market factors

Market factors strongly influence reclassification attempts and the likelihood of approval, as discussed at the micro- and meso-levels. Market factors arise most at a local (country) level, with regional and global influences.

Examples of regional effects include European Union effects and Australasian harmonisation. Examples of global influences include the ripple effect seen with cold remedies in children and the confidence that countries sometimes take from reclassifications elsewhere.

51 Only certain indications or lower strengths become non-prescription, thus a dual prescription and OTC licence exists
In this section I will numerically compare countries in reclassification activity, then compare important barriers and enablers within countries arising in the micro-level chapters and discuss how this experience fits the current literature on reclassification.

11.4.1. Comparative data across core countries

Previous research has compared availability of individual medicines.[31, 49, 50] However, comparing countries’ progressiveness in reclassification is multi-dimensional, and thus I use three tools to provide an overall picture.

Comparisons of a decade of innovative reclassifications (Figure 11-2, Figure 11-3) show the UK, NZ and Japan to be similarly active recently, with the US and Australia less active. The first-in-world comparison (Table 11-1) reveals that, of the five core countries, the UK and NZ were the primary innovators in prescription to non-prescription reclassification 2003-2012. Comparing availabilities and timings, Table 11-3 shows that the UK, NZ and Australia have more of these medicines available without prescription than any other country. Overall NZ and the UK reclassified medicines before other countries, although naproxen’s late UK reclassification differs notably, and the US was occasionally early. While a ripple effect is sometimes seen (e.g. H2-antagonist timing), significant differences are common between countries through delayed or no reclassification.

Figure 11-2 Total number of innovative reclassifications across five core countries 2003-2012

Overall, the UK and NZ are the most progressive countries, with Australia not far behind, albeit more conservative currently. Singapore and Japan show marked current activity but are moderate in their progressiveness and seem to avoid tackling the more complex medicines. The US, despite being the most attractive country to sponsors, has the highest burden of prescription requirements for medicines commonly available without prescription elsewhere.
Table 11-1 A decade of first-in-world innovative reclassifications in core countries (2003-2012)

<table>
<thead>
<tr>
<th>UK</th>
<th>NZ</th>
<th>Australia</th>
<th>Japan</th>
<th>US</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simvastatin 2004</td>
<td>Oseltamivir 2005</td>
<td>Simvastatin 2004</td>
<td>Orlistat 2005</td>
<td>Nil</td>
</tr>
<tr>
<td>Sumatriptan 2006</td>
<td>Famciclovir 2009</td>
<td>Sumatriptan 2006</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>Azithromycin 2008</td>
<td>Calcipotriol 2010</td>
<td>Azithromycin 2008</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tamsulosin 2009</td>
<td>Trimethoprim 2012</td>
<td>Tamsulosin 2009</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Japan is in a progressive phase but from a low base. While Japan has reclassified some medicines that the US has not (e.g. nasal corticosteroids and topical aciclovir), the reverse is also seen (e.g. proton pump inhibitors, EHC, and orlistat). For comparative purposes, two non-core countries have been included in Table 11-3 comparing timing of selected reclassifications, Singapore and the Netherlands, given accessibility of this information. This table shows the relative progressiveness of Singapore, but without reclassifying medicines that are particularly complex or contentious (such as the EHC and chronic treatments). The Netherlands has been particularly inactive recently. Without centralised reclassifications of pantoprazole and orlistat, the Netherlands would be considerably behind the other countries studied.
Table 11-2 Innovative reclassifications by date 2003-2012 in five core countries

<table>
<thead>
<tr>
<th>Year</th>
<th>NZ</th>
<th>Australia</th>
<th>UK</th>
<th>US</th>
<th>Japan</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>EHC</td>
<td>Fluconazole</td>
<td>Omeprazole</td>
<td>Omeprazole</td>
<td>Loratadine *</td>
</tr>
<tr>
<td></td>
<td>Fluconazole</td>
<td>Orlistat</td>
<td>Simvastatin</td>
<td>Hyoscine patch</td>
<td>Minoxidil (women)*</td>
</tr>
<tr>
<td>2005</td>
<td>Aclometasone</td>
<td>Pantoprazole</td>
<td>Chloramphenicol</td>
<td>Oral azelastine</td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td>Sumatriptan</td>
<td>Oseltamivir</td>
<td>Sumatriptan</td>
<td>Amorolfine nail</td>
<td>EHC</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Triamcinolone mouth</td>
</tr>
<tr>
<td>2007</td>
<td>Omeprazole</td>
<td></td>
<td>Orlistat</td>
<td></td>
<td>Aciclovir dermal</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Flavoxate</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Isoconazole vaginal</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Tranexamic acid</td>
</tr>
<tr>
<td>2008</td>
<td>Omeprazole</td>
<td>Naproxen Azithromycin</td>
<td>Nicotine patch</td>
<td>Minoxidil (stronger)</td>
<td></td>
</tr>
<tr>
<td>2009</td>
<td>Famciclovir</td>
<td>Zolmitriptan Chloramphenicol</td>
<td>Orlistat</td>
<td>Tamsulosin</td>
<td>Loxoprofen</td>
</tr>
<tr>
<td>2010</td>
<td>Calcipotriol</td>
<td>Chloramphenicol</td>
<td>Domperidone*</td>
<td>Tranexamic acid</td>
<td>Beclometasone nasal</td>
</tr>
<tr>
<td>2011</td>
<td>Cholera and ETEC oral vaccination</td>
<td>Famciclovir</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2012</td>
<td>Influenza vaccination Trimethoprim</td>
<td></td>
<td></td>
<td></td>
<td>EPA for hypertriglyceridaemia</td>
</tr>
</tbody>
</table>

Source: As for previous chapter listings

* Innovative extended indication rather than new reclassification

EHC = emergency hormonal contraception
ETEC = enterotoxigenic *Escherichia coli*
EPA = Eicosapentaenoic acid

Surprisingly, my findings have similarities with Bowden’s 1993 review.[30] He considered NZ was “leading” in type and quantities of reclassifications, noted the UK’s efforts (but did not position the country exactly) and found the US lagging behind, with Australia slowing and possibly reversing. He also reported deficiencies in information on when medicines have reclassified in different markets.

The USGAO found Australia and the UK had considerably more reclassifications from 1995 to 2008 than the US (19352, 50 and 31, respectively). However, these included all down-schedulings, e.g. pharmacy-only to general sales, and me-too, limiting comparison.

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52 67 medicines were up-scheduled during this period also
### Table 11-3 Comparison of timing of selected reclassifications across countries up to and including 2012

<table>
<thead>
<tr>
<th>Medicine or class of medicines</th>
<th>UK</th>
<th>NZ</th>
<th>Australia</th>
<th>Singapore</th>
<th>Japan</th>
<th>Netherlands</th>
<th>US</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhaled SABA</td>
<td></td>
<td></td>
<td>1976/1984*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrocortisone 1%</td>
<td>1987</td>
<td>1990</td>
<td>1997 or later</td>
<td>?</td>
<td></td>
<td>1991</td>
<td></td>
</tr>
<tr>
<td>Mebeverine</td>
<td>1997&lt;1999</td>
<td>≤2000?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermal moderate potency corticosteroid</td>
<td>2001</td>
<td>2005</td>
<td>2000</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EHC</td>
<td>2001</td>
<td>2001</td>
<td>2003</td>
<td></td>
<td>2005</td>
<td>2006</td>
<td></td>
</tr>
<tr>
<td>Statin</td>
<td>2004</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chloramphenicol eye</td>
<td>2005</td>
<td>2009</td>
<td>2010</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triptan</td>
<td>2006</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oseltamivir</td>
<td>2006</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azithromycin</td>
<td>2008</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tamsulosin</td>
<td>2009</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tranexamic acid (oral)</td>
<td>2010&lt;2010</td>
<td>2009</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcipotriol</td>
<td>2010</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral cholera and travellers' diarrhoea vaccine</td>
<td>2010</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Influenza vaccination</td>
<td>2012</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trimethoprim</td>
<td>2012</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

See following page for explanatory notes and sources of information for this table.
Early Australian reclassifications are presented as a date range for the various States and Territories

† Orciprenaline, a non-selective beta agonist also known as metaproterenol, was reclassified in the US in 1982, but reversed in 1983[648]

‡ Hydrocortisone 1% with oxytetracycline (but not alone) is a category II product in Japan, a historical situation

** Tranexamic acid was reclassified in Australia in 2000 and reverted to prescription in 2007 because of TTH and no sponsor interest

†† Tranexamic acid in Japan is a lower dose and different indication to the UK (liver spots not menorrhagia)

Note: The US and UK have influenza vaccinations provided by pharmacies through different mechanisms.

