Working Papers in Health Policy and Management

Volume 4

Ewout van Ginneken

Implications of future EU policy on the provision of medicines and on actors in the European pharmaceutical sector

November 2010

Department of Health Care Management

Technische Universität Berlin

Ewout van Ginneken

Implications of future EU policy on the provision of medicines and on actors in the European pharmaceutical sector

Working Papers in Health Policy and Management

Volume 4

November 2010

Dr. Ewout van Ginneken is a research fellow in the Department of Health Care Management at the Berlin University of Technology, Germany.

This volume is a revised and updated version of Dr. van Ginneken's dissertation, which was originally published in April 2009.

EDITOR-IN-CHIEF / HERAUSGEBER DER SCHRIFTENREIHE
Prof. Dr. med. Reinhard Busse

EDITOR / REDAKTEUR
Matthew Gaskins

PUBLISHER AND DISTRIBUTOR / VERLAG UND VERTRIEB
Universitätsverlag der Technischen Universität Berlin
Universitätsbibliothek
Fasanenstr. 88 (im VOLKSWAGEN-Haus), D-10623 Berlin
Tel.: +49 30 314 76131; Fax.: +49 30 314 76133
e-mail: publikationen@ub.tu-berlin.de
http://www.univerlag.tu-berlin.de/

ISBN 978-3-7983-2235-6
ISSN 1867-6287

Contents

Overview of figures and tables 1
Abstract (German) 2
Abstract (English) 9
Introduction 15
Objectives 16
Scope of the thesis 17
Research strategy, methods used and structure of thesis 17
Methodological background 21

PART I: REVIEW 22
1 Conceptual model of the European pharmaceutical market 22
2 The European pharmaceutical market: A description 28
2.1 Supply side 29
2.1.1 European pharmaceutical industry 29
Industry structure 30
The Pammolli Reports on the competitiveness of the European pharmaceutical sector 34
2.1.2 Wholesalers 36
2.1.3 Pharmacies 40
2.2 Demand side of the pharmaceutical market 43
2.2.1 Prescribers 43
2.2.2 Patients 45
2.2.3 Payers 47
3 The European Union 51
3.1 European Union policy process and actors 52
3.2 European Union industrial policy 53
3.2.1 European Union pharmaceutical policy: A history, 1960–2000 54
3.2.2 European Union pharmaceutical policy, 2001–2005 58
3.2.3 The G10 process 60
3.3 European Union social policy 69

3.3.1 The European legal frameworks for cross-border health care 70
3.3.2 Access to cross-border pharmaceuticals 73
3.4 European Union health policy 76
3.5 The European Court of Justice (ECJ) 79
3.5.1 The ECJ and cross-border health services 79
3.5.2 The ECJ and pharmaceutical market liberalization 82
3.6 European Medicines Agency (EMEA) 83
4 National pharmaceutical policies in the EU 86
4.1 Regulation for the entire national pharmaceutical market 89
4.1.1 Market authorization 91
4.1.2 Pharmacovigilance 92
4.1.3 Distribution and classification of pharmaceuticals 94
4.1.4 Advertising 96
4.2 NHS/SHI regulation with a potential impact on entire national market 97
4.2.1 Direct price controls and profit controls 97
4.2.2 Measures regulating prescribing and dispensing 100
Stimulating the use of generics 100
Rationalization of prescribing 101
Remuneration of community pharmacies 102
4.3 NHS/SHI pharmaceutical regulation 103
4.3.1 Measures regulating the reimbursement of pharmaceuticals 103
Positive and negative lists (selective listing) 103
Co-payments (cost-sharing) 105
Prescribing budgets 105
4.3.2 Reference pricing schemes 106
4.4 Pharmaceutical policy in the new Member States (EU12) 107

PART II: SCENARIOS 110
5 Methodology 110
5.1 The Delphi technique 110
5.2 The European pharmaceutical policy questionnaire 112
5.3 Expert selection 114
5.4 Conduct of the Delphi questionnaire 115

Anonymity 116
6 Results 117
6.1 Discussion of the results of the Delphi questionnaire 118
The expert opinion 122
6.2 Filling in the scenarios 123
6.2.1 The Expert Scenario 123
6.2.2 The European Crisis Scenario 130
6.2.3 The European Scenario 133

PART III: ANALYSIS 141
7 Analysis 141
7.1 Impact of the Expert Scenario 141
7.1.1 The European pharmaceutical industry 142
Authorization 142
Classification 142
Advertising 143
Pricing, reimbursement post-licensing evaluation and prescribing 143
7.1.2 Wholesalers 145
7.1.3 Pharmacies 147
7.1.4 Demand side (medical care triad) 148
Prescribers 149
Patient/consumer 150
Payers 151
7.2 Impact of the European Crisis Scenario 152
7.2.1 European pharmaceutical industry 152
Authorization, pharmacovigilance, classification and distribution 152
Advertising 154
Pricing, reimbursement, post-licensing evaluation and prescribing 155
7.2.2 Wholesalers 157
7.2.3 Pharmacies 158
7.2.4 Demand side (medical care triad) 159
Prescribers 160

Patient/consumer 161
Payers 162
7.3 Impact of the European Scenario 162
7.3.1 European pharmaceutical industry 163
Authorization 163
Classification 164
Advertising 164
Pricing, reimbursement, post-licensing evaluation and prescribing 165
7.3.2 Wholesalers 165
7.3.3 Pharmacies 166
7.3.4 Demand side (medical care triad) 168
Prescribers 168
Patient/consumer 168
Payers 170

Discussion 172
REFERENCES 181
APPENDIX A 190
APPENDIX B 193
APPENDIX C 196

Overview of figures and tables

Figure 1: Schematic structure of the thesis 21
Figure 2: Stakeholders in the European pharmaceutical market: functions 27
Figure 3: Prescriptions dispensed per capita in selected European countries, 1996 44
Figure 4: Pharmaceutical expenditure (€) per capita through pharmacy, 2004. 46
Figure 5: Market structures for payer/purchaser organizations and European examples .. 49
Figure 6: Assumption of health care costs abroad, options listed 1 through 3 that may include individually purchased pharmaceuticals 75
Figure 7: Competences in the national pharmaceutical market. 89
Figure 8: Competences in the national pharmaceutical market combined with an expected shift between 2006 and 2025 (rated 1–5), based on expert opinions 122

Table 1: Competing policy objectives regarding pharmaceuticals 25
Table 2: Size of the market for pharmaceuticals, 1989–2003. 28
Table 3: Production value, pharmaceuticals (NACE 24.4), constant million, €, 1995–2001. 32
Table 4: Leading pharmaceutical corporations (turnover) worldwide, 2005. 33
Table 5: Leading pharmaceutical corporations (turnover) in Europe, 2005. 33
Table 6: Number of pharmacies in the EU15. 41
Table 7: Share of diagnoses with prescription in selected European countries, 1996. 45
Table 8: The Commission's adoption of G10 Medicines recommendations. 65
Table 9: A non-exhaustive list of European Community action in the European pharmaceutical market, 1965–2004. 68
Table 10: EU mandate on health policy in the Treaty establishing the European Community 77
Table 11: Pharmaceutical expenditures in several EU Member States, 1985–2005. 87
Table 12: Community code. 90
Table 13: Examples of price comparison measures in Europe 99
Table 14: Incentives to promote generics in the EU. 101
Table 15: Comparative definitions of reference price in selected EU schemes 106
Table 16: Category of respondents. 117
Table 17: Delphi questionnaire results. 119
Table 18: The Expert Scenario in numbers 124
Table 19: The European Crisis Scenario in numbers. 131
Table 20: The European Scenario in numbers. 134

Abstract (German)

Der europäische Arzneimittelmarkt steht seit vielen Jahren im Fokus der Politik. Sowohl die Finanzierung von Gesundheitssystemen als auch der Zugang zu solchen werden auf nationaler Ebene durch steigende Ausgaben für Arzneimittel gefährdet. Der pharmazeutische Sektor ist häufig Gegenstand nationaler Interventionen zur Kostendämpfung, da dieser in der Regel schneller als das Bruttoinlandsprodukt und der gesamte Gesundheitsmarkt wächst. Nationenübergreifend wächst die Rolle der Europäischen Union, die versucht, die Innovations- und Wettbewerbsfähigkeit der strategisch wichtigen europäischen Pharmaindustrie zu stärken. Ziel dieser Dissertation ist es, die wachsende Rolle der EU im europäischen Arzneimittelmarkt, insbesondere in Hinblick auf Akteure und Mitgliedstaaten zu untersuchen. Dies erfolgt in drei Schritten, die im Folgenden zusammenfassend erläutert werden: (1) ein *Review* der Rollen und Trends der Akteure des europäischen pharmazeutischen Marktes, einschließlich der EU und ihrer Mitgliedsstaaten; (2) Entwicklung von *Zukunftsszenarien* für die europäische pharmazeutische Politik; und (3) eine *Analyse* der Auswirkung dieser Szenarien auf die verschiedenen Akteure im europäischen Arzneimittelmarkt.

Im ersten Teil werden die Akteure und der konzeptionelle Rahmen, in dem sie interagieren, dargestellt. Die nationalen Maßnahmen zur Kostendämpfung resultieren in niedrigeren Gewinnmargen auf Anbieterseite (Pharmaunternehmen, Großhandel und Apotheken). Vergleicht man Indikatoren der Wettbewerbsfähigkeit der *forschenden Pharmaindustrie* (Forschung und Entwicklung, Lohn- und Nebenkosten, Anzahl von neuen innovativen Arzneimitteln) zwischen den USA und Europa, liegen diese in Europa (deutlich) unter denen der amerikanischen Konkurrenten. Pharmazeutische *Großhändler* standen in den 1990er Jahren einem dramatischen Konsolidierungskurs gegenüber. Derzeit versuchen sie ihre Konkurrenzfähigkeit durch eine Erweiterung ihres Dienstleistungsangebots (vertikale Diversifikation, bspw. durch Logistikdienstleistungen für Pharmaunternehmen) zu sichern. Die *Apothekenbranche* ist verglichen mit anderen Industriebereichen eine der am stärksten regulierten

Branchen überhaupt. Sie weist zudem eine enorme Heterogenität in der Apothekendichte auf und steht zusätzlich den Herausforderungen neuer Apothekenketten und Online-Apotheken gegenüber.

Verglichen mit der Anbieterseite, ist die Nachfrageseite (Verschreiber, Patienten und Kostenträger) durch eine asymmetrische Informationslage gekennzeichnet. Zwar haben *Verschreiber* (Ärzte) in der Regel mehr pharmazeutisches Wissen als Patienten, dennoch hat sich das Arzt-Patienten-Verhältnis aufgrund neuer Informationstechnologien, die einen schnellen Zugang zu medizinischem Wissen ermöglichen (z.B. Internet), verändert. Innerhalb Europas existieren weiterhin erhebliche Unterschiede hinsichtlich Verschreibungs- und Konsumverhalten von Arzneimitteln, die auf kulturelle Unterschiede und nationale Regelwerke zurückzuführen sind. Für gewöhnlich liegt das Interesse der *Patienten* nicht darin, ein möglichst kostengünstiges Medikamente zu erhalten. Doch durch nationale Maßnahmen wie z.B. Zuzahlungsregelungen wird versucht das Bewusstsein der Patienten dafür zu steigern. Die *Kostenträger* (z.B. Krankenkassen) bieten ihre Leistungen innerhalb eines national stark regulierten Umfelds an und haben bisher selbst keine große Rolle in der Eindämmung von Arzneimittelkosten gespielt, was nicht zuletzt an existierenden Gesundheitssystemstrukturen liegt, in welchen es an Instrumenten zur Einflussnahme auf Preis und Volumen von Arzneimitteln mangelt.

Die regulierenden Instanzen auf dem europäischen Arzneimittelmarkt sind die *europäischen Union (EU)* und ihre Mitgliedsstaaten. Die Arzneimittelpolitik der EU wird überwiegend von Seiten der Industriepolitik beeinflusst. Sie ist bestrebt den Arzneimittelmarkt zu liberalisieren und einen europäischen Binnenmarkt (SEM) zu realisieren. In den vergangenen 40 Jahren zeigte die Arzneimittelpolitik einen beachtlichen Trend in Richtung Europäisierung. Dennoch können die 1995 eingeführten verbindlichen europäischen Zulassungsprozeduren und die Aufsichtsbehörde EMEA als letzte große Errungenschaft bezeichnet werden. Die Europäische Kommission hat sich stattdessen der Umsetzung von Empfehlungen der hochrangigen G-10-Arzneimittelgruppe zugewandt. Sie versucht sich auf die Koordination von Ergebnissen zu konzentrieren, statt auf europäisches Sekundärrecht wie z.B. Richtlinien. Entscheidungen des europäischen Gerichtshofs beziehen sich beispielsweise auf das

Recht an geistigem Eigentum, Markenzeichen, Patentschutz, Parallelimporten und Online-Apotheken. Sie beeinflussen wiederum die Gestaltung nationaler Politik in Richtung einer Liberalisierung nationaler Märkte.

Obwohl Marktzulassung, Pharmakovigilanz, Klassifizierung von Arzneimittel sowie deren Distribution immer mehr von der EU mitbestimmt wurden, erhielten die europäischen *Mitgliedsstaaten* mit Hilfe des Artikels 152 des EG-Vertrags Kompetenzen bei Preisbildung und Vergütungen innerhalb ihrer Gesundheitssysteme. Zudem entwickelten Mitgliedsstaaten innerhalb der letzten 25 Jahre zunehmend gleichartige (von einander kopierte) Maßnahmen, um die steigenden Ausgaben für Arzneimittel zu kontrollieren, die oft kurzfristig wirkten, dann allerdings langfristig ohne Erfolg blieben.

Im zweiten Teil der Arbeit werden Zukunftsszenarien der europäischen Arzneimittelpolitik beschrieben. Dazu wurden Schlüsselbegriffe und Variablen europäischer Arzneimittelpolitik aus Publikationen zusammengestellt. Als nächstes wurde ein Delphi Fragebogen entwickelt, mit welchem 41 europäische Experten bezüglich der erarbeiteten Schlüsselthemen befragt wurden. Die Ergebnisse der Delphi Befragung stellten die Bausteine zur Entwicklung eines konsolidierten *„Experten Szenarios“* dar. Daraufhin folgte eine kontrastierende Gegenüberstellung mit einem eher pessimistischen Szenario *(„Europäisches Krisen Szenario”)* und einem eher „optimistischen“ Szenario *(„Europäisches Szenario“)*:

(1) Das *Experten Szenario*: Im Bereich des europäischen Arzneimittelmarktes, in welchem die europäische Gesetzgebung den potentiell größten Einfluss hat, wird eine weitere Europäisierung vorausgesehen. Marktzulassung, Pharmakovigilanz, Einstufung von Arzneimittel, Großhandelsvertrieb und Werbung zeigen einen graduellen Trend in Richtung europäischer Konvergenz. Regulierung und Implementierung von Preisbildung, Abgabe, Verschreibung und Vergütung von Arzneimitteln verbleiben vornehmlich auf nationaler Ebene. Die von den Experten erwartete Europäisierung der vergleichenden Evaluation von Arzneimittel stellt dahingehend eine Ausnahme dar, da sie innerhalb der einzelnen Gesundheitssystems stattfindet, wo eher eine Dominanz der nationalen Kompetenzen vorausgesehen wird.

(2) Das *Europäische Krisen Szenario*: Der europäische Prozess erfährt einschneidende Rückschläge. Hauptsächliche Ursachen hierfür liegen im stockenden Expansionsprozess, einem vorhandenen Imageproblem, einer andauernden europäischen Verfassungskrise und einer pharmazeutischen Krise, die durch ein von der europäischen Zulassungsprozedur genehmigtes Arzneimittel ausgelöst wird. Dies führt zur Rückbesinnung auf nationale Regulierungen und einer Einfrierung des europäischen Prozesses.

(3) Das *Europäische Szenario*: Durch die erfolgreiche Ratifizierung des europäischen Verfassungsvertrages wächst das Vertrauen der Bürger in das europäische Projekt. Das finanzielle Gleichgewicht der einzelnen Gesundheitssysteme wird jedoch durch immer mehr grenzüberschreitende Patienten gefährdet. Um dem entgegenzutreten erarbeiten die einzelnen Mitgliedstaaten einen gemeinsamen europäischen Leistungskatalog. Dieser führt zu einer Europäisierung der verschiedenen nationalen Gesundheitssysteme, welche ironischerweise nicht durch die europäische Kommission, sondern durch die Mitgliedstaaten selbst initiiert wurde.

Die im dritten Teil der Arbeit behandelten Auswirkungen der Szenarien auf die unterschiedlichen Akteure stellen sich wie folgt dar: trotz der europäischen Bemühungen die *Pharmaindustrie* wettbewerbsfähiger zu machen, ändert sich in Zukunft eher wenig an der wirtschaftspolitischen Lage der forschenden Pharmaindustrie. In keinem der Szenarien scheinen größere Veränderungen hinsichtlich freierer Preisbildung und Vergütungsentscheidungen (d.h. weniger Möglichkeiten Investitionen zu refinanzieren) wahrscheinlich. Dennoch ermöglicht die Größe des europäischen Marktes mit zunehmend harmonisierten Märkten Synergieeffekte, z.B. Marktzulassung und Marketing betreffend.

Für die *Generika-Industrie* stellt sich die Zukunftsaussicht durchaus positiver dar. Zunehmende nationale Maßnahmen mit dem Ziel den Generika-Gebrauch zu stimulieren, erleichtern der Generika-Industrie den Zugang zu vornehmlich ‚unreifen' generischen Märkten. Dennoch erhöht der sich weiter europäisierende Arzneimittelmarkt den Wettbewerbsdruck über nationale Grenzen hinaus und führt zu einem internationalen Konsolidierungsprozess auch innerhalb der Generika-Industrie. In-

nerhalb des *Europäischen Krisen Szenarios* könnte dieser Wettbewerbsdruck allerdings langfristig geringer bleiben.

Auch *Biotechnologieunternehmen*, für die das Europäische Zentrale Marktzulassungsverfahren obligatorisch ist, haben großes Interesse an einer Weiterentwicklung des europäischen Marktes. Es wäre für sie finanziell sehr aufwändig, für neue Produkte Marktzulassungsverfahren in allen 27 Mitgliedstaaten einzeln durchlaufen zu müssen (wie im *Europäischen Krisen Szenario* angenommen). Biotechnologieprodukte werden jedoch auch zunehmend eingeschränkten Vergütungsentscheidungen unterworfen, die auf vergleichender Evaluation von Arzneimittel basieren. In Anbetracht ihrer hohen Kosten für Forschung und Entwicklung ist der Unternehmenserfolg dieser Unternehmen von Refinanzierung der Forschungs- und Entwicklungskosten besonders abhängig.

Im *Großhandelssektor* wird sich eine internationale Konsolidierungstendenz – sowohl horizontal als vertikal– weiter fortsetzen. Der nationale Großhandel wird in zunehmendem Maße auch über die Staatsgrenzen hinaus operieren, was durch harmonisierende Arzneimittelmärkte ermöglicht wird. Der Großhandelssektor wird darüber hinaus versuchen, seine Dienstleistungspalette zu erweitern und nach Partnern unter Pharmaunternehmen suchen. Nur unter dem *Europäischen Krisen Szenario* sind sie in der Lage, ihre führenden nationalen Positionen infolge unterschiedlicher nationaler Regelwerke und Warenangebote beizubehalten.

Apotheken werden in Zukunft mit vielen Herausforderungen konfrontiert sein, die zu einer Veränderung des gesamten Sektors führen werden. Sie sind in zunehmendem Maße der europäischen Marktliberalisierung und nationalen Maßnahmen zur Kostendämpfung ausgesetzt. In der Annahme, dass sich das *Europäische Krisen Szenario* nicht verwirklicht, ist es also wahrscheinlich, dass das „goldene Zeitalter“ der Apotheken zu einem Ende kommt. Resultate dieser Veränderungen könnten unterschiedliche Eigentümerschaften (z.B. Krankenversicherer, Nicht-Apotheker), neue vertikale Kombinationen, Apothekenketten, Abschaffung von Staatsmonopolen (wo noch präsent) und ein größerer Marktanteil von Online-Apotheken (auch ermöglicht durch eine europäisch harmonisierten Produktpalette) sein.

Die Nachfrageseite des europäischen pharmazeutischen Marktes zeigt noch sehr große Divergenz zwischen den Mitgliedsstaaten. Die *Verschreiber* stehen allerdings überall unter wachsendem Druck, rational zu verschreiben, was ihre Verschreibungsfreiheit in zunehmendem Maße einschränkt. Wenn Mitgliedsstaaten das Kostendämpfungspotenzial des rationalen Verschreibens ausschöpfen, werden sich die Unterschiede im Konsum von Arzneimitteln zwischen Mitgliedsstaaten wahrscheinlich im Laufe der Zeit angleichen. Der beobachtete Vertrauensverlust im Arzt-Patienten Verhältnis wird wahrscheinlich weiterhin anhalten, nicht zuletzt da Informationen aus dem Internet (leider auch von zweifelhaften Quellen) leicht verfügbar bleiben werden. Das *Europäische Szenario* verstärkt dabei die Notwendigkeit, sich auf europäischer Ebene den gemeinsamen Herausforderungen in einen Europäischen Gesundheitsmarkt zu stellen, während unter einem *Europäischen Krisen Szenario* die Notwendigkeit weniger ausgeprägt ist.

Die *Patientengruppen* sollten ihre Organisationen stärken, um die stark ausgeprägten Informationsasymmetrien zu vermindern, und sich auf Europaebene eine leistungsfähige Teilnahme zu sichern. Die zusätzlichen Erwartungen der Nationalregierungen, dass Patienten einen Teil ihrer Behandlungskosten übernehmen, betont die Notwendigkeit, die Entwicklungen hinsichtlich Gerechtigkeit (Fairness) des Zugangs zu überwachen. Im Moment scheint es weiterhin ein Potenzial für grenzüberschreitende Lieferungen von preiswerteren oder in den Heimatstaaten nicht abrechenbaren Arzneimittel zu geben. Patientengruppen können diese Möglichkeiten in der Zukunft stärker berücksichtigen und diese Informationen an ihre Mitglieder weitergeben. Durch die sich dadurch wahrscheinlich anschließenden Rechtsstreite könnten sie so eine bahnbrechende Rolle in der Schaffung eines klaren europäischen Regelwerkes spielen. Das dies, wie im *Europäischen Szenario* angenommen, letztendlich zu einem paneuropäischen Gesundheitssystem führt, ist nicht undenkbar, allerdings spielen dabei noch eine Vielzahl anderer Faktoren eine Rolle.

Sowohl im *Experten Szenario* als auch im *Europäischen Krisen Szenario* ist die Auswirkung auf die *Kostenträger* eher geringfügig, da sie in ihrer Entwicklung eher von Entscheidungen nationaler Art abhängig sind. Dies beinhaltet bereits sichtbare Initiativen, die zu mehr Wettbewerb im Versicherungsmarkt geführt haben. Würde sich

dagegen das *Europäische Szenario* durchsetzen, könnten Arzneimittel eine katalysierende Rolle im Hervortreten eines europäischen Gesundheitsmarktes spielen, was wiederum zu einem europäischen Krankenversicherungsmarkt, in dem internationale Versicherungskonzerne Policen für einen europäischen (Basis-) Leistungskatalog anbieten, führen könnte. Diese Entwicklung könnte eine internationale Konsolidierung der Krankenversicherer auslösen.

Obwohl im *Experten Szenario* das (europäische) pharmazeutische Regelwerk insgesamt zunehmend europäisch geprägt wird, behalten die einzelnen *Mitgliedsstaaten* die Entscheidungskompetenz hinsichtlich Preisregulierung und Vergütung. Jedoch werden nationale Gesetzgebungen, die nicht-abrechenbaren Arzneimittel und Arzneimitteldistribution unter verstärkter europäischer Beobachtung stehen. Folglich sollten Mitgliedsstaaten ihre gesetzlichen Rahmen prüfen und sie in Übereinstimmung mit europäischem Recht bringen. Die Erwartung, dass abgesehen von den nicht-abrechenbaren Arzneimitteln auch der Generika-Markt zunehmend liberalisiert wird, sollte Mitgliedsstaaten motivieren ihre Preispolitik zu untersuchen, um so einen wettbewerbsfähigen Generika-Markt zu ermöglichen. Die Erwartung, dass eine vergleichende Evaluation von Arzneimitteln zunehmend auf Europaebene stattfinden wird, heißt nicht notwendigerweise, dass die nationalen Entscheidungskompetenzen bei der Arzneimittelvergütung vermindert werden. Eine verstärkte Zusammenarbeit der Mitgliedsstaaten bei der europäischen (vergleichenden) Arzneimittelevaluierung könnte zu einer deutlichen Effizienzsteigerung führen.

Falls sich das *Europäische Szenario* mit einem paneuropäischen Gesundheitssystem durchsetzt, könnten Mitgliedsstaaten zu einer weiteren Zusammenarbeit in Hinblick auf einen europäischen Basiskatalog gezwungen werden, möglicherweise mit zusätzlichem Raum für nationale Kataloge. Anstatt die Idee eines europäischen Basiskataloges kategorisch abzulehnen, wäre es für die europäischen Mitgliedsstaaten sicherlich vorteilhafter, sich auf diese Entwicklung vorzubereiten.

Abstract (English)

The European pharmaceutical sector has received continuous political attention for many years. On a national level, rising expenditures on drugs pose a threat to financing and accessing health care. The pharmaceutical sector, which is frequently growing faster than the GDP and the health sector as a whole, has been the subject of many national cost-containment strategies. On a supranational level, the European Union (EU) has an increasing role. Not only does the EU ensure the satisfactory delivery of public health, it is also concerned with encouraging the innovativeness and competitiveness of this strategically important sector. The main objective of this thesis is to examine the impact of future EU regulation and policy on the various stakeholders in the European pharmaceutical market, with a focus on industry and Member States. To achieve this goal, research was conducted in three steps: (1) a review of the roles, historical contexts and trends of the actors in the European pharmaceutical market, including the EU and Member States; (2) the development of future scenarios for EU pharmaceutical policy and (3) an analysis of the impact of these scenarios on the various stakeholders in the EU pharmaceutical sector.

The first section discusses all actors using a conceptual framework. Stringent cost-containment measures result in smaller profit margins for suppliers of pharmaceuticals (the pharmaceutical industry, wholesalers and pharmacies). When compared to the US, the European innovative pharmaceutical industry lags behind in competitiveness on such factors as research and development (R&D), labour costs and the number of new chemical entities launched. In the wake of the dramatic consolidation trend in the 1990s, European wholesalers tried to cope with the competitive environment by expanding their range of services (e.g. logistics for industry). The pharmacy sector is one of the most heavily regulated sectors and there are substantial differences across Europe in the number of pharmacies per capita. The pharmacy sector is also facing the challenge of competing with pharmacy chains and internet pharmacies

The demand side of the pharmaceutical market (prescribers, patients and payers) is characterized by information asymmetry, in comparison with the supply side. Although a prescriber (doctor) has more pharmaceutical knowledge than a patient, new technologies, particularly the internet, help patients access detailed medical information, which has changed the doctor-patient relationship. Across Europe, prescribing practices and the consumption of pharmaceuticals differ greatly along cultural and national boundaries. Traditionally, there is little incentive for patients to choose less expensive pharmaceuticals, but national policies, such as co-payments, try to increase patient interest. The payer (e.g. sickness funds) must design an insurance policy in a heavily government-regulated environment and thus far have not played a major role in the containment of pharmaceutical costs. This may be due to the existing health care structure in which payers may lack the tools to influence the price and volume of pharmaceuticals.

The regulators in the European pharmaceutical markets are the EU and Member States. European pharmaceutical policy has been dominated by EU industrial policy, which seeks to liberalize the market and create a single European market (SEM) for pharmaceuticals. A remarkable Europeanization trend has been observed over the last 40 years; however, the introduction of legally binding European authorization procedures in 1995 and the establishment of a governing body (the European Medicines Agency, EMEA) may be considered the last major accomplishments. Instead, the European Commission devotes itself to the recommendations of the G10 Medicines Group and focuses on coordinating results rather than secondary legislation, such as directives. The judgements of the European Court of Justice concerning, for example, intellectual property rights, trademarks, patent protection, parallel trade and internet pharmacies have affected national policies and liberalized national markets.

Although market authorization, pharmacovigilance, classification and distribution have gravitated towards European regulation, Member States have kept the competence inside their health systems with regard to pricing and reimbursement following Article 152 of the Treaty establishing the European Community (TEC). Over the last 25 years, Member States have increasingly adopted similar measures to cope

with rising pharmaceutical expenditures, which often showed short-term rather than long-term effects.

The second section describes future scenarios for pharmaceutical policy. Key issues and variables of European pharmaceutical policy were selected from published literature. Next, 41 European experts were selected to participate in a Delphi questionnaire. The results of the questionnaire were used to fill in the Expert Scenario, which was then contrasted with a more pessimistic scenario (the European Crisis Scenario) and a more optimistic scenario (the European Scenario).

(1) The Expert Scenario: Further Europeanization is predicted for the European pharmaceutical market in areas where Europe has most competence and European law has the largest influence. Authorization, pharmacovigilance, classification, distribution and advertising show a gradual trend towards European regulation. Pricing, dispensing, prescribing and reimbursement remain predominantly a national competence and, as a result, limited Europeanization is expected. However, post-licensing evaluation, which takes place within national health care systems as a competence of the Member States, is an exception and it is not expected to remain a solely national matter. It is increasingly adhering to European regulation.

(2) The European Crisis Scenario: There are many major setbacks in the European process, which are largely caused by stalls in the expansion process, a pervasive image problem, an enduring European constitutional crisis and a crisis involving pharmaceuticals authorized through a common European procedure. Due to the number and the magnitude of obstacles, the end result will be a return to national regulation and a freezing of the European process.

(3) The European Scenario: Citizens will have greater trust in the European project after the successful passing of the European Constitution. Member States increasingly suffer from border-crossing patients. This threatens the financial balance of their health care systems and action is required. Member States will collectively develop a common European benefit basket, leading to a Europeanization of the various national health care systems. Ironically, this will not be instigated by the European Commission, but by Member States.

The third section analyses the impact of these scenarios on the various actors. Despite European efforts to make the pharmaceutical industry more competitive, current problems facing the innovative industry may remain in the future. In each of the scenarios, it seems unlikely that pricing will become less restrictive or that reimbursement decisions will be changed. In the absence of such developments, there may be less opportunity to make returns on investments. Nevertheless, the sheer size of the increasingly harmonized European markets may enable synergy in terms of marketing and market launching.

The outlook may be more positive for the generic industry. They will be helped by favourable generic policies (e.g. generic substitution and faster market access) and the existing potential of immature generic markets. Competitiveness is also likely to increase as a result of increasing pressure from foreign competitors, leading to greater international consolidation. There will likely be less competitive pressure under the European Crisis Scenario.

Highly innovative new biotechnology firms (NBFs), which require centralized authorization, have a vested interest in the continuous development of a European market. They may lack the means to file 27 different authorization procedures, which would be the case under the European Crisis Scenario. However, biotech products are also subjected to restrictive reimbursement decisions that are increasingly based on cost-effectiveness studies. Considering their high R&D costs, biotech products are especially vulnerable.

The European wholesaling sector will continue to consolidate internationally, both vertically and horizontally. Wholesalers not only purchase and distribute within national boundaries, they also increasingly engage in cross-border purchasing and distribution, enabled by converging pharmaceutical markets. The wholesaling sector may cope by expanding their range of services and by searching for partners in the pharmaceutical industry. Only under the European Crisis Scenario are they able to retain their leading national position, mostly owing to divergent national frameworks and product ranges.

Pharmacies will be faced with many challenges, leading to a completely different operating environment. They are increasingly the subject of European market liberalization and national cost-containment policies. It seems likely that their golden days will gradually come to an end, based on the assumption that the European Crisis Scenario does not materialize. The result will be a variety of forms of ownership (e.g. insurer-owned and non-pharmacist-owned pharmacies), new vertical combinations, the chaining of pharmacies, the abolishment of state monopolies and the emergence of internet pharmacies enabled by increasingly harmonized products sold in Europe.

There are significant differences between Member States in terms of the demand side of the European pharmaceutical market. Prescribers will be under growing pressure to prescribe conservatively and their freedom to prescribe as they see fit may be increasingly challenged. Differences in consumption patterns are likely to converge over time when high consumption countries realize the cost-containment potential of rational prescribing. Furthermore, the observed loss of trust in the patient-prescriber relationship is unlikely to abate. Information is readily available on the internet and it will only increase, unfortunately not always from credible sources. The European Scenario reinforces the necessity to organize at the European level in order to effectively face common challenges. Such a necessity is not emphasized under the European Crisis Scenario and, therefore, may be less essential.

The various patients groups should improve their organizations in an effort to counter information asymmetry and to participate more effectively in discussions on a European level, discussions that may have far reaching consequences. The growing expectation, on behalf of national governments, that patients should be increasingly responsible for pharmaceutical costs stresses the need to monitor developments regarding equity of access. There seems to be, as of yet, the potential to obtain cheaper and, in the home state, non-reimbursed pharmaceuticals through the cross-border delivery of pharmaceuticals. Patient groups can look into such opportunities and inform their members. They could play a pioneering role, also through litigation and the articulation of these options and force clarity in these frameworks. It is con-

ceivable that this would lead to the emergence of a European health care system as assumed in the European Scenario, but it depends on many factors.

The impact on the payer is negligible in both the Expert Scenario and the European Crisis Scenario. Payers will develop in accordance with decisions made at a national level. Their development is likely to contain visible national trends, which would result in some form of managed competition in the insurance market. Furthermore, in the event that the European Scenario materializes, pharmaceuticals would play a catalysing role in the emergence of a European health market and, possibly in the future, a European health insurance market in which international insurers offer health insurance policies for a basic European health basket. This could also provoke an international consolidation trend between health insurers.

Although the Expert Scenario predicts a Europeanization of the European pharmaceutical framework regarding, for example, authorization, classification (although nationally implemented) and wholesaling, Member States would retain regulatory authority on vital decisions concerning their respective health care systems. However, all national legislation that interferes with non-reimbursed medicines is likely to encounter intensified European scrutiny. Furthermore, the regulatory framework for the pharmacy and wholesaling sector is expected to liberalize over the next 20 years. Therefore, Member States should assess their respective pharmacy and wholesaling frameworks in an effort to improve their adherence to European law. The expected liberalization of the generic market, with the exception of non-reimbursed medicine markets, should motivate Member States to assess their pricing policies in order to facilitate a competitive generic market. The possibility that post-licensing evaluation will become increasingly regulated at the European level would not necessarily threaten the national competence of a particular Member State. Therefore, for efficiency's sake, it is in the best interest of Member States to collaborate in this field. If the European Scenario materializes and a European health care system develops, Member States could be forced into collaborating on a basic European benefits basket, possibly with additional national catalogues. Instead of categorically refusing the idea, it would be prudent to study the various options and potential outcomes in order to be prepared.

Introduction

The European pharmaceutical sector has received continuous political attention for many years. On a national level, the rising expenditures on drugs pose a threat to financing and accessing health care. The pharmaceutical sector, which at times is growing faster than the GDP and the health sector as a whole, has been the subject of many national cost-containment strategies.

Although pharmaceutical policy is primarily considered a national concern (pricing and reimbursement), the role of the European Union is expanding. Not only does the EU ensure the satisfactory delivery of public health, it also encourages innovation and competition. The pharmaceutical sector, a high growth and innovation-intensive industry, is a main provider of employment, the main contributor to the European trade balance and, consequently, it is of high strategic importance. Subsequent reports drafted for the Directorate-General for Enterprise and Industry state that Europe is lagging behind in competitiveness when compared with the US (Gambardella et al. 2000; Pammolli et al. 2004). Indicators like research and development (R&D), size of the European industry and growth rate point out that the European pharmaceutical sector is losing out to its main competitors. Furthermore, EU policy and European law, including the Four Freedoms (the free movement of goods, workers, capital and services), EU competition law and the EU Social Chapter, have resulted in the expansion of regulations, such as anti-trust laws and an increasingly harmonized marketing authorization procedure. The rulings of the European Court of Justice (ECJ) also significantly influence the organization of the health care systems of Member States.

Although the ultimate goal of the EU is the creation of a single European market (SEM), the plan has been modified in an attempt to liberalize the market. Member States are unwilling to give up their regulatory authority out of fear the outcomes will negatively impact domestic industry (i.e. job loss) and their respective health care systems (i.e. more reimbursable products and/or higher prices for pharmaceuticals), depending on state-specific goals. The persistency of this fear is exemplified by the use of the subsidiarity principle.

The High Level Group on Innovation and Provision of Medicines (G10), constituted in March 2001 by the European Commission, resulted in a series of recommendations regarding the European pharmaceutical sector. This report examined how the EU can achieve the seemingly dichotomous goal of innovation (competitiveness) and provision (accessibility) and it provides a direction for EU policy. The G10 recommendations can be seen as a break from the traditional approach, which stresses harmonization in favour of a more realistic approach of co-ordinating national results instead of the underlying rules themselves. However, it remains unclear how the G10 recommendations and traditional EU policy will affect the various stakeholders in the European pharmaceutical sector. This uncertainty weakens national support and threatens to constrain the development of a single European market for pharmaceuticals.

This thesis seeks to estimate the impact of the increasing role of EU policy on the Member States in the European pharmaceutical market. What are realistic and feasible scenarios for the future of pharmaceutical policy? What will be the implications for the delicate balance between the social nature of health services and national competence on the one side and internal market legislation and European competence on the other? What will be the impact on the organization of the pharmaceutical sector? This thesis will also attempt to answer whether EU policy will result in more competitive industry and better pharmaceutical provision. Do national governments have legitimate reasons to be concerned about the impact of EU policy on national policy? Will EU policy lead to job loss, more expensive medicines and restricted access because of changes to the list of reimbursed pharmaceuticals?

Objectives

The main objective of this thesis is to examine the impact of future EU regulation and policy on the various stakeholders in the European pharmaceutical market, with a focus on industry and Member States.

Scope of the thesis

This thesis includes all EU Member States. However, since the EU has only recently begun expanding eastward, emphasis is placed on the original EU15 Member States and their historical contexts. Furthermore, all actors in the pharmaceutical market are included but emphasis is placed on supply side actors and Member States. The period 1960 to 2025 is used as the timeframe.

In achieving this goal, research was conducted in three steps:

1. A **literature review** of the roles, historical contexts, characteristics and visible trends of the actors in the European pharmaceutical market, including the European Union and Member States
2. The development of **future scenarios** for EU/Member State pharmaceutical policy
3. An **analysis** of the impact of these scenarios on the various stakeholders in the EU pharmaceutical sector

Research strategy, methods used and structure of thesis

This thesis takes a qualitative approach. A literature review provides the background information for the scenarios. A scenario is a compilation of trends that provide a possible outcome for the future. Scenarios are useful tools for uncovering new information and showing how interacting sets of trends may lead to a range of conditions (Garrett 1999). The following fundamental components are involved in creating scenarios, as described in the World Health Organization (WHO) commissioned "Health futures: A handbook for health professionals" (Garret 1999):

- Clarifying issues
- Acquiring information
- Analysing the system
- Describing the past and present
- Imagining future trends
- Framing the scenarios
- Filling in the scenarios
- Evaluating the scenarios
- Applying the results

Such a structured approach decreases the chance that important issues are overlooked, therefore, contributing to the validity and reliability of the research. Applied to the three-step approach, the following plan was developed and implemented:

Part I: Literature review

Tasks:

- *Clarify issues*: Which issues need to be addressed and which issues will be given priority? This step was necessary to ensure that nothing was overseen and that the scope of the research was clear. This step is described in the introductory chapter.
- *Acquiring information*: A literature review was conducted and search criteria were drafted, which were applied accordingly:
    - Searching grey sources of information. Searching the internet using conventional search engines
    - Searching online databases. Searching PubMed, EconLit, IBSS, Decomate II and Medline
    - Searching European Commission documents and ECJ rulings
    - Manual search of relevant journals such as Pharmacoeconomics, Health Economics, Journal of Health Economics, Health Planning and Management, and Health Policy
    - Systematically tracing back relevant references
- *Analysing the system*: In this step, information was analysed in order to understand the structure or system under consideration (Garret 1999). Activities consisted of determining the structure of the pharmaceutical market, identifying which input variables are important and identifying the actors and the strategies that they used. What are their goals, activities, resources, limitations, behaviours, interests, mechanisms, schemes and relations? The results of this step created the conceptual framework of the pharmaceutical market presented in Chapter 1.
- *Describing the past and present*: A review was written on the current state of the European pharmaceutical market, including actors (Chapter 2), the European Union and European pharmaceutical policy (Chapter 3) and national pharmaceutical policy (Chapter 4). This review provided the foundations for the scenarios.

Part II: Building scenarios

Tasks:

- *Imagining future trends and events*: A list of uncertainties and trends for the future was formed through systematic scanning of social, economic, technological and political factors. Then, projections were made of current trends in key variables. The results of this component include any projections regarding trends in key variables, in addition to the generated list of possible future trends and events. Applied to the European pharmaceutical market, trends and/or events were the full adoption of G10 recommendations or more national autonomy, which made the key variable ranging from EU regulation to national regulation.
- *Framing the scenarios*: This step involved making assumptions. These assumptions are often expressed as conditional phrases, such as "if G10 recommendations are adopted" or "if SEM for medicines could be achieved, the future would look like …". A base scenario (a scenario based on current trends) was constructed, which was then contrasted with a more pessimistic and a more optimistic scenario. Another approach would have been to generate two axes of uncertainty (a spectrum), using the information uncovered at the previous step (imagining future trends and events). These axes could then have been used to build a matrix (two axes crossing), which would result in four different quadrants and four different scenarios. However, in order to conduct a feasible research and analysis, this approach was discarded. The Delphi technique was used to make assumptions. It is a method of obtaining a reliable consensus from a group of experts through a series of questionnaires interspersed with controlled feedback (Garret 1999). In the Delphi questionnaires, experts were asked to predict the nature of selected topics, for example, in 2010, 2015 and 2025. After two rounds, a consensus on the various trends became apparent, providing the foundations of a (base) scenario. The chosen methodology is discussed in detail in Chapter 5 and its results are outlined in Section 6.1.
- *Filling in the scenarios:* The scenarios were filled in after a decision was made about the frame. The frame was set according to the assumptions and key variables predicted for the future. The construction process involved finishing these assumptions and discussing what would happen if the assumed conditions, in fact, developed in the future. This included outcomes on key issues, those addressed in *Clarify Issues* (Step 1), as well as narrative descriptions (Section 6.2), for which the literature review was consulted (Chapters 3 and 4).

Part III: Analysis

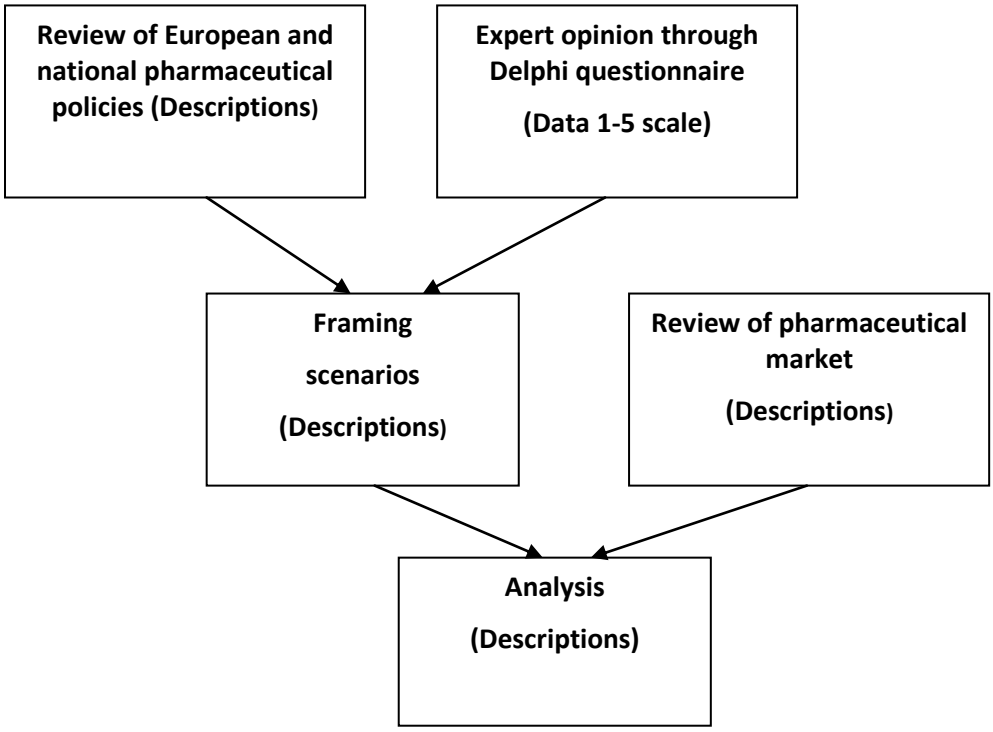
Tasks:

- *Evaluating the scenarios:* The impact of the scenarios on the various stakeholders was made on key issues (Chapter 7) through systematic analysis and the interpretation of the scenarios and using the information from Step 1. What threats and opportunities could these imagined scenarios present?
- *Applying the results*: After the scenarios have been created and their implications identified, the results of work can finally be applied (Garret 1999). In the application stage, the results of the evaluation were interpreted, after which advice and recommendations were given in the form of a discussion.

