The Pharmaceutical Industry in Australia

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1. Introduction

This paper is concerned with describing and explaining some key structural characteristics of Australian pharmaceutical markets and their associated supply chains. It begins with an overview of the three commercial sectors involved in the supply of medicines to patients: (i) the pharmacists who are the retail outlet for consumers, (ii) the wholesalers that are typically used by suppliers to distribute medicines and (iii) the companies that provide the medicines, either as manufacturers or importers or both. Each sector is described in terms of its relative size, concentration and involvement with the Pharmaceutical Benefits Scheme (PBS).

The extent of market concentration within the pharmacy and wholesale sectors is relatively easy to ascertain but is more difficult to determine for the manufacturing sector. To address this, Section 3 draws upon datasets assembled by the Centre for Strategic Economic Studies (CSES) to measure concentration within PBS treatment markets drawing on the definitions of these markets based on the Anatomical Therapeutic Classification (ATC) and various concentration indexes. The relationship among concentration, the number of suppliers, the size of treatment markets, patent status of medicines and other factors are explored using regression analysis. A comparison is made between concentration in Australian markets and those in the USA and Japan. The same data sources are also used to measure the degree of specialisation among PBS suppliers and the relationship between a company's specialisation, the number of markets it supplies and its overall size is explored econometrically.

The extent to which companies can supply medicines to Australian pharmaceutical markets is governed by the operations of two government agencies. The authority regulating whether a medicine can be sold in Australia is the Therapeutic Goods Administration (TGA) and its operations are described in terms of the regulatory approvals process and compared to the equivalent organisations in the USA and Europe. Using data from the TGA, overseas regulatory authorities and the PBS datasets, the lags imposed by the operations of the TGA and the PBS are quantified and their progress over time assessed.

The other government agency, the PBS, is the subject of a companion PIP Working Paper (Sweeny 2007a).

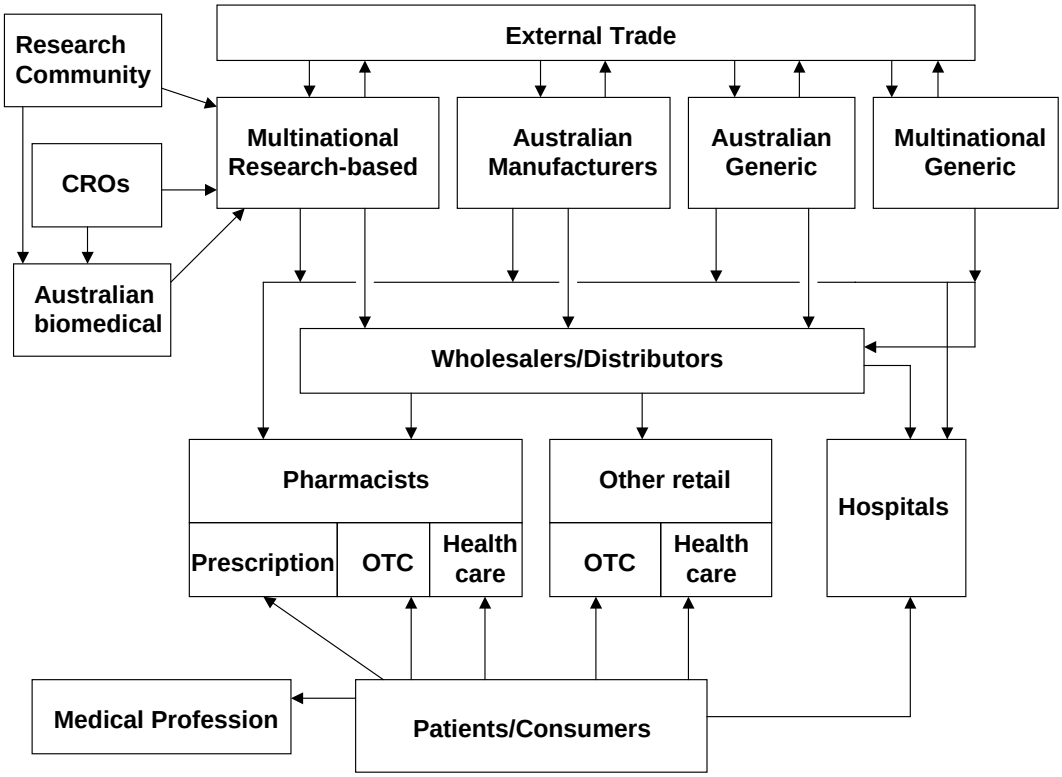
2. The pharmaceutical supply chain in Australia

Despite its importance within the economy, the picture of the pharmaceutical sector in Australia is surprisingly incomplete. Over the past few decades the Productivity Commission and its predecessors have regularly examined various aspects of the sector (Industries Assistance Commission 1974, 1976, 1986, Industry Commission 1996, Productivity Commission 2001, 2003) and several other studies have also contributed to the picture (Australian Economic Analysis 1998, DITR 2002, Parry and Thwaites 1988). Nonetheless there remain significant gaps in our understanding, particularly in some of the key stages of the pharmaceutical supply chain.