SABA = Short-acting beta agonist inhaler
EHC = Emergency Hormonal Contraceptive

Information sourced from Medicines Classification Committee meeting minutes in NZ, National Drugs and Poisons Schedule Committee and Advisory Committee on Medicines Scheduling records in Australia, the Proprietary Association of Great Britain ‘POM to P’ list (accessed 14 April 2013; UK), the Consumer Healthcare Products Association "Ingredients & Dosages Transferred From Rx-to-OTC Status (or New OTC Approvals) by the Food and Drug Administration Since 1975" (accessed 16 February 2013; US), the AESGP list of OTC medicines (accessed various dates until 16 February 2013), the Pharmaceutical and Medical Devices Agency website (Japan; accessed November 2012), The Health Sciences Authority website (Singapore; accessed 11 Dec 2012) Bowden M. Schedule 3 medicines and the prescription to non-prescription switch: a survey of community pharmacists. Sydney: University of Sydney; 1993. Personal communication Jeltje Luinenburg, Koninklijke Nederlandse Maatschappij ter bevordering der Pharmacie (KNMP), 1 Mar 2013. Supplementary sources included local country persons, e.g. Australian Self Medication Industry; Professor Nahoko Kurosawa, Japan. Best efforts have been made to provide accurate dates, but these may reflect committee meeting dates, gazettal dates, or market launch dates, and rely on sources.

Medicines were selected on: Main reclassifications 2000-2012 in the core countries, and five selected old reclassifications to show variation and similarities – SABAs, mast cell stabilisers, nicotine replacement, H2-antagonists and hydrocortisone 1%.

Key:

- Prescription or not marketed
- Reclassified ≥ 10 years after first country in table reclassified
- Reclassified < 10 years after first country in table

I found the US was less progressive in reclassification than other core countries in recent activity. Even in the 1990s the US typically followed two or more core countries in reclassification, with vaginal antifungals the only exception of the medicines considered. Across selected medicines (Table 11-3) Japan has reclassified four medicines that the US has not, and the US has reclassified five medicines that Japan has not. Like the USGAO[49, 50] and Gilbert, et al.[31] I found variability. However, by using the first-in-world measure, and considering innovative reclassifications over time, I found the UK was more progressive than Australia and similar to NZ; this contrasts to Gilbert, et al. and USGAO, but is consistent with commentators' views.[24, 100]

11.4.2. Country factors

All countries vary considerably in their mix of barriers and enablers, including the strength and importance of different barriers and enablers (Table 11-4). The UK stands out for having multiple enablers, and Australia stands out for having multiple barriers. The most important enablers arising from interviews include government policy (UK and Japan), regulatory support (UK, NZ, US),
individuals (NZ), scheduling (NZ, Australia, Japan, the UK), and market size (US and the UK). Innovation also seemed to emerge from interviews for NZ and the UK (not shown).

Table 11-4 Comparison of key enablers and barriers across the five core countries*

<table>
<thead>
<tr>
<th></th>
<th>NZ</th>
<th>Australia</th>
<th>UK</th>
<th>US</th>
<th>Japan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medicine schedules</td>
<td>+++</td>
<td>++</td>
<td>+</td>
<td>--</td>
<td>+/-</td>
</tr>
<tr>
<td>Advertising for OTCs</td>
<td>+</td>
<td>--</td>
<td>++</td>
<td>+</td>
<td>+/</td>
</tr>
<tr>
<td>Population size</td>
<td>--</td>
<td>-</td>
<td>++</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Self-medication culture</td>
<td>+/-</td>
<td>+/-</td>
<td>+++</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>Regulator/committee open to ideas</td>
<td>+++</td>
<td>-</td>
<td>++</td>
<td>+/</td>
<td>+/-</td>
</tr>
<tr>
<td>Regulator/committee confidence in pharmacy</td>
<td>++</td>
<td>-</td>
<td>++</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Regulator/committee confidence in consumers</td>
<td>++</td>
<td>-</td>
<td>++</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Individuals</td>
<td>++</td>
<td>+/-</td>
<td>+/-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Politics and government support</td>
<td>0</td>
<td>-</td>
<td>++</td>
<td>-</td>
<td>+/-</td>
</tr>
<tr>
<td>Prescription copayments</td>
<td>--</td>
<td>+</td>
<td>--</td>
<td>+</td>
<td>--</td>
</tr>
<tr>
<td>Pharmacy organisation involvement</td>
<td>++</td>
<td>+/-</td>
<td>+++</td>
<td>0</td>
<td>++</td>
</tr>
<tr>
<td>Medical support</td>
<td>0</td>
<td>--</td>
<td>+/-</td>
<td>+/-</td>
<td>--</td>
</tr>
<tr>
<td>Proactivity in individual pharmacies</td>
<td>-</td>
<td>-</td>
<td>--</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>Pharmaceutical industry environment</td>
<td>-</td>
<td>+</td>
<td>++</td>
<td>+++/</td>
<td>+/-</td>
</tr>
<tr>
<td>Industry confidence in committee</td>
<td>++</td>
<td>--</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Working with regulator</td>
<td>++</td>
<td>-</td>
<td>+++</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Working with stakeholders</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Cost and effort of doing applications</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>---</td>
<td></td>
</tr>
<tr>
<td>Market exclusivity and transparency</td>
<td>---</td>
<td>--</td>
<td>+</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Pharmacy house-brands</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regional influence</td>
<td>+/-</td>
<td>+/-/0</td>
<td>--</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Patch protection</td>
<td>-</td>
<td>--</td>
<td>-</td>
<td>---</td>
<td></td>
</tr>
</tbody>
</table>

*Barriers are represented by –, enablers by +, and mixed factors by +/-; quantity represents strength of effect based on interviews and documents. Sometimes a factor was discussed but appeared to have little or no effect (represented by 0). Where a cell is blank, the factor did not arise, suggesting it is not an important barrier or enabler. This chart is subjective, according to how participants have communicated the factors, and how I have interpreted the data. The table is not exhaustive.

Barriers often overshadowed or undercut enablers. The US has the most attractive non-prescription market because of its size, culture and potential market exclusivity, yet is hobbled by an increasingly costly, time-consuming process and an all or nothing scheduling system. Scheduling, which should (and apparently does) enable Australian reclassification, seems over-powered by committee constitution, individuals, events, politics, and rigidity, resulting in greater risk-averseness than apparent in many other markets. Some of these effects were echoed in Europe. In addition, advertising limitations and house-brands in Australia reduce potential post-recategorization markets.
The Japanese government policy, pharmacy organisation and regulator proactivity, pharmacist-only scheduling and market exclusivity have helped Japan gain lost ground compared with other countries. However, powerful doctor pressure, culture, pharmacy effects and cost differentials to consumers make some reclassifications difficult and limit returns for companies post-reclassification. Cost differentials to consumers were important barriers in most countries, especially in the Netherlands, where doctors incur no patient payment and prescription subsidy stopped upon reclassification.

Significant enablers and barriers will be discussed under the arising Principles, below.

11.5. General Principles of Reclassification in Developed Countries

General principles emerged from the findings at the micro-, meso- and macro-levels (Panel 11-2). These principles may inform future reclassification interest at a country, regional or global level. Arising from developed countries, their applicability to developing countries would require future research.

Panel 11-2 General Principles of Reclassification in Developed Countries

1. Alignment of the right enablers and absence of significant barriers facilitates reclassification
2. Every country has its own unique mix of enablers and barriers, some of which are dynamic
3. Some factors can both enable and hinder reclassification at the same time.
4. Some countries prefer to follow, others are comfortable as leaders. This preference can vary over time.
5. A myriad of factors at a global, regional and local level affect sponsors pursuit of reclassification
6. Clear, consistently active government policy and/or regulator proactivity enables reclassification
7. Reclassification requires judgement, and therefore different committees will make different decisions on some medicines
8. A pharmacy-only or pharmacist-only schedule enables reclassification
9. Multiple pharmacy factors affect reclassification
10. Individuals can influence reclassification
11. More evidence is needed to inform reclassification (but excessive evidence requirements pre-reclassification inhibit reclassifications)
12. Culture affects reclassification
13. Medical opposition to reclassification hinders reclassification
14. The prime influence of the health system funding on reclassification is the consumer cost differential between the prescribed medicine and the non-prescription medicine
15. The easy, lucrative reclassifications have been done
16. Immediate generic entry discourages reclassification
17. Banning advertising impairs reclassifications
1. **Alignment of the right enablers and absence of significant barriers facilitates reclassification**

Many factors align in the UK and NZ to allow reclassification to progress (Table 11-4). However, reclassification progress is not directly proportional to the number of enablers, as seen by NZ being similarly progressive to the UK despite having more barriers, and the US having fewer reclassifications than Australia despite apparently having more enablers. Reclassification progressiveness depends on the number, mix and strength of factors.

The finding of the multidimensional nature of reclassification activity suggests limited value to looking, as Gilbert, *et al.*[31] and the USGAO did,[49, 50] at the numbers of reclassifications and comparing them with countries’ schedules.

2. **Every country has its own unique mix of enablers and barriers, some of which are dynamic**

Reclassification variability arises from a palette of factors. All countries studied for this research showed a different mix of factors, and I suspect no two countries share the exact same configuration. The meso-level of analysis (Chapter 6) illustrates this concept, showing differences between two similar countries attempting to harmonise, and variation over time. Table 11-4 reflects perceived factors around the time of interviews. Significant differences even occurred between the two more progressive countries studied: the UK and NZ (Table 11-4). Comparing countries of similar population size, or heritage, still shows significant differences.