Methodological background

It is important to note that the analysis in Part III is based on certain hypothetical assumptions. These assumptions, which were made while framing the scenarios, are based on the interpretations of the data provided by international experts in the European pharmaceutical policy questionnaire. To boost the validity of these scenarios, experts have been selected according to several criteria and questioned on a variety of pharmaceutical policy-relevant topics (see Part II). The interpretations of the data (see Figure 1 for a schematic depiction), which came in the form of numbers on a five-point Likert scale, was done using the knowledge and findings of an extensive review of European and national policies (see Chapters 3 and 4 of Part I). In Part III, these scenarios are interpreted in the light of the findings from Chapters 1 and 2 (Part I). To increase the transparency of the analysis, references are used where the analysis bases itself on previous research and on references from Part I of this thesis.

Figure 1. Schematic structure of the thesis.



PART I: REVIEW

1 Conceptual model of the European pharmaceutical market

The pharmaceutical market is a complex market shaped by competing policy goals and interests and frequent public intervention. The number of conflicting actors makes this market an extremely intricate system. Not only do different policy goals and perspectives exist between the various actors in the market, differences also exist within actors. National governments, for example, have to fulfil both health care and industrial policy goals. Due to the high number of actors, it is useful to organize them according to a conceptual model. Therefore, this chapter will discuss a simple model of the European pharmaceutical market, which is used as the basis for analysis and is based on the pharmaceutical value chain and the medical care triad. Next, the other actors are identified together with their policy perspectives and functions. The model clearly demonstrates that the European pharmaceutical market, in fact, consists of three markets on different levels (Schut 1993). The vertical chain of producer, wholesaler and pharmacist forms the supply side of the pharmaceutical market or the pharmaceutical value chain, while consumers (patients), prescribers (physician) and payers comprise the demand side. European and national regulations impact all levels.

The value chain consists of several links (see Figure 2). The first link consists of the manufacturers, the pharmaceutical industry and the importers of pharmaceuticals. Manufacturers and importers form the first market, from where they deliver their products to wholesalers. There are roughly three types of manufacturers: manufacturers of innovative pharmaceuticals, manufacturers of generics and new biotechnology firms (NBFs).

Innovative, branded pharmaceuticals are mostly on-patent, which allows the company to sell the product without competition and regain investments made in costs it made in R&D. As soon as the pharmaceutical loses its patent, other producers can produce the drug, set their own price and try to compete for market share. These

off-patent drugs, known as generics, are nearly perfect substitutes and are often more affordable alternatives to patented pharmaceuticals (Mrazek and Frank 2004). The innovative industry has higher R&D costs but it can receive a high return on investment when new drugs are licensed and reimbursed. Another important aspect of this market is that it is highly international. Many innovative companies are multinationals that deliver their products internationally. The generic industry, however, mainly operates within national borders.

In the second market, wholesalers distribute pharmaceuticals to pharmacies. There are two types of wholesalers: full-line wholesaler and short-line wholesaler. While the former provides a full range of drugs and operates on a national or regional level, the latter provides a specialized limited range, often at competitive prices. Not all European countries allow short-line wholesalers (e.g. France and Italy) because there is a perceived public interest (Taylor et al. 2004a). In contrast with globally-operating manufacturers, most wholesalers traditionally conduct business within their domestic market, although there is an observed consolidation trend, fuelled by the pursuit of economies of scale. Various sizes and forms of pharmacies exist within the EU. Most important European variants are community pharmacies and hospital pharmacies. Mail-order and online pharmacies are growing in popularity. Due to public health priorities and its key position in controlling pharmaceutical expenditures, pharmaceutical distribution is subject to strong national regulation. It is worth noting that the lines between manufacturers, wholesalers and community pharmacies become blurred in cases where there is vertical integration between them (Taylor et al. 2004a). This second market has many international characteristics, though not to the same degree as the first market.

In the third market, the drug gets dispensed to the consumer. The physician prescribes the drug and the consumer collects the pharmaceutical and receives reimbursement from the payer. Strong information asymmetry exists between the demand side (consumer, payer and prescriber) and the supply side (manufacturer, wholesaler and pharmacist). Furthermore, it is an insurance market in which the payer has to facilitate access to drugs for the most vulnerable groups in the population, as individual expenses can be quite substantial. The insurance system removes

the incentive for the consumer to opt for less expensive pharmaceuticals, which greatly increases the chances for moral hazard. The prescriber's chief duty is to prescribe the pharmaceutical he/she deems appropriate, regardless of price. This third market is primarily national and is subject to various strict national regulatory frameworks. The medical care triad depicts the health insurance market in a fundamental way to illustrate that payers mediate between the provider and patients. The triad constitutes the bottom part of the model and forms the demand side of the pharmaceutical market.

The pharmaceutical market is far more intricate than these three markets suggest. These markets consist of smaller, highly fragmented markets for specific therapeutic classes of pharmaceuticals in which certain manufacturers are strongly represented and often dominate during the duration of their patents. The pharmaceutical market, therefore, is characterized by monopolistic and oligopolistic market structures. Other relevant classifications are prescription-only medicines (POMs), which mainly consist of publicly reimbursed innovative and generic drugs and over-the-counter drugs (OTCs), also referred to as non-prescription pharmaceuticals. This is not an exhaustive list as more classifications and definitions will be discussed in due time.

National governments and the European Commission are not a direct component of the pharmaceutical value chain, but both have had an increasingly important role within the European pharmaceutical market. National governments and the European Commission exert influence on all levels as the most important policy makers and legislative powers. One cannot conceive a national government or the European Union as one single actor. Both have different departments and institutions, which represent different stakes and views. All these departments and institutions influence the actors according to their specific policy objectives. Generally, there are two main competing pharmaceutical policy interests: health policy and industrial policy (see Table 1). However, there are also two potentially conflicting perspectives within health policy: the health care perspective and the public health perspective.

At the national level, health policy is dictated by the health ministries of Member States. The Ministry of Trade and Industry advocates for industrial policy. At the supranational level, the Directorate-General for Health and Consumer Protection main-

ly advocates for public health policy objectives, less so for health care perspectives. Industrial policy is the domain of the Directorate-General for Enterprise and Industry.

Table 1. Competing policy objectives regarding pharmaceuticals.

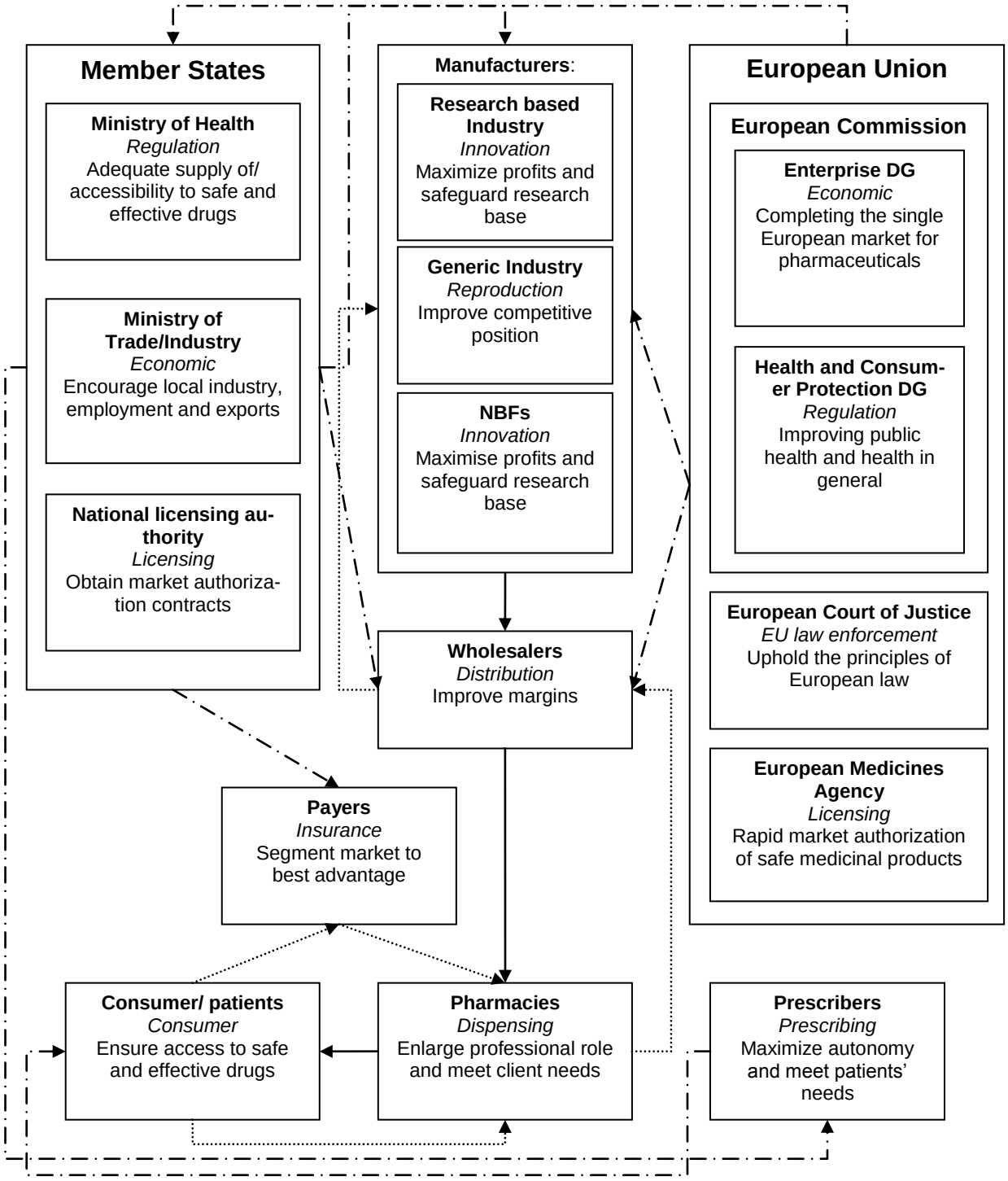
Health policy		Industrial policy
Health care perspective	**Public health perspective**	
Containing cost and improving efficiency in health services and care	Safe medicines	Promoting local research and development capacity
Cost-effective medication	High-quality preparations	Protecting intellectual property rights
Regulating doctor and consumer behaviour regarding medicines	Efficacious treatments	Supporting local scientific community
Generic promotion and/or substitution	Innovative cures	Generating and protecting employment
Improving prescribing	Patient access to medicines	Promoting small and medium enterprise policies
Ensuring access to medicines		Contributing to positive trade balance
		Sustaining the university research base

Source: Permanand and Altenstetter (2004).

The European Medicines Agency (EMEA) and the respective national licensing authorities are responsible for the admission of pharmaceuticals to European markets. A pharmaceutical company can submit a pharmaceutical to more than one Member State through the centralized procedure (EMEA) or the decentralized procedure (through a national licensing authority). When a pharmaceutical company seeks to submit a pharmaceutical to only one Member State, it is accomplished through a solely national procedure (by a national licensing authority). The EMEA is regulated by the DG Enterprise and Industry. The European Court of Justice also wields considerable influence. It is the function of the ECJ to uphold the principles of European law, including the free movement of goods and free competition. Its rulings can significantly impact national policies.

The following chapters of Part I elaborate on the actors of the pharmaceutical market. Chapter 2 describes the supply and demand sides of the European pharmaceutical market, whereas Chapters 3 and 4 discuss the respective roles of the European Union and Member States.

Figure 2. Stakeholders in the European pharmaceutical market: functions and policy objectives.



Based on: Nyfer (1997) and Permanand and Altenstetter (2004).

2 The European pharmaceutical market: A description

In this chapter, the European pharmaceutical market is described according to the model outlined in Chapter 1. This chapter seeks to describe the characteristics and trends of the actors, such as size and market behaviour. The regulation that applies to these stakeholders is discussed in Chapters 3 and 4.

The European pharmaceutical market (see Table 2) is one of the largest in the world, covering roughly between 26% and 30% of the world share in the last decade. Moreover, the pharmaceutical sector provides a significant contribution (over €22 billion in 2001 and over €30 billion in 2004[1]) to the EU trade balance and is the fifth largest industrial sector in the EU, amounting to 2.8% of the total manufacturing production for the EU15 and to 2.71% for the EU25 (Eurostat in: Pammolli et al. 2004). Although roughly the same size at the beginning of the 1990s, the European market is no longer growing at the same rate as the North American market. Nonetheless, European pharmaceutical trade involves many people on different levels and is of considerable economic importance to almost all European Member States.

Table 2. Size of the market for pharmaceuticals, 1989–2003.

	1989	1990	1995	1998	1999	2000	2001	2002	2003
Total (USD billion)									
World	155.3	165.8	280.3	300.6	332.6	357.3	389.4	424.8	491.7
Regional share (%)									
North America	34.0	32.4	31.2	39.2	41.5	44.0	47.2	48.4	46.7
Europe	31.0	26.5	29.6	28.4	26.3	23.7	24.0	25.0	27.5
Africa/ Australia/ Asia	30.0	35.1	32.4	25.1	25.9	25.8	22.9	21.7	21.4
Latin America	5.0	5.9	6.8	7.4	6.2	6.5	6.0	4.9	4.5

Source: IMS International in: Pammolli et al. (2004).

In Europe (2003), the largest markets are Germany (€24 631 million), France (€22 583 million), Italy (€15 592 million), Spain (€10 794 million) and the UK (€10 386 mil-

[1] According to Eurostat on DG Enterprise site, accessed 01/08/2007.

lion). They are the largest global markets after the US (1st) and Japan (2nd; IMS International in: Pammolli et al. 2004). The following sections discuss the supply and demand of the European pharmaceutical market.

2.1 Supply side

The supply side of the pharmaceutical market (i.e. the pharmaceutical value chain) is often referred to as the "golden chain" due to the potential for high profit achieved by manufacturers, wholesalers and pharmacists. However, the operating environment has changed over the last decade. Governments have been putting greater emphasis on cost-containment, which puts pressure on the profit margins of pharmaceutical suppliers. Another important development is new technology, most notably the emergence of life sciences and the rising role of the internet. The former enables new processes of drug discovery and development for the pharmaceutical industry, while the latter is challenging distribution and the pharmacy sector with online pharmacies.

2.1.1 European pharmaceutical industry

Historically, big pharmaceutical industries and major innovations were the domain of German and Swiss companies, a position that was increasingly challenged after the Second World War by firms based in the US and UK. In the years following the war, the pharmaceutical industry experienced a boom, also spurred by new research opportunities created by advances in the field of synthetic drugs. This ushered in the first golden age of the pharmaceutical industry and, as a result, it became known for being a growing innovation-intensive industry, one crucial to a country's economy and public health. However, the thalidomide disaster of the 1960s (see Chapter 3), waning innovation in the 1970s and growing criticism regarding the burden of pharmaceutical cost on health budgets (Feick 2000) contributed to a decline in the industry's image.

The thalidomide disaster highlighted the need for stricter pharmacovigilance. Consequently, national regulatory mechanisms were put in place throughout Europe during the 1960s. In the early years, these regulatory systems mainly safeguarded the quality and accessibility of pharmaceutical provision (i.e. public health perspec-

tive). However, as early as the 1980s, containing pharmaceutical expenditures (i.e. health care perspective) became more and more a policy objective in European States, making the operating environment of the pharmaceutical industry even more difficult. The results were more stringent pricing and reimbursement regimes, which affected the structure of demand in all major markets.

Furthermore, new technological developments in the field of life sciences caused not only a complete overhaul of the processes of drug discovery and development, but higher R&D costs. This development, along with increased pressure from cost-containment policies, caused more globally-operating companies to seek economies of scale, often through mergers, joint ventures and acquisitions and to conduct larger, costlier internationally-based clinical trials. Developments in legislation and in the legal interpretation of intellectual property rights, as well as the recent openness of domestic markets to foreign competition, have influenced patterns of industrial competition and have altered the structure of the industry (Gambardella et al. 2000). These developments suggest an increase in the resources needed to develop new drugs and have led to a reorientation towards core competencies like R&D and innovation, in addition to marketing and distribution.

Industry structure

Two types of pharmaceutical producers exist within the European pharmaceutical industry: manufacturers of patented (innovative) drugs and manufacturers of generic drugs. The innovative industry consists of globally-operating, multinational companies, which cover between 40% and 60% of most national markets in advanced countries (Gambardella et al. 2000). These companies are typically represented in many countries on different continents. Although they have a good share of activities and sales in their respective domestic markets, they also set divisions and activities in other countries and regions, particularly in Europe and the US. These are highly R&D-intensive companies with large R&D and marketing divisions. Investments can be re-earned through patents, which allow companies to have a temporary monopoly.

The generic industry typically exists of smaller national companies, operating almost exclusively in their domestic market. They are specialized in the sales of off-patent (generic) and non-R&D-intensive pharmaceuticals. They conduct mainly manufac-

turing and commercialization activities and do not invest in R&D (Gambardella et al. 2000). Off-patent drugs are free for other companies to produce and, consequently, there is more price competition in their segment and prices can be expected to be lower than in-patent drugs.

In the last twenty years, the so-called new biotechnology firms (NBFs) have emerged among national companies. These research-intensive companies developed from opportunities presented by the life sciences. These companies specialize in biotechnology and their activities range from the discovery and development of new drug compounds to the development of new drug screening and research tools and to the development of technologies in related fields, such as genomics and bioinformatics. In order to develop products, NBFs must compete for financing and the attention of large multinationals, which are the market incumbents and have the necessary sales channel. The multinationals are eager to put the biotech products in their portfolios through biopartnering (EuropaBio 2005).

The European pharmaceutical industry is a high growth manufacturing stronghold in many Member States, with the largest pharmaceutical production in France, which generated a production value of €34 495 million in 2001, followed by Germany with €23 251 million and the UK with €17 224 million (see Table 3).

Table 3. Production value, pharmaceuticals (NACE 24.4), constant million, €, 1995–2001.

Country	1995	1996	1997	1998	1999	2000	2001
France		23554	26002	27891	29868	33065	34495
Germany					20870	22158	23251
United Kingdom		10265	13111	12979	14375	15782	17224
Italy	11954	14696	13732	14703	15843	15342	15674
Spain	6190	6411	6117	6165	6427	6872	7528
Belgium	4143	4033	4051	4041	5059	5672	6655
Netherlands	3283	4069	4601	4853	5217	5494	5489
Denmark	2216	2505	2866	3081	3467	3318	3910
Ireland	1732	1699	2086	2337	3618	3932	3898
Austria	1468		1657	1919	1777	2432	1781
Finland	665	652	732	688	704	755	826
Portugal	921	811	915	740	813	790	729
Slovak Republic	175	197	196	164	144	143	158
Czech Republic	314	295	311	248	244	313	329
US	67394	70671	74917	82214	95446	117460	114039

Source: Eurostat and OECD in: Pammolli et al. (2004).

The leading pharmaceutical corporations in the European market are also among the leading corporations in the world (see Tables 4 and 5). After the heavily contested 2004 takeover of the German-French-owned Aventis by the French Sanofi-Synthelabo, the new Sanofi-Aventis is the largest competitor in the European pharmaceutical market, with a market share of 8.5% (2005), followed by the American-owned Pfizer with 7.2% and the Swiss-owned Novartis with 5.9%. The largest ten companies in Europe have a market share of 47.2%.

Table 4. Leading pharmaceutical corporations (turnover) worldwide, 2005.

Rank	Corporation	Millions (€)	Market share (%)
1	Pfizer	39 341	8.4
2	GlaxoSmithKline	28 820	6.2
3	Sanofi-Aventis	24 553	5.3
4	Novartis	23 212	5.0
5	Johnson & Johnson	21 100	4.5
6	AstraZeneca	19 917	4.3
7	Merck&Co	19 516	4.2
8	Roche	16 276	3.5
9	Abbot	13 073	2.8
10	Wyeth	12 230	2.6
	Subtotal	218 039	46.8
	Total worldwide	466 016	100.0

Source: IMS in: GIRP (2005).

Table 5. Leading pharmaceutical corporations (turnover) in Europe, 2005.

Rank	Corporation	Millions (€)	Market share (%)
1.	Sanofi-Aventis	10 051	8.5
2.	Pfizer	8564	7.2
3.	Novartis	7041	5.9
4.	GlaxoSmithKline	7024	5.9
5.	AstraZeneca	5671	4.8
6.	Roche	4559	3.8
7.	Merck&Co	3835	3.2
8.	Johnson & Johnson	3723	3.1
9.	Wyeth	3016	2.5
10.	Lilly	2642	2.3
	Subtotal	56 124	47.2
	Total Europe	118 794	100.0

Source: IMS in: GIRP (2005).

According to the European Federation of Pharmaceutical Industries and Associations (EFPIA) in 2004, the research-based pharmaceutical industry accounted for about 3.5% of the total EU manufacturing value added and for 15% of the total R&D expenditures of EU businesses. Furthermore, the European research-based industry employs 588 000 people, of which 100 500 are in R&D units. R&D investment in 2002 was €20 200 million (up from €7900 million in 1990) and the trade surplus amounted to €36 000 million in 2002. According to the European Generic Medicines Association (EGA), their members (i.e. the European generic industry) employed over 100 000 people in 2003.

The European biotechnology industry is comprised of 1976 companies, mainly in Germany (525), the UK (455) and France (225) and employs 94 000 people, of whom 35 000 are in R&D (EuropaBio 2005).[2]

The Pammolli Reports on the competitiveness of the European pharmaceutical sector

In 2000, a Pammolli report, "Global Competitiveness in Pharmaceuticals: a European Perspective", was drafted for the Directorate-General for Enterprise and Industry (Gambardella et al. 2000) addressing the global competitiveness of the European industry. It states that the European pharmaceutical industry has been a stronghold of the European industry, providing by far the largest contribution to the European trade balance in high-technology, R&D intensive sectors. It is a main source of employment and a producer of pharmaceuticals, which are greatly important in achieving public health policy goals in all countries. For these reasons, the European pharmaceutical industry is regarded as a strategically important area for the welfare of the European Union. However, this sector has begun to show cracks in its foundations. The report shows that the European pharmaceutical sector is losing out to the United States and it provides four conclusions:

1. The European pharmaceutical sector is more labour intensive than the US or Japanese industries. The US and Japanese industries rely on non-labour inputs, such as capital or R&D. Consequently, specialization is less pronounced in R&D activities and non-R&D-intensive firms have a larger presence in European industry. Furthermore,

[2] The 2005 EuropaBio study only surveyed 15 European countries, namely the EU15, excluding Luxembourg and Greece but including Norway and Switzerland. Therefore, this number does not take the new EU accession countries into account.

the European pharmaceutical industry grew less than the US industry in the 1990s, which was mostly due to the growth of American non-labour inputs (including R&D). Also, these developments should not be separated from the effects of national regulatory regimes (e.g. pricing policy).

2. Globally-operating multinationals largely compete for new innovative products or new chemical entities (NCEs), which require substantial R&D investments. In the 1990s, US companies had become clear leaders in NCE sales. European multinationals, on the other hand, tend to have older portfolios of products than US firms. US firms enjoy a comparative advantage when selling their new drugs. The US market grew rapidly in the 1990s after being roughly the same size as the European market at the beginning of the decade. Although these multinationals operate internationally, the bulk of their sales are within their own domestic market.
3. The US also became the leader of innovation in pharmaceuticals during the 1990s, whereas Europe remains unable to produce a full-fledged industry of innovation-specialized companies and technology suppliers. Furthermore, European companies increasingly rely on the US for sources of research capabilities and innovation. The US biotechnology industry created a large number of new jobs and produced many new world-class drug companies (e.g. Amgen, Chiron, Genzyme), several new drug tool companies and a stream of revenues in the form of royalties from licenses or R&D contracts and collaborations.
4. While some are more competitive than others, national European markets need to improve in overall competitiveness. This is demonstrated by the data on prices and market share after patent expiration as illustrated in the report. In a competitive market, a price drop, often caused by the entry of cheaper generics, is a typical consequence of patent expiration but in many European markets, there is no substantial change. This nurtures inefficient behaviour and a lack of competitiveness.

The Pammolli report was one of the main reasons for the instalment of the G10 Medicines Group. The European Commission adopted the vision displayed in the report on headlines. Strengthening the competitiveness of European pharmaceutical industry has since been an important EU industrial policy objective (see Chapter 3).

A 2004 update by Pammolli et al. made clear that the European pharmaceutical industry is still behind in R&D and in other factors, excluding labour (e.g. on capital). Even if the European industry has experienced a substantial reduction in the share of

labour cost on the value of production in 2000 and 2001, the European industry is still labour-intensive compared to the US. Moreover, the share of added value over production is still lower in Europe than in Japan and the US. US firms still lead in terms of innovative activities, sales and geographical diffusion of NCEs launched in the market place. Although European corporations have increased their market shares and the share of total sales from newly introduced products, they are still behind US firms.

These patterns were, as far as the biotechnology sector is concerned, confirmed in the 2005 report "Biotechnology in Europe: 2005 Comparative Study" drafted for the European Association for Bioindustries (EuropaBio). The report states that the European biotechnology sector does not compete with the US sector in terms of any measurable value (e.g. number of employees, R&D, revenues and venture capital raised, with the notable exception of company numbers) and that European entrepreneurs establish companies at a 50% higher rate than the US. The report identifies "the financing gap" as the main obstacle for a competitive European biotechnology industry, which results in a high amount of collapsed companies after three to five years.

2.1.2 Wholesalers

The wholesaling sector has undergone the same trends as those in the pharmaceutical industry sector. Due to competitive pressures, stringent national market regulation and decreasing profit margins (approximately 27% since the beginning of the 1990s), a dramatic consolidation trend occurred in the last decade, which slowed down to some extent between 2000 and 2004 (Clement et al. 2005). This trend leaves winners with a new strategic orientation and large market shares. In the early 1990s, there were approximately 600 nationally operating full-line wholesalers in the EU15 countries, compared to 151 as of 2004 (Clement et al. 2005). There are considerable differences in the number of wholesalers in each country. Of the 600 national full-line wholesalers in 1992, 70% were based in Italy and Spain (Taylor et al. 2004a), but the consolidation trend is visible throughout Europe. For example, from 1992 to 2002, the number of wholesalers in Italy went down from 259 to 149, from 25 to 16 in Germany, from 19 to 11 in France, from 20 to 14 in the UK, from 41 to 27 in Bel-

gium and from seven to four in the Netherlands. In Poland, a new accession country, the number went down from 600 to 250 in the same period (Long 2002).

The effect of this development is that in many European markets the three largest wholesalers have huge market shares varying from roughly 40% to 95%. In 2002, the actual percentages varied from about 36% (Spain), 43% (Italy), 62% (Germany), 75% (France), to as high as 85% in the UK (Long 2002). This makes the wholesale market in many of the Member States an oligopoly. As of 2004, the EU22[3] had 673 regional and national full-line wholesalers (cf. EU15 holds 418 of this total), which operate a network of 1458 warehouses (Clement et al. 2005). The European countries that still have a relatively high number of wholesalers, mainly the new Member States, will probably continue to observe the consolidation trend, whereas further concentration may be met with anti-trust law in the markets of other Member States.

Another strategic response to coping with increased competitive pressures is vertical integration (where legally permitted), which creates new combinations and blurs the traditional division between actors in the pharmaceutical value chain. Many combinations are observed: integration between wholesalers and the pharmaceutical industry with the pharmaceutical company owning the wholesaler (e.g. Italian manufacturer Angelini and Italian wholesaler Adivar) or a wholesaler having generic production facilities, wholesalers owning their own pharmacies (e.g. OPG in the Netherlands) or pharmacy associations owning their own wholesaler (e.g. Sanacorp in Germany). An example of far-reaching vertical integration is the retail chain Boots,[4] which maintains manufacturing, purchasing, distribution and retailing capabilities. Another interesting example is the planned takeover of the mail-order pharmacy DocMorris by the wholesaler Celesio, in the hopes of facilitating the establishment of the first pharmacy chain in the German market (IHT 2007). Celesio expects that pharmacy chains, which are forbidden in Germany, will become a reality through the liberalizing effects of EU law. This also applies to other countries, such as Austria and Spain.

[3] EU25 minus Cyprus, Malta and Slovakia

[4] In July 2006, Boots Group and wholesaler Alliance UniChem merged to create Alliance Boots.

As the process of horizontal and vertical integration reaches its limits in some countries, wholesaling companies will also seek a competitive advantage by increasing the range of services beyond their traditional logistics function. These additional services create an added value for manufacturers as well as for distribution partners (retail pharmacies) and they may be provided for free. For example, full-line wholesalers increasingly offer pre-wholesaling services (e.g. warehousing, storage, distribution and financial administration) to pharmaceutical manufacturers (Clement et al. 2005).

While these companies began as national wholesalers, many of them are also entering foreign markets through takeovers and mergers. According to the European Association of Pharmaceutical Full-line Wholesalers (GIRP 2003), the leading pan-European companies (those present in more than 10 European countries) are: Alliance UniChem, Celesio and Phoenix. Other major, more domestically-oriented European companies are Anzag, Noweda and Sanacorp (Germany), Cerp Rouen (France), OPG (Netherlands), United Drug (Ireland) and Galenica (Greece). In 2004, the three leading European wholesaling companies held a market share of 43.4% in the EU15 and a 46.5% market share in the EU22 (Clement et al. 2005). Although major wholesalers purchase pharmaceuticals on a European level, the wholesaler-pharmacy relationship is conducted within national boundaries. Even in the case of multinational wholesalers, pharmacies are supplied by the locally based subsidiary. This is not only because of differing controls on product price mark-ups (Taylor et al. 2004a), but also because of different packaging, leaflets and language requirements due to previously non-harmonized national legislation.

Parallel trading

Parallel trading is now well-established among the main European wholesalers. Initially, wholesalers were reluctant to participate in this trade, mainly fearing profit loss and a bad relationship with their supplier (i.e. the pharmaceutical industry), which actively opposes parallel imports. Wholesalers find themselves backed by the EU and its support for parallel trade. However, an ECJ ruling challenged the Commission's ability to force the pharmaceutical industry to provide unlimited volumes of medicines to parallel importing wholesalers; in 1996 it overturned a European Com-

mission fine worth 3 Million ECU on the Bayer Group for limiting the supply of Adalat (also see 3.4.2).[5]

The benefits of parallel trade in terms of benefits for patients and health budgets are heavily debated. Three major studies have dominated public debate on parallel trade. The first study, commissioned by the parallel trade-promoting European Association of Euro-Pharmaceutical Companies (EAEPC)[6] and carried out by the York Health Economics Consortium, found evidence that parallel imports have indirect competitive effects by forcing down the price of domestic counterparts, resulting in direct and indirect savings from parallel trade (West and Mahon 2003). A second study by the London School of Economics (LSE), partially funded by the pharmaceutical company Johnson and Johnson, draws an opposing conclusion. It states that benefits to patients and health care systems are negligible and that the main beneficiaries are the parallel-importers (Kanavos et al. 2004). In an attempt to settle these opposing views, the EAEPC commissioned the University of Southern Denmark to review the theoretical arguments and empirical evidence. The report concludes that parallel distribution generates considerable savings, direct saving to both patients and health payers, up €441.5 million in 2004 in Denmark, Germany, Sweden and the United Kingdom. Furthermore, the level of savings and differences between countries depend, to a large extent, on the way countries have incentives in place to stimulate the use of imported products over local product and also in the way measures are in place (e.g. claw backs) so that savings are passed on to the health system and eventually to the patient. To overcome the losses through parallel trade, manufacturers have developed defensive strategies, such as controlled supply of raw materials (licences), restrictive distribution agreements, product differentiation, multiple small batches and supply restrictions, i.e. limiting sales to win market share (Enemark et al. 2006)

[5] Case T-41/96 R. Bayer AG vs. The Commission of the European Communities (Adalat).

[6] The European Association of Euro-Pharmaceutical Companies (EAEPC) is the professional and representative body of pharmaceutical parallel trade in Europe that is aimed at promoting the free movement of medicinal products. Its membership amounts to over 70 firms from 16 countries in the European Economic Area (EEA).

2.1.3 Pharmacies

The pharmacist has traditionally been responsible for the safe dispensing and, in some cases, manufacturing of medicines. Herein, his/her role is strictly separate from the doctor's responsibility of prescribing the pharmaceutical. However, some considerable exceptions exist and have existed. For example, until the late 1940s, many English GPs dispensed the medicines they prescribed. GPs in more rural areas in Austria were also involved in dispensing. In the Netherlands, there are still about 490 pharmacy-owning GPs, which are called *Apotheekhoudende Huisartsen* (RIVM 2004a). This number is down from about 636 in 2000 (RIVM 2004b), which was about 6% of the total number of GPs in the Netherlands and they were mainly established in rural areas.

There are about 117 000 community pharmacies across the EU15 Member States (see Table 6). In each country, there are significant differences in the number of pharmacies per capita. Greece, for example, has more than seven times as many pharmacies per million inhabitants than the Netherlands. Belgium also has about five times more pharmacies per million inhabitants than the Netherlands. In general, Southern European countries have more pharmacies than Northern European countries. In most countries community pharmacies outnumber hospital pharmacies by 12:1 (Belgium, Denmark) to 25:1 (Spain and Germany). In the Netherlands, this ratio is about 6:1 (Taylor et al. 2004a).

Significant developments are the chaining of pharmacies and the emergence of mail-order pharmacies. Where permitted, pharmacies are chaining in varying degrees in Belgium, Ireland, Italy, the Netherlands and the UK. The development of mail-order and online pharmacies was highly controversial and continues to be opposed by many pharmacists, who think that medicines should be dispensed under supervision in a conventional pharmacy and fear decrease in revenues. However, after initial warnings concerning the purchase of medicines over the internet (PGEU 1999), the Pharmaceutical Group of the European Union (PGEU), which represents community pharmacists in 29 European countries including most EU Member States, approves of online pharmacies and wants to collaborate on the development of e-health and e-enhanced pharmacy applications (PGEU 2001).

Table 6. Number of pharmacies in the EU15.

	Number of pharmacies	Pharmacies per million inhabitants (ranking)
Austria	1086	134.1 (14)
Belgium	5273	517.0 (2)
Denmark	1556	293.6 (6)
Finland	795	152.9 (13)
France	22 689	383.9 (4)
Germany	21 590	263.0 (9)
Greece	8348	787.5 (1)
Ireland	1186	320.5 (5)
Italy	16 382	287.4 (7)
Luxembourg	79	197.5 (12)
Netherlands	1600	101.3 (15)
Portugal	2778	277.8 (8)
Spain	19 439	493.4 (3)
Sweden	1889	212.2 (10)
United Kingdom	12 311	207.6 (11)
EU15 total	117 000	

Source: Paterson et al. (2003).

The notion that all national and European regulation should apply equally to online services is key. A Finish study from 2005 (Mäkinen et al.) illustrated that internet pharmacies often work under illegal conditions and it distinguished three groups of online pharmacies operating in Europe: legally practising online pharmacies, (often illegal) lifestyle pharmacies and (always illegal) rogue sites. Examples of the first legally practising internet pharmacies are new online pharmacies such as the Dutch company DocMorris,[7] the largest online pharmacy on the German market and Pharmacy2u,[8] the largest mail-order and online pharmacy in the UK. Some of these emerging online pharmacies in various constructions are affiliated with pharmaceutical industry, insurance companies or wholesalers.

[7] See: www.docmorris.com
[8] See: www.Pharmacy2U.co.uk

Furthermore, there are two dimensions that need to be taken into account when discussing internet pharmacies: internet pharmacies that work on a national level (i.e. within national boundaries) and pharmacies that engage in cross-border activity. In the latter case, a whole new complicating dimension applies as national pharmaceutical markets are still divergent with regard to regulatory framework and, as a result, issues such as what is on sale, which pharmaceutical receive authorization, how is it classified and how leaflets are labelled. This could pose serious difficulties especially with regard to the free movement rules. For example, if market authorization was obtainable online, manufacturers would then be able to obtain authorization in the Member State with the least stringent legislation and release products without authorization into the markets of Member States (De Clippele 2004). Furthermore, the existence of barely legal and non-regulated internet pharmacies, which supply drugs from unknown sources that are possibly counterfeits, could pose grave safety risks for consumers. Needless to say, this is an unacceptable situation for Member States.

The situation surrounding DocMorris may shed some light on these complex problems. DocMorris was established in the Netherlands in 2000 in order to circumvent restrictive regulations concerning mail-order pharmacies and prescription drug prices in Germany. In its short history, DocMorris has had to overcome many problems posed by German legislation and the fierce resistance, often through litigation, of the German Pharmacists' Association (ABDA). DocMorris managed to force a breakthrough in the German pharmaceutical retail market by using a favourable ECJ ruling from 11 December 2003,[9] based on the free movement rules and an already planned change of German legislation in 2003 concerning mail-order services to its advantage. The ECJ made clear that cross-border mail-order pharmacy services are compatible with EU law, but also held that a national prohibition on mail-order sales of prescription drugs can be justified. This did not affect DocMorris as the German prohibition was (as planned) abolished in 2004 by the amended German Pharmaceutical Act. Nevertheless, DocMorris continues to see strong opposition in the German

[9] Case C-322/01, 'Deutscher Apothekerverband eV versus DocMorris NV

market, especially in their attempts to establish a pharmacy chain, which is problematic under current German ownership regulations.

2.2 Demand side of the pharmaceutical market

The demand side of the pharmaceutical market is characterized by information asymmetry in comparison with the supply side. But also on the demand side, i.e. within the medical care triad, information asymmetry exists. In general, a doctor has more pharmaceutical knowledge than a patient. However, new technologies, such as the internet, help patients access detailed medical information, which has changed the doctor-patient relationship. The payer must design an insurance policy often in a heavily government-regulated environment and deal with agency problems, such as moral hazard.

2.2.1 Prescribers

The prescriber, a specialist or general practitioner (GP), is responsible for prescribing the right pharmaceutical, which is a crucial role in the provision of pharmaceutical products. Historically, the doctor's main priority and interest is to provide the best possible advice and treatment and, if necessary, to prescribe a medicine of good quality, irrespective of costs. However, developments in pharmaceutical expenditures raised awareness among both policy makers and professionals that a rational prescribing behaviour could be a method of cost-containment. Therefore, many national governments now have measures or collaborating initiatives aimed at influencing prescribing behaviour (see Chapter 4).

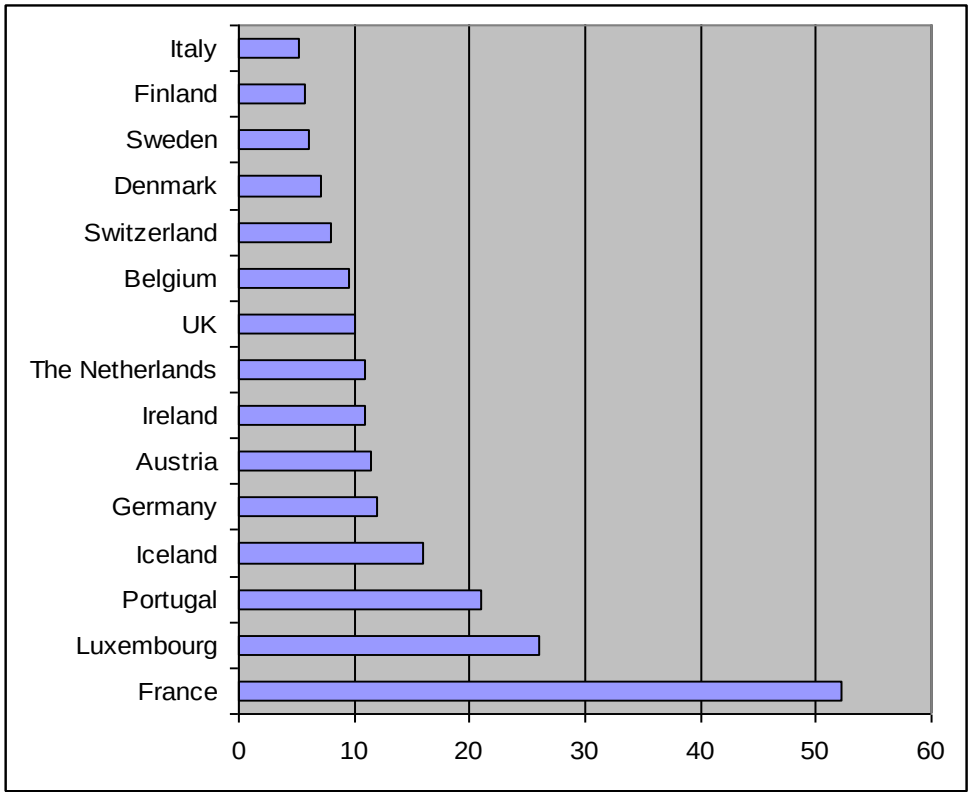
A doctor's knowledge of pharmaceutical products may exceed that of a patient, but there is still huge information asymmetry compared to the supply side of the pharmaceutical market. This makes doctors a possibly profitable marketing target. This is supported by direct visits from pharmaceutical company detailers. Since the 1992 EU directive, national governments have constrained the marketing activities of pharmaceutical companies, particularly those targeted at professionals with the aim of plugging their latest products.[10]

[10] Directive 92/28/EEC on the advertising of medicinal products for human use, now integrated in 2001/83/EC on the Community code relating to medicinal products for human use.

Furthermore, there are significant differences in numbers of prescriptions and thus consumption between countries. This is the result of differing cultural attitudes and health care systems (see Figure 3). According to Yuen (1999), France leads with an average of 52.2 prescriptions dispensed per capita in comparison to about five prescriptions dispensed per capita in Italy and roughly six prescriptions dispensed per capita in Finland and Sweden.

Table 7 illustrates the divergence of percentages of diagnoses made followed by a prescription and reflects different prescribing behaviours. In more recent but rough data for 2003, Italy's percentage of diagnoses with prescription was well over 90%. For Belgium and Spain it was more than 80%, for France more than 75%, for England and Germany around 70% and for the Netherlands slightly over 60% (IMS Health in: Nefarma 2004).

Figure 3. Prescriptions dispensed per capita in selected European countries, 1996.



Source: Yuen (1999).

Table 7. Share of diagnoses with prescription in selected European countries, 1996.

	% diagnoses with prescription
Netherlands	56
Germany	70
UK	74
Spain	79
France	83
Belgium	87

Source: IMS Health in: PriceWaterhouseCoopers (1999).

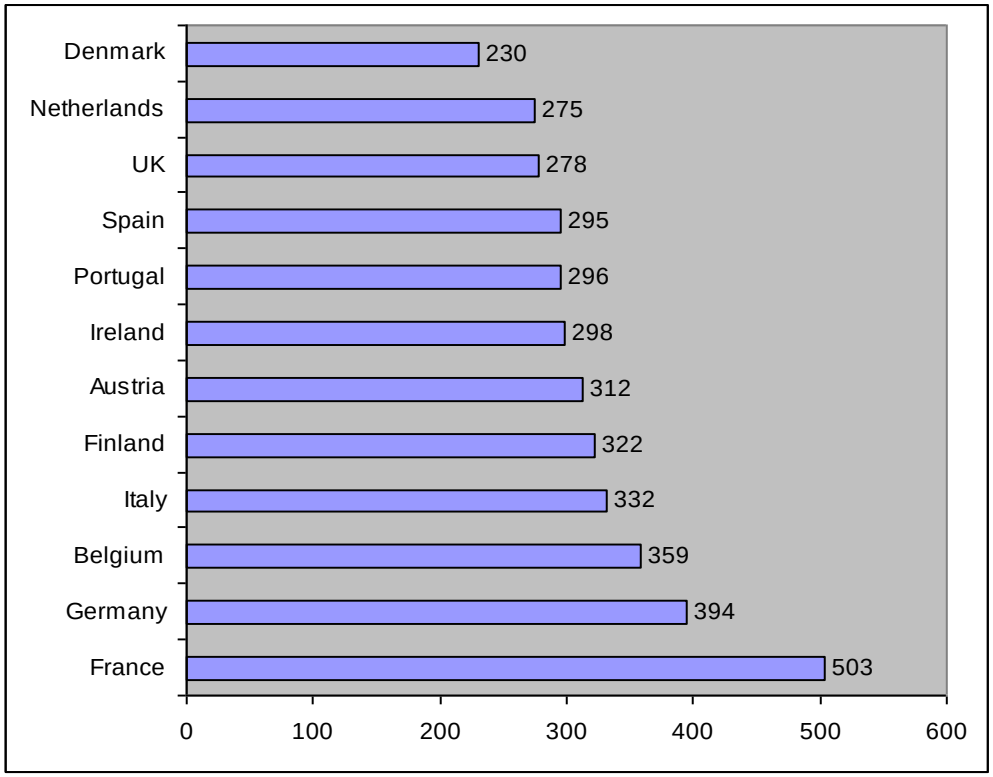
2.2.2 Patients

Due to developments on the patients' side, the doctor-patient relationship is changing. Patients become more involved in their choice of treatment and have access to an abundance of medical information, largely due to the internet. Another important development is the observed loss of trust in the medical profession. There is an emerging trend across Europe to put more information and more power in the hands of patients with regard to accessing and using medicines (Bradley et al. 2004). A case in point is the fact that more pharmaceuticals have been made available over-the-counter in many countries and, therefore, have to be paid for out of pocket, which increases patient responsibility.