The relationship among the players in the pharmaceutical sector is illustrated in Figure 1. Consumers with medical conditions (patients) treatable with

pharmaceuticals either seek this treatment from doctors in general practice or hospitals, or they self-medicate. If the condition requires a prescription pharmaceutical, the doctor provides the prescription to the patient and this can only be filled at a community pharmacy. If the pharmaceutical treatment does not require a prescription, these can be purchased from either a pharmacist or from other retail outlets, such as supermarkets. Some pharmaceuticals must be administered within a hospital and medicines will form a part of many (if not most) hospital treatments.

Figure 1 The pharmaceutical sector in Australia



The ultimate supply of medicines in Australia is dominated by the research-based multinational pharmaceutical companies, and these have varying degrees of involvement in domestic manufacturing, wholesaling, distribution and R&D. Other foreign-owned companies manufacture and supply generic brands of medicines. A few Australian companies act exclusively as manufacturers, but most combine manufacturing with extensive wholesaling and distribution and other health-related activities.

A significant part of the supply of pharmaceuticals in Australia is sourced overseas, while both multinational and Australian manufacturers participate in the export of pharmaceutical products with varying degrees of transformation. The Australian biomedical research community as well as local biomedical companies have developed links with the multinational companies and to a lesser extent with Australian companies, while most of the R&D done by companies in Australia is clinical trials, involving specialist clinical research organisations (CRO).

2.1 Patterns of medication use

In Australia, the sale of medicines is governed by legislation at both Commonwealth and State levels. All products for therapeutic use are regulated by the Therapeutic

Goods Administration (TGA), which is an agency within the Commonwealth Department of Health and Ageing. The TGA controls both regulated (or scheduled) medicines, which are included within the *Standard for the Uniform Scheduling of Drugs and Poisons*, and listed medicines, which are unscheduled. The Standard is maintained by the TGA but takes force in legislation at the State level (Department of Human Services 2006).

As an example, the *Drugs and Poisons Schedule* for Victoria is reproduced as Table 1, and the most important classifications so far as restrictions on the sale of medicines are concerned are

S4 Prescription-only medicines
S3 Pharmacist-only medicines
S2 Pharmacy-only medicines

The S2 and S3 medicines are classified by the TGA as over-the-counter (OTC) medicines and include

- Non-prescription analgesics such as aspirin or paracetamol
- Most topical antifungals
- Most cough and cold remedies
- Hayfever treatments
- Antiseptics
- Sunscreens

Listed medicines are considered to be relatively benign and include a range of complementary (or traditional or alternative) medicines such as vitamin, mineral, herbal, aromatherapy and homoeopathic products. These are often included in industry estimates of OTC sales.

Table 1 Drugs and Poisons Schedule, Victoria

S1	Unscheduled
S2	Pharmacy Medicine – Substances, the safe use of which may require advice from a pharmacist and which should be available from a pharmacy or, where a pharmacy service is not available, from a licensed person.
S3	Pharmacist Only Medicine – Substances, the safe use of which requires professional advice but which should be available to the public from a pharmacist without a prescription.
S4	Prescription Only Medicine – Substances, the use or supply of which should be by or on the order of persons permitted to prescribe and should be available from a pharmacist on prescription.
S5	Caution – Substances with a low potential for causing harm, the extent of which can be reduced through the use of appropriate packaging with simple warnings and safety directions on the label.
S6	Poison – Substances with a moderate potential for causing harm, the extent of which can be reduced through the use of distinctive packaging with strong warnings and safety directions on the label.
S7	Dangerous Poison – Substances with a high potential for causing harm at low exposure and which require special precautions during manufacture, handling or use. These poisons should be available only to specialised or authorised users who have the skills necessary to handle them safely. Special Regulations restricting their availability, possession, storage or use may apply.
S8	Controlled Drug – Substances which should be available for use but require restriction of manufacture, supply, distribution, possession and use to reduce abuse, misuse and physical and psychological dependence.
S9	Prohibited Substances – Substances which may be abused or misused, the manufacture, possession, sale or use of which should be prohibited by law except when required for medical or scientific research, or for analytical teaching or training purposes with the approval of the Secretary to the Department of Human Services.