3. **Some factors can both enable and hinder reclassification at the same time.**

Some factors emerged as both aiding and limiting reclassification in the same market. The pharmacy-only category helped reclassifications become approved, but could hinder sales which could then limit company interest in future reclassifications. Protocols and questionnaires for supply were suggested to encourage reclassifications, but also might discourage supply. Low-cost consumer healthcare discouraged consumers from purchasing non-prescription medicines, reducing potential market size, but also provided a safety net for reclassifications in some countries. If medicines available without prescription are also reimbursed on prescription, this may discourage self-medication (reducing market potential), but if reimbursement is lost on reclassification prescribing may shift to alternative funded options and/or prevent companies pursuing reclassifications.

4. **Some countries prefer to follow, others are comfortable as leaders. This preference can vary over time.**

International diffusion of reclassification information occurred (as noted by others).[26] The UK and NZ were the most progressive of all countries studied. Participants described the UK as the “leader”, several considered NZ to be “leading”, and some mentioned Australia’s earlier leadership. One participant considered the US a pioneer “on a good day”, and called Australia a leader because of non-prescription inhaled SABAs (reclassified in the 1970s and 1980s).[649]
The term leading means being advanced or ahead, and could imply that more is better. I have used ‘progressive’ to avoid that suggestion. I will briefly mirror the use of leading or leader by some participants and commentators[24, 26, 30, 34, 204, 333] to denote that some countries seem comfortable with ground-breaking decisions (and leading), while others are not. Being a leader can imply having followers,[650] and on this basis the UK stands out. While the UK, US, Canada, Australia, Germany and NZ reportedly influenced decisions in other countries, the UK was the most influential. UK decisions encouraged committees, and provided ideas for reclassifications and processes. Reclassifications happened elsewhere because they had occurred in the UK.

NZ’s influence seemed slight outside Australia and has diminished recently with Australia. NZ’s progressiveness has been less obvious than high-profile UK reclassifications,[29, 539, 651-655] probably because it is small and remote. The small market limits pharmacovigilance findings, and might raise doubt about the thoroughness of the reclassification consideration. Additionally, NZ controls such as pharmacist-only and mandating training are uncommon elsewhere. As at February 2013, other countries have not followed NZ in reclassifying oseltamivir, calcipotriol, or trimethoprim, and only Australia has followed with oral famciclovir.

Although limited by barriers, the US seemed comfortable with ground-breaking decisions, perhaps emboldened by extensive pre-reclassification research. This appearance is confirmed by the 2013 reclassification of transdermal oxybutynin,[656] and the home HIV test[53] approval.[657] The US may return to their 1990s leadership[34] if they overcome the general sales barrier (e.g. with technology and/or BTC).

Singapore and Japan were clearly followers, while Australia in recent years appeared not to want to be particularly progressive or to follow other countries that were (e.g. sumatriptan Panel 5-2). Leaders can also be followers.[650] NZ was a follower, particularly of the UK.

Some UK reclassifications have not been emulated[54], including simvastatin, azithromycin and tamsulosin. Follower countries may disagree with the UK decision, or environments may differ. Local barriers or lack of success in the UK may prevent applicant interest elsewhere.

Further UK slowdown of innovative reclassifications (particularly with centralised European reclassification) could affect its leadership, as recently reported.[100] NZ’s influence may increase through further innovative reclassifications, particularly if researched, and if pharmacist-supply becomes more common internationally. Committee member changes could again affect decisions in NZ or Australia, but would probably minimally affect the UK without government policy changes. The future joint Australia-NZ regulatory agency with a single Australasian classification committee, will probably affect progress and international influence of both countries.

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53 The HIV test is not a medicine so is not included in progressiveness measures
54 To the best of my knowledge, and based on AESGP OTC availability data
Some commentators believe the UK leads in reclassification.[24, 26, 34, 333] Other research places NZ and/or Australia ahead.[31, 50] The WSMI highlighted Australia, Germany, the UK, and US as leaders in 2009.[26] Although no rationale was provided. My finding that the UK leads reclassification with NZ close behind reflects three sets of data, and reported influence on other countries.

5. A myriad of factors at a global, regional and local level affect sponsors pursuit of reclassification

An important inhibitor for reclassification is whether or not a sponsor wants to pursue it. Companies consider global, regional and local factors, and effects on their prescription business. Most considerations are financial. For example, expensive US statin reclassifications were attempted by two sponsors[112] because the potential rewards of reclassification and three years’ market exclusivity were highly attractive. An application in Australia was never submitted, GSK lost interest in NZ, and low UK sales of non-prescription simvastatin led to product withdrawal. Company considerations are discussed above (11.2).

6. Clear, consistently active government policy and/or regulator proactivity enables reclassification

Government policy in the UK and Japan prompted other enablers and stimulated many reclassifications. Given the well-known[24, 26, 28, 30, 34, 658] long-standing and significant role of policy in promoting UK reclassification, it may surprise observers that another country (NZ) can become as active without it, especially given NZ’s small market. However, with or without positive government policy, a proactive regulator enabled reclassification in all the more active countries (the UK, NZ, Japan and Singapore), suggesting it is a prerequisite for progressiveness. In the US particularly and Europe to a lesser extent, regulator work with industry before and during the application was considered enabling amid barriers to reclassification. Conversely, regulator conservatism and political concerns apparently limited reclassification in Australia. This variation between countries in regulatory support and government policy has received little attention in the mainstream literature, although in 1995 Francesco opined that policy and regulator proactivity helped the UK reclassification move ahead of the US, and a paternalistic government approach in Europe restricted reclassification.[34] He suggested that regulator proactivity can be ascertained by frequency of reclassifications, and my research supports this suggestion somewhat, looking across more countries. However, my research suggests that regulatory proactivity may sometimes be outweighed by other barriers, e.g. lack of BTC schedule in the US.

Cranz reported widespread European political support for self-medication in 1998,[135] and the EU Council (1999) reportedly supported reclassifying medicines outside traditional areas, e.g. for diabetes and asthma in a collaborative care model.[26, 134] However, I found continental Europe conservative with no mention of current political support, suggesting the EU Council’s support was possibly short-lived, weak or not enacted.
Abraham and Davis considered that excessive pharmaceutical industry influence of the UK regulation of new (prescription) drugs reduced approval times and increased safety-related withdrawals compared with the US.[343] While I found reclassification differences between the UK and US, no participants suggested that the UK was unsafely reclassifying medicines, or that the pharmaceutical industry excessively influenced reclassification\(^\text{55}\). Literature concerns following UK reclassification are limited to increased chloramphenicol use,[659] and one case report suggesting poor practice (by a GP and pharmacist with chloramphenicol).[660] No UK reclassification from the last 15 years or more has been reversed.

Achanta, et al. reported some participants perceived an “aggressive thrust towards deregulation by the industry at the risk of public health”.[341][p6] He did not state the perspective this came from, how frequently it was raised, or in which country or countries this view was aired. My only related findings occurred in Australia where two participants mentioned a push by industry and one participant reported a reclassification application that omitted an important safety issue.

7. **Reclassification requires judgement, and therefore different committees will make different decisions on some medicines**

All selected countries used committees to consider reclassifications. Best illustrated in the meso-level chapter, committees may differ. Committee criticism arose most in Australia, possibly because many participants had been on the committee, providing insight, or because of the NZ-Australia comparison. However, because the criticism came from a range of participants and meeting records supported some concerns, I believe it arose because the committee performance was a strong inhibitor of Australian reclassification. Similar concerns arose from Europe, particularly concerns about the representative members being influenced from above. Indeed, a CHMP member reportedly stated at a conference that some CHMP members encountered a rather hostile environment in their own country towards reclassification and self-care.[96]

The judgement aspect is increased by uncertainty, and many participants discussed a need for more evidence. Sometimes relying on reclassifications in forerunner countries helped the judgement. However, even in the US, where considerably more pre-reclassification evidence is expected in many reclassifications than elsewhere, judgement is needed:

> “Rational people, and rational authorities looking at exactly the same database, whether it’s OTC or prescription can and do come up with different regulatory decisions…. it’s not been a question of who was right and who was wrong, or did somebody miss something…. the most wonderful randomised controlled kind of trial can tell you what the benefits are in a certain population, and what the risks are. But they can’t tell you what the risk tolerance in your population is for that level of risk and that level of benefit. That’s not a scientific decision, that’s a judgement… and what you’re judging is the risk tolerance within your community. And one of the ways we try to do it is with the advisory committees, having consumer

\[^{55}\text{However, no questions were asked specifically on this topic}\]
representatives, and having patient representatives... They bring the technical knowledge, they bring to the discussion the perspective of, I as a patient, who actually at the end of the day is going to be taking the risk... You can have different levels of tolerance within different communities. And so why should that be upsetting to people if one regulatory authority says ... it’s not only the tolerance of the toxicological risk. But what we find more is the tolerance for the lack of knowledge...