Furthermore, the consumption of pharmaceuticals varies widely across cultural and national boundaries. Different attitudes toward pharmaceuticals exist, which can represent their respective cultural values. These result in differences up to twice the total drug consumption per capita within the EU (see Figure 4). For example, total drug consumption through pharmacies in France is €503 per capita, whereas in Denmark this number is only €230. Belgium consumes pharmaceuticals worth €359, which is 1.3 times more than its neighbour, the Netherlands (€275). It is important to note that these differences are jointly determined by a price and volume component. Hence, both factors are subjected to country-specific national frameworks (e.g. price and volume regulation) and are not necessarily determined by cultural factors alone. Another determinant worth mentioning is the level of generics entering the

market, which varies significantly between Member States and could have a mitigating effect on pharmaceutical expenditures. Nevertheless, it does provide an indication of the magnitude of the differences in consumption patterns in the EU.

Figure 4. Pharmaceutical expenditure (€) per capita through pharmacy, 2004.



Source: SFK (2006).

There are many studies on the differences in pharmaceutical consumption patterns between countries, nationalities and ethnic groups. Data from the European Surveillance of Antimicrobial Consumption (ESAC), for example, show that in 2002 France ranked first among the EU25 Member States with an outpatient antibiotic use of 32.22 defined daily doses (DDD) per 1000 inhabitants, compared to 9.83 DDD per 1000 inhabitants in the Netherlands, the lowest consumer. The study shows that differences in selection pressure account for geographic variation in resistance. Countries in Southern and Eastern Europe generally consume more antibiotics than countries in Northern Europe and higher rates of antibiotic resistance exist in the high-consuming countries (Goossens et al. 2005). However, some interesting regional differences occurred. Belgium, for example, ranked sixth among the EU25

with an outpatient antibiotic use of 24.54 DDD per 1000 inhabitants, 2.5 times that of the neighbouring Netherlands. This springs from different attitudes toward disease. Deschepper et al. (2002) found that Belgians worry more about disease and were more used to leaving the consultation room with a prescription. Belgians rated their upper respiratory tract diseases often as bronchitis, whereas the Dutch mostly rated similar symptoms as a cold or the flu and never as bronchitis. For the most part, Belgians more frequently consulted a doctor when ill and were prescribed antibiotics more often, whereas patients in the Netherlands took home remedies, sometimes in combination with OTC medicines.

Traditionally, there is no direct incentive for patients to take cheaper pharmaceuticals and moral hazard belongs to the problems with which the payers are faced. However, national policies try to increase patient interest and responsibility through measures such as co-payments and reference pricing (see Chapter 4).

On the macro level, patient groups are generally not as well-organized as other actors. They lack financial means and their influence on pharmaceutical policy making is limited. Patient organizations are often fragmented along disease areas with possibly conflicting interests. This potentially makes patient organizations vulnerable to the marketing efforts of the pharmaceutical industry, through the funding of patient groups. This is a newer development in Europe but well-established in the United States. Although this may seem like a strange alliance, it is a logical partnership between two actors with a shared interest. Access to the newest treatments (which benefits patients) requires a positive reimbursement decisions (which benefits pharmaceutical industry). However, pharmaceutical industry and patient organizations are unequal partners in terms of funding and information and this can have serious consequences when grants and joint projects with pharmaceutical companies distort and misrepresent their own agendas (Herxheimer 2003).

2.2.3 Payers

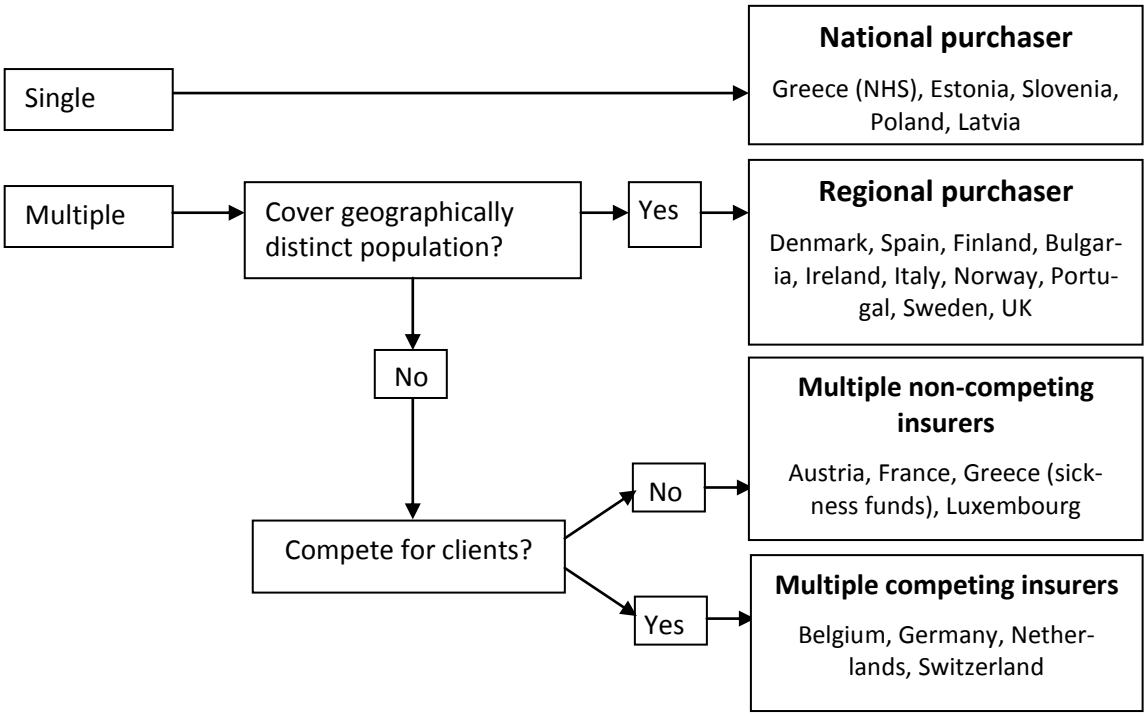
Because the costs of pharmaceuticals can rise substantially, payers must facilitate access to drugs for the most vulnerable groups in the population. Payers in the European pharmaceutical market come in many forms (see Figure 5). A payer can be a sickness fund, an integrated part of a NHS or a private insurer and it may operate on

various levels (e.g. national, regional) or in a single payer or multiple payer system. It may also compete with other payers, have public or private features and it may reimburse the patient or the provider.

During the 1970s and 1980s, the payer/purchaser functioned mainly as a financial intermediary providing or reimbursing the necessary services for the population. In the 1980s, increased pressure on costs led countries to implement cost-containment policies that aimed at integrating a form of market mechanisms into their systems. During the 1990s, payer/purchasers received more planning and management authority (Busse et al. 2007). In the UK, for example, which operates a tax-based NHS, there is a separation between the purchaser and provider ("the purchaser/provider split") for the purpose of creating an internal market where providers compete for contracts with the payers. These various experiments with active purchasing and selective contracting, in which the payer seeks the best offer in terms of value for money and quality for its clients (patients), mainly focused on establishing competition between health service providers, rather than providers of pharmaceuticals.

Thus far, payers have not played a major role in the containment of costs for pharmaceuticals, largely because of the existing health care structure in which they may not have an incentive (e.g. in a strictly financial intermediary function) or simply due to a lack of instruments used to exert influence on pharmaceutical costs. In other words, payers are faced with agency problems. Payers cannot get relevant parties to do what efficiency requires. Consequently, people with more generous insurance spend more on medical care than people with less generous insurance (moral hazard) and providers that pay on a fee-for-service basis may provide more care due to supplier-induced demand than they would if they were not paid per task (Cutler and Zeckhauser 2000). This can, depending on the health care system, directly apply to pharmaceutical provision.

Figure 5. Market structures for payer/purchaser organizations and European examples.



Source: Adapted from Kutzin (2001) and Busse et al. (2007).

Since spring 2004, health insurers in the Netherlands have gained some influence over the price of generics through participating in yearly negotiations (the so-called "covenant") together with the Ministry of Health, pharmacists and producers of generics. The aim of this covenant is to lower discounts for pharmacists in favour of consumers. In 2004, this resulted in a 40% reduction of generics in the market and a pledge by the manufacturers to price new generic medicines 40% below the price level of the corresponding original brand name medicine (SFK 2007). On the longer term, plans exist to further enhance the role of the insurer in order to create a countervailing power on the demand side of the pharmaceutical market. After building up the necessary pharmaceutical expertise to counter information asymmetry, insurers will receive more freedom to purchase pharmaceuticals for insured patients, making them responsible for pricing medicine through negotiation, rather than the government.

Another initiative can be found in Germany where since 2007 sickness funds may sign discount contracts (called *Rabattverträge*) with pharmaceutical companies for individual drugs. Under this system, pharmacies are legally obligated to substitute a

prescribed drug for a generic drug if the patient's sickness fund has such a discount contract. The legal requirement to substitute drugs has been criticized in some studies because it may compromise prescribing quality and patient safety (Pruszydlo et al. 2008; Quinzler et al 2008).

3 The European Union

Pharmaceutical policy is a very complicated interplay of various actors, which includes national governments, industry, wholesalers, pharmacists, doctors, payers and patients (see Chapter 1). Often these stakeholders have conflicting interests that can vary from country to country. This makes it hard for national governments to achieve their respective policy goals. Although pharmaceutical policy is largely determined at the national level, there is, nevertheless, a considerable amount of EU legislation that exerts influence on the policies of Member States, mainly through the use of regulations, directives and decisions.[11]

As will become clear in this chapter, the role of the EU has been expanding in this area mainly resulting from the legal duty to advocate the principles of European law, including the free movements of goods and free competition. This is visible in the Community's attempt to liberalize the market for pharmaceuticals. In recent years, the European Commission has modified its efforts to harmonize national policies into a more realistic co-ordination approach because countries were not and continue to be unwilling to give up their regulatory authority. They fear the outcomes for domestic industry (e.g. jobs) and for their respective health care systems (e.g. higher prices for pharmaceuticals), depending on the Member State's predominant policy objective.

The European Union cannot be seen as a single actor with only one policy goal. Rather, it consists of various actors and various policies, including industrial, social and health policies, which each have a distinct influence on pharmaceutical policy and they are advocated by the various Directorate-Generals (DGs). Since these influences and their origins may seem opaque from outside, this chapter takes a closer look at the EU and aims to clarify the different influences of these policies and actors on past and present pharmaceutical provision. The first section discusses the EU policy-making process and its main actors. Sections Two, Three and Four describe three

[11] Regulations are binding in their entirety and are directly applicable in all Member States. Directives bind Member States as to the results to be achieved, but have to be transposed into the national legal framework and, thus, leave a margin for manoeuvre as to the form and means of implementation. Decisions are fully binding on those to whom they are addressed.

main areas of EU policy (i.e. industrial policy, EU social policy and EU health policy). Sections Five and Six examine two important EU actors: the European Medicines Agency (EMEA) and the European Court of Justice (ECJ).

3.1 European Union policy process and actors

The EU consists of three pillars: the European Community, which has its origins in the European Economic Community (EEC), the Common Foreign and Security Policy and Police and Judicial Co-operation in Criminal Matters, which was created after the amendments introduced by the Amsterdam and Nice treaties. Hence, the latter two play a more intergovernmental role and, consequently, the Commission and the European Parliament play less of a role. This thesis focuses on the first pillar because it is where most EU policies originate. The activities and responsibilities of the EU are outlined in various European treaties (e.g. the Treaty of Rome, the Single European Act, the Treaty of Maastricht).

Governance and political leadership is provided by the European Council. It is the highest political body of the EU and it consists of the President of the European Commission and the heads of states/governments of Member States, who are assisted by their foreign ministers. The Council has a rotating presidency, with the leader of each Member State serving for a period of six months. During the presidency, the country's representatives chair the meetings of the European Council and the Council of Ministers. The European Council usually has quarterly summits.

The European Commission is the executive body of the EU and it is responsible for initiating legislation and the daily management of the EU. Whereas the Council mainly reflects national interests, the Commission is intended to solely represent common European interests. Its main functions are (1) to propose legislation to Parliament and the Council; (2) to manage and implement EU policies and the budget; (3) to enforce European law (with the Court of Justice); and (4) to represent the European Union on the international stage, for example, by negotiating agreements between the EU and other countries. The Commission is currently composed of 27 commissioners responsible for different areas of policy, one from each Member

State. The President and the commissioners are nominated by the Council and have to be confirmed by the European Parliament.

The European Parliament (EP) reflects the interests of the European people and consists of 785 members, who are elected every five years by EU citizens. The EP forms one half of the EU's legislature. Its main functions are (1) passing European laws (jointly with the Council); (2) democratic supervision of EU institutions, including the Commission; (3) and budgetary authority over the e EU budget (shared with the Council).

The Council of the European Union, formerly known as the Council of Ministers, constitutes the second half of the EU legislature. The Council is a platform for national ministers to meet and represent the interests of their respective Member State and specific areas of policy. The Council meets in different formations (e.g. areas relevant to pharmaceutical policy are Social Policy, Health and Consumer Affairs, and Competitiveness). The Council's main responsibilities are (1) to pass European laws jointly with the European Parliament; (2) to co-ordinate the broad economic policies of the Member States; (3) to conclude international agreements with non-EU countries and organizations; (4) to approve the EU's budget, jointly with the EP; (5) to develop the EU's foreign and security policy; (6) and to co-ordinate co-operation between national courts and police forces in criminal matters.

The European Court of Justice (ECJ) and the Court of First Instance form the judicial branch of the EU. The former will be examined and analysed in more detail in Section 3.5.

3.2 European Union industrial policy

The observation that the European Union leans toward industrial policy rather than health policy has its origins in the factual competences the European Economic Community (EEC), the predecessor of the EU, has had since its inception in 1957 through the Treaty of Rome. The main aim of the EEC was to bring about economic integration between the founding nations Belgium, France, Germany, Italy, Luxembourg and the Netherlands. The EEC sought to lay the foundations of "an ever closer union among the peoples of Europe" with "the constant improvement of the living

and working conditions of their peoples" and to "ensure the economic and social progress of their countries by common action to eliminate the barriers which divide Europe". Its central aims included the need for steady expansion, balanced trade and fair competition through the establishment of a customs union with a common external tariff, common policies for agriculture, transport and trade (common commercial policy) and the enlargement of the EEC to include the rest of Europe. Pharmaceutical policy, as a result, leans towards an industrial policy perspective, which is also illustrated by the fact that most legislation regarding pharmaceuticals emanates from the long-established DG Enterprise-Pharmaceuticals Unit, not from DG SANCO. European pharmaceutical policy is, therefore, mainly aimed at the establishment of a common market for pharmaceuticals with common (rapid) authorization procedures.

3.2.1 European Union pharmaceutical policy: A history, 1960–2000

European involvement in the pharmaceutical market dates back to the early 1960s, when the thalidomide disaster took place. Thalidomide, developed by the German firm Grünental, was sold as a sleeping aid and as a remedy for pregnant women to combat morning sickness. Prescription-free thalidomide, also known under various brand names including Contergan in Germany and Softenon in Belgium, Finland and Spain, was a bestseller in 1961–62 with 20 million tablets sold per month. It was not before long until some horrible side effects became apparent. Thalidomide caused birth defects and an estimated 8000 malformed children were born in Europe (Scherer 2000), from which an estimated 4000 cases in Germany alone. The thalidomide disaster, one of the biggest drug tragedies of recent history, raised awareness that in order to safeguard public health, no medicinal product must ever again be marketed without prior authorization. It highlighted the need for better standards and authorization procedures not only in European states, but also at the European Community level.

In 1965, the first European Community pharmaceutical directive (Directive 65/65/EEC) was adopted. Its purpose was to establish and maintain a high level of protection for public health through rules on the development and manufacturing of medicines, to establish guidelines for the post-marketing monitoring of drug safety

and to establish safety, efficacy and quality as the sole grounds for market approval. Thus, one can say that the first Community involvement in the European pharmaceutical market had a strong public health policy perspective (protection) but, in the meantime, it also aimed to establish European standards necessary for the common market.

Ten years later, two important directives (75/318/EEC and 75/319/EEC) introduced the mutual recognition of the respective national marketing authorization procedures in Member States and provided the first step towards creating a Community-wide single European market for pharmaceuticals. Directive 75/318/EEC created the mutual recognition procedure (MRP), which was intended to enable and speed up the free movement of medicinal products within the Community based on scientific criteria for quality, safety and efficacy. This new procedure was facilitated by Directive 75/319/EEC, which set up a Committee for Proprietary Medicinal Products (CPMP), a single authorization and administration body for the Community market, comprising representatives from each of the Member States.

Mutual recognition, also known as the CPMP procedure, encouraged manufacturers with an existing authorization for at least one Member State to seek marketing authorization for a drug simultaneously in five or more recipient Member States (out of the then nine Member States). This allowed companies to submit applications without regulatory staff in every country, thus enhancing smaller national manufacturers to compete more globally. However, the mutual recognition procedure hardly improved the situation. It caused delays as recipient Member States sought (non-binding) arbitration from the CPMP on nearly every occasion. If arbitration had an undesired outcome for a recipient Member State, it could still refuse authorization under Article 36 of the 1957 Treaty establishing the European Community (TEC), which gives members exception to the free movement rules where public health is at stake. Consequently, the procedure was not popular with industry. Only 41 applications were made in the eight years it was in place and the procedure was mostly used for – for industry less important – generics or “me-too” products. Of the 41 applications, 28 (70%) received a favourable opinion. The 41 applications led to 175 authorizations and 65 final refusals (Cartwright and Matthews 1991).

Clearly, the CPMP procedure was not accepted by Member States and was unattractive to industry. In 1983, therefore, the EU created the multi-state procedure, in which the minimum number of recipient states was reduced from five to two (out of the then ten Member States). The procedure was introduced by Directive 83/570/EEC, which soon proved to be troublesome. Although there was an increase in the number of applications submitted, Member States raised objections to all but one of three hundred applications (Abraham and Lewis 2003). It does not come as a surprise that the manufacturers remained sceptical about the advantages of the multi-state procedure. The vast majority of applications prior to the introduction of the decentralized procedure in 1995 were submitted via national approval routes (Abraham and Lewis 2000).

The 1985 White Paper "Completing the Internal Market" provided the intentions of the European Commission regarding the completion of the single European market. These intentions were strengthened by the Single European Act (SEA) of 1986, which laid out plans to establish a single European market for the movement of all goods, services and capital by 1992. In another attempt to further rationalize the authorization process, the 1987 Directive 87/22/EEC introduced the concertation procedure. The concertation procedure was compulsory for biotechnology and voluntary for high technology products and forced manufacturers to simultaneously submit their applications to the CPMP and one Member State, which acted as a rapporteur. The CPMP could then recommend an EU-wide license, after considering possible objections by other Member States. However, as with the multi-state procedure, CPMP arbitration was still non-binding and could be ignored by Member States. They both failed to fulfil expectations, although the concertation procedure was more successful in terms of applications submitted and agreements over labelling (Jones and Jefferys 1994).

Meanwhile, a European restrictive pricing policy was discussed and was successfully opposed and fought by the EFPIA. In 1989, however, the European Commission introduced Directive 89/105/EEC, known as the Price Transparency Directive, in order to counter price differentials in medicinal products between Member States, which were, according to Chambers & Belcher (1994), up to five times on the prices of sin-

gle products. The Price Transparency Directive required Member States to adopt verifiable and transparent criteria for setting pharmaceutical prices and their inclusion in national health systems. The Directive is limited in its aim. It does not regulate European-wide price controls and profit caps, nor does it seek to harmonize the rules of the various national reimbursement schemes. However, it could be seen as the first Community involvement in terms of pricing and reimbursement.

Further SEM-relevant legislation with regard to wholesale distribution (Directive 92/25/EEC), the classification of pharmaceuticals (92/26/EEC), labelling and packaging (Directive 92/27/EEC), advertising (Directive 92/28/EEC) and patent protection (Regulation 1786/92) followed. Despite this legislation, intra-EU price differentials were not reduced. In a 1994 Communication, the European Commission expressed concerns that part of the pharmaceutical industry in the European Union was losing global competitiveness, which would have serious economic and social consequences for Europe (European Commission 1994).

Some of the key actions identified in the 1994 Communication were put into action. A major change took place in January 1995. Member States became bound by CPMP opinions in both the multi- state procedure and the concertation procedure, as outlined in Directive 93/39/EEC. Member States can only question CPMP opinion if a potentially negative impact on public health can be proven. In accordance with expert advice from the CPMP, the European Agency for the Evaluation of Medicines (EMEA[12]) was established under Regulation 2309/93 and began administering these new procedures in February 1995. To mark these changes, the multi-state procedure was renamed the *decentralized* procedure and the concertation procedure the *centralized* procedure.

The response to this 1994 Communication by both the European Parliament (Resolution of 16 April 1996) and the Council (Resolution 96/C 136/04) was to stress the importance of working towards a European industrial policy for pharmaceuticals. In their view, this could be reached by completing the internal market, creating a stable and predictable environment for the protection of patient health, ensuring rapid

[12] EMEA now stands for the European Medicines Agency and is referred to as such in the thesis

access to the market and encouraging therapeutic innovation. However, no progress was made after the introduction of these documents.

In 2000, the Commission ordered a detailed assessment of the EMEA's procedures and operations, a commitment made in Article 71 of Regulation 2309/93, which was undertaken by external consultants Cameron McKenna and Arthur Andersen Consulting (European Commission 2000). On the basis of this assessment, the Commission drafted a discussion document (European Commission 2001a), which eventually led to the adoption of a proposal for a comprehensive reform of the EU pharmaceutical legislation in July 2001, often referred to as Review 2001 (European Commission 2001b). The review contained the following objectives: to guarantee a high level of public health protection for Europeans, to complete the internal market in pharmaceutical products, to meet the challenges of EU enlargement and to rationalize and simplify the system as much as possible.

The proposal for reform particularly concerns Regulation 2309/93, which provides the legislative framework for regulating medicinal products and resulted in Directive 2001/83/EC on human medicines and Directive 2001/82/EC on veterinary medicines (European Commission 2001a, 2001b). Directive 2001/83/EC on the Community code relating to medicinal products for human use dated 6 November 2001 (later amended by the 2004 Directive 2004/27/EC) replaced and consolidated the first pharmaceutical, Directive 65/65/EEC, with all its relevant amendments, the two landmark directives 75/319/EEC and 75/318/EEC and their respective amendments and the 1992 Directives on wholesaling (92/25/EEC), classification (92/26/EEC), labelling and packaging (92/27/EEC) and advertising (92/28/EEC).

3.2.2 European Union pharmaceutical policy, 2001–2005

EU pharmaceutical policy thus far shows that progress has been made using secondary legislation such as directives and regulations. This has led to the harmonisation of national practices and the establishment of a centralized licensing procedure under the auspices of the EMEA. In the field of pricing and reimbursement, however, the 1989 Price Transparency Directive is the only accomplishment of Community policy in 40 years. The Transparency Directive was intended to be the first step towards European regulation in national price and profit control. The Commission nev-

er proposed any form of regulation for price controls and has viewed this as primarily a national matter. This is not surprising for a variety of reasons. Firstly, the European Commission's main goal is to liberalize the market and is decidedly leaning towards industrial policy. This aim is incompatible with installing some sort of price control or profit caps. Secondly, even if the Commission had wanted to introduce profit and price controls, there are huge practical problems. Setting the appropriate margin for retail price control is particularly difficult given the fact that pharmacy costs differ considerably from one Member State to another, as do the methods of retail price control (OECD 2002). Lastly, the 1992 Maastricht Treaty formally established the principle of subsidiarity (also see Section 3.4) in EU law, effectively making it even more problematic for the Commission to interfere with national policy.

In short, there remains no SEM for medicines. After some progress, it has reached a standstill, which mainly stems from the conflict between the principle of subsidiarity and the rules of SEM regulation, i.e. free movement rules. The former enables Member States to retain the competence to determine national health care policy by delimiting policy competence to the lowest level at which it can be effectively undertaken, while the latter demands the free movement of goods, including pharmaceuticals. What follows is a conflict between Member States, who defend the right to set their own prices and make their own reimbursement decisions and the European Commission, which has the legal duty to liberalize the market and demands that there be no obstacles in their circulation within the EU. In other words, competing policy objectives and competences exist between national (cost-containment) and supranational (market liberalisation and free movement rules) policymakers.

In addition to this standstill, it became clear to the European Commission that the European pharmaceutical industry was losing out to its main competitors, mainly the US and, to a lesser extent, Japan. The 2000 report "Global Competitiveness in Pharmaceuticals: a European Perspective" drafted for the Directorate-General for Enterprise and Industry pointed out that Europe is lagging behind in competitiveness when compared to the US (Gambardella et al. 2000). Indicators for this assessment include research and development (R&D), size of the European industry, size of European pharmaceutical markets and growth rate. The pharmaceutical sector, a high

growth and innovation-intensive industry, is a main provider of employment and the main contributor to the European trade balance; through its products, it helps to achieve health goals and is thus of high strategic and economic importance. National price and profit regulation were said to have protectionist effects on the European pharmaceutical industry and reduce the incentive for innovation.

The High Level Group on Innovation and Provision of Medicines (G10 Medicines Group) was established in March 2001 in response to the findings of the Pammolli Report. The G10 Medicines Group, set up by former Commissioner for Enterprise Erkki Liikanen and former Commissioner for Health and Consumer Protection David Byrne, explored possible directions for future EU policy, with achieving the seemingly dichotomous goal of innovation (competitiveness) and provision (accessibility) in the pharmaceutical sector. Although the G10 process integrated a stronger public health perspective through the involvement of DG Health and Consumer Protection, national health ministers and interest groups, it is discussed in this section as it is mainly driven by the Community's internal market aspirations and, as a result, has a strong industrial policy perspective. The G10 group was created with the recognition that the Pharmaceutical Review on its own would not be sufficient to tackle the competitiveness problems currently facing the pharmaceutical industry and rather these problems required national action. Therefore, in May 2002, the G10 process resulted in a series of recommendations without direct legislative Community action.

3.2.3 The G10 process

Methodology

The G10 Medicines Group, consisting of health and industry ministers, representatives of the pharmaceutical industry and patient groups used the Lisbon Method in which the Commission served as a facilitator to help the members develop practical recommendations. Three working groups were created: provision, single market and innovation. These working groups produced a consultation paper containing key issues and broad conclusions, which was issued for public consultation to reach a wider group of stakeholders. Consultation often resulted in critical and conflicting responses. In addition to the consultation exercise, the G10 Medicines Group undertook two other measures to increase transparency: the creation of a special web-

site,[13] containing all the documents used, a forum, the progress of the G10 Medicines Group process and a programme of workshops to examine specific issues in more detail. The goal of this methodology was to reach a consensus within the G10 Medicines Group on a recommendation package. This goal led to a final set of 14 recommendations that were published and presented to President Prodi in May 2002 (European Commission 2002). The recommendations concentrated on five areas: (1) benchmarking; (2) competition, regulation, access and availability in markets; (3) stimulating innovation and improving the EU science base; (4) patients; and (5) enlargement.

Benchmarking: competitiveness and performance indicators

1. The use of benchmarking

The Commission should develop a comprehensive set of indicators in order for comparisons between the EU and its major competitors to be a basis for establishing the best practices.

Competition, regulation, access and availability in markets

2. Access to innovative medicines

European institutions and Member States should secure better access to and availability of innovative medicines through improved licensing legislation, in order to enhance market introduction and should improve the use of modern telecommunication infrastructure (telematics) and techniques to facilitate the operation of the Community regulatory system.

3. Improve timing of reimbursement and pricing negotiations

Regarding national competence, Member States should try to improve time taken between the actual marketing authorization and pricing and reimbursement decisions in order to have procedures that are both effective and ensure speed of access.

4. Developing a competitive generic market

[13] G10 website: http://ec.europa.eu/enterprise/phabiocom/p3.htm

The European institutions and Member States need to secure a competitive generic market through improvements in the licensing process. This should be achieved through finding an appropriate balance between providing intellectual property protection for innovative medicines and easy access to the generic market through the introduction of a Bolar provision.[14] However, Member States still determine the degree of generic penetration.

5. Developing a competitive non-prescription market

In order to develop a competitive non-prescription market, Member States should review where appropriate, amend mechanisms and concepts for moving medicines from prescription to non-prescription status and allow the same trademark to be used for the products moved to non-prescription status.

6. Full competition for medicines neither purchased nor reimbursed by the state

The Commission and Member States should secure the principle that a Member State's authority to regulate prices in the EU should extend only to those medicines purchased or reimbursed by the state. Full competition should be allowed for medicines not reimbursed by state systems or medicines sold into private markets.

7. Relative effectiveness

Although mechanisms to establish relative cost and clinical effectiveness are primarily a matter of national competence, the Commission should facilitate the exchange of national experience on health technologies (HTA) and new information technologies.

[14] A Bolar provision enables commercial testing, using and making (not selling) of on-patent pharmaceuticals prior to patent expiry. Through this exemption of exclusive patent rights, manufacturers can obtain marketing approval before the patent has expired and secure more rapid market access. It is named after the US court case Roche Products Inc. v. Bolar Pharmaceutical. Co. (Fed. Cir. 04/23/1984).

Stimulating innovation and improving the EU science base

8. Creation of virtual institutes of health

The creation of the European virtual institutes of health should be stimulated, connecting all existing competence centres on fundamental and clinical research into a European network of excellence.

9. Install incentives for research

The Commission and Member States should support and co-ordinate the conduct of clinical trials on a European scale and establish a database of trials and clinical research results. They also should put in place an effective policy in terms of incentives, support areas of funding that are less attractive due to restricted size of the expected market (i.e. orphan and paediatric drugs) and support the development of a biotechnology strategy in Europe, for which the completion of Directive 98/44/EEC on the Legal Protection of Biological Inventions is important.

Patients

10. Enhanced information

Restrictions on advertising prescription medicines to the general public should remain in place; however, there should be no restrictions on advertising non-prescription and non-reimbursed medicines. There should be a practical and workable distinction between advertising and information through guidelines agreed on by both Member States and the European Commission.

11. Review of patient information leaflets

Legislation relating to patient information leaflets should be reviewed taking into account views of users and regulators of industry.

12. Pharmacovigilance

Systems of post-marketing surveillance should be optimized to ensure that co-ordinated processes are in place to gather data on adverse events and patient safety.

13. Funding for patients groups

The Commission should consider providing core funding for European patient groups to enable them to participate independently in debates and decision-making on health matters in the EU.

Enlargement

14. Take full account of enlargement

Although it is difficult to predict the impact of enlargement on the pharmaceutical market, in this recommendation, the G10 Medicines Group stresses that the Commission should take full account of enlargement consequences and issues.

In July 2003, the European Commission (2003) welcomed the analysis and approaches proposed by the G10 group in Commission Communication COM (2003) 383 "A Stronger European-based Pharmaceutical Industry for the Benefit of the Patient –A Call for Action". The Commission divided the G10 recommendation into five broad themes resembling the five themes used by the G10 group (see Table 8). In order for these recommendations to be realized, the Commission developed an extensive set of key actions, some linked to programmes already in place and ostensibly put patients' issues on the top of their list:

- Benefits for patients: improving patient information on medicines, strengthening the role of patients in public health decision-making through the support of consumer groups and strengthening European supervision of medicines (pharmacovigilance). Also included in this section is the recommendation to review national approaches to cost and the clinical effectiveness of medicines.
- Developing a competitive European-based industry: examining ways of improving access to innovative medicines, the need to speed up national negotiations on reimbursement and pricing, greater price competition for medicines that are not part of the state sector and measures to develop competitive generic and non-prescription markets.
- Strengthening the EU science base: examining ways to develop incentives for research, including the use of virtual institutes for health and biotechnology, as an ad-

dition to the Sixth Framework Programme for Research and Technological Developments (FP6).[15]

- Medicines in an enlarged European Union: examining ways to the challenge the enlargement by providing a level playing field for intellectual property protection and providing support for accession countries to implement the new legislative framework.
- Member States learning from each other: introducing benchmarking through a set of agreed EU performance indicators (supply, demand & regulatory framework, industry outputs and macroeconomic factors) as a basis for monitoring the implementation of recommendations and to exchange best practices. It was proposed that this could function under the Health Monitoring Programme (1998-2003) and activities planned by Eurostat as part of their development of a Systems of Health Accounts.

Table 8. The Commission's adoption of G10 Medicines recommendations.

European Commission Communication COM (2003) 383	**G10 Medicines recommendations number**	**Corresponding with G10 Medicines theme[16]:**
Benefits to patients	7,10,11,12,13	Patients
Developing a competitive European-based industry	2,3,4,5,6	Competition, regulation, access and availability in markets
Strengthening the EU science base	8,9	Stimulating innovation and improving the EU science base
Medicines in an enlarged European Union	14	Enlargement
Member States learning from each other	1	Benchmarking: competitiveness and performance indicators

Source: own compilation.

The European Commission remained preoccupied with the competitiveness of the European pharmaceutical sector. A clear decline in applications for marketing authorizations in 2002 and 2003 led the Commission to believe that there might be a worldwide crisis concerning innovation in the pharmaceutical sector. Against this

[15] The Sixth Framework Programme (FP6) for Research and Technological Developments (2002-2006) was a collection of the actions at EU level to fund and promote research, leading to the creation of the European Research Area (ERA).

[16] In the G10 report, recommendation seven concerning "relative effectiveness" is classified under "competition, regulation, access and availability in markets". The Commission, however, categorises it under "benefits to patients". This is the only major difference with the G10 and it seems to further underline the expressed emphasis of the Commission on patient benefits.

backdrop, DG Enterprise commissioned Charles Rivers Associates to conduct a study. This study aimed to investigate: (1) whether there is an innovation crisis in the pharmaceutical sector; (2) the reasons behind any crisis and (3) tools available to kick-start innovation.

The outcome of the study was that the recent decline in applications does not reflect a crisis in innovation. Recent history of applications (and the close relationship between applications and authorizations) suggested that a recovery in authorizations was likely to occur in 2004/2005. However, the report came with a range of recommendations broadly in line with the 2000 Pammolli report findings and recent policy proposals in the EU, concerning faster market access, streamlining the regulatory process and the level of market exclusivity. Furthermore, the report stressed the importance of clearing the (observed) bottleneck of Phase III development, by helping companies to accelerate the entry of products in the market and the importance of improving Europe's attractiveness as a locus of innovation on the medium term (European Commission 2004a).

In 2004, Pammolli et al. published an update of their 2000 report called "European Competitiveness in Pharmaceuticals", in which they concluded that their initial findings still apply: "As a whole, Europe is still lagging behind in its ability to generate, organize and sustain innovation processes and productivity growth in pharmaceuticals". The report concluded that the failure of the continental European pharmaceutical industry to achieve a substantial acceleration in productivity cannot fully be explained by factors which are sector specific, but should also be explained by relatively low dynamism in Europe in terms of reforming some of its key capitalist institutions (e.g. labour and capital markets, education, welfare). Also, the uneven geographical distribution of research activities in pharmaceuticals, together with the observed differences in price levels for innovative drugs and reimbursement schemes between Europe and the US and across European countries seems to call for renewed transatlantic dialogue concerning the political economy of the pharmaceutical industry.

In March 2004, the Directive 2004/27/EEC amended the Community code regarding medicinal products for human use, specifically new requirements for the use of

Braille on packaging and in leaflets. Furthermore, Regulation 726/2004 repealed the well-known Regulation 2309/93, which outlined the EU market authorization procedures, although the general principles of 2309/93 remained in place. It mainly sought to improve the centralized and decentralized procedure by creating faster procedures, expanding the mandatory list of pharmaceutical products (centralized procedure) and harmonizing the data protection period further (decentralized procedure). Regulation 726/2004 applied from 20 November 2005.

The Commission's unrelenting preoccupation with the competitiveness of the pharmaceutical industry is maybe best reflected in the installation of the DG Enterprise and Industry unit Competitiveness in the Pharmaceuticals industry and Biotechnology. This unit's overall goal is to promote innovation and competitiveness in biotechnology and pharmaceutical industries, with particular attention to the completion of the Single Market and health and consumer protection. In June 2005, Vice President and Commissioner for Enterprise and Industry Verheugen and Commissioner for Health and Consumer Protection Kyprianou established the Pharmaceutical Forum,[17] which involved yearly meetings in the period 2006 up to 2008. The Pharmaceutical Forum follows up on issues sill outstanding from the G10 Medicines process. It thus formed three expert groups called Information to Patients, Relative Effectiveness and Pricing and Reimbursement.

The process put forward in the aftermath of the G10 recommendations could be seen as a break from the traditional approach of harmonisation through European legislation (also see Table 9) in favour of a more feasible approach of co-ordination of national results and, through this, respecting the subsidiarity principle and the national competence. Much will depend on Member States and their willingness to cooperate. Are they willing to accept coordination and, consequently, guidelines and benchmarks, not just for industrial matters but for health policy matters?

[17] The Forum is jointly chaired by Vice-President Verheugen and Commissioner Kyprianou, Ministers from each invited Member State. In addition to Member States, three representatives from the European Parliament are members. The remaining membership is made up of senior representatives of all actors in the pharmaceutical market.

Table 9. A non-exhaustive list of European Community action in the European pharmaceutical market, 1965–2004.

Year	Important developments	Concerning
1965	Directive 65/65/EEC	Establishment of rules for the development and manufacture of medicines and guidelines for the maintenance of a high level of protection for public health
1975	Directive 75/318/EEC	Establishment of the Committee for Proprietary Medicinal Products (CPMP) to facilitate mutual recognition
	Directive 75/319/EEC	Introduction of mutual recognition of respective national marketing authorization procedures
1983	Directive 83/570/EEC	Creation of the multi-state procedure, in which the minimum number of recipient states was reduced from five to two
1985	White paper "Completing the Internal Market"	Laid down Commission proposals concerning the completion of the internal market.
1986	Single European Act (SEA)	Act outlining plans to establish a single European market for the movement of all goods, services and capital by 1992
1989	Directive 89/105/EEC	"Price Transparency Directive" created in order to counter price differentials for medicinal products between Member States
1992	Directive 92/25/EEC	Wholesale distribution
	Directive 92/26/EEC	Classification
	Directive 92/27/EEC	Leaflets and labels
	Directive 92/28/EEC	Advertising and sales promotion
	Regulation 1786/92	Patent protection
1993	93/39/EEC	CPMP opinions in both the multi-state procedure as the concertation procedure became *binding* on Member States introduced as of 1995
	Regulation 2309/93	Establishment of the EMEA. Started operations in February 1995 and introduced centralized procedure
1996	Resolution 96/C 136/04	Call by the European Council for an industrial policy for the pharmaceutical sector in the European Union.
2000	Report "Global Competitiveness in Pharmaceuticals: a European Perspective" (Pammolli-report)	Report which indicated that the European pharmaceutical industry is losing to its main competitors, particularly the United States

	Release of "Evaluation of the operation of Community procedures for the authorization of medicinal products"	Cameron McKenna and Andersen Consulting report on review of medicines licensing
2001	Memo/01/267	Reform of European Union pharmaceutical legislation
	Directive 2001/83/EC	Community code concerning medicinal products for human use
2002	G10 Medicines report	Final report of the G10 process
2003	COM(2003) 383 A stronger European-based pharmaceutical industry for the benefit of the patient – a call for action	The Commission's answer to the G10 recommendations in which it adopted its views and drafted an extensive set of key actions for the future European pharmaceutical market
2004	Release of report "Innovation in pharmaceutical sector"	Report by Charles River Associates on a possible crisis in innovation in the pharmaceutical sector, including reasons and potential remedies
	Report on "European competitiveness in pharmaceuticals"	An update on the 2000 Pammolli report that shows that Europe's pharmaceutical industry is still behind its US counterparts
	Directive 2004/27/EC	Amending Directive 2001/83/EC on the Community code concerning medicinal products for human use. Includes changes to the label and package leaflet requirements: Braille on the packaging and leaflet to be made available in formats for the blind and partially sighted
	Regulation 726/2004	Adjustments on Community procedures for the authorization and supervision of medicinal products for human and veterinary use and the establishment the European Medicines Agency

Source: own compilation.

3.3 European Union social policy

The European Community's social policies mainly aimed at workers working across borders and guaranteeing their social security benefits in an increasingly Europe-wide labour market. The potential loss of social security benefits constituted barriers for those segments of the labour force that wanted to work abroad. Through the Treaty of Rome, the EEC was committed to "ensur[ing] the economic and social progress of their countries by common action to eliminate the barriers which divide Europe". The influence of EU social policy on the provision of statutory health services, which includes pharmaceuticals, has to be dealt with in the broader context of social

security, including statutory health services and the historical development of patient mobility. This field of EU policy is the domain of the powerful (when compared to DG Health and Consumer Protection) DG Employment, Social Affairs and Equal Opportunities. Although reimbursement levels and decisions are the competence of the Member States, there is a relevant amount of EU legislation and, perhaps even more importantly, ECJ rulings to which Member States must adhere, in case a patient decides to seek reimbursement for the costs of health services incurred abroad.

Previously, it was considered a solely private matter if anyone (e.g. a temporary visitor, a long-term resident or a migrant worker) required treatment abroad. In other words, the costs were incurred individually with or without some form of travel insurance or arrangement through the employer. However, in the 1970s, the then European Economic Community recognized that the principle of free movement of people was meaningless if only those in full health could take advantage of this freedom (Bertinato et al. 2005).

Therefore, the Community set up a social security coordination system outlined in Council Regulation (EC) No. 1408/71 and 574/72[18] that established a series of mechanisms by which individuals can obtain health care abroad based on the principle of the free movement of persons. In 2004, Regulation (EC) No. 883/04[19] was adopted, which in time will replace Council Regulation (EEC) No. 1408/71. This new regulation will eventually modernize the framework and incorporate important case law.[20]

3.3.1 The European legal frameworks for cross-border health care

In the area of health care, the primary aim of Council Regulation (EC) No. 1408/71 is to guarantee access to care in the state of residence for migrant workers and their families; however, Article 22 of Regulation 1408/71 also states the eligibility for re-

[18] Council Regulation (EEC) No. 1408/71 of the Council of 14 June 1971 on the application of social security schemes to employed persons and their families moving within the Community; consolidated version of 5 May 2005; Council Regulation (EEC) No. 574/72 of 21 March 1972 fixing the procedure for implementing Regulation (EEC) No 1408/71 on the coordination of social security schemes for persons moving within the Community, consolidated version of 5 May 2005.

[19] Regulation (EC) No. 883/2004 of the European Parliament and of the Council of 29 April 2004 on the coordination of social security systems, OJ L 166, 30.4.2004; however, this regulation has not been fully implemented and, therefore, Council Regulation (EEC) 1408/71 is referred to in this thesis.

[20] For example, prior-authorization was addressed to align it with the jurisprudence of the ECJ on "undue delay" in the Watts Case (Case C-372/04).

imbursement for treatment in another Member State than the state of residence or affiliation. This eligibility for cross-border health services is subject to the following conditions:

- Occasional care: when temporarily in another Member State, a person is entitled to (publicly contracted) care if it becomes medically necessary during their stay. To prove his/her entitlement in the home state and in order to receive care in the host state, the patient should carry a European Health Insurance Card (EHIC)[21] and show it to a publicly contracted health care provider in the host state.
- Planned care: patients moving to another Member State specifically to obtain care need to obtain prior authorization (certified by an E112 form) from their competent institution in their home state and submit it to the competent authority (depending on the Member State e.g. a sickness fund or provider) of the host state. This authorization has to be given if the treatment is part of the benefit package at home but cannot be given within a medically justifiable time limit.[22]

It is important to note that under Council Regulation (EC) No. 1408/71, the patient is treated in the host Member State as if he or she is a resident of that Member State. In other words, the reimbursement conditions and tariffs of the state of treatment apply, which will then have to be reimbursed by the payer of the home state.

The situation for cross-border health care has changed dramatically since 1998. The European Court of Justice rulings in the Kohll/Decker and subsequent ECJ cases[23] made clear that national health systems and their available statutory health services do not operate in isolation from other Member States, but that they also must adhere to rules concerning the free movement of goods and services (see 3.5 for a more detailed discussion of these cases). These rulings created an alternative

[21] The EHIC's predecessor was form E111, which had to be submitted in the host state. The EHIC was introduced in 2004 to revise and simplify the coordination mechanism for occasional care by replacing all existing paper forms required for occasional care (E111, E110, E119 and E128).

[22] Following the Watts case (Case C-372/04), the ECJ ruled that in order to refuse an E112 authorization on the grounds of waiting times, the public health service must establish that the waiting time does not exceed a medically acceptable period with regard to a patient's condition and clinical needs, i.e. no fixed time limit, but rather a waiting time that relates to an individual patient's condition.

[23] Case C-158/96, Kohll; Case C-120/95, Decker; Case C- 368/98, Vanbraekel; Case C-157/99, Geraets-Smits/Peerbooms; Case C-385/99, Müller-Fauré/Van Riet; Case C-56/01, Inizan; Case C-08/02, Leichtle.

framework, interwoven with 1408/71 and described below, not based on free movement of persons, but on the free movement of goods and services:

- Concerning *non-hospital services* received abroad, the ECJ ruled that pre-authorization was not considered necessary, as the ECJ did not regard the need to maintain the financial balance or the quality of the health services as a justification for this barrier to the free movement rules. The court reasoned that it was unlikely that a substantial rise in cross border mobility to obtain non-hospital services abroad would occur and threaten the system, since coverage would be limited to the levels and conditions of the country of insurance affiliation.
- In the case of *hospital services*, the ECJ did accept certain barriers to the free movement of health services. Access to hospital services can indeed by subjected to a pre-authorization (thus an E112 form), considering the importance for Member States to maintain balanced and accessible hospital services through a system of planning and contracting. However, authorization to receive treatment in another Member State may only be refused if the same or equally effective treatment can be obtained for the patient, without undue delay, from a contracted health provider at home.

It is important to note that non-hospital treatment provided under this legal framework, from now on to be referred to as the Kohll/Decker procedure, will be covered on the terms offered by the state of insurance, as opposed to the state of treatment under the EHIC and E112 schemes. Through its rulings, the ECJ has developed a fairly coherent body of jurisprudence regarding cross-border health services. It aimed to strike the right balance between the social nature of health services and the national competence on the one hand and internal market legislation and the European competence on the other. It remains to be seen, however, whether the current balance will remain dominant over the next years as each ruling seems to open up more questions necessitating an interpretation in the form of a new ruling. For example, there is no European definition of *hospital* or *non-hospital* treatment and *undue delay*, which may well lead to valid differences in interpretation, opening up the possibility for patients (as seen before) to start legal proceedings in order to receive pre-authorization for care that may not be covered or available and reimbursed at home.

3.3.2 Access to cross-border pharmaceuticals

The parallel-existing frameworks described above provide four options, of which three can be used to obtain reimbursement for a prescription-only medicine (POM) abroad (see Figure 6).[24]

1. The first option, using the EHIC card, only applies to occasional care on a temporary stay abroad (e.g. holidays). The patient is treated in the host Member State as if he or she is a resident of that Member State, which implicates that reimbursement conditions, benefit baskets and tariffs of the state of treatment apply. This option could motivate patients to go abroad on holidays or a daytrip, for example and feign the immediate need for a certain pharmaceutical treatment that is not provided or reimbursed in the home system. The potential to shop around for pharmaceuticals with an EHIC is considerable, although distances, travelling costs and information on availability constitute serious barriers.
2. The second option, enabled through the ECJ rulings, is planned non-hospital care abroad without using an authorization. In this case, patients are restricted to the terms and benefits of the home state. This means that they cannot obtain reimbursement for pharmaceuticals abroad that are not included in the benefit basket at home (i.e. the positive list for pharmaceuticals). This also implies that possible higher tariffs in the state of purchase will not be covered by an additional reimbursement (as under EHIC and E112). This is of course a rather theoretical situation as it seems unlikely for a patient to go abroad for a pharmaceutical that can be obtained in the home state without extra costs. Although, under certain circumstances, for example, if a foreign pharmacy is much closer than the pharmacy in the home state, the patient may settle for a (small) out-of-pocket payment. If, however, this particular pharmaceutical is cheaper abroad, the patient would in theory be entitled to receive reimbursement up to the higher home state tariff and possibly make a profit[25] or bypass a co-payment. Whether this option is used in practice and known to the public is hard to say because no data or case studies are available. Another interesting development in this regard is the increasing number of internet pharmacies operat-

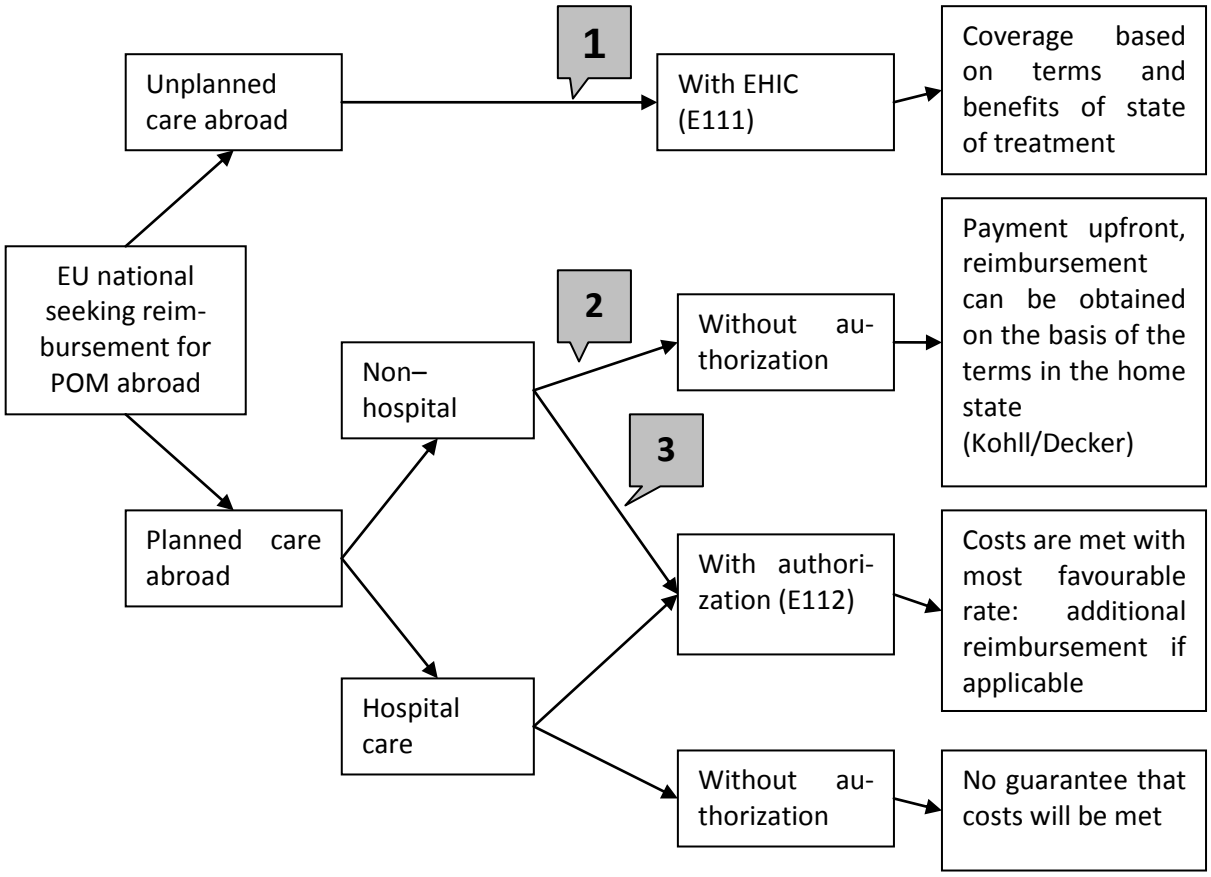
[24] Hospital treatment will often include pharmaceutical treatment, however, the focus of this thesis is the extramural provision of pharmaceuticals that citizens can obtain individually. Furthermore, one could interpret cross-border contracts, which are bilateral agreements mostly taking place between health insurers and health care providers as a fifth option to receive cross-border care. Both are, however, predominantly beyond the scope of this thesis.

[25] This is the result of the Vanbraekel ruling (Case C- 368/98)

ing internationally that make an (expensive) journey abroad unnecessary. However, the development of this practice is faced with many obstacles. Some pharmacies will not (or are not permitted) to recognize a foreign prescription, although this may change in the future when a new health services directive will likely also contain mutual recognition of prescriptions. There still exist differences in labelling language, pharmaceuticals on the market and the way that Member States enable internet pharmacies, even though this may violate European case law.

3. The third option requires the patient to seek authorization to get a reimbursed pharmaceutical abroad. When granted, a patient should be eligible to receive reimbursement at the most favourable rate – the home state rate or the host state rate. This option could be used to obtain reimbursement for pharmaceuticals that are not covered at home, but the authorization may likely be refused. If a consumer seeks reimbursement for pharmaceuticals that are also provided at home, a positive authorization decision seems very unlikely in case of a more expensive rate than at home.

Figure 6. Assumption of health care costs abroad, options listed 1 through 3 that may include individually purchased pharmaceuticals.



Source: Adapted from Assumption of Healthcare Abroad, DG Employment, Social Affairs and Equal Opportunities.

The options described above, of which some more hypothetical or theoretical than others, are all not very well known to the public, providers and some payers mainly due to a lack of information. It seems though that there is potential for patients to obtain reimbursed medicines that are not included in the state of insurance, primarily through the EHIC. In addition, there seems to be the possibility to make a profit if the (also in the home state provided and reimbursed) pharmaceutical is cheaper abroad, mainly through the Kohll/Decker procedure. In other words, there may be a financial incentive to seek out those pharmaceuticals that are reimbursed at home but are available and cheaper abroad. This practice may still be illegal depending on the national framework and it seems that there is still a need for further clarification, which may be given in the next years provided there are ECJ rulings dealing with cross-border pharmaceuticals.

3.4 European Union health policy

The European Union's involvement in health policy and health care services has always played a relatively minor role in the course of European integration. As stipulated in Article 152 of the Treaty Establishing the European Community (TEC), Community action in the field of public health shall fully respect the responsibilities of the Member States for the organisation and delivery of health services and medical care. Furthermore, it is widely accepted that health care services are subject to the subsidiarity principle. Nevertheless, there is a considerable amount of EU legislation, mainly emanating from the implementation of non-health EU policies, which also has repercussions for several topics relevant to governing, financing and delivering health services (e.g. medical devices, public procurement and the mobility of health professionals). In regard to health services and pharmaceuticals, the 1992 Maastricht Treaty (formally the Treaty of European Union), which reformed the existing treaties and the Treaty establishing the European Community (TEC) in particular, expanded the EU's mandate on health policy (see Table 10) with two new provisions.

First, Article 3(o) empowered the Community to "contribute to the attainment of a high level of health protection" for its citizens. Secondly, Article 129 also ensured a high level of health protection in the implementation of all Community policies and activities and outlined specific areas of competence for this objective, namely the prevention of diseases through promoting research on their causes, their transmission and their prevention and through encouraging cooperation between Member States. These two provisions were renewed and renumbered through the Treaty of Amsterdam into Article 3 par. 1 (p) and Article 152, respectively.

Table 10. EU mandate on health policy in the Treaty establishing the European Community.

Article, new version (since the Treaty of Amsterdam[26])	Article, old version (the Treaty of Maas-tricht)	Content/significance for public health
3 par. 1 (p)	3 (o)	A contribution to the attainment of a high level of health protection
30	36	Restriction of the free movement of goods on the grounds of health
39 par. 3	48	Restriction of the free movement of workers on the grounds of public health
46 par. 1	56	Restriction of the right of establishment on the grounds of public health
95 par. 3	100 (a)	Attainment of a high level of health protection in the approximation of laws
95 par. 6	100 (a)	Extension of the approximation period in the absence of danger to human health
95 par. 8	100 (a)	Obligation of Member States to notify specific public health problems in the field that have previously been the subject of harmonisation matters
137	118	Improvement to the working environment for the protection of worker health and safety
140	118c	Prevention of occupational accidents and diseases
152	129	Public health competences
153	129a	Health protection as part of consumer protection
174 par. 1	130 (r)	Protecting human health as part of environmental policies
186	135	Including public health provisions to the provisions on the association of overseas countries and territories

Source: Wismar et al. (2002).

[26] The Treaty of Amsterdam (1997) was not the last amendment. The TEC was last amended by the Treaty of Nice (2001), which entered into force 1 February 2003. The Treaty of Lisbon, signed on 13 December 13 2007, amends the existing treaties of the European Union (EU) and is due to come into force in 2009 if it is successfully ratified by all European Union Member States.

The limitations of the Community sphere of competence are set out in the subsidiarity principle (Article 5 of the TEC), which was established in EU law by the Treaty of Maastricht (1992) and entered into force on 1 November 1993. The subsidiarity principle can be applied only to non-exclusive Community competences (i.e. where shared competence exists, such as public health) and to legislation introduced for the first time. The present formulation, last amended by the Treaty of Nice (2001), entered into force on 1 February 2003 and states:

> *In areas which do not fall within its exclusive competence, the Community shall take action, in accordance with the principle of subsidiarity, only if and in so far as the objectives of the proposed action cannot be sufficiently achieved by the Member States and can therefore, by reason of the scale or effects of the proposed action, be better achieved by the Community. Any action by the Community shall not go beyond what is necessary to achieve the objectives of this Treaty.*

It makes clear that the Community can only become active when their objectives cannot be achieved by the Member State (the sufficiency criterion) and when Community action brings added value over and above what could be achieved by the Member State (the benefit criterion).

With regard to EU health competences, the subsidiarity principle is visible in Article 152 of the TEC. It states (paragraph 4c):

> *…excluding any harmonisation of the laws and regulations of the Member States.*

and (paragraph 5):

> *Community action in the field of public health shall fully respect the responsibilities of the Member States for the organisation and delivery of health services and medical care.*

Therefore, most Member States have assumed that health services fall within their spheres of competence, on the basis of Article 152 of the TEC. However, it became increasingly apparent that EU policies (e.g. competition law, advocating the Four Freedoms) do interfere with Article 152 because they may not necessarily respect the responsibilities of the Member States regarding their respective health systems. As far as a European level health policy is concerned, the competence is rather confined to public health policy, advocated by the Directorate-General for Health and

Consumer Protection, which is also commonly referred to as DG SANCO.[27] Examples include preventing human illnesses and diseases as well as food safety. Also, DG SANCO is leading the efforts to clarify (without specific legal action) the framework for cross-border care, as discussed in Section 3.3. However, its influence on pharmaceutical markets and provision is small when compared to DG Enterprise.

3.5 The European Court of Justice (ECJ)

The European Court of Justice (ECJ) was set up in 1952 in Luxembourg. It has the last word on matters of EU law in order to ensure its equal application across the European Union and Member States. Each Member State appoints one judge for a renewable term of six years. Through its interpretations of Community law, the ECJ wields considerable influence on the complicated interplay between the European Union, Member States and health services, as well as topics relevant to market liberalisation, such as parallel importing, repackaging, intellectual copyrights and rebranding. National differences in the degree and sort of pharmaceutical market regulation may prove vulnerable to litigation in the distribution of pharmaceuticals, for example. A discussion of all case law concerning the various topics affecting the pharmaceutical market is beyond the scope of the thesis. Instead, this section focuses on the court's decisions on cross-border health care, which have significant effects on the cross-border provision of health (see Section 3.3) and provides illustrative examples of pharmaceutical market liberalisation.

3.5.1 The ECJ and cross-border health services

Three important ECJ judgements that greatly impacted the organisation of national health care are Kohll (C-158/96) and Decker (C-120/95), 1998, Geraets-Smits/Peerbooms (C-157/99) and Vanbraekel (C-368/98), 2001 and Müller-Fauré and Van Riet (C-385/99), 2003.[28]

Mr. Kohll and Mr. Decker both held Luxembourg citizenship but were refused reimbursement by their Luxembourg health insurance. Mr. Decker sought reimburse-

[27] From the French words *santé* (health) and *consommateurs* (consumers).

[28] This list is non-exhaustive. More recent rulings dealing with border crossing health services which affirm and clarify the previous rulings include, for example, Case C-56/01 (Inizan), Case C-08/02 (Leichtle), C-145/03 (Keller) and Case C-372/04 (Watts).

ment for a pair of eye glasses (goods) he had bought in Belgium using a prescription from a Luxembourg ophthalmologist, whereas Mr. Kohll demanded reimbursement for a dental treatment (services) his daughter had received in Germany. Neither had obtained pre-authorization from their home insurance institution as requested under the E112 procedure. In the Decker case, the court affirmed that national security schemes should also respect Article 28 of the EC Treaty on the free movement of goods. In the Kohll case, the ECJ concluded that the requirement of prior authorization constituted a violation of Articles 49 and 50 of the EC Treaty, which ensure the free movement of services. A refusal, the ECJ continued, could only be justified on the grounds of maintaining a balanced medical service accessible to all, guaranteeing the financial balance of the social security system, or overriding reasons in the general interest (e.g. health protection). The ECJ found none of the above justifications for a refusal applicable, as reimbursement at the level of the home state would in no way threaten the financial balance or the quality of the health services in the home state.

The Kohll and Decker cases sparked intense political and scientific debate on the meaning and implication of their rulings. Many questions remained, such as on the scope (whether it includes hospital care) and implications for national health systems. It was evident that there was a need for further clarification, which was soon provided by the ECJ rulings in the Geraets-Smits/Peerbooms and Vanbraekel cases, all of which concerned the reimbursement of hospital costs incurred in a Member State other than the home state.

Dutch citizens Mrs. Geraets-Smits and Mr. Peerbooms were both refused reimbursement by their Dutch sickness funds for the costs of their hospital treatment abroad for multi-disciplinary Parkinson treatment in Germany and experimental coma patient treatment in Austria, respectively. Neither had obtained prior authorization for these –in the Netherlands unavailable– treatments and they tried using the procedure based on the free movement of services established in the Kohll case to get a refund after returning home. The ECJ ruled identically in both cases, drawing on previous case law and reiterating that hospital treatment is a *service* according to the EC Treaty and through stating that the Netherlands had violated the free movement

rules by refusing authorization. However, the ECJ accepted that a Member State can justify certain restrictions for treatment through a pre-authorization if such a restriction is necessary in order to maintain a balanced medical and hospital service accessible to all and to guarantee the financial balance of the social insurance system. The ECJ then continued to elaborate on what constitutes a fair and proportional pre-authorization procedure, stating:

> *Authorization to receive treatment in another Member State may be refused only if treatment which is the same or equally effective for the patient can be obtained without undue delay from an establishment with which the insured person's insurance has an agreement.*

Mr. Vanbraekel tried to obtain reimbursement for orthopaedic surgery that his late wife, Mrs. Descamps, a Belgian resident with Belgian health insurance, had received in a French hospital. However, upon her return to Belgium, the Belgian court concluded that she was wrongfully denied authorization. The question that faced the Belgian court was whether she should be reimbursed at the Belgian tariff (as the Kohll ruling would imply for treatment without authorization), which was significantly higher, or the lower French tariff, as Council Regulation (EEC) No. 1408/71 implies. Eventually the ECJ was consulted and ruled that lower rates of reimbursement for treatment delivered abroad can discourage people from applying for authorization and medical treatment abroad and, because a violation of the free movement rules occurred, additional reimbursement covering this difference must be granted to the insured.

This jurisprudence was reaffirmed in the Müller-Fauré/Van Riet judgment of 13 May 2003, concerning the reimbursement of orthodontic treatment outside the Member State of affiliation without prior authorization. The court made clear that patients are generally entitled to reimbursement for non-hospital services (no need for prior authorization), whereas a pre-authorization for hospital services may be justified. In the judgement, the ECJ once more explicitly stated the conditions that Member States must fulfil in order to ensure that their health care systems are compatible with Community law.

These rulings created a parallel framework to meet the costs of health services incurred in another Member State. The original framework (i.e. the procedures estab-

lished under EC Regulation 1408/71, which includes procedure E112 for planned care and procedure E111, now the European Health Insurance Card, EHIC, for care that becomes medically necessary during an occasional stay) was initially set up to facilitate the free movement of migrant workers. Hence, the procedure was based on the free movement of persons. The new framework, which evolved in the aftermath of the Kohll/Decker case, is based on the free movement of services and goods.

The cases exposed a contradiction in the treaties: free movement of goods and services but a de facto exclusion of medical goods and services from these principles. Member States still organize their own social security systems with country specific conditions. The ECJ ruled that the free movement rules regarding services and goods also apply to the health services in the European Union and that this should be facilitated by Member States. However, the ECJ also made clear that public health and social security remain the preserve of Member States from both a legal and a political perspective.[29] The result is a rather complicated framework for the reimbursement of cross-border services (see Section 3.3.1), especially from the perspective of European citizens. Nevertheless, these ECJ rulings increased the opportunities for European citizens to receive reimbursed health care goods (pharmaceuticals) and services (prescriptions, pharmacy services) across borders.

3.5.2 The ECJ and pharmaceutical market liberalization

The ECJ rulings have been encouraging parallel importing, which has resulted in the removal of divergent national intellectual property rights regarding copyrights, trademarks and patents. Furthermore, unnecessary national licensing regimes that prevent generic competition have been challenged by the free movement rules. In the absence of harmonization measures, the ECJ has been generally reluctant to act against national rules and regulations regarding price and profit regulation as well as reimbursement (selective lists). Ironically, the price differentials resulting from national divergence keeps parallel trade attractive. Also, Member States are free to

[29] In the *Smits and Peerbooms* (C-157/99) judgement of 12 July 2001, the court stated that "according to case law, Community law does not detract from the power of the Member States to organize their social security systems. In the absence of harmonisation at Community level it is therefore for the legislation of each Member State to determine the conditions concerning the right or duty to be insured with a social security scheme. Nevertheless, the Member States must comply with Community law when exercising that power" (paragraphs 44-46 of the judgement).

determine selling methods, provided that they do not discriminate against imported products (ECJ 1995). However, an ECJ ruling challenged the Commission's ability to force the pharmaceutical industry to provide unlimited volumes of medicines to parallel importing wholesalers when it overturned a 1996 European Commission fine worth 3 million ECU on the Bayer Group for limiting the supply of Adalat. From 1989 to 1993, the retail price of Adalat (a cardiovascular drug) was approximately 40% lower in France and Spain than in the UK. This motivated French and Spanish wholesalers to export large quantities of the pharmaceutical to the UK, leading to losses up to €115 million for the British subsidiary. The Bayer Group countered this development by reducing the supply of medicines to Spanish and French wholesalers. The ECJ ruled that the Commission had failed to prove a violation of European competition law as no evidence was found of an agreement between Bayer and its Spanish and French wholesalers to limit parallel exports of Adalat to the UK.

However, a review undertaken by Hancher (2004) demonstrates that the ECJ has been generally unwilling to reverse its pro-internal market, pro-parallel import view, especially where it concerns unnecessary obstacles to free movement as a result of nationally divergent property rights. This may be at odds with the G10 process, which acknowledges the importance of property rights to industry and aims to find an appropriate balance between providing intellectual property protection for innovative medicines and easy access to the generic markets.

3.6 European Medicines Agency (EMEA)

The EMEA is responsible for the coordination of the scientific resources that evaluate and supervise medicinal products for both human and veterinary use. To this date, there have been three procedures for the mutual recognition of marketing authorization by Member States: the CPMP procedure (1976-1985), the multi-state procedure (1985–1995) and the decentralized procedure (1995 to the present). The first two were very similar to each other and represent what is often characterized as the "weak" European regulatory state and they were not overly successful in terms of applications admitted. Major changes occurred in 1995 with the constitution of the decentralized procedure combined with the centralized procedure through the EMEA, which is often characterized as the "strong" European regulatory state (Abra-

ham and Lewis 2000). These changes mark the beginning of a revolution in European pharmaceutical regulation and made market authorization increasingly the responsibility of the London-based EMEA. In 2004, adjustments were made to the centralized and the decentralized procedure through EC Regulation 726/2004, which repealed the well-known EC Regulation 2309/93 and aims to provide, in the words of the EMEA, "a more robust, modern and effective regulatory framework for pharmaceuticals in Europe" (EMEA 2005).

Changes made to the centralized procedure include the following:

- an expansion of the list of products for which the centralized procedure is mandatory (in addition to new biotechnology and orphan drugs, all new products indicated for treatment of AIDS, cancer, diabetes and neurodegenerative diseases)
- accelerated procedures through shortened deadlines in the different steps of the overall procedure
- "fast track" procedures for products of major interest to public health and therapeutic innovation
- a strengthening of the role of the European Medicines Agency as a scientific advisor (e.g. it may request the European Commission impose financial penalties on authorization holders)

Some important changes to the mutual recognition decentralized procedure are:

- harmonization of the data protection period with the period provided for the centralized authorized products (i.e. 10 years), with a possibility for a one year extension under certain conditions
- improvement of the procedure (i.e. definitions, legal status and improvement on arbitration mechanism applicable when Member States disagree over a certain authorization) by ensuring that the objections related to the serious risk of public health are evaluated properly and that necessary follow up measures are taken.

The centralized drug approval through the EMEA procedure has been reasonably successful and will include generic products in the future. Approval of a drug requires acceptance in all other EU Member States. In the national decentralized process, a company can apply for approval in one Member State. When it receives approval it can –with the expectation of quick authorization– apply to the market in

other Member States. In case of an objection by a Member State, the EMEA solves the dispute.

Despite its relative success, there also has been criticism. Concerns have been raised about the review process, which supposedly approves drugs that may have little clinical benefit despite their higher prices (Mossialos et al. 2004). Consequently, approved drugs are not likely to meet the expectations of patients who believe that these new drug signify substantial improvements in treatments (Garattini and Bertele' 2002).

Furthermore, there are concerns about the operation of the EMEA (Garattini and Bertele' 2004). First, the EMEA is regulated by DG Enterprise, not by DG Health and Consumer Protection whose objectives would perhaps be more aligned with the interests of patients and less with the interests of industry. Secondly, while the EMEA and decentralized national licensing agencies are primarily financed through fees from industry for market authorization, it can provoke competition for funds. Ideally, the decentralized route would become obsolete and remove the competition. In addition, the European Commission recently suggested that the management board of the EMEA should include representatives from the pharmaceutical industry, providing a possible source for conflicts of interest.

The EMEA does not have an internal staff capable of carrying out evaluations of submitted products, as, for example, its US counterpart, the Food and Drug Administration (FDA). Instead, it contracts national medicine agencies to perform evaluations and report back their findings. Companies can nominate a national agency when applying through the centralized procedure, which may lead them to choose those more likely to give their product a favourable report (Garattini and Bertele' 2001). This practice could stimulate national agencies to compete with other agencies on rapid authorization and favourable reports.

All of these factors contribute to the fact that the EMEA has been accused of favouring industry in its operations. An alleged swift approval, rather than strict assessment as a prime objective, has been criticized by various authors (e.g. Abraham and Lewis 2000; Bertele' and Li Bassi 2004; Garattini and Bertele' 2001, 2004).

4 National pharmaceutical policies in the EU

The national pharmaceutical market forms an important part of health care systems, not only in economic terms but also in terms of public health. The national regulatory mechanisms in Europe were put in place in the aftermath of the thalidomide disaster, showing an analogy with the European Community developments in the early 1960s. In the early years, these regulatory systems mainly safeguarded the quality and accessibility of pharmaceutical provision, but, as early as the 1980s, the containment of pharmaceutical expenditures became more and more a policy objective in European states. The rising expenditures on drugs put pressure on the national health budgets, which posed a threat to the financing and accessibility of health care. Pharmaceutical expenditures, which frequently are growing faster than GDP and total health expenditure (see Table 11), have been the subject of many national cost-containment strategies.

The degree to which cost-containment measures are adopted reflects how much focus is given to industrial policy (e.g. nourishing a science base, employment and strategic issues), public health policy (e.g. safe medicines, patient access, high quality preparations and innovative cures) and health care policy (e.g. cost-containment, generic promotion, cost effective medication). However, even Member States like Germany and the UK, who support strong industry and historically have been more willing to make a trade-off in favour of industrial policy, are cutting back on pharmaceutical expenditures.

Before a medicine is dispensed, it has to be admitted to a national market through the responsible authorization agencies. This can be achieved through the EMEA (centralized procedure) or through a national medicine agency (decentralized procedure and exclusively national procedure). As soon as the product is licensed, various national regulations – often transposed European directives – apply to the medicine on issues ranging from packaging, advertising and distribution to pharmacovigilance. It is important to note that referring to “national policy” in this regard may be misleading, as the actual policy is the sum of transposed EU directives and national regulation. This will be discussed in greater depth in the following sections.

Table 11. Pharmaceutical expenditures in several EU Member States, 1985–2005.

	Total expenditure on pharmaceuticals (% of total health expenditure)					Total expenditure on pharmaceuticals (% of GDP)				
Year	**1985**	**1990**	**1995**	**2000**	**2005**	**1985**	**1990**	**1995**	**2000**	**2005**
Austria		9.0	9.2	11.9	12.0		0.8	0.9	1.2	1.2
Belgium	15.7	15.5	16.7		17.1	1.1	1.1	1.4		1.8
Czech Rep.		21.0	25.1	23.4	25.1		1.0	1.8	1.5	1.8
Denmark	6.6	7.5	9.1	8.8		0.6	0.6	0.7	0.7	2.0
Finland	9.7	9.4	13.0	15.2	15.8	0.7	0.7	1.0	1.1	1.3
France	16.2	16.9	15.0	16.5	16.7	1.3	1.4	1.6	1.7	1.9
Germany	13.8	14.3	12.9	13.6	15.1	1.2	1.2	1.3	1.4	1.6
Greece		14.3	15.7	17.8	18.5	1.0	0.9	1.4	1.4	1.7
Hungary			25.0		30.5			1.8		2.6
Italy		20.3	20.7	22.0	20.3		1.6	1.5	1.8	1.8
Luxembourg	14.7	14.9	12.0	11.0	8.4	0.8	0.8	0.7	0.6	0.7
Netherlands	9.3	9.6	11.0	11.7		0.7	0.8	0.9	0.9	
Poland					28.0					1.7
Portugal	25.4	24.9	23.6	22.4	21.6	1.5	1.5	1.8	2.0	2.2
Slovak Rep.				34.0	31.9				1.9	2.3
Spain	20.3	17.8	19.2	21.3	22.4	1.1	1.2	1.4	1.5	1.9
Sweden	7.0	8.0	12.3	13.8	13.7	0.6	0.7	1.0	1.1	1.3
UK	14.1	13.5	15.3			0.8	0.8			

Source: OECD Health Data (2008).

A decision has to be made on whether the pharmaceutical is covered under the health insurance scheme of the respective Member States. In principle, most Member States have universal public coverage (i.e. coverage for the entire population, defined by legal residence or citizenship). In most EU27 Member States, this is accomplished through a contribution-based social health insurance (SHI) system or a tax-based National Health Service (NHS).[30] The reimbursement decision is a crucial

[30] SHI countries include Austria, Belgium, Czech Republic, Estonia, France, Germany, Luxembourg, the Netherlands, Slovakia and Slovenia. NHS countries include UK, Sweden, Ireland, Italy, Latvia, Poland, Portugal and Romania. More precisely speaking, however, each country has a unique mix of sources for health care revenues that consist of both general taxes and social contributions. Furthermore, some systems cannot be strictly described as systems of universal insurance. For certain population

decision for industry. If their products are not reimbursed, patients are not as likely to use it due to high costs, meaning that they will not be able to receive a return on their investment. After admission to the benefit basket, more regulations apply to the pharmaceutical under the respective health scheme (e.g. reference pricing and co-payment measures). Furthermore, other regulations seek to bring down pharmaceutical expenditures by influencing the prescriber (GP/physician) and pharmacist, which does not directly concern the pharmaceutical.

International studies use various ways to categorize pharmaceutical policies: price measures versus volume measures, direct versus indirect measures, demand side versus supply side measures, or coercive versus non-coercive measures. However, these distinctions are often used to describe national cost-containment strategies Therefore, in order to get a more coherent impression of national pharmaceutical frameworks, the measures and regulatory approaches are discussed at the appropriate level as depicted in Figure 7.

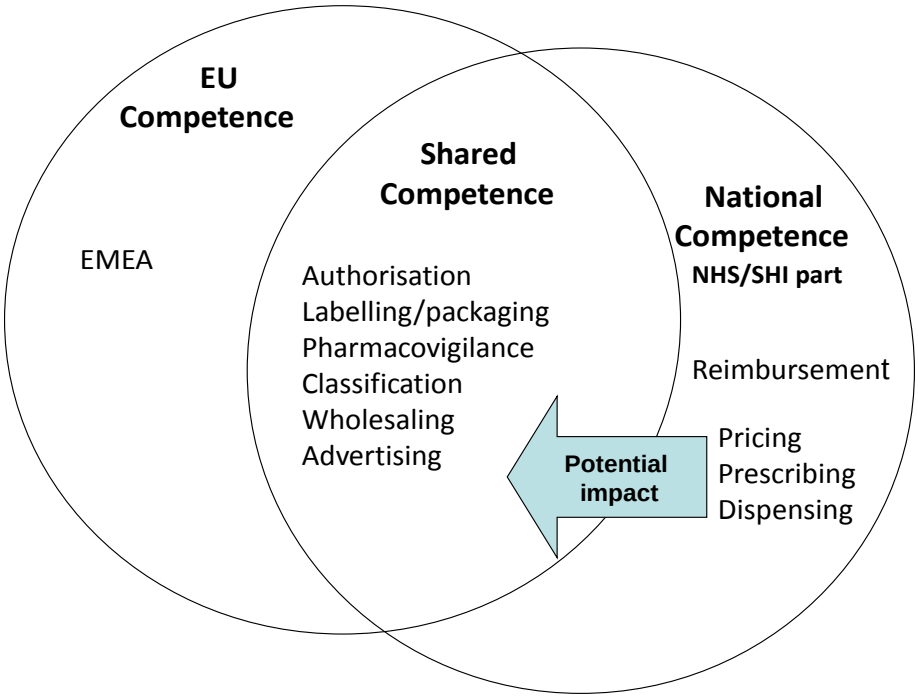
The first section of this chapter deals with regulation that applies to the entire national pharmaceutical market. This includes, following the pharmaceutical down the value chain: marketing authorization (licensing), pharmacovigilance, classification, distribution and advertising. These issues are a shared competence between the European Union and Member States. The second and third sections discuss the various national pharmaceutical regulations and measures under the respective SHI and NHS schemes in Member States, such as pricing and reimbursement. These will be divided into measures with a potential impact on the entire pharmaceutical market (Section Two) and measures that only have an influence within the system (Section Three). Making such a distinction is useful because it highlights the areas of shared competence where the Community can become active, albeit in accordance with the principle of subsidiarity. Within their respective health systems, the competence generally lies with the Member State, following Article 152.[31] However, national reg-

groups, the primary mode (or part) of cover for health care is substitutive voluntary health insurance (e.g. in Ireland and Germany).

[31] The word “generally” was chosen because, as seen before, the organisation of the health systems of Member States must still respect the Four Freedoms. Therefore, the national systems are not completely exempt from Community influence.

ulation that impacts the entire national health market (see arrow in Figure 7) could also fall within the sphere of the EU competence (e.g. pricing regulation that affects non-reimbursed medicines). This implies a field of shared competence. It is specifically in these fields that the EU has used its competence and might possibly use it in the future. This chapter concludes with a section exclusively dedicated to pharmaceutical policy in new Member States. Its significantly different historical backgrounds and recent Western-based reforms warrant a more thorough look into its development and reform processes.

Figure 7. Competences in the national pharmaceutical market.



4.1 Regulation for the entire national pharmaceutical market

The dissonance between the industrial policy-leaning European Commission and health policy-leaning Member States, forces Member States to use the principle of subsidiarity to block European regulation. Although Member States control a significant portion of their respective pharmaceutical markets, the EU still plays a considerable role. The EU regulatory framework, which aims to promote the single Europe-

an market, has strong impact on issues such as manufacturing, authorization, labelling/packaging requirements, advertising rules, wholesale distribution and patent protection. This is achieved through Directive 2001/83/EC,[32] the Community code relating to medicinal products for human use, hereafter to be referred to as the Community code, which integrates many of the previous pharmaceutical directives (see Section 3.2). The contents and scope of the Community code are outlined in Table 12. Member States have regulations in place on these issues, but their authority in these matters has been gradually overtaken due to these directives, which have to be transposed in their legal framework in order to further harmonize pharmaceutical legislation.

Table 12. Community code.

Directive 2001/83/EC on the Community code relating to medicinal products for human use	
Title I	Definitions
Title II	Scope
Title III	Placing on the market
Title IV	Manufacture and importation
Title V	Labelling and package leaflet
Title VI	Classification of medicinal products
Title VII	Wholesale distribution of medicinal products
Title VIII	Advertising
Title IX	Pharmacovigilance
Title X	Special provisions on medical products derived from human blood and plasma
Title XI	Supervision and sanctions
Title XII	Standing Committee
Title XIII	General provisions
Title XIV	Final provisions

[32] Directive 2001/83/EC, later amended by Directive 2004/27/EC, replaces and consolidates the first pharmaceutical Directive 65/65/EEC, with all its relevant amendments, the two landmark directives 75/319/EEC and 75/318/EEC and their respective amendments and the 1992 directives on wholesaling (92/25/EEC), classification (92/26/EEC), labelling and packaging (92/27/EEC) and advertising (92/28/EEC).

4.1.1 Market authorization

In 1995, the establishment of the European Medicines Agency (EMEA) and the centralized procedure altered the authorization process of medicines in the European Union (also see Chapter 3). It leaves pharmaceutical companies that seek market authorization in a Member State with three options: the centralized and the decentralized procedures for EU-wide authorization and the old exclusively national procedure.

The centralized procedure is compulsory for new biotechnology products, orphan drugs and all new products for the treatment of AIDS, cancer, diabetes and neurodegenerative diseases. The application is submitted directly to the EMEA, which checks whether it fulfils all necessary requirements. If so, the EMEA validates the application and the Committee for Medicinal Products for Human Use (CHMP),[33] part of the EMEA and selects two rapporteurs to assess the application. These appointed rapporteurs are individual members of the CPMP and take the preference of the applicant into account. The rapporteurs will act as the coordinators of the assessment report and the contact person for the applicant. At the conclusion of the scientific evaluation, undertaken within 210 days, the opinion of the full membership of the CHMP is transmitted to the European Commission to be transformed into a single market authorization for the whole EU, published in the Official Journal of the European Communities. After the product is licensed through the centralized procedure, the CHMP is responsible for pharmacovigilance until the product is available on the market.

The decentralized procedure (or mutual recognition procedure) applies to the majority of conventional medicinal products and is based on the principle of mutual recognition of national authorizations, granted by national marketing authorities.[34] Through this procedure, the market authorization for one European Member State can be extended to one or more Member States identified by the manufacturer. When problems concerning the recognition of authorizations occur between Mem-

[33] The Committee for Medicinal Products for Human Use (CHMP) was formerly known as the CPMP, Committee for Proprietary Medicinal Products (see Chapter 3).

[34] The concerned national medicines authorities responsible for licensing, classification and pharmacovigilance can be found at www.hma.eu.

ber States, the EMEA (through the CHMP) gets involved and functions as an arbitrator. In such a situation, the opinion of the CHMP is transmitted to the European Commission. If minor or no objections are raised by the Member States, the authorization is published in the Official Journal of the European Communities. The mutual recognition is compulsory for any non-centralized product sold in more than one Member State.

Market authorization exclusively for one country can still be obtained through the medicine agency of that particular Member State. These medicine agencies (also called licensing agencies) also have the national responsibilities of pharmacovigilance and the classification of all authorized products irrespective of procedure. However, as soon as the manufacturer seeks market admission in another Member State, the mutual recognition procedure becomes compulsory. The various European national medicine authorities keep in regular contact on issues of Community interest through the Heads of Medicines Agencies (HMA).

The criteria for the authorization of pharmaceuticals in Europe are based on the EU-wide good clinical practice standards and include proven safety and efficacy, as outlined in Directive 2001/20/EC (see below). Only a small beneficial effect needs to be demonstrated in order to fulfil the efficacy criteria and cost-effectiveness is not included. This implies that a newly licensed pharmaceutical does not necessarily have higher therapeutic benefits. Cost-effectiveness does not become an issue in most countries until the reimbursement decisions on coverage under the SHI/NHS are made. The role of the authorization procedure is mainly to guarantee that the product works, is safe and is of good pharmacological quality. Directive 2003/94/EC of 8 October 2003 lists the principles and guidelines of good manufacturing practice concerning pharmaceuticals. Title IV and V of the Community code cover further legal requirements for manufacturing, labelling and package leaflets.

4.1.2 Pharmacovigilance

After the pharmaceutical is approved, whether according to the centralized, decentralized or national procedure, it undergoes post-marketing surveillance, or pharmacovigilance. Pharmacovigilance is a continuation of the evaluation of the pharmaceutical. Although pharmacovigilance used to be a solely national matter, after the tha-

lidomide disaster, Directives 65/65/EEC and Directive 75/319/EEC, now part of the Community Code relating to medicinal products for human use, forced all actors to collect, collate and exchange adverse drug reactions (ADRs) within the European Economic Area. However, the directives are binding as to the results to be achieved and many of the regulatory requirements were already covered under existing national law. For example, the UK enacted the Medicines Act in 1968. Consequently, many different systems with different reporting patterns were put in place, if not already established.

Furthermore, the new authorization procedures expose approved medicines to much larger populations, more so than under the pre-1995 European situation. These developments raised concern about pharmacovigilance standards in Europe and highlighted the need for a better understanding of the various national systems before pharmacovigilance assessment could be applied to the EU as a whole. Therefore, the EudraVigilance data processing network and management system was launched in December 2001. It has been developed according to internationally-held standards. As a result, the EMEA implemented the electronic data exchange of Individual Case Safety Reports (ICSRs) for marketed medicinal products. The system enables the exchange of pharmacovigilance data between national medicine agencies, the EMEA and the pharmaceutical industry.

Directive 2001/20/EC,[35] the Clinical Trials Directive, has been fully implemented since 1 May 2004. The directive aims to simplify and harmonize the administrative provisions governing clinical trials by establishing a clear, transparent procedure and creating conditions conducive to the effective co-ordination of such clinical trials in the European Community by the medicine agencies involved. This means that from now on, sponsors of clinical trials need to obtain a EUDRACT number from the new EUDRACT database in order to collect all relevant information about suspected serious unexpected adverse reactions (SUSARs). This information is then reported to the appropriate authorities. EudraVigilance does not only cover the post-authorization phase, but also the pre-authorization phase.

[35] Directive 2001/20/EC of the European Parliament and Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use.

4.1.3 Distribution and classification of pharmaceuticals

When a pharmaceutical enters a national market, pharmaceutical wholesalers are subject to national regulation, once again, stemming from the Community code relating to medicinal products. The Code has a full title dedicated to wholesaling (Title VII) and integrates the 1992 directive (92/25/EEC) on wholesale distribution. The Code includes the requirement for the possession of an authorization before engaging in wholesale activity, forces Member States to follow up with the authorization holder and suspend or revoke the authorization if authorization conditions are not met. Member States must ensure that their authorization holders maintain adequate premises, qualified staff, precise recordkeeping, emergency plans for market-withdrawal of pharmaceuticals and information that may trace the distribution path of every medicinal product. Guidelines on good distribution (94/C 63/03[36]) are similar to the guidelines for good clinical and manufacturing practice and are also in accordance with the Community code.

Pharmaceutical products can be dispensed by hospitals, community pharmacies and, depending on their classification and the Member State, drug stores and supermarkets. The European pharmacy sector is a heavily regulated, controlled field. In a study of regulation of professional services in the EU, conducted for the Directorate-General for Competition, Paterson et al. (2003) found that pharmacists are faced with the most extensive, restrictive regulation of all researched professions, which included accountants, lawyers and engineers. Pharmacies must be licensed under national regulation in all EU Member States. Depending on the Member State, the responsible agencies are, for example, the French Départments and German Länder, the Health Care Inspectorate in the Netherlands, the National Agency for medicines in Finland, the health department (Belgium, Denmark and Portugal), the Royal Pharmaceutical Society in the UK and the College of Pharmacists in Spain (Taylor et al., 2004a). In Sweden, pharmaceutical products are sold through a state monopoly and only one state-owned company is carrying out the pharmacy services. Portugal, Austria, Belgium, Denmark, Finland, France, Italy, Spain, Greece and Luxembourg have quite extensive regulations, in which the number of pharmacies is restricted, for ex-

[36] Guidelines on Good Distribution Practice of Medicinal Products for Human Use (94/C 63/03)

ample through economic needs tests and maximum pharmacies relative to population numbers. Ireland, Germany, the UK and the Netherlands do not have these kinds of restricting market entry regulations (Paterson et al. 2003). With the exception of Belgium, Ireland, the Netherlands, Sweden and the UK, only pharmacists can own pharmacies. In the Netherlands, for example, non-pharmacists have been allowed to employ pharmacists since 1999. This paved the way for pharmacies owned by supermarkets, chemists, insurers and industry.

Each Member State has its own medicines classification system, which is set up to ensure that the public benefits from the pharmaceutical while minimizing chances of inappropriate use and harm to the user. Classification is the responsibility of the Medicine Agency[37] (licensing authority) of the concerned Member State. In most European countries (e.g. UK and France), medicines are classified into three categories: prescription-only medicine (POM, also known as Rx), pharmacy-supervised sale (P), or general sales list (GSL). Some Member States do not use the pharmacy-supervised sale category.