"US regulator voice

The background work appears to help US and UK reclassifications. Many ‘first-in-class’ US reclassifications just had one committee meeting.[112] In contrast, multiple considerations were common in NZ and Australia, even when the medicine was reclassified elsewhere. However, extensive pre-work in the US is expensive and time-consuming, preventing applications.

Biases in committee members may arise from the committee constitution, regulator perspective, individuals, reclassification experiences, and political influence. These biases could include weighing losses heavier than gains (as Temin noted in reclassification),[22] status quo bias,[507] experience effects,[511, 512] and organisational influences[514] (see 6.5.2.2). Government policy may influence group norms and hence judgements. The UK’s CHM approved complex reclassifications that many other countries would likely reject. Approval possibly occurred because of political (and often medical) support, the regulatory agency’s background work with the companies to resolve questions, and because PGDs provided confidence in pharmacy.

I found reclassification experiences (historical and recent, and positive and negative) affected further reclassification, examples included analgesic nephropathy in Australia, and the positive experience of oseltamivir in NZ and orlistat in Singapore. Friedman partly attributed FDA conservatism in 1992 to controversy from reclassifying an asthma reliever in 1982 (reversed in 1983).[320]

Committee judgements affect the progressiveness of a country. Approvals may attract further reclassification applications (e.g. NZ), and rejections may discourage reclassification applications (e.g. US), potentially compounding this effect.

Committee constitutions appeared to affect decisions, with representative models in Europe and Australia restricting reclassification, and reportedly needing people with evidence-based skills and coal-face experience. Patch protection arose with the Japanese and NZ committees. ‘Groupthink’ seemed to occur in Australia. Little criticism of the UK’s CHM and NZ’s MCC occurred, possibly because both were progressive. US committee performance received little attention, perhaps because it had not met recently.

The committee constitution should include primary-care practitioners (pharmacists and GPs), a big picture health view (e.g. public health), consumer representation, and an academic with knowledge of non-prescription medicine usage. A regulatory staff member is useful, but should

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56 The first of a class of medicines to be reclassified
not have excessive power. Limiting members’ terms would reduce groupthink and encourage new ideas. Appointees should not represent a particular organisation, but be on the committee to make the right decision for consumers, and use evidence-based decision making skills. Adding relevant experts according to the consideration has merit, but many experts have little experience of reclassification. The committee should be unaffected by politics or media.

Committee inconsistency[21, 51] and non-evidence-based influences[19, 21, 232] on reclassification have been reported in the US and elsewhere. Lyles reported pharmaceutical policy generally was often political rather than evidence-based.[661] Nguyen, et al.[51] and Brass and Hiatt[336] suggested FDA advisory committee improvements, some of which were similar to those I suggested for Australasia. Bowden also recommended evidence-based decision making.[30] A European Medicines Agency representative reportedly noted pressure from media and political lobby groups caused evaluators to become more risk averse.[96] To encourage rational decision-making in reclassification and better inform judgements, Brass, et al. developed a framework for benefit-risk assessment in 2011,[662] adopted by the MHRA.[61]

Using interviews and meeting records for Australasian reclassification identified important differences in committees. Absence of publicly available transcripts or detailed meeting records for reclassifications in most countries makes committee comparison difficult. Other research comparing health committee considerations between countries appears scant, with work comparing UK and US new drug considerations perhaps the closest.[343] Further research could continue to explore committee differences and the ideal committee constitution, and use observers at meetings in different countries considering the same reclassification.

8. A pharmacy-only or pharmacist-only schedule enables reclassification

Scheduling appeared to affect reclassification strongly. An intermediate category (or categories) facilitates reclassification particularly in NZ, Japan, the UK, and Australia (but see below). Absence of such a category impedes some reclassifications, e.g. in the US and for centralised European reclassification57.

“…you can come out at the same place on the science, but when you look at the tools for managing risk that your parliaments have given you, they’re different. And if you’re looking at a certain benefit-risk profile and you don’t have a certain tool to manage that risk, you can’t get to the same place as somebody else who in their country they have tools to manage risk…. Pharmacist-only, versus pharmacy-only, I mean that’s a risk management tool at the end of the day, and we don’t have it, and other countries do.” US regulatory participant

However, Canada’s relative inactivity and Australia’s recent low activity despite a pharmacist-only and pharmacy-only category, demonstrated the multi-factorial nature of reclassification.

57 Portugal removed their pharmacy-only category in 2005
Many commentators have suggested the US would benefit from a BTC schedule,[33, 566, 663, 664] with statin reclassification rejections partly attributed to absence of BTC.[51, 153] Others have called for a European-wide pharmacy category.[35] Detractors of BTC cite concerns including pharmacy ability,[160] lack of evidence,[50, 664] and concern that further down-scheduling would not occur.[50]

Other research has considered BTC availability.[31, 32, 49, 50] Achanta, et al. found US interview participants (primarily academics) believed a BTC category of medicines would help US reclassification.[341] Gilbert, et al.[31] and the USGAO[50] found fewer medicines restricted to prescription where pharmacy-only and/or pharmacist-only schedules were used than in the US without such categories. However, the USGAO considered BTC benefits were unclear because restricting medicines to pharmacies reduced consumer access, while Gilbert, et al. noted potential benefits to consumers, the health system and the pharmaceutical industry of widened access through the pharmacy schedule. The selected countries appeared to affect the outcomes and both studies included only one country with a single general sales category. See the US chapter for further BTC discussion (8.6.3).

Several elements strengthen my finding that the intermediate schedule enables reclassification. Observers from two different markets affected by the absence of intermediate scheduling (the US and Europe58) noted this lack impeded reclassification. My research demonstrates few US or centralised European innovative reclassifications during 2003-2012, supporting the observers’ comments. In markets with an intermediate category, observers typically stated that scheduling greatly enabled reclassification. Furthermore, the effect of scheduling in many interviews was volunteered in response to an open question that made no mention of scheduling, showing it was often top-of mind without any prompting. The views on scheduling came from a range of participants – industry, regulatory, pharmacy, academic and medical participants. Finally, discussion points in Australasian meeting records indicated that the pharmacist-only category was largely enabling (albeit muddied in Australia recently by increasing committee conservatism).

Differing requirements of and practices with intermediate categories between countries adds confusion. Pharmacy-only in NZ allows self-selection, but not in the UK, and in Singapore such medicines are reportedly locked away and supplied only by pharmacists.

The pharmacist-only or pharmacy-only category’s enabling effect seemed greater where participants (and minutes) expressed trust in pharmacy (Table 11-5). Both education and community pharmacy differ considerably around the world,[253] but in the meso-level, committee perceptions were likely behind the apparent differing trust in pharmacy between NZ and Australia.

An unexpected effect was the unusual drugstore category which seemed to reduce the role of the pharmacist and pharmacy staff in supplying non-prescription medicines in both countries with it –

58 As previously mentioned, although most of Europe has a pharmacy-only category, because one or more member states do not have this, it affects centralised reclassification.
the Netherlands and Japan. This finding may be confounded by the dispensing focus, pharmacy and consumer culture, and low-cost doctor visits in each country. In Japan, drugstores (and some pharmacies) often did not stock category one medicines, limiting sales opportunities for medicines in that class and potentially reducing viability for reclassifications to category one (pharmacist-only). Evidence on risks and benefits of the drugstore category at the consumer level is required.

Aronson suggested introducing a separate category “Pharmacist Consultation and Supply, with built-in safeguards” for the UK to control and facilitate wider access to medicines that do not suit pharmacy-only availability.[79] Oseltamivir research showed unique availability was workable, the tools for supply were useful and concerns about the reclassification did not eventuate.[80, 81] I predict that in NZ at least, reclassification under special conditions will enable further complex reclassifications that would struggle to reclassify otherwise. Interest in such availability may be limited by legislation, political will, and alternatives (such as minor ailment schemes, pharmacist-prescribing and PGDs). However, supply barriers, as for oseltamivir,[279] could limit consumer access gains and discourage industry.

Effectively, consumer access to medicines is limited in the US, and in Europe (through centralised reclassification) because of the scheduling system. Further research would inform this consideration, although, given pharmacists’ training, a pharmacist-only availability under strict criteria should logically provide a safer reclassification environment than general sales.

9. **Multiple pharmacy factors affect reclassification**

Many pharmacy factors apparently affect reclassification (Table 11-5). The progressive countries all exhibited pharmacy proactivity, suggesting pharmacy enthusiasm for progress helps as suggested previously.[26, 665] Alternatively, progress in reclassification may motivate pharmacy. The pharmacy sector was most influential in NZ where a pharmacy retailer drove reclassifications.