POMs can only be supplied when recommended/endorsed by a medical practitioner and dispensed through a community or hospital pharmacist. The over-the-counter (OTC) market, medicines for sale without prescription, consists of the P and GSL categories. There are major distinctions between the P and GSL categories in the various Member States. In most countries, medicines in the P category can only be sold under the supervision of a pharmacist. On the other hand, both pharmacists and retail outlets (e.g. chemists or supermarkets) can sell pharmaceuticals from the GSL category. This is not necessarily the case in all countries. For example, in Italy and France the P and GSL categories are only available through a pharmacist, although GSL products may be displayed in areas where they can be selected by customers and advertised to the public (Bond et al. 2004). Deregulation was adopted in the Netherlands, which only had the POM and GSL categories until 2007. This split the OTC category in three (Staatsblad 2007). Apart from the P and GSL (all retail outlets) categories, there is a third intermediate category that can only be sold by pharma-

[37] National medicines authorities responsible for licensing, classification and pharmacovigilance can be found at http://heads.medagencies.org/index.html

cies and chemists and is, therefore, comparable to the Italian and French interpretation of GSL.

The Classification Directive (92/26/EEC[38]), now under Community code Title VI, came into effect in 1992 and, on a European level, harmonizes the criteria that determine whether a product should be sold as an OTC or a POM. It is important to note, however, that these criteria are applied nationally and whether a pharmaceutical receives POM or OTC status varies considerably across Member States. A Europe-wide trend can be observed as the OTC market is expanding in terms of value, volume and range of products (Bond et al. 2004).

4.1.4 Advertising

Following Directive 92/28/EEC, now under Community code Title VIII, public advertising of POMs is prohibited, whereas public advertising of OTCs is allowed in most cases.[39] Most Member States already had a similar distinction and rules in place. As a consequence of the inconsistencies between countries in terms of classification, there are also differences in the ability to advertise pharmaceuticals. Member States have their own frameworks in place that regulate controls on OTC pharmaceuticals. The objectives of these constraints are related to public safety and competition issues. A clear distinction has to be made between advertising and information to patients. In contrast to the European framework for pharmaceutical advertising, the issue of national information provisions did not lead to harmonization between Member States. Several Commission initiatives and repeated public debates focused on the need to address this lack of a Community framework on information to patients; however, no substantial changes to the legal situation have been made in the last 15 years (European Commission 2007).

[38] Directive 92/26/EEC,of 31 March 1992 concerning classification of the supply of medicinal products for human use

[39] Until recently, EU legislation prohibited advertising treatment for chronic insomnia, diabetes and other metabolic diseases, malignant diseases and serious infectious diseases, including HIV and tuberculosis and sexually transmitted diseases. The pharmaceutical review lifted these restrictions.

4.2 NHS/SHI regulation with a potential impact on entire national market

There is a considerable amount of national cost-containment measures, which, depending on how they are applied, can strongly influence the entire pharmaceutical market (outside the NHS/SHI, i.e. non-publicly covered medicines). As outlined in Section 4.2.1, direct price controls and prescribing and dispensing measures can affect the entire pharmaceutical market. A myriad of cost-containment measures were taken in the 1990s, which were often copied from each other, even though reliable information about the successes and failures of measures adopted elsewhere was not gathered (Maynard and Bloor 2003; Guillén and Cabiedes 2003). There are studies that tried to link price level with the regulatory framework, often with significant discrepancies. Some suggest prices are kept lower through a strict regulatory framework (Garattini et al. 1994; Johnsson 1994; Rovira and Darba 2001), while others suggest that in countries with less regulation, prices tend to be lower due to competition (Reekie 1998; Danzon and Chao 2000). This discrepancy reflects the different methodological approaches, including the range of products considered, particularly whether off-patent generics were included, the period covered by the data and the method of calculating the indices (Mrazek and Mossialaos 2004). Furthermore, the total of pharmaceutical spending (not just prices) suggests that the policies adopted in EU countries during the 1980s and 1990s have not been effective in controlling public pharmaceutical spending (Guillén and Cabiedes 2003).

This illustrates the difficulties Member States experience controlling their pharmaceutical expenditures and developing successful pharmaceutical cost-containment policies. This section seeks to provide an overview of the wide variety of pharmaceutical cost-containment regulation in place across Member States. The purpose of this thesis is to look at national policies and Member States in a general, rather conducting country-to-country analysis.

4.2.1 Direct price controls and profit controls

Price control measures aim to contain the rising public expenditures on pharmaceuticals, in other words, the expenditures within the SHI/NHS system. However, these measures may have nationwide impacts and affect the entire national pharmaceuti-

cal market and/or all authorized medicines. This depends on the scope of the regulation in force and when it only affects reimbursed medicines, the cost-containment effects are strictly limited to within the SHI/NHS.

With direct price controls, the government simply sets maximum prices for pharmaceuticals. How these prices are set varies from country to country. They may apply to all medicines or to specific pharmaceutical groups, such as all reimbursed medicines, off-patent (generics) or on-patent pharmaceuticals. At what level these prices are fixed depends on several country-specific factors, including budget limits, prescribing behaviour, patterns of utilization and the importance of the pharmaceutical industry to the national economy (Mrazek and Mossialos 2004). Pharmaceutical prices are controlled in most European countries. The UK and Germany are the only EU15 countries in which in-patent drugs can be freely priced at launch. In France, free pricing for medicinal products defined as "innovative" was introduced in 2003. It does not come as a surprise that these three Member States have the largest pharmaceutical industries in the EU. In the UK, however, prices are moderated indirectly by controlling the profits earned by the pharmaceutical industry. The Pharmaceutical Price Regulation Scheme (PPRS) regulates profits to a band of 17% to 21% on historic capital, with 25% variation on either side. If companies set their prices in such a way that profits are higher than the band, the pharmaceutical company has to reimburse the NHS or reduce the profits. If profits are lower, the company can raise its prices. However, the scheme offers little incentive to be efficient, as such behaviour reduces cost and raises the profits, which then have to be reimbursed to the NHS (Maynard and Bloor 1997).

Member States use different price setting schemes, which, of course, reflect their respective policy priorities. Prices are directly controlled through negotiations with industry (Austria, France, Italy, Portugal, Spain and, more recently, the Netherlands) and fixed by national authorities through a list of factors, including discretionary criteria that are subjective, open to bias and could result in a lack of transparency (Mrazek and Mossialos 2004). Examples of such factors are price comparisons between similar products within a country or comparisons with identical or comparable products in other countries. Examples include the use of international comparisons

of ex-manufacturers price (e.g. Belgium, Denmark, Netherlands, Italy, Portugal) or wholesale price (e.g. Finland, Ireland) (see table 13). The Netherlands, for example, uses the ex-manufacturer's price in their neighbouring countries as a maximum, but regulates the prices of generics through yearly agreements (called 'covenants') with the generic industry, pharmacists and health insurers.

Table 13. Examples of price comparison measures in Europe.

Member State	Price comparison
Belgium	Ex-manufacturer's price in France, Germany, Luxembourg, Netherlands
Denmark	Average European ex-manufacturer's price excluding Greece, Portugal, Spain and Luxembourg, but including Liechtenstein
Finland	Average EU wholesale price
Ireland	Average wholesale price in Denmark, France, Germany, Netherlands, UK
Italy	Weighted average of ex-manufacturer's prices in the EU (excluding Luxembourg and Denmark)
Netherlands	Average ex-manufacturer's price in Belgium, France, Germany, UK
Portugal	Minimum ex-manufacturer's price of identical products in France, Italy, Spain

Source: Mrazek and Mossialos (2004).

Whether price controls are effective in reducing pharmaceutical expenditures is heavily debated. The introduction of stricter price controls is often accompanied with increasing expenditures (Mrazek and Mossialos 2004). Expenditures do not necessarily decrease when prices fall: the volume component or the shift to other medicines can still make up for the lower price. A frequently observed effect is that pricing measures seem to work in the short term, but their effectiveness decreases in the long term. Possible explanations are that industry is able to create "escape valves" by increasing the sales of already commercialized products and that higher prices can be set via product differentiation through new trademarks (Guillén and Cabiedes 2003).

The 1989 European Transparency Directive forces Member States to adopt verifiable and transparent criteria when setting pharmaceutical prices and making reimbursement decisions. It does not regulate European-wide price controls or profit caps, nor does it seek to harmonize the rules of the various national reimbursement schemes.

It does, however, set a 90-day limit for adopting a decision on the price. The Transparency Directive is the only European directive concerning pricing that is in force.

4.2.2 Measures regulating prescribing and dispensing

Stimulating the use of generics

Generics are off-patent drugs usually sold under their chemical name and are possibly manufactured by more than one producers. Consequently, they are more price-competitive. As visible in Table 14, there are various options that stimulate generic use, which are aimed at the demand side of the pharmaceutical market,[40] either directed towards the physician (responsible for the prescription) or towards the pharmacist (responsible for dispensing the pharmaceutical). The number of Member States participating in the generics market has grown over the past few years and is expected to continue to grow in the near future.

In countries that already had promoting policies for generics (Germany, Denmark, the Netherlands and the UK), the generic market (as a percentage of total prescriptions) is notably bigger than in countries that did not have such policies in place (e.g. France, Spain) (Mrazek and Frank 2004). This is illustrated by Simoens and De Coster (2006), who had access to IMS Health and EGA data and distinguished two groups of countries in terms of share of generic medicines by volume in 2004. The first group is made up of countries with a mature generic market, in which the volume of generics exceed 40% of the market share, (e.g. Denmark, Germany, Netherlands, Poland and the UK). The second group consists of countries with developing generic markets, in which generics make up less than 20% of the market share (e.g. Austria, Belgium, France, Italy, Portugal and Spain). The study demonstrates that there is no single approach to developing a generic medicines market, but countries that have promoted generic medicines in the past 10 to 15 years consequently have more mature generic markets than countries that have only recently implemented such policies.

For example, the greatest amount of drug substitution has occurred in the Netherlands (Guillén and Cabiedes 2003). The Dutch government, in alliance with pharma-

[40] There are also supply side policies that can stimulate the use of generics (e.g. reference pricing schemes).

cists and medical organizations, tries to stimulate a more rational prescribing behaviour through the use of electronic prescribing programs in which a computer provides suggestions for a generic substitute (EVS, Electronisch Voorschrijf Systeem).

Table 14. Incentives to promote generics in the EU.

Target	Method	Country
Physician	Generic name prescribing encouraged or required	Finland, France, Germany, Ireland, Italy, Luxemburg, Netherlands, Portugal, Spain (in some regions), UK
	Prescribing budgets	Germany, Italy, Ireland, UK
	Pay agreement linked to prescribing	Spain (local schemes)
	Dissemination of information to promote generics	Belgium, Italy, Ireland, Portugal, UK
	Prescribing guidelines	France, Netherlands, Portugal, UK
	Monitoring prescribing	Austria, Belgium, Denmark, Luxembourg, Netherlands, UK
Pharmacist	Generic substitution	Denmark, Finland, France, Norway, Spain
	Multi-source product selection if prescription is written using the generic name	Italy, Germany, Luxembourg, Portugal, Netherlands, Sweden, UK
	Margins that encourage generic dispensing	France, Netherlands, Norway, Spain, UK
	Dispensing budgets	Denmark

Source: Mrazek and Mossialos (2004).

Rationalization of prescribing

The promotion of generics makes up a great part of the aim of most countries to rationalize their prescribing behaviour, but these attempts does not mean that they are constrained to generics. Some of the methods mentioned in Table 14 (e.g. guidelines, information campaigns and monitoring), can also be used to promote a more reluctant prescribing behaviour, to give advice on drugs and optimal length of treatment for each condition and provide support for more cost-aware decisions, regardless of whether a computerized decision support system is used. All European countries apply prescribing guidelines to some extent and a trend is visible, but not all

countries apply them in a systematic and generalized way (Guillén and Cabiedes 2003).

The criteria that determine how the guidelines are designed differ from country to country. In general, they are not regarded as a substitute for a physician's clinical judgement. In the UK, guidelines are the responsibility of the National Institute of Clinical Excellence (NICE). The NICE guidelines include cost-effectiveness insights and are targeted at both physicians and patients. France uses guidelines drafted by experts and professionals, which are framed as statements about what should not be prescribed (i.e. *les réferences médicales opposables*). In theory, failure to comply results in a fine related to the harm caused and the cost incurred and the extent of deviance; however, most practitioners are not even aware of these rules and their administration is so complex that they have been rarely used as control devices. In Germany, prescribing guidelines were introduced in 1995 and function closely with the negative list. However, these guidelines were not the subject of systematic analysis so the effects on quality and spending are unclear (Maynard and Bloor 2003).

Remuneration of community pharmacies

A percentage of prices is the most common method of remunerating community pharmacies in Europe (e.g. Austria, Belgium, Finland, Greece, Italy, Portugal and Spain). This can make it attractive for community pharmacies in these countries to supply more expensive medicines, which is an undesired situation from a cost-containment point of view. Key to controlling pharmacy reimbursement policies is attempting to eliminate the incentive to sell more and more expensive pharmaceuticals. It has been shown that this can be achieved by removing the link between the remuneration of pharmacists and the price or quantity of drugs. Different schemes are in place. Some countries have margin-ceilings (Spain), use margins that diminish as prices rise (e.g. France and Germany until 2003) or have fixed amounts per dispensation, regardless of drug price (UK, Sweden, Ireland and the Netherlands). The combination of a small price percentage and a dispensing fee is used in Germany. Since 2004, a pharmacy is remunerated 3% of the price of the pharmaceutical and a fixed dispensing fee of €8.10. In Denmark, the Ministry of Health offers a yearly amount to compensate community pharmacies that have low levels of dispensation

(Guillén and Cabiedes 2003). However, the question remains as to why there are still so many countries with a system that contains an incentive to sell more expensive medicines.

4.3 NHS/SHI pharmaceutical regulation

The regulation discussed in this section strictly lies within a Member State's National Health Service (NHS) or Social Health Insurance (SHI) scheme and generally falls within the sphere of competence of the Member State.

4.3.1 Measures regulating the reimbursement of pharmaceuticals

Positive and negative lists (selective listing)

Most European countries appear to conduct a "positive list" or are moving towards introducing a positive list (McGuire et al. 2004). The criteria and schemes, through which pharmaceutical products are approved for reimbursement and put on a positive list, vary from country-to-country. The Transparency Directive 89/105/EEC, however, specifies a 90-day limit for making a reimbursement decision. In most countries, therapeutic benefit is the main criterion, but cost-effectiveness, compared to products already reimbursed, is growing in popularity. Germany is the main exception and still uses a negative list, which lists pharmaceuticals excluded from reimbursement. Newly authorized pharmaceuticals are automatically reimbursed, which makes the Transparency Directive's 90-day limit superfluous. Long-existing plans to shift to a positive list have failed thus far. The UK uses a selective list, which formally still exists as a negative list. Since 1999, advice on cost-effectiveness criteria is given through the National Institute of Clinical Excellence (NICE, see below). Since 1999, pharmaceuticals in France are reimbursed according to their medical effectiveness (Service Médical Rendu, SMR). A reform in 2003 followed the advice of the Commission de Transparence (part of the Haute Autorité de Santé) and reduced reimbursement rates for 617 drugs. Another 84 drugs were removed from the list in the summer of 2003 (Busse and Schlette 2004).

Economic evaluation/post-licensing evaluation

A manufacturer has to provide evidence of the quality, safety and efficacy of their product in order to have their product authorized. However, these three hurdles are

no longer sufficient to ensure a positive reimbursement decision. It is for this reason that throughout the EU and other industrialized nations, there is an increasing interest for complementing pharmaceutical reimbursement procedures by adding a fourth hurdle, which would be demonstrable cost-effectiveness. There are a couple of relevant factors regarding the rise in cost-effectiveness studies for pharmaceutical prices or reimbursement. Apart from the more obvious reasons, such as rapidly growing pharmaceutical expenditures, the increasing number of prescribed items and growing awareness of failing national regulations, a propensity towards prescribing newly introduced drugs is commonly observed throughout Europe. New innovative drugs tend to have higher prices on average than existing products (McGuire et al. 2004), making an examination of their relative cost-effectiveness even more urgent.

A number of EU states are developing or already using post-licensing evaluation systems that include the use of economic evidence in comparative drug evaluation when making reimbursement decisions. The UK pioneered post-licensing evaluation in the EU. Since 1999, the National Institute of Clinical Effectiveness (NICE) has advized the NHS, not only on clinical effectiveness, but also on the cost-effectiveness of new products. The NICE requires companies to hand in evidence of the costs and effects of new products. Recommendations are generally for subgroups of patients and are guided by cost-effectiveness and cost-utility analysis. Whereas the NICE also provides guidelines to physicians and patients (see rationalization of prescribing), health economic evaluation is used as an additional requirement in the reimbursement decision-making process in most European countries. These countries include Belgium, Finland, Norway, Portugal, Italy, the UK, Sweden, Spain and the Netherlands (McGuire et al. 2004; Taylor et al. 2004b). Other countries, such as France, Finland, Norway and Denmark, include cost-effectiveness as supporting evidence for reimbursement or pricing (McGuire et al. 2004). In 2004, Germany established the Institute for Quality and Efficiency in Health Care (IQWiG), which may have an evaluative function in the future (Zentner et al. 2005). Hungary has become one of the first Eastern European countries to signal the introduction of economic evidence as a formal requirement (Taylor et al. 2004b).

Co-payments (cost-sharing)

The majority of European countries use co-payments in which the consumer makes a contribution to the financing of pharmaceuticals (cost-sharing). During the 1980s and 1990s, cost-sharing largely increased, which raised the level of private expenditure on drugs. It aims to increase efficiency by reducing excessive demand and containing overall health costs. In a study prepared for the European Commission DG Employment and Social Affairs, Thomson et al. (2003) distinguished three different forms of cost-sharing in Europe: *co-insurance*, the most common form, requires the patient to be liable for some percentage of the total cost of the pharmaceutical (Belgium, Denmark France, Greece, Luxembourg, Portugal and Spain), *flat-rate payments*, in which the patient pays a fixed fee per item or prescription (Austria and the UK) and *deductibles,* which oblige the patient to bear the initial expense up to a specified amount (e.g. Denmark, Ireland and Sweden). Some countries may also use a combination of the three. Finland, for example, uses combinations of deductibles and co-insurance. Some countries also opt for exemptions or reduced rates for vulnerable population groups. These exemptions and reductions are commonly based on clinical condition, level of income, age or type of drugs. Examples of such groups are low income groups (e.g. Austria, Belgium and Germany), the elderly (e.g. Belgium, Ireland and Spain), children (e.g. Germany and the UK), people with chronic illnesses (Portugal) and people with life threatening illnesses (Belgium). Combinations also exist, such as the elderly with low income (Greece) (Thomson et al. 2003; 2004).

However, its effectiveness as a policy tool is heavily debated in academic circles. In general, co-payments have had very limited success in controlling pharmaceutical expenditures in EU Member States. Also, their deterrent effect may apply to both unnecessary and highly effective treatments (Guillén and Cabiedes 2003). Consequently, it is a sensitive social issue, evoking political debate and patient group and media attention about its feasibility and equity implications.

Prescribing budgets

In some Member States, doctors are allocated prescribing budgets or a practice budget, which includes prescription medicines. Examples of such Member States are the UK, Ireland, Germany, France and Denmark. Various studies on the effects of

budget holdings in the UK (GP fundholding) showed that drug spending is only affected in the short term (e.g. Bradlow and Coulter 1993; Stewart-Brown et al. 1995; Walley et al. 2000). In the UK, primary care trusts (PCTs) were introduced in 1999, replacing the individual GP-fund-holding system. The PCT is responsible for purchasing a wide range of services, including pharmaceuticals. The PCT can only purchase collectively and benefits through savings are also collective. The scheme uses peer pressure to develop corporate affinity among GPs in an effort to control overall prescribing. However, both the reluctant and the generous GP may benefit from cost aware behaviour. This reduces the incentive and might reduce support for prescribing budgets (Walley and Mossialos 2004). In Germany, cash-limited prescribing budgets were collectively set up in 1993. In its nine year history (the scheme was abolished in 2001), the scheme underwent changes and always evoked discussions about cost-containment and the effects on prescribing quality.

4.3.2 Reference pricing schemes

A reference pricing scheme sets limits for pharmaceuticals assigned to the same group of therapeutic substitutes. If a consumer requests or is prescribed a more expensive drug, the consumer has to bear the difference in price. Some authors view reference pricing as a form of cost-sharing, albeit a more voluntary one as reference pricing schemes often provide co-payment-free alternatives. On the demand side, the scheme hopes to raise awareness of the prescribed drug's price and to cause both the patient and doctor to opt for a drug listed at reference price or below. On the supply side, it hopes to cause manufacturers to lower their prices to reference prices. The scheme may be broadly or narrowly defined, including all generics and some patented drugs (e.g. the Netherlands) or just a small selection of generics (e.g. Spain). Furthermore, states use different systems to establish the reference price (Table 15).

Table 15. Comparative definitions of reference price in selected EU schemes.

Country	Introduced	Definition of reference price
Germany	1989	Reference price should not surpass the highest price in the bottom third of the price range for drugs containing the same active substance and having comparable efficacy

Netherlands	1991	Average price of drugs with similar (pharmaco-) therapeutic effects
Denmark	1996	Lowest priced generic equivalent available on the market
Spain	2000	Arithmetic mean of the three lowest cost per treatment day grouped by formulation and calculated by DDD
Belgium	2001	Equal to a price that is 26% lower than the price of the original brand for generic equivalent products
Italy	2001	Lowest priced generic equivalent available on the market
Portugal	2003	Lowest priced generic equivalent available on the market

Sources: Mrazek and Mossialos (2004); Simoens and De Coster (2006).

Although reference pricing seems to have a positive short term effect on pharmaceutical spending (Guillén and Cabiedes 2003), the effects do not result in important long term savings (Lopez-Casanovas and Puig-Jumoy 2000). One explanation is that an increase in the volume and price of drugs outside the reference price system typically nullifies any reductions in pharmaceutical spending from the scheme (Mrazek and Mossialos 2004). In the Netherlands, for example, many manufacturers raised their prices towards the price limit and price increases up to 500% (Snier 1995). Furthermore, manufacturers and wholesalers have been paying bonuses and giving discounts to community pharmacies where their respective products were dispensed, which undermines the system. Also, it is said to prevent payers from effectively negotiating medicine prices. However, France is implementing a reference pricing system without the necessary accompanying controls indicated by the Dutch experience (McGuire et al. 2004). Also, Spain has altered its reference pricing system in an attempt to curb pharmaceutical expenditures, which amounted to +11% in 2003 (Busse and Schlette 2004).

4.4 Pharmaceutical policy in the new Member States (EU12)

Most of the new EU Member States (the EU12)[41] cannot be easily compared to the EU15 countries. Pharmaceutical reform in the new Member States from Eastern Europe[42] began when communist ideology gave way to democracy and market liberali-

[41] The EU12 are Cyprus, Czech Republic, Estonia, Hungary, Latvia, Lithuania, Malta, Poland, Slovakia and Slovenia, who joined in May 2004 and Bulgaria and Romania, who joined in January 2008.

[42] Cyprus and Malta are exceptions, being Southern European democratic countries without a communist history.

zation. Former communist countries went from a supply based, centralized system, often characterized by shortages and inadequate supplies, to a system with a liberalized pharmaceutical sector, with a flood of new imported and affordable pharmaceuticals. Changes meant above all privatization of state industry and the distribution network.

Reform of pharmaceutical regulation based on Western European standards has been driven by the desire for EU access and other measures, such as market authorization, patent legislation, manufacturing standards, licensing requirements, drug pricing and reimbursement. These developments drove the EU12 countries to establish in 10 years what most EU15 countries have been working on the last 40 years. To facilitate this process, the Pan-European Regulatory Forum (PERF) was created for both regulators in the EU15 and the candidate countries (initially the 10 countries that joined 2004) to identify practical arrangements for implementing the EU regulatory framework for pharmaceuticals in anticipation of the "big bang" enlargement of 2004. It went through three stages of development between 1999 and 2004, known as PERF I, PERF II and PERF III and sought to address topics such as quality, safety and efficacy in a European context.

One important consequence of the massive shift to imported drugs was the escalation of pharmaceutical expenditures. For example, in Slovenia the average cost of drugs increased by 70% between 1990 and 1999 (Albreht et al. 2002). Also because of the new imports, the list of available drugs skyrocketed in Hungary from 1300 drugs in 1990 to 10 577 in 2002.

The huge increases in pharmaceutical costs raised the need for cost-containment programs. The EU10 countries adopted approaches widely used in the EU15 (Mrazek et al. 2004), including selective listing with full, partial or no reimbursement (Czech Republic, Poland, Slovakia) and partial coverage according to disease severity (Hungary, Latvia, Slovenia) or type of drug (Poland).

Prices have been regulated by a number of mechanisms including price negotiation (Hungary, Poland, Latvia and Lithuania), international price comparisons (Czech Republic, Estonia, Hungary, Latvia, Lithuania, Poland and Slovenia), setting the ex-manufacturer's price (Slovakia, Lithuania), reference pricing (Czech Republic, Estonia,

Hungary, Lithuania, Poland, Slovakia) and economic evaluation (Estonia, Latvia, Lithuania). As in Western Europe, there are multiple ever-changing and complex approaches (Mrazek et al. 2004). The countries have predominantly focused on reimbursement and pricing in favour of the measures affecting prescribing and dispensing and, in this respect, they follow the patterns observed in Western Europe.

PART II: SCENARIOS

5 Methodology

This thesis aims to examine the possible future of the European pharmaceutical market and questions whether this future will result in greater European or national influence. In Part II, three scenarios for European pharmaceutical policy are developed and described. In Part III, these scenarios will be compared to the findings of the literature review detailed in Part I. This chapter describes the chosen methodology for the framing of the scenarios. In order to make assumptions on the course of the issues and key variables and to be able to frame the scenarios, the Delphi technique was selected as a tool. Section One discusses the Delphi technique and reasons for its selection. In the second section, the Delphi technique is applied to the particularities of the pharmaceutical market leading to the European pharmaceutical policy questionnaire. Section Three elaborates on the process of selecting experts and, finally, Section Four describes how the chosen Delphi design was conducted.

5.1 The Delphi technique

The Delphi technique is a means of obtaining a reliable consensus of opinion from a group of experts through a series of questionnaires that is interspersed with controlled feedback (Garret 1999). In this process, the range of the answers will converge towards the correct and final answer, which is provided by the median scores. The Delphi method was selected because it can generate the results of multiple experts, adding to its scientific value compared to scenarios stemming from one person's ideas, imagination or perception of the studied material. The main alternative is to hold expert meetings using the Nominal Group Technique (NGT), for example, a method similar to the Delphi with the exception of limited group discussion; however, final judgements are made in isolation (Van de Ven and Delbecq 1971). Contributing experts to this thesis come from all corners of the European Union and scheduling a meeting with all of them would not have been financially feasible, particularly considering the limited funding for this project. Even assuming that experts could (and were willing) to participate, group discussion leaves room for a possible bias. In

addition, traditional group meetings are an inefficient and ineffective method of making forecasts and decisions (Green et al. 2007). A systematic review undertaken by Rowe and Wright (1999) looked at several empirical studies that analyse the Delphi technique as a forecasting tool. They found that Delphi groups outperform statistical groups (by 12 studies to two, with two ties) and standard interaction groups (by five studies to one, with two ties). Furthermore, the Delphi technique is an established procedure that has been extensively reviewed in various studies (e.g. Linstone and Turoff 1975; Lock 1987; Stewart 1987; Rowe et al. 1991; Rowe and Wright 1999) and it adds scientific legitimacy to the scenarios.

The Delphi technique was developed by Helmer, Dalkey and Gordon at the Rand Corporation at the beginning of the Cold War to forecast the impact of technology on warfare. Over the years, new applications have been developed such as the Policy Delphi (1970s), which seeks to generate the strongest opposing views on the resolution of a major policy issue and its main objective is not to reach a consensus (Turoff 1970). The Argument Delphi focuses on ongoing discussion and finding relevant arguments, rather than focusing on the output (Kuusi 1999). The Disaggregative Policy Delphi seeks to cluster quantitative expert or interest group responses into similar groups (Tapio 2002) and the Wideband Delphi involves more interaction and communication between experts. According to Garret's definition (1999), the key elements of the Delphi technique are the following:

1. Structuring the flow of information: the contributions of the experts are collected in the form of answers to questionnaires and their comments to these answers when given. No discussion takes place among experts. The panel director then processes the information and filters out irrelevant content. This avoids face-to-face panel discussions on differences in opinion which may lead to biased outcomes.

2. Providing feedback to the participants: the answers are sent back to the experts, who are then asked to review comments (answers). They then can reconsider and revise their original answer. The method prevents the participants from adhering to previously stated opinions and/or conforming to the positions of a group leader. They then complete another questionnaire

which is sent back to the coordinator. Several rounds may be required before a consensus is reached. It is also possible that no consensus is reached but that respondents divide themselves into two or more groups. This is the goal of some Delphi designs, including the Disaggregative Policy Delphi mentioned above.

3. All participants remain anonymous[43]: identities are not revealed even after the completion of the final round and the report is released. This aims to prevent participants from dominating others using their authority or personality, to free them from their personal biases, to minimize undesired biasing effects such as the "halo effect",[44] to allow them to freely express their opinions, to encourage open critique and to admit errors by revising earlier judgments without losing face. Moreover, the results can not be ascribed to the expert by name and no responsibility has to be assumed.

For future studies, a Delphi design is often used to seek expert opinions on purpose, scope, key variables, actors, assumption sets, scenarios, strategies and tactics. The expert opinions are usually expressed through the assignment of weight (e.g. judging by probability, ranking by value) or the expression of choice from several possibilities rather than written answers to questions. The Delphi technique can, therefore, be used for both future research designs that are objective and exploratory and designs that are subjective and normative (Garret 1999).

5.2 The European pharmaceutical policy questionnaire

The aim of this Delphi questionnaire is to reach a consensus within a group of selected experts on whether regulation in the European pharmaceuticals market will take a predominantly European or national course over the next twenty years. In the European policy questionnaire, which was specifically designed for this thesis, experts were asked questions on key issues of pharmaceutical policy in Europe and were asked to estimate the current situation (the Delphi was conducted in 2006) and what they expect the situation to be in 2010, 2015 and 2025. Ten issues were selected

[43] More novel Delphi applications may not guarantee full anonymity, such as the Wideband Delphi.
[44] Halo effect: generalisation from the perception of one outstanding personality trait to an overly favourable evaluation of the whole personality (Merriam Webster Online).

from the review (Part I) and cover the whole range of regulation on all levels of the European pharmaceutical market: authorization, pharmacovigilance, classification, distribution, advertising, pricing, dispensing, prescribing, post-licensing evaluation and reimbursement. The key variable for these issues ranged from “fully national” to “fully European”. An extra category was added that asked the experts’ opinion on these issues.

In order to achieve a high response rate, a very simple and short design with closed answer categories was constructed. Two rounds were expected to be enough to provide a picture of the overall trend expected by the respondents. A preliminary test survey (see Appendix A) was sent to the members of a European network the department of Health care Management at the Berlin University of Technology participates in to check whether the questionnaire, format (tables) and application were clear. Since the response rate was rather disappointing, the introduction was shortened and the expert questions section (see below) was moved to the end of the questionnaire, as to not immediately discourage the respondents.

Some key features of the final first round design (see Appendix B) are:

- The introduction emphasizes that filling out the questionnaire should not take more than a couple of minutes. It also provides a deadline and asks that the questionnaire be forwarded to other experts the recipient may know.
- The questionnaire begins with “category of respondent”. The categories correspond with all actors of the pharmaceutical market indicated in the literature research of the thesis.
- The questionnaire includes a category on how the expert values the current situation, also to see whether there was unacceptable divergence in their estimation.
- The key variable ranges from “fully national” to “fully European”. This was combined with closed answer categories. On the question “Will the following issues predominantly be *regulated* and *implemented* at a European level or at a national level?”, respondents were asked to use a five-category Likert scale: (1) fully national, (2) predominantly national, (3) even or 50/50, (4) predominantly European or (5) fully European.
- A list of expert questions was included in the questionnaire in order to possibly weigh the results and to check whether the right expertise was at hand. In addition,

three categories of answers (1=fully, 2=average, 3=not at all) were provided. They consist of two general questions, “Would you consider yourself an expert in the field of European pharmaceutical policy, both on the European and national level?” and “Are you familiar with the current state of the European pharmaceutical market, including its actors and recent developments?” and two more specific questions, “Are you familiar with European law with regard to European health care, in particular the European Commission’s public health competences (e.g. Article 152)?” and “Are you familiar with European case law, especially Kohll/Decker, Smits-Geraets/Peerbooms and Vanbraekel and its possible consequences?”. The latter two questions were included as European case law was indicated in the literature research (Part I) as having a potential effect which could alter the future course of the European pharmaceutical market.

- The questionnaire contains an optional comments section.

5.3 Expert selection

The experts for the Delphi questionnaire on European pharmaceutical policy were selected from different sources. The questionnaire demands a very broad expertise of national and European pharmaceutical policy and knowledge of all the issues, ranging from authorization to reimbursement. Acquiring the emails of suitable respondents was done through the following methods:

- All authors referred to in the literature research and authors referred to in some standard works on European pharmaceutical policy were searched on the internet and their e-mail addresses were noted down if found.
- The membership directory of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) was consulted. The directory contains the e-mails of its members.
- The websites of various organizations (e.g. NGOs, companies) and interest groups mentioned in the literature research were searched. Some only provided an e-mail address for general information, whereas others contained personal e-mail addresses.
- The previously mentioned methods do not yield a sufficient number of respondents from pharmaceutical industry. E-mail addresses of experts working for the pharmaceutical industry are difficult to acquire by searching the internet. Therefore, all

available business cards at the Department of Health Care Management, TU Berlin, were hand-searched.

After selecting the addressees, around 200 (alleged) experts working for various actors in the European pharmaceutical market were approached. However, academics make up the largest group of addressees and respondents.

5.4 Conduct of the Delphi questionnaire

The conduct of the questionnaire has the aim to achieve the highest possible response rate. Therefore, the questionnaire has the following features:

- The questionnaire was sent by e-mail. More people could be reached this way and it invited respondents to forward the questionnaire to colleagues. This was very successful in some cases and the messages were forwarded to colleagues within and outside their institution of affiliation. As a result, the questionnaire even penetrated institutions that do not publish its e-mails on the internet.
- E-mail is a fast, affordable means of communication for both the sender and the receiver.
- The subject header of the email contained the words “(short!) Delphi questionnaire” and the date of the deadline (see Appendix B and C).
- The questionnaire was sent by e-mail and opens in the message window, not in an attachment. The reader was directly presented with the questionnaire and saw that it is short, which aims to excite curiosity and a spontaneous reply. This is the reason why it was decided against only using attachments that could be filled out and sent back or using an interactive web-based design following a link, after which the respondents would fill out their questionnaire online. Filling out the questionnaire online may be an elegant way to conduct a questionnaire and it has some advantages regarding the processing of the evoked data, but, in the end, the immediate visibility of the email questionnaire through the e-mail preponderated. Furthermore, widely used HTML supporting e-mail programs have no difficulties displaying figures or tables, which make attachments largely unnecessary.
- After receiving and reading the e-mail, respondents were asked to reply to the e-mail and fill out the questionnaire in the new reply e-mail. Although most e-mail programs support HTML-codes and respondents should have had no problems using this procedure, an attachment with the same contents as the e-mail was sent along as backup. It later turned out that some respondents preferred using the attach-

ment, maybe also because some of them encountered problems with their non-HTML -compatible e-mail programs. After ten days, shortly before the original deadline, a reminder message with an extended deadline of ten days was sent, containing the whole questionnaire and attachment so that the respondent did not have to look for the original e-mail.

- As mentioned earlier, the expert questions were placed at the end of the questionnaire in order to prevent the respondents from being discouraged.
- In round two, only the addressees whose results were received and used in Round 2 were approached. Respondents did not have to answer the “category of respondent” and “expert questions” sections again. The results of the first round of “category of respondent” questions were incorporated in the questionnaire in round two.

Anonymity

To ensure the full anonymity of both the addressees and the results, the selected e-mail addresses were inserted in the blind-copy field (Bcc) of the e-mail and then sent simultaneously. By blind-copying the addresses, respondents could not see the addresses of fellow respondents and 200 individual e-mails did not have to be sent.

6 Results

The e-mail questionnaire received a steady flow of responses with small peaks directly after sending the message and after sending the reminder. The first round yielded 41 usable filled-out Delphi questionnaires. Some answers were not used due to illegibility and/or insufficient expertise. The processed results were then anonymously incorporated in a new questionnaire (see Appendix C) and sent again according to almost the same protocol as described under "conduct of the questionnaire". Of the 41 respondents in round one, 27 replied, a response rate of 66%.

The respondents come from various backgrounds (see Table 16), the largest groups being academics, "other" (e.g. consultants, WHO) and the pharmaceutical industry. Two explanations for this unevenly spread result are that (1) the initial mailing list consisted mostly of academics and people from the pharmaceutical industry and (2) most actors lack broad knowledge about other layers of the European pharmaceutical market (e.g. a pharmacist might not know about current developments in authorization or European law) which could have prevented them from responding.

Table 16. Category of respondents.

	R1	R2		R1	R2
Pharmaceutical industry (R&D)	7	5	National government/regulator	3	2
Pharmaceutical industry (generic)			European Union	1	
Wholesaler	1	1	Academic	20	14
Pharmacist			Consumer organization		
Insurer/payer (NHS, Sickness F.)	1	1	Other	8	4

R1=Round 1, R2=Round 2.

In this chapter, the scenarios for future pharmaceutical policy will be filled in. First, the results of the Delphi questionnaire will be discussed (Section One). These results were used as building blocks to fill in a most likely Expert Scenario, which was then contrasted with a more optimistic ("pro-European") and a more pessimistic ("anti-European/national") scenario. The scenarios are found in Section Two.

6.1 Discussion of the results of the Delphi questionnaire

One could say that the median scores of the questionnaire show an extrapolation of current trends. Answers to the question "Will the following issues predominantly be regulated and implemented at a European level or at a national level?" (see Table 17) can be divided into two main groups.

In the first group, the experts foresaw further Europeanization of the European pharmaceutical market, where the European Union and national governments share the competence. Europe has the most competence and European law has the largest potential influence. Authorization, pharmacovigilance, classification, distribution and advertising show a steady and gradual trend towards European regulation.

The second group covers those sectors of the European pharmaceutical market that overlap with the national health systems of Member States. Hence, those parts where the competence of the Member State prevails. Therefore, pricing, dispensing, prescribing and reimbursement remain predominantly a national competence and just a slight increase in European influence is expected.

However, post-licensing is one major exception. Post-licensing evaluation is the use of comparative benefit and cost-effectiveness studies when making reimbursement decisions. It takes place within the national health systems as a competence of the Member States and is not expected to remain a solely national matter. Rather, it is expected to develop into a field with evenly spread responsibility.

The following results attract particular attention. Although the respondents' answers show convergence in the second round and a trend is visible, not all issues arrived at a consensus. In the second round, 66% of respondents from the first round respondents filled out the questionnaire. It is worth questioning whether the 66% showed convergence compared to their first round. However, the answers of the 34% that did not respond in the second round were visible and influenced the 66% that responded and, consequently, they have to be included. In addition, some very different views exist as to how the "today" (2006) situation should be interpreted. Advertising in particular and classification to a lesser extent, shows widely diverging views. Although 41% in the first round seem to think that advertising is a fully national field,

the remainder think it is predominantly national (19%), evenly spread (14%), predominantly European (22%) and even fully European (3%, i.e. 1 respondent, a clear outlier). This is a remarkable score bearing in mind the fact that an advertising directive has existed since 1992 (now integrated in the Community code), which prohibits direct-to-consumer advertising of prescription drugs. An explanation for this spread could be the fact that European countries had similar policies in place even before the 1992 EC involvement regarding advertising and classification. This may affect the visibility and people's awareness of European involvement. The second round still shows disagreement and even more people now view advertising (54%) and classification (58%) as fully national fields. These scores are less convincing than other issues, where a consensus of 90% to even 100% appeared.

Table 17. Delphi questionnaire results.

			EXPECTATION							
Issue	**2006**		**2010**		**2015**		**2025**		**Opinion**	
	Rnd1 (%)	**Rnd2(%)**	**Rnd1 (%)**	**Rnd2(%)**	**Rnd1 (%)**	**Rnd2(%)**	**Rnd1 (%)**	**Rnd2(%)**	**Rnd1 (%)**	**Rnd2(%)**
1. Market authorization (licensing)	1: 08		1:		1:		1:		1:	
	2: 23	31	2: 10		2:		2:		2:	
	3: 45	58	3: 45	73	3: 20	12	3: 05	04	3: 09	04
	4: 25	12	4: 38	20	4: 50	73	4: 45	30	4: 25	48
	5:		5: 08	08	5: 30	15	5: 50	67	5: 66	48
	n=40	n=26	n=40	n=26	n=40	n=26	n=40	n=27	n=32	n=25
2. Pharmacovigilance (post-marketing surveillance)	1: 18	08	1: 08		1: 05		1: 05		1:	
	2: 49	65	2: 15	23	2: 05	08	2: 03	04	2: 06	
	3: 28	27	3: 51	58	3: 33	35	3: 23	11	3: 22	12
	4: 05		4: 23	15	4: 44	50	4: 44	59	4: 25	40
	5:		5: 03	04	5: 13	08	5: 26	26	5: 47	48
	n=39	n=26	n=39	n=26	n=39	n=26	n=39	n=27	n=32	n=25
3. Classification: Rx (prescription only), OTC	1: 38	58	1: 18	20	1: 08	08	1: 03	04	1: 10	08
	2: 38	27	2: 38	58	2: 21	31	2: 21	22	2: 13	17
	3: 15	12	3: 23	15	3: 31	46	3: 23	37	3: 10	13
	4: 05	04	4: 15	04	4: 26	12	4: 28	22	4: 32	38
	5: 03		5: 05	04	5: 15	04	5: 26	15	5: 34	25
	n=39	n=26	n=39	n=26	n=39	n=26	n=39	n=27	n=31	n=24

4. Distribution (wholesaling)	1: 41	31	1: 15	12	1: 03	04	1: 03		1: 03	
	2: 46	62	2: 38	58	2: 36	31	2: 26	22	2: 19	17
	3: 08	08	3: 33	23	3: 33	50	3: 31	29	3: 35	33
	4: 05		4: 13	04	4: 26	12	4: 26	41	4: 23	38
	5:		5:	04	5: 03	04	5: 15	07	5: 19	13
	n=39	n=26	n=39	n=26	n=39	n=26	n=39	n=27	n=31	n=24
5. Advertising (e.g. direct-to-consumer advertising)	1: 41	54	1: 16	20	1: 05	08	1: 03	08	1: 13	13
	2: 19	15	2: 34	36	2: 18	32	2: 16	15	2: 17	30
	3: 14	12	3: 18	12	3: 29	28	3: 24	31	3: 23	09
	4: 22	15	4: 26	28	4: 26	20	4: 29	27	4: 13	17
	5: 03	04	5: 05	04	5: 21	12	5: 29	19	5: 33	30
	n=37	n=26	n=38	n=25	n=38	n=25	n=38	n=26	n=30	n=23
6. Pricing (e.g. pricing and profit controls, reference pricing)	1: 80	88	1: 59	62	1: 34	35	1: 20	26	1: 26	32
	2: 15	12	2: 24	23	2: 37	38	2: 35	37	2: 16	20
	3: 05		3: 07	15	3: 12	20	3: 18	19	3: 23	20
	4:		4: 07		4: 12	08	4: 15	15	4: 13	12
	5:		5: 02		5: 05		5: 13	04	5: 23	16
	n=40	n=26	n=41	n=26	n=41	n=26	n=40	n=27	n=31	n=25

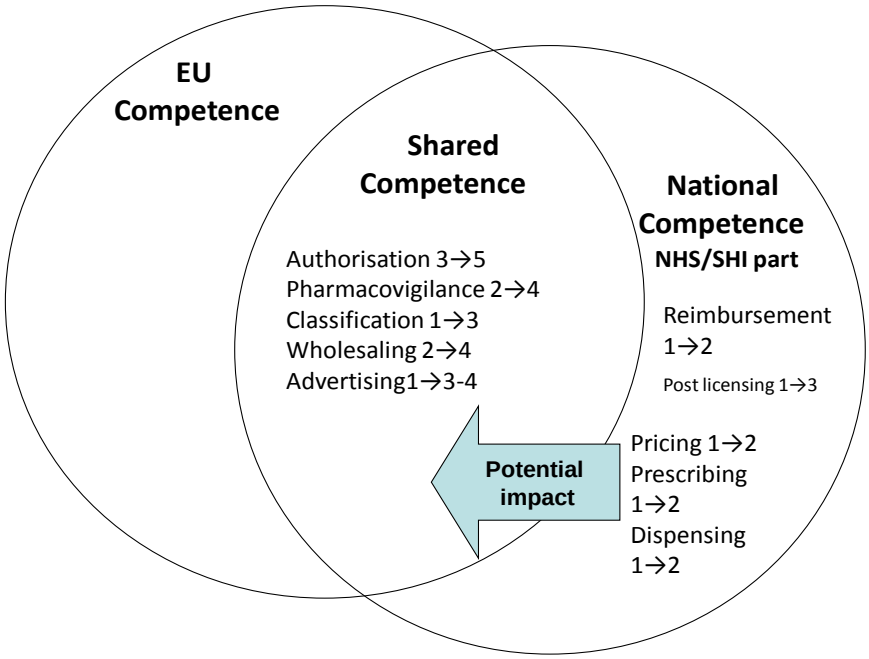
7. Dispensing (pharmacy level): e.g. generic substitution, remuneration	1: 85	92	1: 66	73	1: 44	42	1: 38	26	1: 42	29
	2: 10	08	2: 27	28	2: 34	46	2: 30	52	2: 26	42
	3: 05		3: 05		3: 17	12	3: 20	19	3: 13	08
	4:		4: 02		4: 02		4: 10	04	4: 10	08
	5:		5:		5: 02		5: 03		5: 10	13
	n=40	n=26	n=41	n=26	n=41	n=26	n=40	n=27	n=31	n=24
8. Prescribing: e.g. prescribing guidelines, budgets	1: 90	100	1: 61	85	1: 41	31	1: 26	19	1: 29	17
	2: 10		2: 32	15	2: 34	62	2: 35	56	2: 23	29
	3:		3: 07		3: 20	08	3: 20	19	3: 23	29
	4:		4:		4: 05		4: 15	07	4: 16	13
	5:		5:		5:		5: 03		5: 10	13
	n=40	n=26	n=41	n=26	n=41	n=26	n=40	n=27	n=31	n=24

9. Post-licensing evaluation (comparative benefit/ cost-effectiveness)	1: 73	88	1: 34	35	1: 17	08	1: 10	04	1: 16	08
	2: 23	12	2: 41	65	2: 29	42	2: 25	30	2: 13	13
	3: 05		3: 22		3: 39	50	3: 33	37	3: 13	21
	4:		4: 02		4: 07		4: 25	26	4: 35	42
	5:		5:		5: 07		5: 08	04	5: 23	17
	n=40	n=26	n=41	n=26	n=41	n=26	n=40	n=27	n=31	n=24
10. Reimbursement: by public payers, i.e. scope of benefit catalogue (including positive/negative list)	1: 90	96	1: 70	81	1: 43	50	1: 28	26	1: 32	25
	2: 10	04	2: 20	15	2: 38	38	2: 45	44	2: 28	42
	3:		3: 10		3: 15	08	3: 13	19	3: 22	17
	4:		4:	04	4: 05	04	4: 15	11	4: 10	13
	5:		5:		5:		5:		5: 06	04
	n=40	n=26	n=40	n=26	n=40	n=26	n=40	n=27	n=31	n=24

Will the following issues predominantly be regulated and implemented at a European level or at a national level? **Grey: highest score** 1=fully national, 2=predominantly national, 3=even or 50/50, 4=predominantly European, 5=fully European.