Variable pharmacy behaviour may limit opportunities afforded by pharmacy categories, but resulting effects on reclassification seem greater in some countries than others, suggesting it is overlooked in some countries or over-emphasised in others. While addressing pharmacy variability should improve reclassification opportunities, Australia’s quality programme in pharmacy apparently has not, probably because of committee perceptions. Lamiraud, et al. suggested that consumers take more responsibility and require more information to choose a non-prescription medicine than if consulting the doctor.[188] Further research needs to explore this effect. Additionally, research is needed to ascertain consumer outcomes, e.g. pharmacies could alter their behaviour according to the consumer (as suggested by mystery shopping that found different results for one shopper).[285] Pharmacy assistants’ roles and lack of training arose sometimes, and dovetailed into variable pharmacy behaviour.
Chapter 11

Table 11-5 Variable effects of pharmacy factors on reclassification

<table>
<thead>
<tr>
<th>Pharmacy factor</th>
<th>Enabler</th>
<th>Barrier</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacy education</td>
<td>Strong pharmacy practice education, for new graduates, raised in UK, Australia, NZ, US</td>
<td>Lack of pharmacy practice education until recently, in Japan. Concerns raised in Europe</td>
</tr>
<tr>
<td>Pharmacy interest in reclassification</td>
<td>Seemed higher where dispensing income appeared limited or threatened, e.g. UK, NZ, Singapore</td>
<td>Seemed lower where dispensing provided good income, e.g. Netherlands, Australia, Japan</td>
</tr>
<tr>
<td>House-brands</td>
<td>Galpharm utilised house-brands in their model</td>
<td>Pharmacy house-brands negative in Australia and Canada</td>
</tr>
<tr>
<td>Pharmacy culture</td>
<td>Self-care a traditional pharmacy role, e.g. UK, NZ, Australia</td>
<td>Pharmacy less involved in self-care, e.g. US, Netherlands, Japan</td>
</tr>
<tr>
<td>Pharmacy organisations</td>
<td>Proactive pharmacy organisations, e.g. UK, Japan, Singapore.</td>
<td>Some pharmacy organisations seemed less engaged on reclassification</td>
</tr>
<tr>
<td>Pharmacy practice behaviour variability, and trust</td>
<td>Pharmacy positively viewed in the UK, NZ, and Singapore particularly, and in Australia by some. Helped by PGDs or reclassifications where pharmacists considered to act professionally</td>
<td>Lower trust in pharmacy appeared to reduce reclassification approvals, e.g. Australia, Europe</td>
</tr>
<tr>
<td>Protocols and questionnaires</td>
<td>Tools (e.g. protocols and questionnaires) aid reclassification in many countries, particularly the UK and NZ.</td>
<td>Australian committee concern about enforcing their use. UK concerns about excessive content</td>
</tr>
</tbody>
</table>

UK participants’ concerns about protocols, echoed previous commentary.[7, 281, 666] UK pharmacists seemed mostly positive about protocols (in 1997)[667] and accepted the protocol for tamsulosin,[304], but many omitted part of the simvastatin protocol.[165] NZ and Australian interviews raised no concerns about protocols, mirroring research in NZ[80] and Australia.[486] The UK tools may reflect complex materials, e.g. urine sample check and questionnaire with azithromycin,[116] versus one-page algorithms or questionnaires for NZ reclassifications. Possibly low enthusiasm for these medicines[261, 304] causes commentators to blame protocols. Pharmacists’ work pressure might vary by country or they may perceive the protocol to include unnecessary questions. Queddeng, et al. recommended simplifying the EHC protocol in Australia.[307] Further research into the acceptability, utility and potential improvements of such tools across multiple countries is warranted, particularly given their increasing prevalence.

Lack of privacy in pharmacy and inability to access medical records arose in multiple countries.

Community pharmacy balances the need to be profitable with professional obligations, creating an ethical dilemma,[668] yet commercial conflict for pharmacy arose surprisingly little. Possibly it was not seen as an important barrier or enabler, it was incorporated into ‘pharmacy variability’ or may reflect the participant mix – only four medical voices. Industry worried about pharmacy hindering supplies, perhaps suggesting that at least some pharmacists or assistants were fulfilling
their professional obligation, and/or that consumers would prefer a more anonymous supply without advice or questions.

10. Individuals can influence reclassification

Individuals can help or hinder reclassification. NZ and Australia showed this effect most, but some comments about individuals occurred elsewhere. Individual committee members, politicians, pharmaceutical company employees, experts used by companies, and regulator employees were all mentioned by participants.

Bowden (1993) also observed that individuals’ initiatives have promoted reclassification, but did not elaborate.[30] Nguyen, et al. commented on a committee member’s inconsistency,[51] and Armstrong noted the influence of individuals in the US EHC reclassification.[19] Brass and Hiatt’s proposed improvements to member selection and chair requirements for the US.[336] Kurko, et al. revealed an individual politician’s effect in the Finnish move of NRT to general sales.[232]

11. More evidence is needed to inform reclassification (but excessive evidence requirements pre-reclassification inhibit reclassifications)

Lack of research evidence contributes to uncertainty for committees. Many reclassifications will be easier where informed by evidence, but research adds expense, and committees may argue that their environment differs from that in which the evidence was generated.

A Medline search[59] found no post-marketing surveillance studies for non-prescription simvastatin, tamsulosin, azithromycin or sumatriptan, despite being ground-breaking reclassifications. For simvastatin, low sales disabled the planned studies.[115] Pharmacovigilance through spontaneous reports suffers from low reporting rates, may not differentiate non-prescription supplies, and only provides adverse reaction data, with no indication of potential delayed diagnosis. Doctor reporting of delayed diagnoses resulting from non-prescription use is limited because patients may not report non-prescription use, and there is no official way or encouragement to report these problems. Deaths are probably under-reported.[669] The WSMI considers PMS studies should not be routine, particularly without market exclusivity.[26] The UK has apparently provided quasi-market exclusivity for post-marketing surveillance, but ensuing studies are unpublished as yet. Three years of market exclusivity with post-marketing surveillance studies incentivises Japanese industry to reclassify and conduct research but findings usually remain unpublished. I consider market exclusivity could be a useful incentive elsewhere, but to maximise the benefit, these studies should be well-designed and published.

Lack of evidence extends to the pharmacy sphere – whether a pharmacy-only or pharmacist-only category provides benefit or is a costly inconvenience – and to overall benefits of reclassifications.

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59 As at 28 February 2013
“…we don’t have any hard and fast case studies that we can go to the regulators and say “well look, here’s a long term review of this market and over five years these were the outcomes of this switch.” The consumer got healthier and the government saved $50m.”

Industry participant

Evidence could inform future reclassifications, and improvements to consumer and/or pharmacy materials or conditions for supply. In 2013, Kelly suggested using research from UK reclassifications to inform issues that are holding back European reclassifications.[100]

12. Culture affects reclassification

National, consumer, pharmacy and medical culture often arose in interviews. Participants mentioned the culture of using the doctor versus being self-reliant (contrast Japan with the US), consumer attitudes to medicine-taking (Netherlands versus the US), the importance of the medical profession (Japan versus NZ), and the role and behaviour of pharmacy (the UK versus the US). Consumer rights were prominent in the US. Avoiding conflict in Japan and a ‘can do’ attitude in NZ were considered to affect reclassification. Culture occasionally had international influences, e.g. contraception reclassifications elsewhere affected by US concerns.[670, 671]

“…we talk a lot about prescribing patterns being different [versus other countries] and they are,… but also just the ingesting, the taking of meds, the attitude that patients have, pharmacists have, the society has towards the taking of medications. Towards safety, towards even advocacy for goodness sake. It’s very, very different and it reflects itself, to me, especially in this Rx [prescription] to OTC switch…. the pharmacist doesn’t really tell you anything, or do anything. That’s kind of American, right, let it happen. That’s not the system in Europe.” Academic participant

Culture extended to committees, with some committees apparently more risk tolerant and open to change and uncertainty than others. See the meso-level (6.5.2.2) and judgement (above).

Given the cultural diversity in the selected countries, cultural effects are unsurprising. Hofstede found four key cultural attributes from employee attitude surveys conducted by IBM (1967-1973).[339] His findings differ from mine: e.g. Hofstede found the UK, US, Australia and NZ often scored similarly, but I found they varied in reclassification progress, barriers and enablers. However, Hofstede’s power distance, the distance between high ranking and low ranking people (social inequality), is smaller for NZ than Japan, which is consistent with higher medical profession power in Japan versus NZ. Hofstede rates the US the highest of all countries for individualism, consistent with my findings of strong consumer’s rights. Japan rated considerably lower for individualism and Singapore very low. The EHC availability perhaps reflects this, being reclassified in countries with high individualism, but not in those with mid- or low individualism where tradition and ‘shame’ cultures are stronger. My finding of conflict avoidance, and devolving responsibility to the state for Japan, fits Hofstede’s collectivistic social norms.
Other commentators have mentioned culture, typically regarding the rise of consumerism driving reclassification.[24, 161] Differences in cultural traditions between European countries have been noted to affect attitudes to illnesses and self-medication.[110, 672] A large survey found gastro-oesophageal reflux disease was diagnosed more frequently (self or physician) in the US (27%) versus Europe (19%).[673] The authors suggested differing obesity levels or cultural differences (possibly arising from US advertising) in patient and physician perceptions could be responsible. Additionally usage of OTC and prescription medicines was nearly double per person in the US compared with Europe.

13. Medical opposition to reclassification hinders reclassification

Medical opposition varied by country, with participants (including a doctor) noting funding mechanisms and desire to retain control affected this. Medical support was higher in the UK where capitation funding occurred, and lower where fee for service occurred, particularly Japan and Australia. Furthermore, many committee members considering reclassifications have medical backgrounds. Even in the UK where co-operation with doctors enabled reclassification, antibiotics and medicines for long-term conditions were opposed. These medical concerns need to be explored, and perhaps a new model for such reclassifications with tighter controls, such as proposed by Aronson,[79] and used in NZ for oseltamivir[80, 81] and trimethoprim[159] may overcome these difficulties. The UK’s relatively liberal medical view possibly reflects government policy, capitation funding and incentives to focus on long-term conditions. Additionally, pharmacist prescribing and PGD activity may provide comfort with pharmacists’ increasing roles. Other commentators have raised the importance of medical buy-in for reclassification,[26, 115, 665] but it is difficult to achieve in most countries. Doctor backlash concerns influenced company strategy.

Hunt suggested politics and power stimulated medical negativity to the Canadian H2-antagonist reclassification,[126] and Lyon reported highly politicized reclassification in Europe including physician lobbying,[95] which two academics suggested was funding related.[110] My research suggests a greater effect than the literature indicates, with Japan hindered across most reclassifications, and political negativity from Australian medical organisations. Although not a reclassification, widening availability of immunisations through US pharmacists was difficult,[94] despite obvious potential public health benefits, and some medical control remains.

Consumers continue to see doctors, despite reclassification. Smith and Martin found 78% of purchasers of reclassified medicines had consulted their doctor in the last year.[210] Banks observed UK reclassifications “do not appear to have lessened the dependence of consumers on doctors.”[204][p2] Andrade, et al. found physician visits did not reduce in the US with the reclassification of H2-antagonists, even though chronic prescription usage of the medicine reduced 15%.[201] Doctors need reassurance that they will still see their patients (from an economical, preventive health and diagnosis perspective).
14. The prime influence of the health system funding on reclassification is the consumer cost differential between the prescribed medicine and the non-prescription medicine

Despite vast health system differences, the main factor influencing reclassification arising from health funding was cost to consumers of non-prescription versus prescription supply. These costs, including doctor consultation and prescription charges, vary between and within countries and have differing and sometimes opposing effects. In the UK, Japan and NZ, participants believed low (or no) prescription copayments deterred post-reclassification sales. UK commentators[167, 674] and research[562] support this concept. Additionally, a low consumer cost of prescribed medicines may affect the willingness to pay across all medicines (an anchor bias[675]). This effect received little mention in the US and Australia presumably because non-prescription supply costs less than prescription supply for many people, but others have noted such an effect in the US.[50]

Conversely, low prescription costs could help reclassification as suggested by a couple of participants, my committee experience, and research.[156] Low prescription or medical costs encourages consumers with long-term or high usage of a medicine to visit the doctor to access subsidised medicines, creating a safety net from a committee perspective. In the US no such safety net would exist for the uninsured or underinsured population, providing a second effect of the health system. This safety net effect has not been previously identified, to my knowledge.

The doctor payment mechanism and pharmacy payments may indirectly influence reclassification (see points 9 and 13 above).

An important but contrary effect arises where funders stop reimbursement for medicines post-reclassification, as in the US and Netherlands. Reimbursement can encourage prescription access rather than non-prescription access, and two industry participants opposed it as it sabotages the non-prescription market and takes doctors’ time unnecessarily. Lyon considered Western Europe lagged behind the US in reclassifications’ success because the US stopped reimbursement and Europe did not.[95] However, loss of prescription reimbursement on reclassification reportedly prevented reclassifications in the Netherlands as companies protected their prescription business. Additionally, it may shift prescribing to other reimbursed treatments, so self-care may not increase and government savings may be negligible. This was shown when reimbursement stopped for many OTC medicines in Turkey.[168] Reimbursement changes need to be viewed alongside doctor and prescription copayments generally.

In Japan, participants reported branded products retain a good price and market post patent expiry, discouraging reclassification interest. In contrast, in the US a large price drop and significant shift to generics decimates post-patent branded prescription medicines, stimulating reclassification interest. Confirming these views, 80% of US prescriptions were dispensed as generics in 2011,[676] compared with 20% of Japanese prescriptions in 2009,[677] and WHO reported very low US and UK generic prices.[346]
15. The easy, lucrative reclassifications have been done

In many markets, few easy reclassifications with significant market opportunity remain. Complex reclassifications require considerable preparation, approval is uncertain, supply requirements may be burdensome, and UK returns were reportedly poor, discouraging industry. Collaborative care models are recommended for some complex reclassifications.[26, 121, 643, 664] Examples include the UK’s doctor consultation post-tamsulosin supply,[116] and NZ’s doctor diagnosis (and monitoring if necessary) with calcipotriol.[156] Evidence and doctor experience with such models, government policy, and doctor shortages may encourage committees, regulators and doctors to support a collaborative care approach to assist complex reclassifications. Complexity may be greater than needed to satisfy various stakeholders. Blenkinsopp and Bond questioned the use of guidelines to manage theoretical concerns with H₂-antagonists.[24] Guidelines and protocols should not be unnecessarily excessive, and could be reviewed and simplified after use.

Complex reclassifications are on the cusp of other supply mechanisms such as pharmacist prescribing and PGDs, which can address many medicines at once, and/or may be developed relatively cost-effectively and quickly, and may include subsidised care for consumers. Alternatively, governments or third parties (as in NZ) could drive these reclassifications in countries where the barriers to reclassification are low and flexibility is available.

Low cost doctor visits and prescriptions reduce consumer interest in self-medication for long-term conditions or for higher priced medicines. Additionally, consumer culture (in the UK at least) is to visit doctors for long-term conditions (self-treat for four to seven days only).[560] so a change in consumer mind-set (and/or expansion of funding) is also required.

16. Immediate generic entry discourages reclassification

Market exclusivity (preferably three years or more) has long been desired by industry,[26, 590] yet market exclusivity apparently does not correlate with progressiveness. Little or no market exclusivity occurred in the most active countries (the UK and NZ, respectively), while low progressiveness occurred in the US despite high market exclusivity. These findings reflect the multi-factorial nature of reclassification. However, immediate house-brand entry in Canada and Australia (combined with advertising restrictions) possibly discouraged reclassification. Market exclusivity is important, and even reclassifying by product encouraged reclassifications in the UK; chloramphenicol was driven by sponsors in the UK, but not in NZ or Australia.

“…[there] needs to be some sort of encouragement somehow for companies to want to [reclassify medicines]. And they hold the bulk of the money and bulk of the information and they're the ones that will generally do the investment if there's any additional studies required. So they need to get something back in return... “ International industry participant

Concerns preventing market exclusivity being implemented might include legislative changes, a belief that exclusivity is not warranted (e.g. markets not requiring special studies), and a belief
that exclusivity is unnecessary given the activity occurring without it (e.g. in NZ). Additionally, concerns about higher consumer costs may occur. However, given participant reports of poor returns, and the UK slowdown and reduced sponsor activity in NZ shown in this research, three years’ market exclusivity may be necessary to stimulate reclassification. Longer exclusivity may be necessary for difficult reclassifications or for niche products with small markets. Industry suggested three years in the US may be insufficient given the increasing burden of pre-reclassification studies, echoing others.[590, 678] However, market exclusivity in the US may cause companies to delay reclassification to maximise returns.[220] My participants did not repeat this, but some reported reclassifications at the end of the patent life, which might support this view, disadvantaging consumers. Further consideration is warranted on how to best use this tool.

17. Banning advertising impairs reclassifications

Inability to advertise in Australia (combined with house-brands in pharmacy, transparent process and no market exclusivity) discourages reclassification. Without advertising, it is difficult to create consumer awareness of a reclassification. However, medicines are not ordinary items of commerce and should not be marketed as such.[190] Advertising in the US for non-prescription medicines has been criticised. Advertising needs to be responsible, creating an understanding that the product is not suitable for everyone and that risks exist, as suggested by others.[679] WHO advises that consumer advertising “should help people to make rational decisions”, and include names of active ingredients and major precautions, contraindications and warnings.[98][p24, 25] Further research could usefully ascertain how well consumer advertising in different countries adheres to the WHO advice. In the US, advertising is overseen by the FDA for prescription medicines, and the Federal Trade Commission (FTC) for OTC medicines.[227] Faerber and Kreling found US OTC ads were less balanced then prescription ads, and risk statements were nonspecific, e.g. “use only as directed”.[227] which may have contributed to low consumer awareness of precautions with OTC analgesics.[242] Omitting generic names from advertisements may contribute to the poor knowledge and unintentional overdose which causes nearly half of acute liver-induced failure in the US.[680] It is therefore unsurprising that Tinetti, Chair of the FDA’s NDAC which recommended against reclassifying lovastatin, expressed concern about lack of FDA oversight of OTC ads.[160] Using the WHO advice in industry advertising codes may help inform some consumers who believe that medicines that are non-prescription are harmless.[190, 224] If industry advertised more responsibly, regulators and committees may hold fewer concerns about advertising and post-reclassification safety. However, industry may not want to change given knowledge deficiencies help maintain brand loyalty and encourage consumers to use advertising to inform purchases.[225]

Many of these principles have a financial dimension – returns to companies, payment to doctors, cost differentials to consumers, the cost of reclassification, the financial limitations of generic competition, pharmacy funding, cost benefits to governments driving self-medication policy, and the cost of collecting evidence. Committees worry about consumer costs following reclassification.