These largely confirm the findings of the literature review in terms of actual competences. Furthermore, they seem to continue the "Europeanization" trend as observed in the review of 40 years of pharmaceutical policy. When merging the results of Table 17 with Figure 7 (see Chapter 4), this becomes even more clear (see Figure 8). In those fields where a shared competence between the EU and Member States exists, the experts expect a shift towards European regulation of at least two points on the Likert scale between 2006 and 2025. In fields where the Member States have more competence, only a one point shift in European influence is expected and the overall results suggest that these issues remain predominantly regulated at the national level. One exception is the issue of post-licensing (part of the reimbursement decision) which shows a higher jump of two points towards a field of shared competence. This could be explained by the expectation that European collaboration projects will be initiated by Member States, instead of on a European level. Section Two of this chapter expands on this issue.

Figure 8. Competences in the national pharmaceutical market combined with an expected shift between 2006 and 2025 (rated 1–5), based on expert opinions.



Rating: 1=fully national, 2=predominantly national, 3=even or 50/50, 4=predominantly European, 5=fully European.

The expert opinion

When asked for their opinion, a significant amount refrained, especially in the first round. This may indicate that it was a difficult question to answer. One possible explanation was provided by a respondent who stated under his or her comments section, "my opinion depends on the content of the policy, not where it is promulgated and so that is why I have not expressed any opinion in that column." Although it provides an interpretation of the question, one can still state, irrespective of the contents of the policy, whether it is better to regulate and implement certain issues on a national or European level.

Furthermore, the expectations of the experts seem to resemble the experts' opinions on the desired situation. This could mean two things: (1) the experts approve of the development of the European pharmaceutical market and agree on its course or (2) they filled out the questionnaire to serve their interest. Or, as one respondent

stated in the comments section, "I have the strong feeling that the 'consensus' will depend on the interests of the responders and the mix of responders." Of course the respondent could have been biased; however, the likelihood of the respondent using the questionnaire to impact the future of the European pharmaceutical market is slim, considering the questionnaire was anonymous and this thesis serves no official policy-making purpose.

6.2 Filling in the scenarios

The results of the Delphi questionnaire can now be used to construct three scenarios. The outcomes of the experts' views will be used as the "middle" and "most likely" scenario, called the "Expert Scenario". This Expert Scenario will be contrasted with a more pessimistic scenario and a more optimistic scenario.

In the pessimistic' scenario, which will be referred to as the "European Crisis Scenario", the European process suffers major setbacks, mainly caused by a stalled expansion process, a pervasive image problem and the public's lack of trust in European integration, all of which are worsened by an enduring European constitutional crisis. These developments eventually lead to a return to national regulation and a freeze on the European process.

The optimistic scenario, called the "European Scenario", assumes that after the successful passing of the European Constitution, spurring newly found trust in the European project on behalf of Europeans, Member States will increasingly be burdened border-crossing patients. This threatens the financial balance of their respective health care systems and counter-action is necessary. Member States must gather and try to work out a deal on a European benefit catalogue. This would lead to an Europeanization of the various national health systems. Ironically, this has been instigated by Member States, not the European Commission. The following chapters elaborate on these scenarios.

6.2.1 The Expert Scenario

The Expert Scenario is an extrapolation of current trends (see Table 18). After initial progress using secondary legislation, such as directives and regulations, a standstill in the harmonization process is reached, mainly because of the dissonance between

subsidiarity and a SEM. Instead, the European Commission now favours the coordination of national results along the lines of the G10 recommendations, in which the European Commission acts more as a facilitator. The projects, actions and collaborations resulting from the G10 process, partially already in place or linked to existing programmes, unfold over the next five years. Larger harmonization efforts in certain areas could be possible, even using secondary legislation, in part due to greater convergence of national agendas.

Table 18. The Expert Scenario in numbers.

Issue	Today	2010	2015	2025
Authorization	3	3	4	5
Pharmacovigilance	2	3	4	4
Classification	1	2	3	3
Distribution	2	2	3	4
Advertising	1	2	2	3-4
Pricing	1	1	2	2
Dispensing	1	1	2	2
Prescribing	1	1	2	2
Post-licensing evaluation	1	2	3	3
Reimbursement	1	1	1	2

Will the following issues predominantly be regulated and implemented at a European level or at a national level? 1=fully national, 2=predominantly national, 3=even or 50/50, 4=predominantly European, 5=fully European.

In this scenario, the sectors where European law has the largest influence (roughly the whole European pharmaceutical market minus the diverse national health systems) will slowly move towards a predominantly European level-regulated and implemented system. Those sectors of the health care system that fall mainly under the national competence remain a national competence and hardly shift towards Europe.

Authorization

Authorization will gradually shift from a field of equally shared competence to a solely European matter. The several national licensing agencies will only work for the EMEA, which is based in London and it will no longer be possible to authorize a pharmaceutical for just one national market. The first step will be the removal of the

exclusively national authorization procedure by 2015. The various national licensing agencies will then only serve as solely subcontractors for the EMEA. Secondly, the decentralized authorization procedure will be phased out completely by 2025 after a gradual process of shifting certain therapeutic groups towards the centralized procedure, as done before with biotechnology products and orphan drugs.

Pharmacovigilance

The main European instrument for pharmacovigilance is the Eudravigilance data processing network that came into effect in 2001 and was modernized in November 2005 as a result of the pharmaceutical review (European Commission 2001a). This network, in combination with the Clinical Trials Directive, seeks to harmonize and streamline the exchange of data between national licensing agencies, the EMEA and pharmaceutical companies. However, many different responsible authorities are involved and there are different procedures and responsibilities for products under the centralized and the decentralized authorization procedures (ISI 2006). Therefore, the harmonizing practice has so far been more successful for medicinal products licensed through the centralized procedure (CAPs) than for products licensed through the decentralized procedure. In the next years, the European legal framework will seek to further harmonize regulation, pharmacovigilance practice, product information, communication and cooperation between Member States.

The first result will be an equally shared competence between Member States and Europe by 2010. In the following 15 years, the network will be enhanced and expanded. The abolishment of national authorization and the decentralized procedure will also facilitate harmonization and simplify the system. All national pharmacovigilance systems will start working according to the same protocol and systems by 2015, under the auspices of the EMEA, but national institutions will be left largely intact.

Classification

Title VI of the Community code relating to medicinal products for human use outlines the criteria set to determine whether a pharmaceutical should be classified as a prescription-only medicine (POM) or an over-the-counter (OTC), non-prescription drug. However, these criteria have so far been applied nationally. National variations

also exist as some countries split the OTC category into a pharmacy supervised list (P) and a general sales list (GSL). Thus, one could say Member States have the upper hand in terms of regulation.

Nevertheless, the European Commission regards a more flexible classification process, in particular where it concerns moving medicinal products from POM to OTC status, as essential for a competitive non-prescription market. Therefore, the European Commission will use all its influence to implement the actions as proposed in the G10 recommendations in the next five years. These recommendations include allowing the use of the same trademark for pharmaceuticals moved to non-prescription status and encouraging Member States to review these switching mechanisms.

Classification will develop into a field of shared competence beginning around the year 2010. An amended classification directive introduced between 2010 and 2015 will then establish the categories POM, P and GSL. In other words, the directive follows the European trend by splitting up the OTC category. It is, of course, hoped that this would establish a more flexible and faster switching process, through which more pharmaceuticals receive the non-prescription status (either P or GSL), making more drugs directly accessible to the public at lower level outlets, such as supermarkets. It also includes mechanisms for industry to apply for reclassification. This directive will further harmonize and thus Europeanize the European pharmaceutical market. However, even in this scenario, the classification decision is still applied nationally, but it can be expected that national differences in sale items will become less distinct.

Wholesaling

The wholesaling sector will see a further European harmonization and liberalization trend. Still very much nationally dominated, it will develop into a Euro-dominated field. As of yet, there is only one European directive setting criteria that have to be met by wholesalers, such as adequate premises, qualified staff and emergency plans for market withdrawal. These criteria, however, are enforced on a national level by very different national authorities, varying from federal states (Germany) to a national medicine agency (Finland) to a health inspectorate (the Netherlands). The first

step will be more liberalization Europe-wide through competition law. By enacting a regulation, the supervision of wholesaling a European matter will become the responsibility of the EMEA. The national competent authorities will then operate under the supervision of the EMEA.

Advertising

Although there is a directive that prohibits public advertising of prescription-only medicines (POMs), the differences stemming from nationally applied classification decisions makes it a predominantly national field. Also, Member States individually decide on the methods they use for controlling pharmaceutical advertising and the level of the penalties for breaching their national rules. Advertising will change into an evenly shared competence sector as a consequence of an overall trend towards a more liberal European pharmaceutical market favoured by the industrial policy-leaning European Commission. More therapeutic groups will be open for direct consumer advertising around the year 2015, mainly due to the classification system. The methods for controlling pharmaceutical advertising and level of penalty will be more harmonized. There will be more convergence in advertising between countries by 2025 as a result.

Dispensing, pricing, prescribing and reimbursement

Regulation concerning dispensing pharmaceuticals to the public, pricing, prescribing and reimbursement mainly takes place within the national health system, where the competence largely lies at the national level. Member States decide how this is to be regulated (e.g. on a national level or devolving it to the regions). Therefore, the consulted experts expect little European influence over the next years and the regulatory frameworks will, for the most part, remain a national competence. As Member States take generally more health policy-leaning perspectives, it can be expected that the emphasis remains on cost-containment, that more cost-containment measures will be adopted and that these cost-containment strategies used throughout the EU show more convergence. This would mean more stringent pricing regimes, increased use of generic substitution especially in immature generic markets, conservative prescribing through the use of guidelines and increased requirements

regarding the use and execution of economic evaluations (e.g. post-licensing evaluations) when making reimbursement decisions.

However, some Europeanization is expected but that does not have to mean much more than increased cooperation between countries, maybe even supported or facilitated by the European Commission where it serves its public health goals or suits its market liberalization agenda. Increasing the amount of generics in the market, for example, could curb national expenditures, but could also provide opportunities for the European Commission to promote and facilitate a competitive European generic market.

The European Commission's limited competence in national systems does not mean that the Member States have full control over national pricing and reimbursement schemes. Some of the pricing and reimbursement schemes presently in force in Member States can have a strong influence on the entire pharmaceutical market (i.e. outside the various national health systems). The European Commission respects the authority of Member States in their national health systems and respects their protection of their respective health care budgets; however, the Community pursues full competition for medicines neither purchased nor reimbursed by the state (i.e. categories of medicines that are not reimbursed, often non-prescription drugs and those pharmaceuticals provided outside the state sector, which includes in private hospitals). This should result in a competitive EU-wide single market for non-reimbursed medicines with pan-European prices and less interference from the regulations of Member States.

The definition of what belongs to the national system (i.e. where does the national competence end and where does the European competence begin), will be redefined over the next twenty years. Member States keep full competence in the market where regulation concerns controlling their health care budgets through dispensing and prescribing regulation, for example. This means restrictive pricing and restrictive policies for dispensing and prescribing can only apply to reimbursed pharmaceuticals.

Post-licensing evaluation

One of the more surprising outcomes of the Delphi is the expectation of experts in the field of post-licensing evaluation. The increasing use and importance of clinical effectiveness and cost-effectiveness studies as a fourth hurdle in gaining access to a Member State's list of reimbursed pharmaceuticals is already a Europe-wide trend. In this policy scenario, all Member States will actively use the fourth hurdle and experts expect a larger European role. However, apart from a facilitating role, this seems unlikely to be instigated by the European Commission. The more industrial-policy leaning European Commission is more interested in opening up the markets and creating more liberalization than more restrictive controls, let alone putting restrictions in place that could eventually block off certain pharmaceutical products from being reimbursed in a certain Member State. Furthermore, the Commission recognizes it is primarily a matter of national competence.

Maybe the outcomes are not as contradictory as they may appear at first sight. Not all European regulation and influence has to come from the European Commission. It is very well possible that the experts had more European-level cooperation between national governments and institutions in mind (i.e. initiated at the national level). Or, as one respondent rightly commented in the first round of the Delphi questionnaire, "where you say 'European' it does not necessarily mean European Commission, but it can be collaboration between the EU Member States." One can think of Europe-wide economic evaluations initiated by the National Competent Authorities (NCAs such as the NICE in the UK and the IQWiG in Germany) and even structural cooperation between the NCAs. This cooperation will be increasingly possible as the national cost-containment regulations and practices in this area show more and more convergence.

In their adoption of the G10 recommendations, the European Commission pleads for more exchange of national experience on health technologies (HTA) and is in this way hoping for more speed and transparency in national relative effectiveness assessment systems. The EC supports this view through providing funding for EUnetHTA, the European Network for Health Technology Assessment, which coordinates the efforts of 29 European countries, including 25 EU Member States, in evalu-

ating health technology in Europe. Their reasoning is that a patchwork of different national systems places a huge burden on industry and can delay access to the market. Hence, the European Commission will try to exert influence where it can, keeping in mind its limited competence, but with a different policy perspective than the Member States. The Commission favours faster and easier market access and reimbursement, whereas Member States prefer cost-containment through rational use of efficient pharmaceuticals.

6.2.2 The European Crisis Scenario

In the European Crisis Scenario, we assume that a set of interrelated determinants come together in the upcoming five to 10 years, creating a very difficult environment for the EU pharmaceutical policy to progress. An ongoing constitutional crisis undermines the whole European process. After the failure of the ratification of the European Constitution through referenda in France and the Netherlands in May and June 2005 respectively, as well as the failed ratification of the Treaty of Lisbon (a revision of the European Constitution) through an Irish referendum in June 2008, the prospect of another failed attempt and its possibly severe consequences cripple the successive EU presidencies. Although the successive Member States exercising the EU presidency prioritize an agreement on the European Constitution at the semi-annual European summits, Member States remain divided as to how to solve the ongoing standstill. Instead, Member States keep bickering over the European budget, rebates, the agricultural policy, democratic accountability, enlargement issues (Turkey in particular) and future visions for the EU. The presidency seems unable to find the right moment or correct political and economic opportunity to come up with a feasible plan to start the ratification process anew.

Adding to the problem are low economic growth rates in the European Union and the cumbersome expansion of the new Member States. The Lisbon objective to become “the most competitive and dynamic knowledge-driven economy by 2010” seems further away than ever. The goals of the Treaty of Lisbon were already toned down, partially put on ice and branded “unrealistic” and “too ambitious” and now few European citizens believe in the beneficial effects of a single European market. The new Member States (the EU12), especially Bulgaria and Romania, do not provide

the Union with the energy as was maybe hoped by the founding Member States. On the contrary, they slow down harmonization and have difficulty effectively transposing the *acquis communautaire*, the total body of EU law accumulated thus far, into their respective legislative frameworks.

To make matters worse, a Vioxx-like scandal of a medicinal product authorized through the European centralized procedure legitimizes present criticism of the EMEA and the European procedures. It is evident that the combination of these developments cannot remain without consequences for the European Union in regard to its power to carry out policies and its public image. The European Crisis Scenario unfolds against this difficult background (see Table 19).

Table 19. The European Crisis Scenario in numbers.

Issue	Today	2010	2015	2025
Authorization	3	3	2	2
Pharmacovigilance	2	2	2	2
Classification	1	1	1	1
Distribution	2	2	1	1
Advertising	1	1	1	1
Pricing	1	1	1	1
Dispensing	1	1	1	1
Prescribing	1	1	1	1
Post-licensing evaluation	1	1	1	1
Reimbursement	1	1	1	1

1=fully national, 2=predominantly national, 3=even or 50/50, 4=predominantly European, 5=fully European (not based on expert opinions).

Authorization and pharmacovigilance

In 2009, a statin drug called Cardax is authorized through the centralized procedure and sold and prescribed as a preventive cure for cardiac illnesses, but turns out to have some terrible side effects. Cardax, which was introduced by “company X”, was authorized through the centralized procedure in which the company favoured “Member State Y” as a rapporteur state, expecting a more rapid and favourable authorization procedure than with the medicine agencies of other Member States. Data and market studies led “company X” to believe that “Member State Y” provided

the best chances of getting their product approved. The new pharmaceutical was instantly extremely popular, with market shares up to 45% in Europe. After roughly two years since its introduction, it becomes clear that the widely-used product has life threatening side effects when used in combination with an ACE-inhibitor. A significant increase in cases of cardiac arrythmias causing sudden cardiac death is shown in patients, mostly men over 55, after using Cardax.

All European Member States are affected resulting in huge public outcry. Questions and motions are put forward in all national parliaments and in the European parliament. Already present criticism of the alleged industry-favouring EMEA aggravates soon after. European public opinion and the majority in national parliaments hold the EMEA and the European Commission responsible and accuse the European Commission of neglecting its public health goals and favouring industry goals. In an attempt to appease the outraged and shocked public, Germany and France, two of the Member States most affected in terms of casualties, announce that they will solely authorize new pharmaceutical products through their national authorization procedures for an undetermined period of time. Furthermore, they announce a reassessment of all pharmaceuticals authorized through European procedures and a reassessment for all pending authorization requests.

The German and French action is a major setback for the pharmaceutical policy agenda of the European Commission and for the EMEA and its procedures in particular. It precipitates a status quo for many years to come, with no actual change towards Europe. On the contrary, where possible, Member States will place more emphasis on their national competences and practices. *Europe* and all its connotations, has become a heavily burdened term that the governments and political parties of Member States would rather avoid when courting the Euro-sceptic electorate. Moreover, solid economic growth in the European Area between 2015 and 2020 is seen as proof by national governments and civilians alike that there is no necessity to revitalize the European process.

Pharmacovigilance, in accordance with developments in the field of authorization, will become more regulated at the national level. The plans of the European Commission to further harmonize regulation, pharmacovigilance practice, product infor-

mation and communication and cooperation between Member States will be put on hold.

Classification, distribution, advertising, dispensing, pricing, prescribing and reimbursement

The status quo seems to have the gravest effects for those fields that had the most potential to see a move towards Europe and to become Euro-dominated. Apart from authorization and pharmacovigilance, classification, distribution and advertising could be mentioned in this regard. Regulation regarding pricing, dispensing, prescribing and reimbursement will develop along the lines of the Expert Scenario, in which these issues remain within the national competence. As a result, the national health policy perspective will dominate the policies of Member States. This implies more stringent cost-containment regimes, with restrictive pricing and reimbursement frameworks and a prominent role for clinical effectiveness and cost-effectiveness. One can also think of increased use of generic substitution, rational prescribing and cost-sharing.

The European Commission's limited competence in the health systems of Member States will not be acted upon as described in the Expert Scenario. This is mainly due to the general Europe-wide, Euro-sceptic environment. This means that the European Commission will not take action in those fields that could be seen as a potentially European field, specifically regulation that applies (or has potential influence) outside the boundaries of the national health system. This could, for example, be the case for pricing schemes or dispensing regulation applying to medicines neither purchased nor reimbursed by the state. In the European Crisis Scenario, there will therefore be no developments towards a competitive European, non-prescription market with less interference from Member State regulation and there will be no developments towards an EU-wide single market for non-reimbursed medicines with pan-European prices. Discussion of the division of national and European competences as described in the Expert Scenario is eagerly avoided.

6.2.3 The European Scenario

In the European Scenario (see Table 20), we assume that an unexpectedly far-reaching agreement on an actual European Constitution combined with the highest

economic growth rates in the European Union since the 1990s and a steady drop in unemployment rates from about 8% in 2006 to around 6% in 2011, gradually change the public's overall Euro-sceptic perception of the EU. Furthermore, the new constitution would make it easier to pass legislation as qualified majority voting is abandoned in favour of simple majority voting. Eurostat data show that expansion eastward is, in fact, an important factor in this relative progress, as it proves to be more successful and much less cumbersome than expected. The economic data show high domestic demand in the booming accession countries, providing the EU15 Member States with new, attractive markets for exports and investment. A new European Commission plan drafted in 2010, continuing where the Lisbon objectives and the Partnership for Growth and Jobs left off, will seek to capitalize on this momentum. The new and highly ambitious plan foresees more European harmonization also with the use of secondary legislation.

Table 20. The European Scenario in numbers.

Issue	Today	2010	2015	2025
Authorization	3	3	4	5
Pharmacovigilance	2	3	4	5
Classification	1	2	3	4
Distribution	2	3	4	5
Advertising	1	2	3	4
Pricing	1	2	3	4
Dispensing	1	2	3	4
Prescribing	1	2	3	4
Post-licensing evaluation	1	2	3	4
Reimbursement	1	2	3	4

1=fully national, 2=predominantly national, 3=even or 50/50, 4=predominantly European, 5=fully European (not based on expert opinions).

Moreover, two developments in the European health care sector will have far-reaching consequences. First, better organized empowered patient groups, led by an increasingly aggressive Health Consumer Powerhouse, will reap the benefits of the latest EU case law and spur a rise in European cross-border patients, who (independently, not as part of a cross-border contract) will seek reimbursement for health

services abroad for what is often on the fringes of what is funded in the home state. Second, the growing importance of internet pharmacies, which are enabled by favourable EU case law and increasingly less hampered by restrictive national regulation, will have a catalysing effect on cross-border pharmacy services.

In this scenario, more patients will challenge refusals for reimbursement and exploit legal uncertainties surrounding cross-border care. Successive rulings until 2015 will be in favour of patients, lowering unjustified barrier for providing and receiving care abroad. In these rulings, the ECJ specifically addresses pharmaceuticals as both a service (prescription) and a good. Patients challenge long waiting times, which, in the view of the ECJ, are no longer justified as a tool used for efficient planning, even when the targets of national waiting lists are met.[45] Patients challenge private providers for refusing reimbursement,[46] which eliminates much of the (legal) uncertainty when visiting a foreign provider. Patients challenge refusals for treatment abroad that is not provided in the home state, while arguing that treatment offered at home is verifiably less effective than what is offered abroad.[47] The FP6 HealthBASKET project found this behaviour highly probable and showed that huge differences may exist in the way patients with identical conditions are treated across Member States, which can result in large differences in the choice of technologies, procedures, staffing mix and usage intensity (Velasco-Garrido 2006). This could then motivate European patients to use their legal options to seek statutorily-paid, cross-border health care with the expectation of reimbursement for treatment, for example, with newer technologies or a more broadly-defined treatment that includes services not included at home (Busse and Van Ginneken 2007). In this scenario, it becomes increasingly difficult for Member States to justify an authorization refusal, even for treatments and services, including pharmaceuticals, which are not covered in the national benefit basket.

[45] As was seen in the 2006 Watts judgement, case C-372/04

[46] This development was already apparent in the 2007 Stamatelaki judgement, Case C-444/05.

[47] According to the ECJ in the Smits/Peerbooms decision, authorization refusals on the grounds of effectiveness should be based on what is "sufficiently tried and tested by international medicine" (evidence based medicine) when refusing an authorization. In the Smits/Peerbooms case, the effectiveness of the sought treatments was deemed insufficient to justify reimbursement. A lawsuit would stand a good chance when a treatment is verifiably better according to best medical evidence.

Patients also increasingly use the Kohll/Decker procedure (see Section 3.3.) to obtain pharmaceuticals that are listed in their home state but were dispensed by foreign pharmacies. Using this procedure, patients even have a financial incentive to purchase less-expensive pharmaceuticals abroad, which are then reimbursed with the higher home state tariff. Not only does this enable a profit, it may also imply, for certain Member States, bypassing co-payment. Favourable case rulings, initiated by patients demanding to be reimbursed at the higher home state rate, make this opportunity known to the general public.

A combination of these developments strengthens and increases opportunities for patients to receive non-hospital care and pharmaceuticals in a host state regardless of the state's reimbursement conditions. This undermines the attempts of the European Commission and Member States to secure national competence in the national health systems through a directive that states that non-hospital care in another (host) Member State should be reimbursed according to the same conditions as the home Member State.

The different patient groups in Europe observe this opportunity and draft lists of reimbursed services, pharmaceuticals and specific case law in all Member States to exploit the loopholes and uncertainties in cross-border care. In order to do this more effectively, the national patient groups organise themselves in pan-European patient organizations. A spike in cross-border health care will result, mostly based on case law than on Regulation 1408/71. Patient groups serve as information supplier for patients, using websites with examples and advice on situations in which it is beneficial or disadvantageous to go abroad. Pharmaceuticals play a pioneering role in this development because through the increasing number of internet pharmacies and internet-doctors, a patient does not physically have to go to another Member State (which comes with extra costs that cannot be reimbursed), but can place his/her order from his/her home using a personal computer, regardless of whether an internet-doctor is used from another country.

Member States continue to argue that cross-border patients pose a threat to the financial balance and solidarity of their health systems by maintaining medical and hospital services that are balanced and accessible to all citizens of the EU through

planning and contracting. Although this is a legally legitimate argument,[48] it will become too difficult and too late to reverse the resulting situation. Countries with extensive benefit baskets and/or countries with inexpensive health services and pharmaceuticals see an influx of foreign money coming from foreign health insurance systems (e.g. health insurers and the NHS) and countries with more restrictive benefit baskets and/or more expensive pharmaceuticals will see the money leaking from their health system. In the end, the only rational answer is for Member States to sit together and come up with a deal on a basic European benefit package with similar conditions for co-payments in an effort to remove the incentive to go abroad. This would still leave room for additional benefit catalogues that reflect differences between Member States concerning the cultural and economic environments. The basic European benefit basket should limit people from seeking reimbursement for non-reimbursed services and costs in another country.

Member States will also open up their procurement and contracting mechanisms to foreign providers. The European health market, including the pharmaceutical market, will become increasingly European in nature, in which providers, purchasers and patients increasingly interact on a European level.

Authorization and pharmacovigilance

Under the European Scenario, authorization and pharmacovigilance will develop along similar lines as would occur in the Expert Scenario. Hence, authorization will gradually turn from a field of equally-shared competence to a solely European matter. The several national licensing agencies will only work for the EMEA based in London and it will no longer be possible to authorise a pharmaceutical for just one national market. The first step will be the removal of the exclusively national authorization procedure by 2015. The various national licensing agencies will solely serve as subcontractors for the EMEA. As a second step, the decentralised authorization procedure will be phased out completely by 2025, after a gradual process of shifting certain therapeutic groups towards the centralised procedure.

[48] As was made clear in 2001 with the ECJ rulings in the Geraets-Smits and Peerbooms cases, C-157/99.

As for pharmacovigilance, the EudraVigilance data processing network that came into effect in 2001 combined with the Clinical Trials Directive seek to harmonise and streamline the exchange of data between national licensing agencies, the EMEA and pharmaceutical companies. However, the many different responsible authorities involved and the different procedures and responsibilities for products under the centralised and the decentralised authorization procedure (ISI 2006) are complicating factors. This is why the harmonizing practice has thus far been more successful for medicinal products licensed through the centralised procedure (CAPs) than for products licensed through the decentralised procedure. This will change mainly as a consequence of the developments in the authorization procedures. The abolishment of national authorization and eventually the decentralized procedure will provide greater harmonization and simplify the system in favour of Europe. This means that all national pharmacovigilance systems will start working according to the same protocol and system by 2015, under the auspices of the EMEA, but will leave the national institutions intact. Around 2020, an amendment of the existing regulation will expand the competences of the EMEA and make it the sole body in Europe responsible for pharmacovigilance, which distinguishes the European Scenario from the Expert Scenario.

Classification, distribution and advertising

Under Title VI of the Community code relating to medicinal products for human use, criteria are set which determine whether a pharmaceutical should be classified as a prescription-only (POM) or a OTC drug. However, these criteria have so far been applied nationally. In the next 20 years, classification will develop into a fully European field. An amended classification directive introduced between 2010 and 2015 will establishes the categories POM, P and GSL across Europe. It mainly seeks to enable a single European market for pharmaceuticals and raise the number of non-prescription products, making more drugs accessible to the public through a flexible deregulation of pharmaceutical products. The classification decision will be the responsibility of the EMEA, for which national competent authorities are then contracted to give advice. The pharmaceutical industry will be encouraged to seek reclassification for their products through a new European reclassification mechanism.

These directives will attribute to an almost complete harmonization and, thus, a Europeanization of the European pharmaceutical market and the national differences in sale prices will gradually disappear.

In addition, the nationally-dominated wholesaling sector will undergo further European harmonization and liberalization, as is expected in the Expert Scenario, but even slightly more far-reaching. Wholesaling will develop into a fully Euro-dominated field. As of yet, there is only one European directive that sets the criteria for wholesalers, such as adequate premises, qualified staff and emergency plans for market withdrawal. These criteria, however, are enforced at the national level by very different national authorities. A first step will be more harmonization between national practices. A regulation will make the supervision of wholesaling a European matter and the responsibility of the EMEA. The competent national authorities will be under direct supervision of the EMEA, similar to the relationship between national medicine agencies and EMEA in terms of authorization and pharmacovigilance.

Although there is a directive that prohibits public advertising of POMs, the differences stemming from nationally applied classification decisions make it a predominantly national field. As a consequence of the shift to a single European market for pharmaceuticals, advertising will change into a Euro-dominated field in order to facilitate the SEM and new regulation will make the monitoring of advertizements and its associated penalties a European responsibility. As a result, the methods of monitoring advertisement for medicinal products are harmonized and penalties for infringements will become standardized for all Member States.

Pricing, dispensing, prescribing, reimbursement and post-licensing evaluation

As seen above, those fields that have traditionally been the full competence of the Member States have to be adapted to the new European reality. This will force Member States to coordinate their decisions on pricing and reimbursement (including post-licensing evaluation) at the European level through a collaboration of competent national authorities. This is the only way of facilitating a European health market with free flowing services and people without directly giving up all national competences. The harmonizing effect also leads to more coordination of regulation that concerns prescribing and dispensing of pharmaceuticals. It is a gradual process

that first involves the emergence of a European health market between 2015 and 2020, with Europe-wide free pricing for non-reimbursed medicines and generics and a basic European reimbursement package, which eliminates the possible financial incentives to go abroad. On the other hand, it simplifies the procedure of receiving treatment and pharmaceuticals abroad. This will be accomplished through collaboration instigated by Member States. In the subsequent years, more people will favour greater European Commission involvement based on the principle of subsidiarity. The national collaboration process will have provided a high level of harmonization in national practices and will basically pave the way for more European involvement. A logical step in the development of the single European market will be to organize and arrange medicines at a European level, which is now in accordance with the sufficiency criterion (the level best suited to achieve its objectives) and the benefit criterion (value is added). Furthermore, it will build on the positive climate around the European Union in general and it has many organizational advantages. A Euro-dominated pharmaceutical market with a European reimbursement decision will be just one of the results.

The question remains whether restrictive pricing regulation or free pricing for all pharmaceuticals will be the dominant policy perspective of the European Commission. As of now, the European Union has a mainly industrial policy perspective, but this is largely the result of the factual competences of the EU, which mainly stem from the free trade principles (see Chapter 3). When the EU is handed new competences relating to health care policy and public health policy, the policy outcome is expected to change accordingly and provide a better, more balanced representation of the overall perspectives of Member States. Moreover, Member States are not expected to give up competence in their national health care systems if it would be a radical change from their former policies. Hence, this would create a more balanced policy with a stronger health policy perspective and more innovative policies for restrictive pricing, reimbursing and prescribing regulation. In the end, one should not forget that Member States form the European Union.

PART III: ANALYSIS

7 Analysis

This chapter provides a systematic examination of the impact of the three pharmaceutical policy scenarios (i.e. the Expert Scenario, the European Crisis Scenario and the European Scenario) on the actors in the European pharmaceutical market. Therefore, each policy scenario for the future (Part II, Chapter 6) will be compared to the trends and characteristics for each actor as described in the literature review (Part I), as visualized in Figure 1. The observed trends in the literature review are likely to be affected by different policy scenarios, which would especially affect the pace at which these trends evolve. The discussion in the next and final chapter of Part III addresses what these scenarios imply for the provision of pharmaceuticals within the European Union and the competitiveness of European industry (i.e. the goals of the European Commission in this sector).

7.1 Impact of the Expert Scenario

In the Expert Scenario, the supply side of the European pharmaceutical market will generally see a consolidation and harmonization trend that trickles down the pharmaceutical value chain. As a result, international consolidation concerning wholesalers and, at a later stage, pharmacies is a logical consequence of companies trying to keep up with the pharmaceutical industry and wholesalers in order to be on a level playing field with their respective suppliers, particularly in an increasingly liberalized market. Various developments in European and national pharmaceutical policy reinforce these developments. One can think of the increasingly Euro-dominated authorization procedures and classification decisions but also of the levelling effect of parallel trade, which is less hampered by national regulation and national differences.

Although the demand side of the market largely overlaps with the health systems of Member States (the competence stays with the Member States in the Expert Scenario), it is not immune to the European trend and is, to a certain degree, forced to adapt to the changing realities of the supply side. The next paragraphs analyse the

impact of the Expert Scenario on the various actors of the European pharmaceutical market.

7.1.1 The European pharmaceutical industry

In the Expert Scenario, the European policies that mainly affect the pharmaceutical industry are authorization, classification, advertising, pricing, prescribing, reimbursement and post-licensing evaluation. These policies will be briefly discussed to provide an overview of the impact of the Expert Scenario on the pharmaceutical industry, which includes the innovative industry, generic manufacturers and NBFs.

Authorization

After the abolishment of the strictly national procedure, authorization will be carried out through European procedures only by 2015. This implies that national differences in, for example, availability, administration and packaging will gradually fade out. Pharmaceuticals will no longer be tailored to the needs of specific populations (national or regional) and there will be no pan-European differences in sale prices. This means that generic manufacturers, who are still strongly regionally-embedded and mainly operate along national boundaries (Gambardella et al. 2000; Pammolli 2004), will have to look out for European partners to produce, market and distribute their generics since they will face increased competition from other European generic manufacturers. Hence, it can be expected that a consolidation trend as part of a general consolidation of the pharmaceutical industry (see Chapter 2) can be expected to persist, maybe even accelerate due to increased competition. NBFs are already bound to the centralized procedure, so there will be no impact on the way they seek authorizations for their products.

Classification

The EU legislation concerning classification mainly seeks to facilitate a competitive non-prescription market. The European OTC (P and GSL) market is already expanding in terms of value, volume and range of products, despite differences in the exact products available and the regulations governing their distribution, supply and use (Bond et al. 2004). This is an interesting development for all manufacturers of non-prescription medicines, especially since the P and GSL categories will presumably be applied across Europe between 2010 and 2015. Producers will have a large stake in

getting their products switched from the P to the GSL category, which is more accessible to the public. They will have the necessary mechanisms at their disposal to apply for a reclassification of their product, against European-wide criteria, albeit nationally applied. One can expect the industry to adjust to this development, which is actually a lucrative opportunity, by developing new strategies and, for example, diversifying the range of their products and package sizes, all aimed at receiving the GSL status. It is also in line with the ongoing trend towards self-medication, in part due to the increased expectation of Member States that citizens bear more of their health care costs themselves (Bradley et al. 2004) and the European Commission's efforts to support a competitive non-prescription market as first articulated in its response (European Commission 2002) to the G10 report (European Commission 2001).

Advertising

In the Expert Scenario, more therapeutic groups will be open for direct consumer advertising. In addition to this, a growing non-prescription market through deregulation also implies more pharmaceuticals that allows direct consumer advertising, which could lead to an even further increase in advertising expenditures on top of the already very high marketing expenditures that sometimes exceed the R&D budget (OECD 2008). On the other hand, the abolishment of the strictly national authorization procedure, but also a more harmonized classification decision, will gradually remove national differences in the categories in which pharmaceutical products are sold in certain Member States. This increasing convergence will make it easier to instigate larger pan-European marketing campaigns, which can be expected to bring about synergy effects. Another advantage for the pharmaceutical industry in this regard will be the increased harmonization in the methods for controlling pharmaceutical advertising and the establishment of a harmonized penalty system instead of the old system that was fragmented along national boundaries.

Pricing, reimbursement post-licensing evaluation and prescribing

Since the Member States will retain full control over their national health system where it concerns the state (publicly covered) sector, there will be more emphasis on cost control and curbing health care budgets, which is in line with the current trend

(see Sections 4.2 and 4.3). Furthermore, the increasing convergence with regard to the methods used for cost control (Maynard and Bloor 2003; Guillén and Cabiedes 2003), the pharmaceutical products that are available and the use of economic evaluation and post-licensing evaluation (through European collaboration of National Competent Authorities) are likely to result in reimbursement decisions increasingly being made along the same lines and, thus, having similar outcomes. Member States that had relatively free pricing (e.g. Germany and the UK) will also increasingly regulate prices for innovative drugs. Member States will then use the full repertoire of volume and price measures in order to circumscribe the number and price of pharmaceuticals that are reimbursed through the system. This implies that it will become more difficult, mainly for the innovative industry, to win back their increasingly costly investments in R&D (through new technologies), especially in those cases where the new pharmaceutical has no proven extra clinical or administering benefit. Furthermore, this has considerable consequences for the sequence in which manufacturers launch their products in the European market (i.e. countries with relatively free pricing in the first place) as this influences the prices in other countries and price comparisons. In the literature review, it became clear that the pharmaceutical industry is quick at adapting to new situations so it can be expected to come up with various strategies to deal with this new reality. Apart from the already visible consolidation trend, one can think of even more emphasis on drugs with blockbuster potential (e.g. lifestyle drugs and drugs for diabetes and cardiac illnesses), a further switch to the US and new cheaper emerging markets (e.g. new EU Member States and Asia) as centres of research and operating activities in search of increased efficiency and productivity, larger marketing expenditures and increased financing of well-disposed clinical trials. Research has shown that pharmaceutical companies tend to go where there is a strong market (Pammolli et al. 2004; OECD 2008). It is interesting to note that some new Member States (e.g. Poland, Hungary, the Czech Republic and Slovenia) already show an increased specialization in pharmaceutical manufacturing (Pammolli et al. 2004).

On the other hand, new opportunities will arise through the sheer size of the European market as a whole, in which all national markets are gradually opened up

through EU law. What arises is a formidable market of 487 million people with large growth potential, especially in the EU12 Member States. In this market, a liberalized OTC market with free price setting throughout the EU, later followed by an increasingly European generic market, will emerge in which manufacturers compete on price. This development will make these markets particularly more competitive. For the generic industry, chances lie in favourable national policies that increase the amount of generics that enter the market and favourable EU policies that promote the wide use of Bolar provisions to ensure faster market access after patent expiration (European Commission 2002). This tougher competition should spur the competitiveness of the European generic industry and not 'nurture' inefficiency (Gambardella et al. 2000). Tougher competition can also be expected in the marketing of generic products. The innovative industry will try to retain market share even more by using their brand and trying to give it a strong position in the market prior to patent expiration.

7.1.2 Wholesalers

In the field of wholesaling, the current consolidation and integration trends (Clement et al. 2005) will be reinforced by increased harmonization in national pharmaceutical policies and liberalization of pharmaceutical markets. On the one hand, the areas in which European wholesalers can cooperate increase with every development that harmonizes the national regulation concerning the distribution, use and supply of pharmaceuticals. Since the pharmaceutical products that are on sale in the various EU countries are expected to become increasingly similar, it is likely that wholesalers collaborate in the purchasing and distribution of pharmaceuticals. On the other hand, the merger and acquisition trend is, of course, not a voluntary one but is also precipitated by fiercer competitive pressures.

A minority of countries do not allow for short-line wholesalers because it is thought to contradict the public interest when wholesalers only specialize in certain therapeutic groups or pharmaceuticals in their assortment (Taylor et al. 2004a). However, EU law will gradually open up these markets and limit national interference. This will add to the trend observed in some Member States of highly specialized wholesalers carrying a limited range of products at very competitive prices (Taylor et al. 2004a),

which are especially active in those markets that are expected to gradually turn predominantly European over the next two decades (e.g. the non-prescription and generic markets).

Member States show differences in their legal frameworks with regard to the distribution chain and integration. It can be expected that these differences will slowly dissolve through the workings of EU law. This will eventually make vertically-integrated combinations in the pharmaceutical value chain (i.e. combinations between pharmaceutical industry, wholesalers and pharmacies) a widespread European practice. Furthermore, the observed merger and acquisition trend (Clement et al. 2005) will continue and have a levelling effect on the huge differences between wholesalers per capita in the various Member States. This will result in oligopolistic market structures, as already observed in the more developed EU Member States and in most Member States by 2015. The consolidation trend increases the purchasing power of the wholesalers, through which they will be able to negotiate more effectively with their suppliers.

Parallel trading is expected to become more well-established, not only through favourable case law, harmonized markets, effective national incentives and smaller price differentials, but also because larger wholesaler combinations can face the industry at eye level. Before, wholesalers were reluctant to engage in parallel trading fearing profit loss and a bad relationship with the pharmaceutical industry, of which they were highly dependent. Needless to say, the pharmaceutical industry is a known adversary of parallel trading because they fear profit loss in high-priced countries (see also Section 3.5.2 for the discussion of case law). This development contributes to more competitive pressure and a levelling effect on price differentials, together with other aforementioned trends with harmonizing effects.

Although these large wholesaler combinations purchase pharmaceuticals on a European level, the supplier relationship with pharmacies will at first remain conducted at basically a national level through locally-based subsidiaries. However, more border-crossing services are also likely to develop when European markets for certain pharmaceutical groups develop (OTCs and generics pioneering this development).

7.1.3 Pharmacies

As seen in the literature review, the future of European pharmacies is strongly interwoven with the future of wholesalers and they will basically follow the same trends. Pharmacies have a special role in the value chain, being on the dividing-line of the private free market that supplies them and the public, heavily regulated market they serve. Since it is such a regulated environment (Paterson et al. 2003), there is tremendous opportunity for market liberalization and the EU will push through its agenda wherever it can. Ongoing market liberalization will make market-entry regulation easier, which enables other forms of ownership and new combinations in the pharmaceutical value chain. The market will be opened up, for example, through enabling non-pharmacists to open pharmacies, by gradually abolishing state monopolies where present or allowing the takeover of pharmacies across national borders. The EU perspective will not conflict with the national agendas since cheaper pharmaceuticals, through lower profit margins for pharmacists, are perfectly in line with national health care policy.

At present there are huge national differences in the number of pharmacies per million inhabitants, with differences of up to seven times within the EU15 (Paterson et al. 2003; Taylor et al. 2004a) but a strong consolidation trend aiming to reap the merits of economies of scale will counter these differences to a certain degree and larger chains are the result. Chaining will give pharmacies a better position in their negotiations with suppliers, but will also avail them in an increasingly cost-conscious environment in which they are confronted with progressively stringent national cost-containment policies. One can think of Member States promoting generic substitution but also of direct negotiations between governments and pharmacy organizations, as seen in the Netherlands for example. At first, chaining takes places within national boundaries, yet it is also very likely that the international takeover trend visible in the pharmaceutical industry and followed by the wholesalers, will eventually trickle down to the pharmacies as well. It seems likely that the DocMorris case described in this thesis will become an example of increased importance.