250
Additional to discovering reasons behind international variation, I also found that significant barriers in all studied countries inhibit consumer access to medicines. Many proposed reclassifications arising from multi-stakeholder working parties in the UK,[121, 681] and Europe,[26] have not occurred or been rare in developed markets. Safety and practice changes might have affected several proposed reclassifications e.g. COX-2 inhibitors and hormone replacement therapy. However, my findings suggest that sponsors see little potential return. Additionally, approval of many such reclassifications is currently unlikely in most markets including the US, despite the fact that recent (e.g. last decade) reclassifications in the five core countries have not been reversed, nor have major safety concerns been published for these medicines in the non-prescription setting. The European centralised reclassification may be holding the UK back, but do so poor sales of complex reclassifications.

This research considers barriers to reclassification across different countries. Overcoming some hurdles requires encouragement for companies e.g. ensuring considerations are evidence-based, the process is not unduly slow and cumbersome, and returns are not immediately jeopardized by generic entry. Alternatively, non-sponsors (such as pharmacy organisations) could drive reclassification, following the NZ example, although costs, legislation and company resistance might preclude that in many countries. The third-party attempt by Wellpoint in the US to reclassify non-sedating antihistamines only came to fruition when the companies wanted to reclassify.[29] While government-driven reclassifications have occurred, I found little interest in doing this.

11.6. Should non-sponsors drive reclassification?

Many participants believed it was reasonable for non-sponsors to drive reclassification but the industry held important concerns about implications for them, and could pursue legal avenues to prevent this in some countries (particularly in the US). Non-sponsors may be better positioned than industry to consider greatest consumer need and best molecule to meet that need. There is no restriction to a pipeline of company products, concerns about generic entry, and advertising may not be necessary. Multiple challenges exist for a non-sponsor driving reclassification; depending on the market some may be insurmountable. Unlike NZ, most markets are unlikely to want to reclassify medicines without consumer-labelling. However, third party reclassification has resulted in increased availability to four different medicines to NZ consumers. The most significant public benefit could come from the increased availability of the influenza vaccination. Achanta, et al. found mixed views on whether regulators should unilaterally reclassify medicines, but did not consider third-party reclassification.[341]

11.7. Discussion of overall findings

As this is the only research to systematically elucidate why reclassification varies using a range of voices across a range of countries, comparator studies are limited.

The little research considering international differences in reclassification has generally focused on specific areas: criteria used;[30-32] medicines availability comparisons;[30, 31, 49, 50] and effects of
differing schedules.[31, 49, 50] Findings from these studies have been compared with my findings in relevant discussions above (Principle 8, and 11.4.1). Case studies have compared reclassifications in different countries.[19, 21, 29] Cohen also identified different drivers behind reclassifications between countries,[21, 29] different judgements between countries, and inconsistency in reclassifications.[21] He also reported the industry desire to maintain prescription status during the patent life and that lack of BTC category limits US reclassification. Commentators’ views have largely been included in discussion under various principles. However, Lyon, an experienced industry employee reported that consumer self-selection and de-reimbursement increased sales in the US compared with Western Europe, and resulting low sales in Western Europe limited companies’ interest.[95] I found greater complexity than this, e.g. de-reimbursement can hinder reclassification, culture is important, and other health system costs may affect the potential market.

11.8. Strengths and limitations

11.8.1. Strengths

This study is the largest of its kind to my knowledge. I examined five core countries and four secondary countries, using interviews with 79 stakeholders, extensive document analysis and my own experience. I researched reclassification numbers to document variability, categorising these in a novel way (using ‘innovative’ reclassifications, ‘first-in-world’ reclassifications and comparing dates across key reclassifications). No previous comparisons have been as thorough. I explored stakeholder views on barriers and enablers they perceived to affect reclassification. The wide range and high quality of key informants ensured that most relevant voices were included. Participants included committee members, and representatives of regulatory agencies, industry, academia and pharmacy, medical and consumer groups. Only five requests failed to achieve an interview. When a UK/Europe medical participant withdrew, UK submission documents from medical organisations were analysed instead.

Multiple countries were selected for diversity in population size, health system, scheduling systems and culture. My focus on five countries provided reasonable depth. Adding data from four other countries helped to confirm factors or show differences in other countries, e.g. the house-brands effect in Australia was echoed in Canada but differed in the UK. Extensive document analysis for Australasia demonstrated changing progressiveness over time, and regional effects, both researched for the first time.

My long-standing involvement in reclassification, pre-research conversations with regulators and pharmacists in other countries, observation of an Australian meeting, and involvement in a European reclassification attempt, helped the research. This ‘insider’ knowledge and connections helped in setting up interviews, knowing who to interview, understanding the language of reclassification, and building rapport and encouraging sharing of information.
I triangulated findings with documents including meeting records for Australasia, and my own experiences in reclassification. All core country chapters and the Europe section were sent for comment to a knowledgeable participant well-versed with the country at question, with resulting feedback incorporated.

In qualitative research (especially given the heuristic involvement of self) subjectivity is expected and is often embraced.[350, 358, 682] Bias (or intuition) helps a researcher to know “when to look, where to look, and how to look.”[524][p44] However, subjectivity can cause limitations.

11.8.2. Limitations

My experiences in (and perspective on) reclassifications, as a pharmacist and a New Zealander will have affected my interviews, analysis and reporting. A researcher weights his or her work in words chosen and how messages are conveyed.[683] I conducted all interviews, was the only person to see all transcripts and analysed and reported findings with guidance from supervisors. Using a second researcher to conduct or analyse interviews would have been outside the heuristic methodology.[358]

I have attempted to be true to participants’ voices in using their interviews and quotes. I was curious about what they thought and why, and found their viewpoints valid, reasonable and understandable. I systematically documented all potential enablers and barriers and considered all in analysis and reporting. I often provided the frequency of viewpoints for a somewhat objective indication of importance. I included viewpoints arising from only one or two participants that seemed ‘salient’. [684]

Although offered a transcript copy, most participants declined, and only one made changes.

Sharing information and ideas encourages participants to share their thoughts.[358, 682] I asked about barriers and enablers before sharing information to minimise my contamination with these important top-of-mind questions. Another interview with a different interviewer, different shared experiences, or on a different day would elicit a different conversation, but the main findings may not have changed greatly. Highly experienced participants with years of reclassification experience probably kept and stated their underlying views despite our shared experiences. Triangulation confirmed some findings. An additional brief written questionnaire may have facilitated comparison, but would have reduced interview time and required more of participants.

Participants may self-edit.[682] Some participants were presenting their personal view, but their organisation and experiences may affect their perspective. Participants may hold different views to another person from the same or a similar organisation. My findings are not exhaustive, and I did not seek data saturation. Given the relatively few people in each country with the desired knowledge and experience in the field, data saturation may not be possible, and given the scope of the research, I traded depth for breadth.[350] Data saturation as a concept may be an illusion – what we know is always incomplete, provisional and ever-changing. I generally interviewed the person most involved in reclassification in each organisation. I did not interview consumer participants or medical participants in all core countries, partly because of time limitations and refusals. Consumer participants had limited knowledge of reclassification. Interviewing more medical participants may have added value, but the
breadth did not permit this, given these participants knew less about reclassification variability than others interviewed. Given the range of participants and their collective knowledge, I anticipate that the main barriers and enablers probably arose for the core countries.

Protection of participants means I cannot always be as transparent as a reader might want. Potentially I may have looked more favourably at the MCC or NZ than other committees or countries owing to past allegiances, but I have provided NZ with many suggestions for improvement.

Changes during the extended period of research may have affected findings. However, this allowed time for consideration between phases of interviews. Such a period is not surprising in an extensive comparative international project. Abraham and Davis spent six years conducting comparative UK-US research examining new medicine approvals and rejections using numerical comparisons and key informant interviews.[343]

Lists of reclassifications were unavailable for some countries, so various sources were used. Dates may vary according to the source of information, e.g. the year the committee agreed to reclassify the medicine, the reclassification agreement was reported, the gazettal occurred, or the medicine was marketed. While not ideal, this still allows a comparison of approximate dates.

My measure of 'innovative' reclassifications was occasionally difficult to apply (one or two reclassifications in some countries) partly because of a lack of published research. Occasional different judgements would not have changed overall findings. Three other pharmacists (in Australia or NZ) provided feedback on uncertain reclassifications with majority vote (of four) deciding outcomes. Having a medical perspective might have provided further benefit. Comparing all reclassifications would have been less informative because of TTH (affecting many little-used substances) and 'me-too' reclassifications, and 'first-in-class' provides difficulties also (2.3.2.12). Therefore, the new 'innovative' reclassification measure provided more useful information than alternatives.