Another significant development with catalysing potential for the occurrence of European pharmacy chains with European prices is the rise of internet pharmacies.

However, this mainly applies to the OTC pharmaceuticals and non-reimbursed prescription pharmaceuticals (i.e. those medicines for which the patient carries the financial responsibility). If an internet pharmacy in Member State A offers certain POM pharmaceuticals at a lower price than Member State B, a patient in Member State B does not have an incentive to order the product in Member State B because his/her payer will reimburse anyway. It is important to mention that the European Commission supports a mutual recognition of pharmaceuticals in a proposed 2008 directive for cross-border health services. It could, therefore, be a different case when Member State payers start to develop (or are given the instruments and freedom to develop) policies that will give patients some participation in the discounts they receive. This would correspond with similar regulations for pharmacists that are allowed to keep some of the discounts they receive when they manage to purchase medicines at a discount.

However, this seems unlikely in this scenario since it could also threaten the domestic pharmacy sector (i.e. the national provision of medicines) and this is not in the interest of the Member States. For OTCs and costly non-reimbursed pharmaceuticals (e.g. anti-malaria prophylaxis, which is not reimbursed in the insurance policies of most countries), it can become very profitable to look around. This is possible if we assume mutually recognized prescriptions. Additionally, in this particular field (i.e. outside the national, publicly-covered system) Member States cannot do much to control or regulate this practice. Patient and consumer groups could function as facilitators in making this possibility visible to the public. The competitive pressure internet pharmacies impose on traditional pharmacies can result in lower national prices and internet pharmacies can have a levelling effect on European price differentials in the longer term.

7.1.4 Demand side (medical care triad)

The demand side of the European pharmaceutical market will be faced with more policies focused on cost-awareness, which aim to keep health care affordable and accessible over the next twenty years and further in the future. This can be achieved if Member States adopt similar strategies concerning pricing, prescribing and dispensing, as discussed in Chapter 4; however, new initiatives will also emerge, often

part of larger health care reforms that aim to generally restructure the funding of health care and introduce more market competition. This could be some form of managed competition with limited government interference. In this development, the payers/purchasers of health care (e.g. health insurer, sickness fund, Primary Care Trust) will have larger stakes in controlling health care costs and are likely to bear more direct financial responsibility herein. It is, therefore, very well possible that payers will play a larger role in controlling pharmaceutical expenditures in the future than they do at present.

It is also on this side of the pharmaceutical market where the most divergence between Member States continues to exist. Whereas the supply side is less fragmented and increasingly organized on a European level, the demand side represents 27 different Member States and thus 27 health systems. Furthermore, it represents a myriad of cultural and personal attitudes towards prescribing practices and pharmaceutical consumption. These differences exist not only nationally but also on a regional, cultural and individual level. This applies to both prescribers (doctors, GPs and physicians) and patients.

Prescribers

In general, taking into account the differences in consumption and prescribing across national and cultural boundaries, doctors will be under increasing pressure to prescribe rationally and, by doing so, have a larger responsibility in controlling health care cost. It can be expected that their ability to prescribe what they deem appropriate will be increasingly challenged through guidelines, electronic formularies and the use of prescribing data. In this practice, huge national differences exist between Member States (see Section 4.2.2), so there will be frontrunners and stragglers, but the trends are already visible. Also, more Member States with high levels of prescription per capita will realize that there is huge potential for savings. The frontrunners in general are the western and mainly northern Member States, whose prescribing policies show more innovative and restrictive policies in this regard compared to southern, traditionally high-consumption countries. These policies will be adopted by the EU12 countries when their health care systems develop towards the EU15 average in terms of quality. Twenty years from now, the differences per Member State

will be levelled for the most part. Another development will be the increasing loss of trust in the doctor-patient relationship, also due to more power and information in the hands of patients with regard to accessing and using medicines (Bradley et al. 2004). This development, in combination with restrictive cost-containment policies, will negatively impact the reputation of the medical profession. It will be in their interest to construct these formularies and policies. It could also lead to greater international collaboration and more European collaboration, in particular of professional medical organizations that will look to safeguard their autonomy in prescribing as they see fit.

Patient/consumer

In an IAPO (International Alliance of Patients' Organizations) survey, including input from patients from ten EU Member States, patients rated timely access to the best treatment and information, the right to participate in decision at the individual patient level and patient involvement in policy-making among their top priorities (IAPO 2006). This is reflected in this scenario for the future of the European pharmaceutical sector. As described in Section 2.2.2, the doctor-patient relationship is changing, which can be ascribed to developments in the environments of patients. Patients become more involved in their choice of treatment and have various ways to access a sheer limitless amount of medical information, mainly through the internet. Furthermore, the doctor–patient relationship is characterized by strong information asymmetry, but this unequal relationship will be countered to a certain degree through patient empowerment.

The myriad of European patient groups will also organize themselves better, on both a national and European level, to keep up with the Europeanization trends on the supply side of the European pharmaceutical market in order to enable them to participate independently in the decision-making process on health matters in the European Union. It will be of key importance in this age of rapidly growing, freely-accessible medical information that patient organization groups, in dialogue with the relevant European and national institutions, play a pioneering role in the establishment of a standardized European certifying system for good quality health information web sites, with, for example, quality labels and a multilingual web portal.

Already there are regional and national networks in place and others are developing but, in this scenario, the expectation is that around 2010, these networks should work toward some kind of standardized European system. This can all take place within the frameworks of the G10 Medicines Group plan concerning information to patients, the EU's e-Health action plan (European Commission 2004b) and the 2006 MedIEQ (Quality Labelling of Medical Web Content Using Multilingual Information Extraction) project, co-funded by the European Commission under the public health programme. However, patient organizations have to play a pioneering and pro-active role in this process.

In an increasingly cost aware environment, patients will also be expected to have an increased responsibility for paying for their medicines and may be encouraged to care for minor ailments with OTC remedies, paid for out-of-pocket (Mossialos et al. 2004). Apart from good information, this further illustrates the need for powerful patient organizations that monitor developments that could have negative effects on the equity of access. Another development will be the expectation that patients will increasingly be subjected to marketing efforts from the pharmaceutical industry. Not just through direct-to-consumer advertising, a result of increased competition and a larger OTC market and more therapeutic groups open to advertising, but also through new methods, such as funding for patient groups (Herxheimer 2003).

Patient organizations are relatively poor and have little independent funding, which can make them easily seduced by the rich pharmaceutical sector. When these relationships exist, they must be fully acknowledged and open. All patient groups should have readily available guidelines, maybe standardized on a European level, on how to interact with the pharmaceutical industry. In this light, it would be a good idea to apply the recommendations from the G10 Medicines Group to the funding of patient organizations. However, there are important issues at stake, such as equity of access, appropriate use and detection of adverse events (Bond et al. 2004).

Payers

Under this scenario, little convergence in national practices with regard to insurance form is expected and national health insurance systems will develop in ways decided at a national level. In other words, this is the result of a general health care policy,

rather than the impact of the European pharmaceutical policy. It is up to the individual Member States whether this is some sort of managed competition under public or private law or a NHS. However, it can be expected that innovative policies will be developed in most Member States to counter agency problems and, by doing so, it will give them more responsibility in the containment of costs.

7.2 Impact of the European Crisis Scenario

The European Crisis Scenario foresees a gradual return to national competence where possible. The process of an increased Europeanization and consolidation of the distribution chain will be halted by the shift towards national competence and less foreign competitive pressures, as occurs in the other scenarios. This will inevitably have grave effects for all the actors of the European pharmaceutical market, from which the supply side actors will be particularly affected. Changes and stagnation are, therefore, most visible in those fields that undergo a Europeanization trend in the other scenarios (i.e. those fields that have shared competences between the EU and Member States). This includes authorization, pharmacovigilance, classification and distribution. The fields where the national competence is predominant will see a development that is similar to the Expert Scenario, but in a national, rather than a European context. In comparison to the Expert Scenario, there will be more divergence between countries, resulting in frontrunners and stragglers that are further apart in the way they implement policies than in the Expert Scenario, where the European process has a strong harmonization effect. In the following paragraphs, the impact of the European Crisis Scenario will be examined in detail.

7.2.1 European pharmaceutical industry

Authorization, pharmacovigilance, classification and distribution

Under the European Crisis Scenario, authorization, pharmacovigilance, classification and distribution will gradually return to being national competences. The failure of the European authorization procedures becomes clearly visible between 2015 and 2020 when the EMEA and its procedures will be dismantled. What remains are 27 strictly national authorization procedures with different protocols, different data exclusivity periods, a myriad of pharmacovigilance systems and a nationally-applied

classification decision based on domestically determined criteria. The diverging effect of these developments will have huge consequences for the pharmaceutical industry and the way products are brought to the national markets.

The larger, traditional, innovative multinational companies historically already possess subsidiaries in most countries, often the result of mergers and acquisitions. These national subsidiaries and agencies will now have to concentrate on maintaining, or maybe even expanding, the capacity to file for authorization procedures and meeting the requirements of the national regulatory frameworks. Hence, for the innovative pharmaceutical industry, this scenario implies higher administration costs and even more pressure on their R&D budgets compared to a scenario in which administration and industry friendly European procedures emerge as the European standard.

On the other hand, one could think that it could also provide opportunities to exploit pharmaceuticals in higher priced states, such as states in which the pharmaceutical industry is an important provider of jobs. In any case, this will be difficult in the more developed EU15 countries considering the assumption that developed European states will all be forced to adopt stringent cost-containment policies in order to curb health care expenditures and relieve national budgets. An interesting development would be further specialization into pharmaceutical manufacturing (Pammolli et al. 2004), which has already started in Central and Eastern European countries. This may result in a relocation of the manufacturing sector of the pharmaceutical industry, which would not only serve as a production facility with low labour costs, but also as a growth market where national governments are willing to develop a favourable industry-friendly climate, including lenient pricing regimes, to attract and retain big pharmaceutical companies, tailored to the purchasing power in these countries.

Manufacturers of generic pharmaceuticals, which are still very much nationally organized, will have the smallest burden to bear. The several national generic markets will not develop into a dynamic, Europe-wide generics market with a standardized regulatory framework. The lack of convergence and standardization means that potential competition from other countries will face a serious barrier and disadvantage

that varies from country to country when accessing a national market. Through this, the generic industry can hold on to its dominant national positions for a longer period of time than under the other scenarios. However, the concentration trend will still be inevitable, mainly as a result of pressure from national pricing regimes, but it could be severely slowed down due to less foreign competition.

Smaller pharmaceutical companies that do not a have an agency or subsidiary in the various European states and companies, for whom the central European procedure was obliged (often small non-European NBFs), will have to initiate authorization procedures in all the different European States, which is a clear competitive disadvantage in their quest to get their products on the market. In this process, pharmaceutical outsourcing companies such as Parexel will play a key role and show incredible growth potential when their expertise and infrastructure is consulted, but increasing use of partnerships with multinationals (e.g. biopartnering) also seems likely.

This increased administrative effort to cope with the various regulatory frameworks implies extra costs and it is possible that not in every European country an authorization application is made. Poorer and smaller European countries may be deprived of some new products. It is not unthinkable, however, that smaller countries follow the example of Luxembourg and will adopt the authorization decisions of other European countries. Also, smaller scale cooperation on authorization between certain European states could prove necessary in order to safeguard access to expensive innovative pharmaceuticals.

It is important to note that the lines between innovative, generic and NBF companies will become even more blurred over the next twenty years, making combinations of the developments described above possible.

Advertising

In the European Crisis Scenario, the national differences as to which pharmaceutical products are sold in which category in certain Member States are expected to diverge as a result of national variations in market authorizations and classification decisions. The increased divergence will make tailor-made national advertising cam-

paigns a necessity, much like the present situation and two groups of countries will become visible.

The first group, consisting of the more developed EU15 countries, will place more emphasis on self-medication as a means to cut costs and will, therefore, favour flexible deregulation of pharmaceuticals. Citizens of these countries already have years of experience and have long been encouraged to employ self medication. Therefore, the number of non-prescription pharmaceuticals open to advertising is likely to increase. The ban on advertising POMs will be prolonged since it is assumed to stimulate the demand for expensive POMs.

The second group will mainly consist of Eastern and Central European countries with less developed health care systems. Their populations are not as used to a culture of self medication, may not be aware of its dangers and will therefore be protected by conservative classification decisions (i.e. pharmaceuticals are more likely to be kept on POM or P status). However, as previously assumed, the Eastern and Central European countries are interested in attracting pharmaceutical industry as a locus of manufacturing and innovation. It could mean that the research-intensive pharmaceutical industry is enticed by lenient advertising regulation. Concretely, this could mean that certain POMs may be advertised. In this case the governments make a health/industry policy trade-off in favour of the pharmaceutical industry. This is comprehensible keeping in mind that these countries have strong growth economies combined with not fully developed health care systems where the health budget does not pressure the national budget to the same degree as in Western European countries. There are opportunities in both groups depending on the state and therapeutic class and overall spending on advertising will likely increase.

Pricing, reimbursement, post-licensing evaluation and prescribing

As far as regulation within a state's health care system is concerned, the European Crisis Scenario will develop along the same lines as the Expert Scenario. However, there are two major differences. First, we assume in the Expert Scenario that the pharmaceutical markets show convergence through the harmonizing effects of increasingly Europe-dominated regulation over authorization, pharmacovigilance, classification and distribution. This is not the case in the European Crisis Scenario where

these markets are expected to develop in ways that increase the differences between them, which also restricts the opportunities to collaborate. Secondly, in the European Crisis Scenario the influence of EU legislation is no longer an important factor, as opposed to the European Expert Scenario. This means that there is no European liberalization of the markets outside the state sector, hence no development towards a competitive, European non-prescription market and no movement towards some sort of competitive European generic market. As a result, the European states will have strong influence over the entire national pharmaceutical market, as described in Sections 4.2 and 4.3.

It is expected that developed European health care systems will take a stronger health policy perspective in which containment of costs is key and that the newer, less developed European States, mostly Eastern and Central European countries, are more likely to make a trade-off in favour of industrial policy. This is an assumption that requires strong economic growth in these countries and initial investments in the access to health care before switching to a stronger industrial perspective since many Eastern European countries have systems where patients are often struggling with comparably high co-payments as of 2008 (e.g. Poland, Slovenia, Estonia).

In the former, we see the trend as described in the Expert Scenario, which means that the trend of copying methods used for cost control will set the standard (Maynard and Bloor 2003; Guillén and Cabiedes 2003), of which economic evaluation, generic penetration and restrictive pricing will be expected to become integral parts. This implies that it will mainly become more difficult for the innovative industry to win back their investments in R&D, which are already accelerating in terms of costs. In general, the aforementioned factors will not create a favourable long-term environment for the innovative pharmaceutical industry (including NBFs) in the EU15 countries and further relocation of operations seems to be the solution.

In the latter, new opportunities for the pharmaceutical industry will arise in the booming new European countries where favourable reimbursement and pricing policies only add to the already attractive emerging economies with low labour costs, growing markets and an abundance of well-educated scientists and engineers. In this scenario, the relocation from the EU15 to the US, Eastern and Central European

countries and other comparable emerging economies (e.g. in Asia) may take place with an accelerated pace.

For the more nationally-organized generic industry, chances lie in favourable national policies that would increase the level of generic penetration. They could be one of the winners in this scenario, with less foreign competitive pressure as markets are diverging and a shared interest with national government (generic penetration).

7.2.2 Wholesalers

For wholesalers, the European Crisis Scenario will not have grave consequences on the short term. However, consolidation trends among European wholesalers towards pan-European wholesalers will be hindered when compared to the Expert Scenario, in which the current consolidation trends and integration (Clement et al. 2005) will be accelerated through increased harmonization in national pharmaceutical policies and the opening up of national pharmaceutical markets through EU law.

The differences that Member States show in their legal frameworks with regard to integration, mainly where the wholesaler-pharmacist relationship is concerned, will not gradually dissolve but will develop according to the policy objective in the respective country. In other words, some countries will implement –if not already in place– market liberalization policies similar to those emanating from European law, resulting in large vertically-integrated combinations in the supply chain, whereas other countries will keep or increase the restrictions in their legal framework.

The observed horizontal integration trend will have a levelling effect on the huge differences between wholesalers per capita in the various Member States. However, the huge national differences will not disappear at the same rate as under the Expert Scenario. The strictly nationally-regulated health systems will make it easier for wholesalers to retain their leading national positions for a longer period of time. Going abroad is not yet a competitive necessity and does not have the same financial advantages as the other scenarios, where collaboration in more fields is possible (e.g. purchasing, storing, marketing and distribution).

Nevertheless, depending on the state of the development of the national pharmaceutical market, the national wholesaling market will show an increasingly oligopolis-

tic structure. In this process there are frontrunners that, as of today, have already reached this stage (mainly northern countries from the EU15), a midfield (southern Europe) and trailers (new accession countries). Pan-European collaboration between the developed nations with similar frameworks remains attractive on a smaller scale and scope.

The operating environment for parallel trading will become more difficult and complex. Since market authorizations are granted on the national level, the differences concerning what is on sale (e.g. packaging sizes, administering form) vary between countries, which will increase the impediments to import pharmaceuticals that are on sale in another country. Furthermore, the national frameworks of each individual country determine whether parallel trading is allowed. In this scenario, the wholesale combinations that do engage in these activities, where legally permitted, mainly operate in a national setting and, as a result, have less negotiating power vis-à-vis the multinational pharmaceutical industry. Therefore, they can be expected to encounter difficulties with the pharmaceutical industry when they pursue parallel importing. The pharmaceutical industry would want to avoid a situation in which their products are purchased at a foreign subsidiary with lower prices. Even though the wholesalers are expected to hold on to their leading role on the national scale, they do face the difficulty of coping with a much larger, internationally-oriented industry with a stronger negotiation position.

7.2.3 Pharmacies

There are huge national differences in the European Member States in the number of pharmacies per capita and the regulatory environment in which they must operate (Paterson et al. 2003; Taylor et al 2004a). It is expected that under the European Crisis Scenario, depending on the policy perspectives of the individual Member States, more (national) market liberalization will enable new combinations in the pharmaceutical value chain with the hope that it increases efficiency and drives down profit margins (i.e. a stronger health care perspective). One can think of the chaining of pharmacies but also of non-pharmacists being permitted to open and/or own pharmacies. On the other hand, some Member States can be expected to take a stronger public health perspective and keep more restrictive regulations in place

with regard to market entry, such as pharmacy ownership (e.g. state monopoly or solely pharmacists), the number of pharmacies (e.g. through economic needs tests and pharmacies per capita).

However, also under the European Crisis Scenario, larger chains are developing, which is hoped to give pharmacies a better negotiation position in their dealings with suppliers, but also to help them cope with increasingly stringent national cost-containment policies. One can imagine Member States promoting generic substitution, but also direct negotiations occurring between governments and pharmacy organizations.

Another significant development with far reaching potential is the emergence of internet pharmacies. However, this development will mainly take place domestically since pharmaceutical markets and their regulations take a national course, which makes cross-border internet pharmacies virtually impossible.

7.2.4 Demand side (medical care triad)

The demand side of the European pharmaceutical market will be characterized by diverse national policies adapted to different national settings and priorities that represent a myriad of cultural, national, regional and personal attitudes towards prescribing practices and pharmaceutical consumption. The countries may also be divided into two general groups along the same lines as described above.

One group, mostly consisting of the EU15 Member States, will roughly follow the developments as described under the Expert Scenario, i.e. they follow the ongoing trend and will expand their cost-containment policies aiming at affordable and accessible health care through cost and volume measures. The strategies, new and pre-existing, will often be copied from other countries and applied to their own domestic situation.

The other group, mainly the new accession countries, will lead to a policy trade-off in favour of industrial policy. Reforming regulation based on Western European standards has been driven by the desire of EU access (Mrazek et al. 2004) and mainly included measures such as market authorization, patent legislation, manufacturing standards, licensing requirements as well as drug pricing and reimbursement. The

implemented cost-containment measures have predominantly focused on reimbursement and pricing rather than measures affecting (rational) prescribing and dispensing (Mrazek et al. 2004).

Prescribers

In the first group, doctors will generally face increasing pressure to prescribe rationally and thus will have a role in controlling health care costs, following the expectations of the Expert Scenario. Member States with high levels of prescription per capita will realize that there is huge potential for savings. It is likely that the doctor's ability to prescribe what they see fit will be constrained through guidelines, electronic formularies and the use of prescribing data. In this process, huge national differences exist between Member States, so there will be frontrunners and stragglers. Add to this development the observed loss of trust patients have in their doctors (Bradley et al. 2004) and one can see that the medical profession will be under increased strain. It will be in their interest to cooperate to construct these formularies and policies. International collaboration is foreseen at this point in the Expert Scenario, but it cannot be expected to be at the same degree as in the European Crisis Scenario with its diverging national health systems.

In the second group, these volume measures will not be implemented to a large degree until the full range of pricing and reimbursement measures are exhausted and the health care systems are on a EU15 level. In the meantime this practice nicely fits the governments' policies to provide an attractive manufacturing, operating and research base for the pharmaceutical industry. This is expected to take at least the next twenty years. The doctors will therefore enjoy more freedom in their prescribing habits and will not be subjected to extensive restrictive prescribing measures. However, the increasing loss of trust in the doctor-patient relationship is a trend here, although not to the same degree as the consumers of more developed EU Member States. This can be explained through (although gradually dissolving) differences in education levels, cultural attitude towards pharmaceuticals and access to information.

Patient/consumer

In the first group of Member States, the patients will roughly see the same developments as in to the Expert Scenario, although not in a European context, i.e. circumscribed to the national setting. Hence, the doctor-patient relationship will become a situation in which patients become more involved in choice of treatment and have various ways to access an abundance of medical information, mainly through the internet. This will decrease the existing information asymmetry in the doctor–patient relationship to a certain degree. Therefore, patient groups will also better organize themselves, mainly domestically, in order to allow them to participate independently in the decision-making process on national health decisions. Furthermore, the development towards mainly nationally standardized certifying systems for health information web sites of good quality will be of key importance. The patient groups will have to play a pioneering, active role in that development. Already there are regional and national networks in place and others are developing. This will result in fully-operational national systems by 2015. The development towards a European standardized system as described under the Expert Scenario will largely be put on ice.

Furthermore, in an increasingly cost aware environment, patients will be expected to have an increased responsibility in paying for their medicines and will be encouraged to care for minor ailments with OTC remedies paid for out-of-pocket (Mossialos et al. 2004). This also further illustrates the need for powerful patient organizations with access to the decision-making process that monitor developments that could negatively affect equity of access to pharmaceuticals.

In the second group, the development towards full-fledged patient organizations still has a long way to go. The patients and their organizations will have to go through the same emancipation process as in the first group of Member States. This is expected to take longer due to cultural, political and economical factors.

Both groups, however, will be faced with increased marketing efforts from the pharmaceutical industry. Not just through direct-to-consumer advertising, which can be expected to be more common in second group of countries as a result of more therapeutic groups open to advertising, but also through new strategies, such as funding for patient groups.

Payers

As under the Expert Scenario, not much convergence in national practices with regard to the organization of payers is foreseen. National health insurance systems will autonomously develop in ways decided upon at a national level as a result of discussions and decisions on their respective health systems that reflect country specific characteristics (e.g. concerning the economical, political and cultural environment). Whether this is some sort of managed competition, under public or private law, or an NHS is up to the Member State and is not a result of the European Crisis Scenario.

7.3 Impact of the European Scenario

In the European Scenario, both the supply side and demand side of the European pharmaceutical market undergo a strong Europeanization trend. On the supply side, this takes place at a faster pace and with further reaching consequences than under the Expert Scenario because pharmacovigilance matters and classification decisions are decided on a supranational level. At first Member States will retain full control over their national health systems where it concerns the public sector. This implies more emphasis on cost control and curbing health care budgets and thus an extrapolation of current trends (see Sections 4.2 and 4.3). When you add the increasing convergence in methods used for cost control (Maynard and Bloor 2003; Guillén and Cabiedes 2003), the range of available pharmaceutical products and the use of economic evaluation (through European collaboration of the national competent authorities) to this development, reimbursement decisions will increasingly be taken along the same lines. Furthermore, the market in general, the non-prescription and generic markets in particular and national benefit catalogues will become more European in nature, also forced through cross-border health care. The first step will be a European benefit catalogue that takes out the incentive for patients to go abroad for (reimbursed and/or in their home-state unavailable) pharmaceuticals. As a result, it will become a logical consequence to arrange pricing, reimbursement, post-licensing and prescribing on a European level between 2020 and 2025. What will result is an emerging SEM for medicines with the free movement of all pharmaceuticals, including innovative POMs, generic medicines and non-prescription drugs all at pan-European prices (before taxes such as V.A.T).

On the demand side, a development towards a European health market with European health insurers emerges. For this, litigating consumers and border-crossing pharmaceuticals play a pioneering and catalysing role. In the next paragraphs, the impact of the European Scenario on the various actors of the European pharmaceutical market will be described in more detail.

7.3.1 European pharmaceutical industry

In the European Scenario, the European policies mainly affecting the pharmaceutical industry are authorization, classification, advertising, pricing, prescribing and reimbursement and post-licensing evaluation. These fields for the most part overlap with the developments of the Expert Scenario. This will be discussed briefly in the following pages with greater emphasis on the differences between scenarios.

Authorization

As under the Expert Scenario, authorization will be carried out through European procedures only by 2015 and a gradual phasing out of the decentralized procedure will take place between 2015 and 2020, using the centralized procedure by 2025. This implies that national differences with regard to what is on sale, how it is administered, how it is packaged and the contents of leaflets, among other concerns, will gradually disappear as newer products enter the market and substitute older products over time. Pharmaceuticals will gradually no longer be tailored to the needs of a particular Member State and the availability of pharmaceuticals will be largely consistent across Europe. This practice will have a profound influence on the innovative industry because it is now dealing with one large market and only one market authorization has to be filed.

As a result, generic manufacturers, who are still strongly regionally and domestically embedded and mainly operate along national boundaries, will have to look out for European partners to produce, market and distribute their generics because they will have to compete with all other European generic manufacturers looking for a share of the European market, despite the fact the market is still growing. Hence, the consolidation trend towards a competitive European generic industry can be expected to persist and maybe even accelerate. There will be no direct impact on NBFs as the centralized procedure has already been compulsory for their products.

Classification

The EU legislation relating to classification mainly seeks to facilitate a competitive non-prescription market, which has been expanding in terms of value, volume and range of products. An amendment of the classification directive will first implement the P and GSL categories across European Member States between 2010 and 2015. Where the Expert Scenario differs from the European Scenario is that a new regulation will make the EMEA the institution responsible for making a centralized and binding European classification decision around 2020. In interplay with the solely European central authorization, this has a stronger harmonizing effect on the pharmaceutical market than under the Expert Scenario. Producers will have a large stake in getting their products deregulated from P to the easier, accessible GSL category and will have the mechanisms at their disposal to apply for a reclassification of their product, at first through nationally applied Europe-wide criteria and later through the European centralized classification decision around 2020. As under the Expert Scenario, one can expect the industry to adjust to this development by developing new strategies and, for example, differentiating the range of their products aimed at receiving the GSL and P status. It is also in line with the ongoing self-medication trend and the increased expectation of Member States that citizens inevitably will have to bear a larger part of their health care costs.

Advertising

The harmonizing effect of the centralized European market authorization and classification decision will turn advertising into a Euro-dominated field, with a European monitoring and penalty system under the auspices of the EMEA. Moreover, more therapeutic groups will be open for direct consumer advertising, also as a result of an expanding non-prescription market and the deregulation of pharmaceuticals to P and GSL categories. Hence, more pharmaceuticals will exist for which direct consumer advertising is allowed and will possibly result in higher advertising expenditures. However, the convergence trend that is even more rapid than under the Expert Scenario across Member States will make it easier to instigate larger pan-European marketing campaigns which should enable efficiency gains for the marketing of pharmaceuticals that sometimes exceed the R&D budget (OECD 2008).

Pricing, reimbursement, post-licensing evaluation and prescribing

The European Scenario foresees increasingly converging national markets with a limited number of reimbursed pharmaceuticals that go through a Europe-wide post-licensing evaluation. This national practice results in emerging and eventually fully European markets for non-reimbursed, generic and innovative medicines. This implies that it will mainly get more difficult for the innovative industry to win back their increasingly expensive investments in R&D, especially when a new pharmaceutical has no proven extra clinical or administering benefit. It may become more lucrative to focus on OTCs with blockbuster potential or specific groups of lifestyle drugs. It will force the pharmaceutical industry to abolish their market launching strategies (e.g. which Member State first?) as these strategies will effectively become useless in a SEM with centralized reimbursement decisions where there are few possibilities left to manipulate and influence the prices. A further relocation in search of productivity and efficiency gains to emerging economies (e.g. new accession countries, Asia) or more lucrative markets (e.g. USA) as a locus of research and operating activities, becomes an attractive alternative. Also, larger marketing expenditures and increased financing of (well-disposed) clinical trials will seek to influence government and public opinion.

The European generic industry will face threats and opportunities in the emerging generic market. On the one hand, through favourable national policies, the degree of generic penetration is expected to rise and the market they serve will be extended to all Member States. On the other hand, fiercely competitive foreign manufactures will also attempt to attain a slice of the huge European market and prices will be driven down. The increasing competitive pressure will result in winners and losers (i.e. mergers and acquisitions) and an accelerated consolidation trend will become visible.

7.3.2 Wholesalers

For European wholesalers, the current trends of consolidation and integration will be reinforced by increased harmonization in national pharmaceutical policies, liberalization of pharmaceutical markets, increased competitive pressure and eventually the emergence of a SEM for medicines. These results are similar to the results of the Expert Scenario. The areas in which European wholesalers can cooperate increase

with every development that harmonizes the national situations. For example, wholesalers can be expected to collaborate in the purchasing (stronger negotiating position) and distribution of pharmaceuticals. This leads to a strategic relocation from the national market to the European market.

Furthermore, EU law will gradually open up the wholesaling markets and limit government barriers concerning market-entry. This will add to the development of specialized wholesalers that carry a limited range of products at very competitive prices (Taylor et al. 2004a), which as of yet are not legally permitted in every Member State. The specialized wholesalers will be initially active in the markets that gradually turn European, first the OTC and generic markets and later the entire pharmaceutical market including POMs. This will have a levelling effect on pan-European drug prices. Parallel trading is expected to become a widespread practice, playing a catalysing role in the harmonization of pharmaceutical price levels through competitive pressure, as observed in some studies (West and Mahon 2003; Enemark et al. 2006). This development contributes to the removal of European price differentials.

Furthermore, more market liberalization will make vertically integrated combinations in the pharmaceutical value chain (i.e. combinations between pharmaceutical industry, wholesalers and pharmacies) a widespread European phenomenon. The strong consolidation trend has a levelling effect on the huge differences between wholesalers per capita in the various Member States. This will result in oligopolistic market structures in most Member States by 2015.

7.3.3 Pharmacies

As previously observed under the Expert Scenario, the future of the European pharmacies is strongly related to future developments in the European wholesaling sector. Pharmacies basically undergo the same trends. The EU will push through its market liberalization agenda, helped by litigating (foreign) pharmacy chains in search of market share. This eventually deregulates market-entry regulation, enables other forms of ownership and makes new combinations in the pharmaceutical value chain possible. What emerges is a more harmonized European pharmacy environment characterized by gradually abolished state monopolies (where present), international consolidation, market entry and ownership by foreign pharmacy chains. There is no

conflict between EU-initiated market liberalization with national agendas since cheaper pharmaceuticals achieved through lower profit margins for pharmacists is perfectly in line with national health (care) policy. This harmonizing effect also combats the huge national differences in pharmacies per capita as it leads to a strong consolidation trend mainly through chaining. Chaining will give pharmacies a better negotiation position in their dealings with suppliers. Chaining first takes places within national boundaries and European chains will be established. Convergence will occur faster than under the Expert Scenario when national situations converge.

As described under the Expert Scenario, internet pharmacies have the catalysing potential to affect the occurrence of European pharmacies and overall European prices. Pharmacies have to compete with foreign pharmacies for market share, which is possible as a result of a harmonized market. However, in the beginning this mainly applies to the non-reimbursed prescription pharmaceuticals (i.e. pharmaceuticals for which patients are financial responsible), such as OTCs and costly non-reimbursed pharmaceuticals like anti-malaria prophylaxis. Patient and consumer groups may make this opportunity visible to the public. The competitive pressure internet pharmacies impose on traditional pharmacies can result in lower national prices and internet pharmacies from cheaper countries can create a levelling effect on European price differentials in the long term.

However, when the harmonization of the pharmaceutical market advances and when payers have more influence on their products and the development of pharmaceutical policies, payers will encourage or obligate patients to get their POMs at selected, possibly foreign or self-owned internet pharmacies. Taking over or opening up (internet-) pharmacies seems a logical step in building up the necessary expertise.

When pharmaceuticals become regulated at the European level by 2025, regulation will be put in place stemming from former national policies that regulate the national provision of medicines. This will include a regulation that safeguards the public function of pharmacies (i.e. ensuring a minimum per million inhabitants or area).

Lastly, these developments have huge consequences for the responsibilities of pharmacists. Through the deregulation of medicines and the emergence of internet pharmacies, personal advice on pharmaceuticals, one of the traditional roles of the

pharmacist, will be increasingly taken away and put in the hands of the patients. Furthermore, many future pharmacists will be employed instead of owning their own pharmacies. On the other hand, they will increasingly obtain the legal instruments and responsibility to correct inaccurate prescriptions and substitute cheaper generic equivalents.

7.3.4 Demand side (medical care triad)

The demand side of the European pharmaceutical market will undergo markedly different developments compared to the Expert Scenario. Empowered patient groups reap the benefits of favourable case law, which eventually results in a European health care market and a true SEM for pharmaceuticals. This precipitates the emergence of a European basic health care catalogue and later a European health insurance market for patients, in which combinations of consolidated European health insurer offer insurance policies to all European citizens.

Prescribers

As in the Expert Scenario, the freedom of doctors to issue prescriptions will be restricted and a loss of trust is observed. This results in a difficult work environment for medical professionals. The Expert Scenario also discussed the various ways Member States design their policies. Those cost-containment policies aimed at the prescribing habits of doctors will be increasingly adopted by less developed Member States when their rapidly developing health care systems reach the EU15 level in terms of quality, quantity and funding of services.

This may jeopardize the autonomy and reputation of the medical profession. It will be in their interest to construct cost-containment policies and alter the outcomes of these policies to the best of their ability. Therefore, since the European health care market will gradually become European, doctors will have to organize themselves better, which shall lead to more European collaboration of European professional medical organizations looking to safeguard their autonomy in prescribing what they deem suitable for the patients.

Patient/consumer

Empowered patients and better organized patient organization play a pioneering and crucial role in the development and realization of the European Scenario and the

emergence of a European health care market, which is described in more detail under the European Scenario in Chapter 6. European patients and their organizations are an integral part of the European Scenario as it is they who interfere with the efforts of Member States to maintain the competence in their respective health care systems, show a spike in pan-European patient mobility and challenge refusals for reimbursement at home for services incurred abroad using favourable case law and harmonized European pharmaceutical markets to their advantage. Furthermore, it is the patients that speed up the establishment of a European health system when they progressively use (possibly foreign) internet pharmacies to purchase pharmaceuticals, initially non-prescription medicines and gradually more POMs.

Funding will be of key importance in establishing a European partner that can participate independently and on eye-level in the decision-making process on health matters in the European Union. In the European Scenario, this funding mainly stems from the EU and national governments, which aspire to cut the increasingly observed partnership between patients and the pharmaceutical industry. This will allow patient groups in taking up a pro-active role in the establishment of a standardized European certifying system for health information web sites of good quality, which takes place within the frameworks of the G10 Medicines Group plan concerning information to patients, the EU's e-Health action plan (2004) and the 2006 MedIEQ (Quality Labelling of Medical Web Content Using Multilingual Information Extraction) project.

The need for thorough and accurate information on the product and its appropriate use is strongly related to another challenge the European patient groups will face, namely the increased responsibility patients will receive in paying for their own medicines, also facilitated by the flexible classification of medicines. This development can have negative effects on the equity of access and will thus deserve the full attention of European patient groups.

The emergence of a SEM for medicines influences price levels throughout the EU. Countries with low pharmaceutical prices that were formerly basically subsidized by countries with higher pharmaceutical prices (where industry made the larger share of its profits) are likely to see higher prices as new harmonized prices come into

force. This could have consequences for the equity and access to medicines provided that economic and purchasing power differentials are still present throughout Member States.

Payers

The payer has many faces in the European pharmaceutical market. It can be a sickness fund, private insurer or an integrated part of a NHS; it can have public or private features and it can reimburse the patient or the provider. In the next twenty years, convergence will not occur to the same extent as other actors in the pharmaceutical market because of the national health care structure and regulation in which they operate. However, in most Member States there is a visible trend towards containing costs through health insurance reform in which health insurers receive more instruments for cost control, often through the introduction of some degree of managed competition, such as in Switzerland, the Netherlands and Germany.

In the European Scenario, payers are expected to develop more and more into European players in order to facilitate the European market when the basic European benefit catalogue is in full effect. When patients observe that foreign health insurers offer cheaper policies covering the basic European health catalogue, they will once again insist on their right to the free movement of services and take out insurance from that foreign insurer. This of course poses a large threat to where health insurers and health care providers purchase their care. It is, therefore, likely that insurers will increasingly be more cost-aware in anticipation of the European health market, which is also in line with national cost-containment policy. Hence, sickness funds and/or private insurers will campaign to get more instruments to influence the expenditures in their health care systems, for example, through more selective contracting with health care providers (already a widespread practice) and by being directly responsible for the purchase of pharmaceuticals, thus influencing pharmaceutical prices. This will take place in anticipation of the single European market for health insurance that will gradually emerge, in which the insurers are subjected to strong foreign competition and are increasingly expected to behave as market players. In this European health market, the European Union acts more as a facilitator that sets the rules concerning the benefit baskets, quality of care, patient rights and

accessibility than as an actively-controlling and managing institution. It may then turn out that this is easiest to regulate under a private set-up, which could lead to a privatization of the European health sector. After that, the European consolidation trend, as mainly seen in the supply side of the pharmaceutical market, will become commonplace among health insurers.

Discussion

Methodological discussion

To ensure the scenarios were as strong as possible and to enhance the validity and reliability of these scenarios, a structured approach was chosen consisting of several fundamental components, following the methodology of the WHO-commissioned handbook "Health Futures" (Garret 1999). This approach is described in more detail in the introduction of this thesis. In addition, the input of multiple European experts was incorporated through the use of the Delphi technique. Although groups are generally more accurate than individual experts, group processes can often lead to suboptimal judgements (Rowe and Wright 2001). Rowe and Wright (2001), therefore, defined several principles for using expert opinion in forecasting, which have implications for the selection of experts. The specific principles applying to expert selection are (1) use experts with appropriate domain knowledge, (2) use heterogeneous experts and (3) use between five to 20 experts. The former two were achieved by selecting the experts with the right (publishing) track record and by including expert questions in the survey to filter out those who, in fact, lack the necessary expertise. Even though academics constituted the largest group of addressees and respondents (14 out of 27 in the second round), this group is highly heterogeneous in terms of background (e.g. law, economics and public health) and expertise (e.g. varying from pricing/reimbursement to authorization). Other additional categories of experts included members of the pharmaceutical industry (five out of 27 in the second round), national government regulators (two out of 27 in the second round) and an "other" category (e.g. consultants, NGOs – four out of 27). This research consulted more than 20 experts. According to research (cf. Armstrong 1985), accuracy ceases to improve by higher numbers. However, this number will depend on the number of experts available but also on the nature and quality of the feedback provided (more in-depth feedback may suggest a smaller panel). One of the key aims of this Delphi application, which was set up to cover a very wide range of issues on different levels under very divergent spheres of influence, was to receive a high number of respondents. The varying estimations of the "today" scenario (2006) seem to

underscore the difficulty in providing answers and justifies the consultation of a large number of experts. Maybe the relatively high percentage (34%) of respondents that bowed out after the first round provides further evidence of this assumption. The argument that a high number of participants may decrease the effectiveness of processing the information and giving feedback does not apply here since feedback only consisted of the aggregated scores (i.e. no text), which had no influence on the feedback load. Furthermore, although 27 respondents participated in the second round, the respondent sample varied from 23 to 25 participants per issue (e.g. authorization, pricing), which is fairly close to the optimal 20 participants. Lastly, the chosen Delphi application was tested in a preliminary test round and described in detail in Chapter 5. The application can be repeated, albeit with possibly different respondents and a later timeframe (i.e. 2006 would clearly not represent the "today" scenario).

It is advisable to be cautious when filling in scenarios and to be very aware of their methodological shortcomings. A clear methodological limitation of a Delphi study is the difficulty to repeat and duplicate this study with the same experts and the same timeframe, both which negatively affect its reliability. Research has shown, however, that that a degree of reliability is possible using the technique, such was found in the research of Felsenthal and Fuchs (1976), Dagenais (1978) and Kastein et al. (1993). The validity of a Delphi study depends on the quality of its design as much as on the nature of its panellists (Rowe and Wright 1999). The Delphi scenario is the main methodology when assessing possible futures and, therefore, the main instrument to make prospective policies. The uncertainty and complexity surrounding the course of European health policy warrants a scenario study (also see Chapter 5 for more information on the choice and conduct of the Delphi technique in this thesis).

The interpretations of the data generated by the Delphi questionnaire, which came in the form of numbers on a five-point Likert scale, was done using the knowledge and findings of an extensive review of European and national policies put in their historical perspectives. Both this review and the Delphi information fed into the construction of these scenarios (also see Figure 1). In the analysis, the impact of these

scenarios was compared to the observed trends from the literature review with regard to the actors in the pharmaceutical (described in Chapters 1 and 2).

Discussion of outcomes

The impact of the three scenarios constructed in the previous chapters led to a couple of obvious questions. First of all, how likely are these scenarios to unfold as described in Chapter 6? The experts showed convergence with regard to most regulatory issues as surveyed in the Delphi. They also fit the current set of trends, showing one exception for the issue of post-licensing-evaluation. To realize alternative scenarios to this baseline scenario, the Expert Scenario was contrasted with a more pessimistic and a more optimistic scenario. Compared to the Expert Scenario, the European Crisis Scenario is a far bolder scenario, in which potentially far-fetched assumptions (e.g. a constitutional crisis and a pharmaceutical disaster) leads to an unlikely but not impossible scenario. It is worth noting that it was a pharmaceutical disaster (thalidomide) that spurred the first supranational involvement with pharmaceuticals in the European Community. Why could the same thing not happen in the opposite direction, i.e. starting from a relatively advanced European framework? The European Community has also changed since its foundation in 1957, particularly with respect to its size, as it now encompasses 27 Member States. Maybe supranational legislation is no longer the appropriate level to regulate issues in such a huge market. The European Scenario may not be as far-off as the European Crisis Scenario. Its development mainly takes place along the lines of the Expert Scenario, but at a much faster pace, assisted by a Europe-positive climate. It is worth looking at this scenario because certain aspects (e.g. the strong pro-active role of the consumers leading to an increasing European nature of health markets) may very well take place and could, therefore, provide leads for a possible future (albeit maybe not in 20 years from now). The review of Part I of this thesis made clear that major change is possible on the longer term. Similarly, in 1965 it may have sounded very improbable that there would be European authorization procedures only 30 years (1995) down the road.

The next question that arises is what are the main lessons to be learned from these scenarios, particularly the Expert Scenario? When looking at the scenarios, a couple

of things become clear. The supply side of the European pharmaceutical market will likely see a consolidation trend that trickles down the value chain and markets will increasingly be harmonized through EU legislation.

Despite European efforts to make the pharmaceutical industry more competitive, the current problems facing the innovative industry may not alter much in the future. In none of the scenarios it seems likely that there will be much change with regard to less restrictive pricing and reimbursement decisions in the richer countries of the EU (i.e. fewer opportunities to retrieve investments). The expectation that post-licensing evaluation will become widely used also through more European collaboration of national competent authorities (e.g. NICE, IQWiG and Commission de Transparence) will unsettle the European innovative industry, to say the least. On the other hand, the sheer size of the European market, combined with increasingly European authorization and classification decisions making way for synergy effects regarding marketing and market launching, will make the EU a progressively indispensable market for the innovative industry. If the EU seeks to foster the science base that the pharmaceutical innovative industry provides, it will have to come up with innovative policies and incentives (e.g. for science in general, framework programmes) in coordination with Member States that can compensate for the less regulated pharmaceutical markets, the US in particular and the cheaper labour of emerging markets. This may require more than the proposed policies. For the generic industry, the outlook may be more positive. They will not suffer as much as the innovative industry in bringing their products to the market. They will be helped by favourable generic policies, growing generic markets, especially the potential of immature generic markets and will profit from faster market access through Bolar provisions. On the other hand, competition is likely to increase as a result of increasing foreign competitive pressure, leading to more (international) consolidation. The generic market may see a strategic shift from the national market to the European market. Only under the European Crisis Scenario may this development be impeded to a certain extent. However, the EU goal of a competitive generic market with freer pricing seems a realistic aim for the future (as opposed to the market for POMs). Highly innovative NBFs have a vested interest in the continuous development of a

European market but are faced with the same competitiveness problems as the innovative industry. The loss of the (obligatory) centralized procedure under the European Crisis Scenario would effectively obstruct market access to (mainly smaller, less attractive) European countries as they are small in size and do not always possess the means to file a (national) authorization procedure, for which they often seek a multinational partner. For them to survive, that is avoiding takeovers, a large European market with centralized procedures is vital. However, biotech products are also subjected to increasingly restrictive reimbursement decisions, which are increasingly based on cost-effectiveness studies. This makes them especially vulnerable considering their high R&D costs.