I do not pretend to have a deep knowledge of countries apart from NZ. I spent time trying to understand pharmacy and the health system in the core countries, and was aided in having worked briefly in community pharmacies in Australia and the UK, and having visited pharmacies in each of the core countries. I read background material and had further informal conversations with participants (email or at conferences) to aid my understanding. Using a local participant to check each chapter should have avoided major misunderstandings.

In Japan, the language barrier made interviews less informative in the time available (e.g. time for translation or explaining a question), background information or relevant academic papers in English is uncommon, and marketed medicines and the health system differ from other countries. Therefore I visited pharmacies and drugstores in Japan collaborated with a Japanese academic, and had help from a Japanese community pharmacist particularly in compiling the list of reclassifications and deciding which reclassifications were innovative. Email communications supplemented interviews, and I checked key diagrams or information with selected participants.
11.9. Summary of chapter

In studying five core countries, and four others, I found important differences in reclassification and exposed many reasons for these differences. Product, company and market factors affect progressiveness in reclassification in complex ways. These factors affect the decision to attempt reclassification, and the likelihood of reclassification approval. I found that multiple enablers are required for a country to become progressive.

Every product consideration can differ, and countries differ with each other, and over time. This chapter developed a multi-dimensional approach to considering progressiveness. I then used progressiveness measures alongside interviews to find the UK is the leader in reclassification. I have developed principles of reclassification based on my findings from a deliberately diverse group of developed countries, which may help countries reviewing their reclassification processes. Non-safety barriers occur even in very progressive countries, the UK and NZ, and should be addressed where possible and desirable, including through market exclusivity and utilising the pharmacist. Given the multiple barriers, reclassification could be driven by others, as I have demonstrated in NZ, particularly as more patents expire.
Chapter 12. Conclusions

The goal of this research was to ascertain why developed countries vary in prescription to non-prescription reclassification. Reflexivity underpins my research to address this goal. My starting position was that I believe that, on balance, reclassification with relative safety is desirable. Some readers might consider this stance too liberal. They might suggest that down-scheduling loses the opportunities that each medical visit presents for maintaining and improving personal and population health.[641] Readers might also believe that reclassification could increase harmful effects from medicines through increased use or inappropriate use. I personally hold concerns about inappropriate use of medicines, would not favour the reclassification of some medicines that others would, and advocate using protocols and restrictions (including pharmacist-only supply) to reduce harm. Therefore, some e.g. in industry may consider me excessively restrictive in my approach to reclassification. Others will have a similar perspective to mine. However, all people have predispositions, and to manage them as a strength rather than a problem, I have reflected critically on the centrality of my predispositions to my heuristic analysis. My knowledge and experience have facilitated this study. I have retained throughout the research a curiosity about viewpoints of others and the differences between countries. I have sought to make my methods transparent, triangulate findings, represent diverse perspectives from key informants, and include evidence for my interpretations.

I found variability between developed countries in reclassification arose from a complex range of factors which blended uniquely for every country examined. These factors affect one of two areas: whether the medicine is likely to be able to reclassify in that country, or whether a sponsor (or other party) wants to pursue reclassification in that country.

Regional effects on reclassification variability have emerged, both positive and negative, and from a company and country perspective. My NZ-Australia meso-level research provided insight into differences that can occur between similar countries and changes over time in reclassification. This research highlighted the effect of differing committee constitutions, individuals and experiences. The requirement for a European centralised process is limiting UK reclassification. Where regionalisation occurs, implications need to be carefully considered. Allowing regionally-linked countries to continue to make their own decisions as in NZ and Australia currently may be less limiting than the European situation. However, with NZ and Australia planning a joint scheduling committee, this research reflects on how stakeholders perceive the two countries are performing in reclassification. Both countries could improve their committee constitution. The findings of this project provide an opportunity to take the best from both countries and adapt useful initiatives from elsewhere into the design of the new Trans-Tasman committee and process. Suggestions have been provided at the meso-level.

Some countries look internationally to benchmark themselves, or adapt ideas from other countries that are progressive in reclassification. I have provided multiple measures (including a new
innovative reclassification measure) across a selection of developed countries that vary in population size, scheduling, and health system. I have also suggested principles for reclassification for countries to use when considering barriers and enablers in their own health system. In portraying how the studied countries have aided reclassification, ideas have emerged which regulators may choose to implement or adapt, knowing some stakeholders’ views from a country using the enabler.

Given the rising pressure on health systems, countries may want to learn from those that have enabled reclassification. Indeed, countries that are currently more active in reclassification (NZ, Japan and Singapore) clearly learnt from the UK. The UK and Japan demonstrate the benefits on furthering reclassification through consistent, active government policy and a proactive regulator. Japan rewards companies undertaking post-marketing surveillance following reclassification with three years’ exclusivity. Such research, if conducted well and published could contribute understanding of real-life usage in different markets, inform further down-scheduling and allow evidence-informed changes to labelling and reclassification conditions.

My research supports the enabling role of a pharmacist-only and/or pharmacy-only category in reclassification. Use of such a category would facilitate wider consumer access to medicines in the US and Europe. Evidence of consumer outcomes may help to resolve the uncertainty in the US of whether to introduce a BTC category. Where an intermediate category occurs, pharmacy improvements would help further reclassifications. Such improvements include: raising performance in some pharmacies; a better understanding from consumers as to pharmacy’s role and responsibilities; and appropriate clinical learning and communication skills in undergraduates and graduates in all countries.

Every country appeared to have significant non-safety related barriers preventing reclassifications. Dutch women had to wait 20 years longer than other countries to treat vaginal candidiasis effectively without a prescription; Americans had to wait over a decade to get a safer antihistamine available without a prescription; and influenza vaccination remains prescription-only in most countries. Consumers and the health system may be burdened for medicines that could be self-managed, or pharmacist-managed.

It therefore seems reasonable to reduce barriers to reclassification that are not safety-related. This is consistent with my original standpoint of supporting reclassification with a focus on relative safety. Based on my findings (and arising from the Principles of Reclassification in the macro-level chapter), I now outline the framework of an ideal reclassification environment. A country would ideally have government policy support, a proactive regulator, proactive pharmacy organisations, and a tiered non-prescription scheduling system (including pharmacist-only) to provide flexibility for different medicines. The reclassification process should not be excessively time-consuming or costly. Non-sponsor applications and regulator-stimulated reclassifications would be workable. Three years of market exclusivity with robust data collection and publication to aid further reclassification decisions would occur. The committee would be carefully designed (experts not representatives) and selected to ensure high quality decision making by informed well-performing members who are open to different
ideas and conscious of safety. Pharmacists and doctors would be open to the concept of reclassification and would enter into constructive debate. Pharmacy would perform well (perhaps through encouragement and penalties), and be proactive with new reclassifications, and consumers would be well-informed and empowered in health. Advertising would be allowed for reclassified medicines, and industry would take a responsible approach. Regional effects would not stymie an individual country from innovating. Where doctor-prescribed medicines cost less than self-medicating, limited non-prescription sales potential probably limits reclassification. However, any change in reimbursement or consumer copayment strategy needs to be viewed from a larger population health perspective, and risks would probably outweigh benefits. There is no single country that meets all of these criteria, the closest may be the UK.

With few ‘easy’ reclassifications remaining, some reclassifications are entering a ‘grey zone’ between pharmacist prescribing and reclassification (simvastatin, azithromycin, tamsulosin, calcipotriol and trimethoprim). Using specially-trained pharmacists in community pharmacies to deliver more complex medicines under protocols, e.g. antihypertensives, could provide important access. Such availability may help address under-treatment in the community, encourage patients to become more involved in their own care, and receive more timely treatment, and give doctors more time to manage complex patients. NZ probably best exemplifies this ‘grey zone’, with exemption to prescription and mandatory training. The current reclassification model may not work for companies marketing medicines for chronic conditions. Pharmacy or the regulator may be better placed to progress these complex reclassifications, as they may be able to reclassify an appropriate suite of medicines enabling individualising treatments. However, consumer demand is unclear, and safety needs to be carefully considered. Some countries may have neither the mindset nor the legislation in place to enable such supplies, and the inability to add to medical records in most countries remains an important barrier. Alternative means of increasing access through pharmacists (and non-pharmacists) in the UK, US and Canada suggest that mechanisms other than reclassification might be easier to implement in some countries. Evidence of consumer outcomes for complex reclassifications and these other mechanisms of availability is desirable to inform further such widening of access.

Reclassification often occurs under uncertainty where assumptions and judgements are necessary, but uncertainty is common in health,[685] and should not provoke automatic reclassification rejection. Safety remains important. Greater consumer usage and outcome data is needed across the different scheduling environments to understand the effect of each shift, inform committees and address concerns. Research may show that concerns are not warranted, providing confidence to committees, or may show that concerns are warranted, consequently changing, slowing or halting reclassification. Committee membership and functioning seem to need consideration in some countries at least (as suggested throughout the chapters). Further research could involve observing different committees considering the same reclassification.
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264


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