The European wholesaling sector is expected to see an international consolidation trend, both vertically and horizontally and increased foreign competition. This implies that wholesalers not only purchase and distribute within national boundaries, but increasingly engage in cross-border purchasing and distribution. Hence, what before was known as parallel trade, will become well-established through favourable law and converging pharmaceutical retail markets. The wholesaling sector is well-advised to keep carving out their niche by differentiating their range of services (e.g. logistics) and search for partners, as pharmaceutical companies will increasingly seek to self-distribute their products in the hope of increasing efficiency. Another coping strategy is specialization on a limited range of products at competitive prices. It is likely that EU market liberalization will increasingly enable this practice. Only under the European Crisis Scenario are they able to retain their leading national position mostly owing to the more divergent national regulation and product range requiring national distribution channels.

Pharmacies will be faced with many challenges in the next twenty years leading to a completely different sector. They are increasingly the subject of European (market liberalization) and national attention (huge profits, i.e. large cost-containment potential) and it seems likely that their golden days will gradually come to an end on the assumption that the European Crisis Scenario does not materialize. As of yet the pharmacy market is one of the most regulated sectors in Europe, leaving enormous potential for EU market liberalization, also provided that (possibly foreign) newcom-

ers litigate. The result will be different sorts of ownership (e.g. insurer-owned, non pharmacist-owned), new vertical combinations, chaining of pharmacies, abolishment of state monopolies and the emergence of internet pharmacies. The emergence of DocMorris in the German pharmacy sector could well be exemplary for many national pharmacy sectors across Europe of what they will have to cope with in the future. The increasingly harmonized range of products on sale in Europe will progressively enable cross-border pharmacy services, especially when mutual recognition of prescriptions becomes a fact. Internet pharmacies also pose challenges to legislators and policy makers as counterfeit drugs coming from rogue websites make their way into the distribution channel. The European Commission may use this example as an increased need for a SEM for medicines, as this would make pharmacovigilance more efficient. The Member States, on the other hand, will retain strong remit over pharmacy services concerning the way reimbursed medicines are dispensed (e.g. generic substitution). But one can also think of new incentives and measures to make cheaper pharmaceuticals attractive to consumers and to give payers the instruments and thus a financial stake in cheaper pharmaceuticals, in order to avoid profits from cheaper pharmaceuticals remaining in the distribution chain. This could be arranged, for example, through insurance policies that give discounts when cheaper pharmaceuticals (e.g. generic/parallel import) are used or through enabling insurers to purchase their own pharmaceuticals and operating their own pharmacies.

The demand side of the European pharmaceutical market still shows huge differences between Member States when compared to the supply side. It will largely remain within the national competence, especially where it concerns reimbursed pharmaceuticals. This implies a continuation of observed trends.

The prescribers of pharmaceuticals will be under growing pressure to prescribe rationally and their freedom to prescribe as they see fit may be increasingly challenged through guidelines, electronic formularies and prescribing data. Although significant differences exist between Member States in consumption patterns, roughly along the lines north-south and east-west, it is likely that these will cease to exist over time when new accession countries develop towards EU15 average and when high con-

sumption countries realize the cost-containment potential of rational prescribing. Furthermore, the observed loss of trust in the patient-prescriber relationship is not likely to abate. Information is readily available on the internet and will only increase, unfortunately also from dubious sources. The strongly organized prescribers are also well advised to organize at a European level, as their counterparts from other Member States see the same challenges regarding freedom to prescribe. Looking at the impact of the other scenarios, the European Scenario only reinforces the necessity to organize at the European level, while under a European Crisis Scenario the need may be less essential or obvious.

The various patients groups should bolster their organizations, not only nationally but also on a European level, in order to participate more efficiently in the current European-level discussions that may have far-reaching consequences for them. This will also help to counter the strong information asymmetry, especially now as supply side actors become larger and larger and European affairs increasingly become important to the organization and delivery of health care services. Only then can they fully reap the possibilities with which they are provided by an increasingly European market. First, patients should demand health information websites of good quality. Especially since it is likely that patients have more choices to make and will be increasingly subjected to marketing efforts by the industry, often from dubious sources with an unclear distinction between patient information and advertising. They should play a leading role and be in dialogue with relevant European and national policy makers in the establishment of a European certification system, which is possible within current initiatives and frameworks. Second, the increased expectations by national governments that patients bear an increasing part of the costs, especially as treatments are more expensive and health expenditures are rising, stresses the need for patient organizations that monitor developments regarding quality and equity of access and intervene in the public debate when needed at the highest level. It may be interesting to have a more thorough look at the European Scenario as this scenario deals with consumers playing a more proactive role. There seems to be the potential to obtain cheaper pharmaceuticals and those that cannot be reimbursed in the home state through the cross-border delivery of pharmaceuticals. Pa-

tient groups should look into these opportunities and signal them to their members. They could play a pioneering role, also through litigation and articulation of these options and force clarity in these frameworks. Whether this would lead to the emergence of a European health system with a European benefit basket, as described in more detail in the European Scenario, depends on many factors. However, there are conceivable developments that could make this an inescapable solution.

This consideration automatically leads us to the role of the payer of pharmaceutical products. In the Expert Scenario and the European Crisis Scenario, the impact of these scenarios on the payers is negligible. Payers will develop in ways decided at a national level. Their development is likely to contain already visible national trends to bring some form of managed competition in the insurance market and, therefore, the instruments that go along with it, such as selective contracting, more financial responsibility and competition for customers. Under most current frameworks the insurer has scant influence on the containment of pharmaceutical prices as they just pay what is prescribed. This could be solved by some of these innovative policies. It is probable that in the future, payers in Europe will become more powerful players instead of merely administrative payers of services as still visible in many countries today. In addition, would the European Scenario materialize, pharmaceuticals would play a pioneering and catalysing role in the emergence of a European health market and, possibly later, a European health insurance market in which international insurers offer health insurance policies for a European basic health basket. This could also provoke an international consolidation trend between health insurers.

What does all this imply for the Member States? Should they fear the continuous Europeanization of the European pharmaceutical market? Although the European pharmaceutical framework in the Expert Scenario will turn European with regard to authorization, classification (although nationally implemented) and wholesaling, for example, the Member States will fully retain the regulatory overhand on vital decisions in their respective health systems. This is especially visible with regard to pricing and reimbursement, as overwhelmingly expected by the experts. However, all national legislation that interferes with non-reimbursed medicines is likely to undergo intensified European scrutiny. Furthermore, the regulatory framework for the

pharmacy and wholesaling sector is expected to be liberalized over the next twenty years. Therefore, Member States should assess their regulatory frameworks to bring it more in line with European competition law and the Four Freedoms sooner rather than later. The expectation that in addition to the non-reimbursed (e.g. OTCs) markets also the generic market will increasingly be liberated should motivate Member States to assess their pricing policies in order to facilitate a competitive generic market with free pricing. This basically also fits the national cost-containment agenda. In short, in the Expert Scenario it seems that all vital decision (e.g. pricing, reimbursement and classification decisions) regarding the publicly covered part of the system are safeguarded. The expectation of the experts that national competent post-licensing evaluation authorities will be increasingly regulated on a European level does not have to imply that this takes away the national competence to make their own decisions. Anyway, it makes sense for Member States to support this collaboration (as supported by current EU policy) because it will help them carrying out this task more efficiently, especially small Member States that lack funds to justify such an agency. If the European Scenario materializes and a European health system develops as a result of external factors from outside the sphere of influence of Member States, Member States could be forced into a European collaboration on a basic benefit basket. This could be the start of a pan-European health insurance policy that could still leave room for national divergence through additional national catalogues, tailored to national needs relating to economic and cultural factors. Instead of categorically refusing the idea, it may be better to study it in order to be prepared.

REFERENCES

Abraham J, Lewis G. Regulating medicines in Europe. Competition, expertise and public health. London, Routledge, 2000.

Abraham J, Lewis G. Europeanization of medicines regulation. In: Abraham J, Lawton Smith H, eds. Regulation of the pharmaceutical industry. Houndmills, Palgrave Macmillan, 2003, 42–81.

Albreht T, Cesen M, Hindle D, Jakuboswski E, Kramberger B, Petric VK, Premik M, Toth M. Health Care Systems in Transition: Slovenia. Copenhagen, European Observatory on Health Care Systems, 2002.

Armstrong JS. Long range forecasting: from crystal ball to computer, 2nd ed. New York: Wiley, 1985.

Bertele' V, Li Bassi LA. A Critique to the European regulatory system. Journal of Ambulatory Care Management. 2004, 27(2): 98–104.

Bertinato L, Busse R, Fahy N, Legido-Quigley H, Mckee M, Palm W, Passarani I, Ronfini F. Policy Brief: Cross-Border Health Care in Europe. Copenhagen, World Health Organization on behalf of the European Observatory on Health Systems and Policies, 2005.

Bond CM, Orru PO, Leder JM, Bouvy M. The over-the-counter pharmaceutical market. In: Mossialos E, Mrazek M, Walley T, eds. Regulating pharmaceuticals in Europe: striving for efficiency, equity and quality. Copenhagen, European observatory on health systems and policies, 2004: 260–278. (http://www.euro.who.int/document/E83015.pdf) Last Access: 14 November 2008

Bradley C, Holme Hansen E, Kooiker S. Patients and their medicines. In: Mossialos E, Mrazek M, Walley T, eds. Regulating pharmaceuticals in Europe: striving for efficiency, equity and quality. Copenhagen, European observatory on health systems and policies, 2004: 158–177. (http://www.euro.who.int/document/E83015.pdf) Last Access: 14 November.2008

Bradlow J, Coulter A. Effect of Fundholding and Indicative Prescribing Schemes on General Practitioners' Prescribing Costs. British Medical Journal. 1993, 307: 1186–1189.

Busse R., Schlette S, eds. Health Policy Developments. Issue 2: focus on health and aging, pharmaceutical policy and resources. Gütersloh, Bertelsmann Foundation Publishers, 2004.

Busse R, Schreyögg J, Gericke CA. Analyzing Changes in Health Financing Arrangements in High-Income Countries: A Comprehensive Framework Approach HNP Discussion Paper Series. Washington DC, World Bank, 2007.

Busse R, Van Ginneken E. Benefit baskets and tariffs. In: Wismar M, Palm W, Figueras J, Ernst K, Van Ginneken E, eds. Cross-Border Healthcare: Mapping and Analysing Health Systems Diversity. Report prepared for the European Commission DG Health

and Consumer Protection. Brussels, European Observatory on Health Systems and Policies, 2007: 163–189.

Cartwright AC, Matthews BR, eds. Pharmaceutical product licensing: requirements for Europe. Chichester, Ellis Harwood, 1991.

Chambers G, Belcher P. The Consumption of Medicines in the European Union. In: Mossialos E, Ranos C and Abel-Smith B, eds. Cost Containment, Pricing and Financing of Pharmaceuticals in the European Community: The Policy-Makers' View. Athens, LSE Health and Pharmetrica S.A., 1994.

Clement W, Tuma M, Walter E. The European Pharmaceutical Wholesale Industry: Sructure, Trends and socio-economic Importance. Vienna, Institut für Pharmaökonomische Forschung (IPF).

de Clippele F. Legal aspects of on-line pharmacy. Acta chirurgica Belgica. 2004, 104: 364–370.

Cutler D, Zeckhauser R. The Anatomy of Health Insurance. In: Culyer AJ and Newhouse JP, eds. Handbook of health economics. Amsterdam, Elsevier, 2000: 563–643.

Dagenais F. The reliability and convergence of the Delphi technique. The Journal of General Psychology. 1978, 98: 307–308.

Danzon PM, Chao LW. Does regulation drive out competition in pharmaceutical markets? Journal of Law and Economics. 2000, 43(2): 311–357.

Deschepper R., Vander Stichele RH, Haaijer-Ruskamp FM. Cross-cultural differences in lay attitudes and utilisation of antibiotics in a Belgian and a Dutch city. Patient Education and Counselling. 2002, 48(2): 161–169.

Enemark U, Møller Pedersen K, Sørensen J. The economic impact of parallel import of pharmaceuticals. Odense, CAST - Centre for Applied Health Services Research and Technology Assessment, University of Southern Denmark, 2006.

EFPIA. The Pharmaceutical Industry in Figures: 2004 Edition. Brussels, EFPIA, 2004. (www.efpia.org/6_publ/default.htm) Last Access: 14 October 2006

EGA. EGA Fact Sheet No. 3. Generic Medicines and Evaluation. Brussels, EGA, 2003. (www.egagenerics.com/doc/fs_innovation.pdf) Last Access: 14 May 2006

EMEA Summary of the annual report of the European Medicines Agency 2005. EMEA, London, 2005. (http://www.emea.europa.eu/pdfs/general/direct/emeaar/SummaryAnnualReport2005.pdf) Last Access: 14 November 2007

Green K, Armstrong JS, Graefe A. Methods to Elicit Forecasts from Groups: Delphi and Prediction Markets Compared. Foresight: The International Journal of Applied Forecasting. 2007, 8: 17–20.

EuropaBio. Biotechnology in Europe: 2005 Comparative study. Lyon, Biovision, 2005.

European Commission. Completing the internal market. White paper from the commission to the European Parliament. Brussels, European Commission, 1985.

European Commission. Communication on the outlines of an industrial policy for the pharmaceutical sector in the European Community. Brussels, COM(93)718 of 2 March 1994.

European Commission. Evaluation of the operation of Community procedures for the authorization of medicinal products. Evaluation carried out on behalf of the European Commission by McKenna C, Arthur Andersen Consulting. Brussels, European Commission, 2000.

European Commission. Review of pharmaceutical legislation, discussion document, final version. Brussels, European Commission, 2001a.

European Commission. Memo/01/267 'Reform of EU Pharmaceutical legislation'. Brussels, European Commission, 2001b.

European Commission. G10 Medicines Report. High Level Group on Innovation and Provision of Medicines: recommendations for action. Brussels, European Commission, 2002.

European Commission. Commission A Stronger European-based Pharmaceutical Industry for the Benefit of the Patient – A Call for Action. Brussels, European Commission, Communication COM 383, 2003.

European Commission. Innovation in the Pharmaceutical sector. Brussels, European Commission, 2004a.

European Commission. e- Health, making healthcare better for European citizens: Am action plan for a European e- Health Area. Brussels, European Commission, 2004b.

European Commission. Draft report on current practice with regard to provision of information to patients on medicinal products. Brussels, European Commission, 2007.

European Council. Resolution 96/C 136/04 of 23 April 1996 designed to implement the outlines of an industrial policy in the pharmaceutical sector in the European Union. Brussels, European Council, 1996.

European Parliament. Report on the Communication from the Commission to the Council and the European Parliament on the outlines of an industrial policy for the pharmaceutical sector in the European Community, adopted by the European Parliament on 16 April 1996.

Feick J. Marktzugangsregulierung: nationale Regulierung, internationale Harmonisierung und europäische Integration. In: Czada R, Lütz S, eds. Die politische Konstitution von Märkten. Opladen, Westdeutscher Verlag, 2000, 228–249.

Felsenthal DS, Fuchs E. Experimental evaluation of five designs of redundant organizational systems. Administrative Science Quarterly. 1976, 21: 474–488.

Fraunhofer Institute Systems and Innovation (ISI) Research. Assessment of the European Community system of Pharmacovigilance. Karlsruhe, ISI, 2006.

Gambardella A, Orsenigo L, Pammolli F. Global Competitiveness in Pharmaceuticals: A European Perspective. Report for Directorate-General for Enterprise, European Commission. Brussels, European Commission, 2000.

Garattini L, Salvioni F, Scopelliti D, Garattini S. A comparative analysis of the pharmaceutical market in four European countries. Pharmacoeconomics. 1994, 6(5): 417–423.

Garattini S, Bertele' V. Adjusting Europe's drug regulation to public health needs. Lancet. 2001, 358: 64–67.

Garattini S, Bertele' V. Toward new legislation of drugs in Europe. Expert Review of Pharmacoeconomics and Outcomes Research. 2002, 2: 89–94.

Garattini S, Bertele' V. The role of the EMEA in regulating pharmaceutical products. In: Mossialos E, Mrazek M, Walley T, eds. Regulating pharmaceuticals in Europe: striving for efficiency, equity and quality. Copenhagen, European observatory on health systems and policies, 2004: 80–96. (http://www.euro.who.int/document/E83015.pdf) Last Access: 14 November 2008

Garrett MJ. Health Futures. A handbook for health professionals. Geneva, World Health Organisation (WHO), 1999.

GIRP. Pharmaceutical key-figures 2003. Brussels, GIRP, 2003.

(http://www.girp.org/girppublication/DataIMS-GIRP2003.pdf) Last Access: 14 November 2008

GIRP. Pharmaceutical key-figures 2005. Brussels, GIRP, 2005.

Goossens H, Ferech M, Vander Stichele R, Elseviers M, ESAC Project Group. Outpatient Antibiotic Use in Europe and Association with Resistance. Lancet. 2005, 365: 579–587

Guillen AM, Cabiedes L. Reforming pharmaceutical policies in the European Union: a 'penguin effect'? International Journal of Health Service. 2003, 33(1): 1-28.

Hancher L. The European Community dimension: coordinating divergence. In: Mossialos E, Mrazek M, Walley T, eds. Regulating pharmaceuticals in Europe: striving for efficiency, equity and quality. Copenhagen, European observatory on health systems and policies, 2004: 55–79. (http://www.euro.who.int/document/E83015.pdf) Last Access: 14 November 2008

Herxheimer A. Relationships between the pharmaceutical industry and patients' organisations. BMJ, 31 May 2003, 326: 1208–1210.

IAPO. A survey of patient Organizations' concerns. Perception of health care. International Alliance of Patients' Organizations. 2006.

Cullen A, von Schapter E. Celesio to buy Doc Morris to build German pharmacy chain. International Herald Tribune. 27. 4. 2007. (http://www.iht.com/articles/2007/04/26/news/bxdoc.php) Last Access 16 November 2007

Jones K, Jefferys D. EMEA and the new pharmaceutical procedures for Europe. Health Trends. 1994, 26 (1): 10–13.

Jonsson B. Pricing and reimbursement of pharmaceuticals in Sweden. Pharmacoeconomics. 1994, 6(1): 51–60.

Kanavos P, Costa-i-Font J, Merkur S, Gemmill M. The economic impact of pharmaceutical parallel trade in European Union member states: A stakeholder analysis. LSE Health and Social Care, London School of Economics and Political Science, 2004.

Kastein MR, Jacobs M, Van der Hell RH, Luttik K, Touw-Otten FWMM. Delphi, the issue of reliability: a qualitative Delphi study in primary health care in the Netherlands. Technological Forecasting and Social Change. 1993, 44: 315–323.

Kutzin, J. A descriptive framework for country-level analysis of financing arrangements. Health Policy. 2001, 56: 171-204.

Kuusi, O. Expertise in the future use of generic technologies. Epistemic and methodological considerations concerning Delphi studies. Helsinki, Government Institute for economical research VATT, 1999.

Linstone HA, Turoff M. The Delphi method: techniques and applications. London, Addison-Wesley, 1975.

Lock, A. Integrating group judgments in subjective forecasts. In: Wright G, Ayton P, eds. Judgmental Forecasting. Chichester, Wiley, 1987: 11–30.

Long DM. Presentation to the International Federation of Pharmaceutical Wholesalers Conference September 2002: Worldwide Pharmaceutical and Wholesaling Trends. Monaco, 2002 (http://www.ifpw.com/2002gmm/presentations/Long.ppt) Last Access: 16 November 2008

Lopez-Casasnovas G, Puig-Junoy J. Review of the literature on reference pricing. Health Policy. 2000, 54(2): 87–123.

Macarthur D. Drug Distribution in Europe: Trends and Driving Forces. Waltham, MA: Decision Resources Inc., 1996.

Mäkinen MM, Rautava PT, Forsström JJ. Do online pharmacies fit European internal markets? Health Policy. 2004, 72 (2): 245–252.

Maynard A, Bloor K. Regulating the pharmaceutical industry. British Medical Journal. 1997, 315: 200–201.

Maynard A, Bloor K. Dilemmas in regulation of the market for pharmaceuticals. Health Affairs. 2003, 22(3): 31-41.

McGuire A, Drummond M, Rutten F. Reimbursement of pharmaceuticals in the European Union. In: Mossialos E, Mrazek M, Walley T, eds. Regulating pharmaceuticals in Europe: striving for efficiency, equity and quality. Copenhagen, European observatory on health systems and policies, 2004: 130-143. (http://www.euro.who.int/document/E83015.pdf) Last Access: 16 November 2008

Mossialos E, Walley T, Mrazek M. Regulating pharmaceuticals in Europe: an overview. In: Mossialos E, Mrazek M, Walley T, eds. Regulating pharmaceuticals in Europe: striving for efficiency, equity and quality. Copenhagen, European observatory on health systems and policies, 2004: 1–37. (http://www.euro.who.int/document/E83015.pdf) Last Access: 16 November 2008

Mrazek M, Frank R. The off patent pharmaceutical market. In: Mossialos E, Mrazek M, Walley T,eds. Regulating pharmaceuticals in Europe: striving for efficiency, equity and quality. Copenhagen, European observatory on health systems and policies, 2004: 245–259. (http://www.euro.who.int/document/E83015.pdf) Last Access: 16 November 2008

Mrazek M, de Joncheere K, Petrova G, Mossialos E. The pharmaceutical sector and regulation in the countries of central and eastern Europe. In: Mossialos E, Mrazek M, Walley T, eds. Regulating pharmaceuticals in Europe: striving for efficiency, equity and quality. Copenhagen, European observatory on health systems and policies, 2004: 323–333. (http://www.euro.who.int/document/E83015.pdf) Last Access: 16 November 2008

Mrazek M, Mossialos E. Regulating pharmaceutical prices in the European Union. In: Mossialos E, Mrazek M, Walley T, eds. Regulating pharmaceuticals in Europe: striving for efficiency, equity and quality. Copenhagen, European observatory on health systems and policies, 2004: 114–129. (http://www.euro.who.int/document/E83015.pdf) Last Access: 16 November 2008

Nefarma. Jaarverslag 2003. Een naslagwerk van de toekomst. The Hague, Nefarma, 2004. (www.nefarma.nl/files/nefarma_jaarverslag_2003.pdf) Last Access: 16 November 2006

Nyfer. Speciale studie nr. 11: Geneesmiddelen: Handel of zorg? Breukelen, Nyfer, 1997.

OECD. The cost of pharmaceuticals. Paris, OECD, 2002.

OECD. Pharmaceutical Pricing Policies in a Global Market. Paris, OECD, 2008.

Paterson I, Fink M, Ogus A, et al. Economic impact of regulation in the field of liberal professions in different Member States. Final Report. Study for the European Commission. Vienna, Institute of advanced studies (HIS), 2003.

Permanand G, Altenstetter C. The politics of pharmaceuticals in the European Union. In: Mossialos E, Mrazek M, Walley T, eds. Regulating pharmaceuticals in Europe: striving for efficiency, equity and quality. Copenhagen, European observatory on health systems and policies, 2004: 38–54. (http://www.euro.who.int/document/E83015.pdf) Last Access: 16 Nvember 2008

PGEU. The Internet and Medicines. Enjoy the Internet: but don't risk your health! Brussels, PGEU, 1999. (www.pgeu.org/Portals/6/documents/before/99.805E%20internet_leaflet.pdf) Last Access 16 November 2008

PGEU. Statement on the development of e-health and e-enhanced pharmacy 2001. Brussels, PGEU, 2001. (http://www.pgeu.org/Portals/6/documents/before/01.06.20E%20PGEU12%20e-^enhanced%20%20pharmacy.pdf) Last Access: 16 November 2007

PriceWaterhouseCoopers. The Dutch Drug Expenditure and policy in a European context: A quick scan comparison of the Dutch expenditure on drugs and the underlying policy in several European countries. The Hague, PriceWaterhouseCoopers, 1999.

Pruszydlo MG, Quinzler R, Kaltschmidt J, Haefeli WE. Medizinische Probleme und Risiken bei der rabattvertragsgerechten Umstellung von Medikationen in Deutschland. Deutsche medizinische Wochenschrift. 2008, 133: 1423–1428.

Quinzler R, Bertsche T, Szecsenyi J, Haefeli WE. Teilung von Tabletten: welchen Einfluss haben die Rabattverträge auf die Verordnungsqualität? Medizinische Klinik. 2008, 103(8): 569–74.

Reekie WD. How competition lowers the costs of medicines. Pharmacoeconomics. 1998, 14(1): 107–13.

RIVM. Stijgende geneesmiddelenkosten: theoretische en praktische inzichten. Den Haag, Sdu, 1999.

RIVM. Nationale Atlas Volksgezondheid. Een ruimtelijk beeld van zorg en gezondheid in Nederland. 2004a (www.rivm.nl/vtv/data/atlas/gnhv_farm_a023.htm) Last Access: 16 November 2007

RIVM. Nationaal Kompas Volksgezondheid. 2004b

(http://www.rivm.nl/vtv/object_map/o1504n21466.html) Last Access: 16 November 2007

Rovira J, Darba J. Pharmaceutical pricing and reimbursement in Spain. European Journal of Health Economics. 2001, 2(1): 39–43.

Rowe G, Wright G, Bolger F. The Delphi technique: a re-evaluation of research and theory. Technological Forecasting and Social Change. 1991, 39(3): 235–251.

Rowe G, Wright G. The Delphi technique as a forecasting tool: issues and analysis. International Journal of Forecasting. 1999, 15: 353–375.

Scherer FM. The pharmaceutical industry. In: Cuyler AJ, Newhouse JP, eds. Handbook of health economics. Amsterdam, Elsevier, 2000.

Schut FT . Verschillende markten binnen de sector gezondheidszorg. In: Lapre RM, Rutten FFH, eds. Economie van de gezondheidszorg. Utrecht, Lemma, 1993.

Snier H. Concurrentie en strategie in de geneesmiddelensector. Dissertation, University of Rotterdam, Eburon, Delft, 1995.

Staatsblad van het Koninkrijk der Nederlanden. Jaargang 2007 /93. Wet van 8 februari 2007 tot vaststelling van een nieuwe Geneesmiddelenwet. ’s-Gravenhage, Sdu Uitgevers, 2007

Stewart TR. The Delphi technique and judgmental forecasting. Climatic Change. 1987, 11: 97–113.

Stewart-Brown S, Surender R, Bradlow J, Coulter A, Doll H. The Effects of Fundholding in General Practice on Prescribing Habits Three Years after the Introduction of the Scheme. British Medical Journal. 1995, 311: 1543–1547.

Stichting Farmaceutische Kengetallen (SFK). Data en Feiten 2006. The Hague, SFK. 2006. (http://www.sfk.nl/publicaties/2006denf.pdf) Last Access: 10 October 2007

Stichting farmaceutische Kengetallen (SFK). Facts and Figures 2008. The Hague, SFK. 2008. (http://www.sfk.nl/algemeen/2008fandf) Last Access: 16 November 2008

Tapio P. Disaggregative Policy Delphi: Using cluster analysis as a tool for systematic scenario formation. Technological Forecasting and Social Change. 2002, 70(1): 83–101.

Taylor D, Mrazek M, Mossialos E. Regulating pharmaceutical distribution and retail pharmacy in Europe. In: Mossialos E, Mrazek M, Walley T, eds. Regulating pharmaceuticals in Europe: striving for efficiency, equity and quality. Copenhagen, European observatory on health systems and policies, 2004a: 196–121. (http://www.euro.who.int/document/E83015.pdf) Last Access: 16 November 2008

Taylor RS, Drummond MF, Salkeld G, Sullivan SD. Inclusion of cost effectiveness in licensing. British Medical Journal. 2004b, 329: 972–975.

Thomson S, Mossialos E, Jemiai N. Cost sharing for health services in the European Union. Report prepared for the European Commission DG Employment and Social Affairs. London, European Observatory on Health Care systems and LSE Health and Social Care, London School of Economics and Political Science, 2003.

Thomson S, Mossialos E. Influencing demand for drugs through cost sharing. In: Mossialos E, Mrazek M, Walley T, eds. Regulating pharmaceuticals in Europe: striving for efficiency, equity and quality. Copenhagen, European observatory on health systems and policies, 2004: 227–244. (http://www.euro.who.int/document/E83015.pdf) Last Access: 16 November 2008

Turoff M. The design of a policy Delphi. Technological Forecasting and Social Change.1970, 2(2): 149–171.

Van de Ven A, Delbecq AL. Nominal versus interacting group processes for committee decision-making effectiveness. Academy of Management Journal. 1971, 2: 203–212.

Velasco-Garrido M, Schreyögg J, Stargardt T, Busse R. Identification of health baskets in nine EU countries. Revue Francaise Affaires Sociales. 2006, 60: 63–88.

Walley T, Murphy M, Codd M, Johnston Z, Quirke T. Effects of Monetary Incentives on Primary Care Prescribing in Ireland: Changes in Prescribing Patterns in One Health Board 1990–1995. Pharmacoepidemiology and Drug Safety. 2000, 9(7): 591–598.

Walley T, Mossialos E. Financial incentives and prescribing. In: Mossialos E, Mrazek M, Walley T, eds. Regulating pharmaceuticals in Europe: striving for efficiency, equity and quality. Copenhagen, European observatory on health systems and policies, 2004: 177–195. (http://www.euro.who.int/document/E83015.pdf) Last Access: 16 November 2008

West P, Mahon J. Benefits to payers and patients from parallel trade. York, York Health Economics Consortium, 2003.

Wismar M, Busse R, Berman PC. The European Union and health services: the context. In: Busse R, Wismar M, Berman PC, eds. The European Union and health services: The impact of the Single European Market on Member States. Amsterdam, IOS Press, 2002: 17-30.

Yuen P. Compendium of Health Statistics, 11th edition. London, Office for Health Economics, 1999.

Zentner A, Velasco-Garrido M, Busse R. Evaluation von Arzneimitteln nach der Marktzulassung: ein internationaler Vergleich. Das Gesundheitswesen. 2005, 67: 583.

Note: All European Union law, including treaties, legislation, case-law and legislative proposals referred to in this thesis can be accessed at: http://eur-lex.europa.eu/

APPENDIX A

Delphi pre-test

From: Ewout van Ginneken

Subject: TU Berlin Dep. of Health Care Management - (short!) Delphi pretest - please reply before JAN 11

Technische Universität Berlin

Delphi questionnaire 'European pharmaceutical policy'

NOTE: this Delphi round is a preliminary test round, to see whether the questionnaire is clear and understandable. Therefore, your feedback is more than welcome and can be given in the comments section at the end of this questionnaire. When results are satisfactory, they will be used and you will be approached again in the second round. When major changes in the questionnaire will be necessary, you will be approached anew. Your cooperation is highly appreciated and should not take more than a couple of minutes. Feel free to forward. Thanks!!

PLEASE REPLY BEFORE JANUARY 12

1 Introduction

This Delphi questionnaire is part of a research project on the future of the European pharmaceutical market. The Delphi technique is a procedure aimed at obtaining a reliable consensus of opinion from a group of experts through a series of questionnaires interspersed with controlled feedback (Garret, 1999). Aim of this Delphi questionnaire is to reach consensus among a group of selected experts on whether regulation in the European pharmaceuticals market will take a predominantly European or national course in the next twenty years. In order to achieve this, the questionnaire will be send to the experts several times, each time adding the results of the previous round. The individual results will not be attributed to the expert by name, i.e. are anonymous.

The survey starts off with questions about your category and expertise before going over to the actual Delphi part of the questionnaire. You can fill out the questionnaire in this document by replying to this message and by answering the questions in a new ('reply') mail. Make sure you send it to: praktikant@ww.tu-berlin.de. Feel free to forward this mail to your colleagues. As a beginning, two Delphi rounds are planned. Additional rounds can be scheduled later. Filling out the questionnaire –and possibly forwarding it– should not take more than a couple of minutes and would attribute greatly to this project.

2 General questions

Category of respondent

Please check the category that describes you best (e.g. use 'x').

Pharmaceutical Industry (innovative)		National government / regulator	
Pharmaceutical Industry (generic)		European Union	
Wholesaler		Academic	
Pharmacist		Consumer organization	
Insurer/payer (NHS, sickness funds)		Other (feel free to specify)	

Expertise

Please answer using numbers 1 to 3.

1= fully

2= average

3= not at all

1. Would you consider yourself an expert in the field of European Pharmaceutical policy, both on the European and national level?	
2. Are you familiar with the current state of the European pharmaceutical market, including its actors and developments?	
3. Are you familiar with European Law in regard to European health care, in particular the European Commission's public health competences (as laid down in e.g. article 152)?	
4. Are you familiar with European case law, especially Kohll/Decker, Smits-Geraets/Peerbooms and Vanbraekel and its possible consequences?	

3 Delphi questionnaire

Please fill out by using numbers 1 to 5 for each year and issue in the corresponding answering box. For category '**today**' give your estimation on the current situation. For category '**opinion**', give your own opinion: what would be desirable?

Will the following issues predominantly be regulated and implemented at a European level or at a national level?

1 = fully national

2 = predominantly national

3 = even or 50/50

4 = predominantly European

5 = fully European

	EXPECTATION				
Issue	**today**	**2010**	**2015**	**2025**	**opinion**
1. Market Authorization (Licensing)					
2. Pharmacovigilance (post marketing surveillance)					
3. Classification: Rx (Prescription only), OTC					
4. Distribution (wholesaling)					
5. Advertising: e.g. direct-to-consumer advertising					
6. Pricing: e.g. pricing and profit controls, reference pricing					
7. Dispensing (pharmacy level): e.g. generic substitution, remuneration					
8. Prescribing: e.g. prescribing guidelines, budgets					
9. Post-licensing evaluation (comparative benefit/ cost-effectiveness)					
10. Reimbursement: by public payers, i.e. scope of benefit catalogue (including positive/negative list)					

Comments (not requested)**:**

Thank you for your cooperation.

Ewout van Ginneken, Reinhard Busse, Christian Gericke, Jonas Schreyögg

Department of Health Care Management

University of Technology Berlin

praktikant@ww.tu-berlin.de

http://mig.tu-berlin.de

APPENDIX B

Delphi round 1

From: Dept. Health Care Management

Subject: TU Berlin / Prof. Busse - (short!!) Delphi questionnaire - please reply before FEB 28!

Technische Universität Berlin

Delphi questionnaire 'European pharmaceutical policy'

PLEASE REPLY BEFORE FEBRUARY 28 and PLEASE FORWARD / DISTRIBUTE

1 Introduction

Aim of this Delphi questionnaire is to reach consensus among a group of selected experts on whether regulation in the European pharmaceuticals market will take a predominantly European or national course in the next twenty years. The questionnaire will be send several times, each time adding the results of the previous round. The individual results will not be attributed to the expert by name, i.e. are anonymous. You can fill out the questionnaire in this document by replying to this message and by answering the questions in a new ('reply') mail. Make sure you send it to: praktikant@ww.tu-berlin.de. Please forward this mail to your colleagues and other contacts. Two Delphi rounds are planned (second round planned for early March). Filling out -and forwarding- the questionnaire should not take more than **a couple of minutes** and would contribute greatly to this project. Thanks for your help!

2 Category

Category of respondent

Please check the category that describes you best (e.g. use 'x').

Pharmaceutical Industry (R&D)		National government / regulator	
Pharmaceutical Industry (generic)		European Union	
Wholesaler		Academic	
Pharmacist		Consumer organization	
Insurer/payer (NHS, sickness funds)		Other (feel free to specify)	

3 Delphi questionnaire

Please fill out by using numbers 1 to 5 for each year and issue in the corresponding answering box. For category '**today**', give your estimation on the current situation. For categories '**2010**', '**2015**' and '**2025**', give your future expectation for these respective years. For category '**opinion**', give your own opinion: what would be desirable (also 1 to 5)?

Will the following issues predominantly be regulated and implemented at a European level or at a national level?

1 = fully national

2 = predominantly national

3 = even or 50/50

4 = predominantly European

5 = fully European

		EXPECTATION			
Issue	**today**	**2010**	**2015**	**2025**	**opinion**
1. Market Authorization (Licensing)					
2. Pharmacovigilance (post marketing surveillance)					
3. Classification: Rx (Prescription only), OTC					
4. Distribution (wholesaling)					
5. Advertising: e.g. direct-to-consumer advertising					
6. Pricing: e.g. pricing and profit controls, reference pricing					
7. Dispensing (pharmacy level): e.g. generic substitution, remuneration					
8. Prescribing: e.g. prescribing guidelines, budgets					
9. Post-licensing evaluation (comparative benefit/ cost-effectiveness)					
10. Reimbursement: by public payers, i.e. scope of benefit catalogue (including positive/negative list)					

4 Expertise

In order to possibly weigh the results, please answer these questions about your expertise, using numbers 1 to 3.

1= fully

2= average

3= not at all

1. Would you consider yourself an expert in the field of European pharmaceutical policy, both on the European and national level?	
2. Are you familiar with the current state of the European pharmaceutical market, including its actors and recent developments?	
3. Are you familiar with European Law with regard to European health care, in particular the European Commission's public health competences (as laid down in e.g. article 152)?	
4. Are you familiar with European case law, especially Kohll/Decker, Smits-Geraets/Peerbooms and Vanbraekel and its possible consequences?	

Comments (not requested)**:**

Thank you for your cooperation.

Ewout van Ginneken, Reinhard Busse, Christian Gericke, Jonas Schreyögg

Department of Health care Management

WHO Collaborating Centre for Health Systems Research and Management

Berlin University of Technology

praktikant@ww.tu-berlin.de

http://mig.tu-berlin.de

APPENDIX C

Delphi round 2

From: Dept. Health Care Management

Subject: TU Berlin / Prof. Busse - ROUND II Delphi questionnaire - please reply before APRIL 21

Technische Universität Berlin

Delphi questionnaire 'European pharmaceutical policy' ROUND II

PLEASE REPLY BEFORE APRIL 21

1 Introduction

Thank you very much for your participation in the first round. Now we would like to ask for your opinion in this second round. Aim of this Delphi questionnaire is to reach consensus among a group of selected experts on whether regulation in the European pharmaceuticals market will take a predominantly European or national course in the next twenty years. In this second round questionnaire, the results of the first round are added. The individual results will not be attributed to the expert by name, i.e. are anonymous. You can fill out the questionnaire in this document by replying to this message and by answering the questions in a new ('reply') mail. If that does not work, please use the attachment. Make sure you send it to: praktikant@ww.tu-berlin.de. Filling out the questionnaire should not take more than **a couple of minutes** and would contribute greatly to this project. In this second round, you **only have to fill out part 3** of the questionnaire. Thanks again for your help!

2 Category

Category of respondents

Results first round after selection (no need to answer) n=41

Pharmaceutical Industry (R&D)	7	National government / regulator	3
Pharmaceutical Industry (generic)		European Union	1
Wholesaler	1	Academic	20
Pharmacist		Consumer organization	
Insurer/payer (NHS, sickness funds)	1	Other (feel free to specify)	8

3 Delphi questionnaire

Please fill out **after taking notice of the results of the first round** by using numbers 1 to 5 for each category and issue in the corresponding (grey) answering box. You can find the results (1 to 5) of the first round (in %) and number of respondents (n) for each answering category and issue under **Rnd1 (%)**. For category '**today**', give your estimation on the current situation. For categories '**2010**', '**2015**' and '**2025**', give your future expectation for these respective years. For category '**opinion**', we ask again to give your own opinion: what would be desirable (also 1 to 5)? You **only have to fill out the grey boxes**!

Will the following issues predominantly be regulated and implemented at a European level or at a national level?

1 = fully national

2 = predominantly national

3 = even or 50/50

4 = predominantly European

5 = fully European

			EXPECTATION							
Issue	**Today**		**2010**		**2015**		**2025**		**Opinion**	
	Rnd1 (%)	**Rnd2**	**Rnd1 (%)**	**Rnd2**	**Rnd1 (%)**	**Rnd2**	**Rnd1 (%)**	**Rnd2**	**Rnd1 (%)**	**Rnd2**
1. Market Authorization (Licensing)	1: 08		1:		1:		1:		1:	
	2: 23		2: 10		2:		2:		2:	
	3: 45		3: 45		3: 20		3: 05		3: 09	
	4: 25		4: 38		4: 50		4: 45		4: 25	
	5:		5: 08		5: 30		5: 50		5: 66	
	n=40		n=40		n=40		n=40		n=32	
2. Pharmacovigilance (post marketing surveillance)	1: 18		1: 08		1: 05		1: 05		1:	
	2: 49		2: 15		2: 05		2: 03		2: 06	
	3: 28		3: 51		3: 33		3: 23		3: 22	
	4: 05		4: 23		4: 44		4: 44		4: 25	
	5:		5: 03		5: 13		5: 26		5: 47	
	n=39		n=39		n=39		n=39		n=32	
3. Classification: Rx (Prescription only), OTC	1: 38		1: 18		1: 08		1: 03		1: 10	
	2: 38		2: 38		2: 21		2: 21		2: 13	
	3: 15		3: 23		3: 31		3: 23		3: 10	
	4: 05		4: 15		4: 26		4: 28		4: 32	
	5: 03		5: 05		5: 15		5: 26		5: 34	

	n=39		n=39		n=39		n=39		n=31	
4. Distribution (wholesaling)	1: 41		1: 15		1: 03		1: 03		1: 03	
	2: 46		2: 38		2: 36		2: 26		2: 19	
	3: 08		3: 33		3: 33		3: 31		3: 35	
	4: 05		4: 13		4: 26		4: 26		4: 23	
	5:		5:		5: 03		5: 15		5: 19	
	n=39		n=39		n=39		n=39		n=31	
5. Advertising: e.g. direct-to-consumer advertising	1: 41		1: 16		1: 05		1: 03		1: 13	
	2: 19		2: 34		2: 18		2: 16		2: 17	
	3: 14		3: 18		3: 29		3: 24		3: 23	
	4: 22		4: 26		4: 26		4: 29		4: 13	
	5: 03		5: 05		5: 21		5: 29		5: 33	
	n=37		n=38		n=38		n=38		n=30	
6. Pricing: e.g. pricing and profit controls, reference pricing	1: 80		1: 59		1: 34		1: 20		1: 26	
	2: 15		2: 24		2: 37		2: 35		2: 16	
	3: 05		3: 07		3: 12		3: 18		3: 23	
	4:		4: 07		4: 12		4: 15		4: 13	
	5:		5: 02		5: 05		5: 13		5: 23	
	n=40		n=41		n=41		n=40		n=31	
7. Dispensing (pharmacy level): e.g. generic substitution, remuneration	1: 85		1: 66		1: 44		1: 38		1: 42	
	2: 10		2: 27		2: 34		2: 30		2: 26	
	3: 05		3: 05		3: 17		3: 20		3: 13	
	4:		4: 02		4: 02		4: 10		4: 10	
	5:		5:		5: 02		5: 03		5: 10	
	n=40		n=41		n=41		n=40		n=31	

8. Prescribing: e.g. prescribing guide-lines, budgets	1: 90		1: 61		1: 41		1: 26		1: 29	
	2: 10		2: 32		2: 34		2: 35		2: 23	
	3:		3: 07		3: 20		3: 20		3: 23	
	4:		4:		4: 05		4: 15		4: 16	
	5:		5:		5:		5: 03		5: 10	
	n=40		n=41		n=41		n=40		n=31	
9. Post-licensing evaluation (compar-ative benefit/ cost-effectiveness)	1: 73		1: 34		1: 17		1: 10		1: 16	
	2: 23		2: 41		2: 29		2: 25		2: 13	
	3: 05		3: 22		3: 39		3: 33		3: 13	
	4:		4: 02		4: 07		4: 25		4: 35	
	5:		5:		5: 07		5: 08		5: 23	
	n=40		n=41		n=41		n=40		n=31	
10. Reimbursement: by public payers, i.e. scope of benefit catalogue (including positive/negative list)	1: 90		1: 70		1: 43		1: 28		1: 32	
	2: 10		2: 20		2: 38		2: 45		2: 28	
	3:		3: 10		3: 15		3: 13		3: 22	
	4:		4:		4: 05		4: 15		4: 10	
	5:		5:		5:		5:		5: 06	
	n=40		n=40		n=40		n=40		n=31	

Comments (not requested)**:**

Thank you for your cooperation.

Ewout van Ginneken; Prof. Dr. Reinhard Busse, Dr. Christian Gericke, Dr. Jonas Schreyögg

Department of Health Care Management

WHO Collaborating Centre for Health Systems Research and Management

Berlin University of Technology