Source: Department of Human Services 2006.

Most prescription medicines in Australia are made available to patients under the Pharmaceutical Benefits Scheme (PBS), which acts both as an insurer, and as a sole purchaser negotiating prices for medicines with suppliers.

Patients in private hospitals pay for the medicines used during their treatment and if these are listed on the PBS they attract the PBS subsidy. Public hospitals are funded by State Governments in the main and they provide medicines to patients free. State Governments are reimbursed for the cost of those medicines listed on the PBS and provided to non-admitted and day-admitted patients in public hospitals. Funding for public hospitals are governed by Australian Health Care Agreements and it is likely that some or all of the cost of providing PBS-listed medicines to longer stay hospital patients will be met by the PBS under future versions of these agreements.

The most comprehensive picture of the use of medicines in Australia is provided by the National Health Survey (NHS) undertaken by the Australian Bureau of Statistics in 1995 (ABS 1999)[1]. This survey found that 59% of the population used one or more medications over a two week period, the most popular of which were pain relievers, skin ointments and creams, medicines for coughs and colds, and medications for heart problems or high blood pressure (Table 2).

Table 2 Medication use by age, 1995

Type of medication used	Number using	0-14	15-24	25-44	45-64	65 and over	Total
	000's	%	%	%	%	%	%
Medication for diabetes	262.2	0.1	0.3	0.5	2.5	5.8	1.5
Asthma medications	1,197.5	8.2	8.1	5.5	5.7	6.5	6.6
Medication for arthritis	621.4	0.1	0.2	1.1	6.4	14.4	3.4
Medication for cough/colds	1,283.8	11.4	7.8	6.7	5.0	3.3	7.1
Skin ointments/creams	1,761.6	8.0	12.0	11.1	9.4	7.2	9.8
Stomach medications	730.3	0.7	1.5	3.0	6.3	11.9	4.0
Laxatives	98.8	0.4	0.1	0.3	0.6	1.9	0.5
Medications for allergies	571.5	1.8	3.4	4.0	3.7	2.3	3.2
Fluid tablets/diuretics	394.8	0.1	0.0	0.3	2.8	12.5	2.2
Medications for heart problems/blood pressure	1,910.3	0.1	0.2	2.2	19.3	49.2	10.6
Medications to lower cholesterol/triglycerides	307.8	0.0	0.0	0.4	4.0	6.3	1.7
Pain relievers	4,265.2	13.9	25.1	30.2	25.2	19.4	23.6
Sleeping medications	265.6	0.2	0.3	0.9	2.1	5.6	1.5
Medications for anxiety, nervous tension, depression	395.9	0.1	0.8	2.2	3.9	4.7	2.2
Tranquillisers or sedatives not included above	79.3	0.2	0.2	0.3	0.6	1.2	0.4
Other medications	3,221.8	9.4	13.1	14.6	24.8	35.5	17.8
Total *	10,671.7	41.6	51.8	57.4	69.6	85.9	59.1
Total persons		3,872.7	2,710.3	5,583.5	3,739.6	2,155.0	18,061.1

* Persons may have reported more than on type of medication so components do not add to totals.
Source: ABS 1999, Table 1.

[1] While the PBS data from Medicare Australia and the DoHA made available to CSES is rich in detail it does not provide information on use of medicines by socio-economic or demographic status. The ABS National Health Survey for 2001 only provides data on medicines for a select range of conditions. Publications from the BEACH survey of GPs (eg Britt et al 2007) only report summary information.

Overall, medicine use rises strongly with age – from 52% of those aged 15-24 to 86% of those aged 65 and over. However there is significant variation in the age profile of medicine use depending on the type of medicine. Asthma medication use is higher among younger age groups, as is the use of medications for coughs and colds, pain relievers, and skin ointments and creams. The incidence of medicines to treat the illnesses of ageing – type 2 diabetes, arthritis, stomach problems, fluid retention, heart problems, high blood pressure, and high cholesterol – all increase rapidly after the age of 45 and particularly after 65. The use of tranquillisers, sedatives and sleeping medications is also more pronounced among older age groups.

People aged 45 and over account for about 32% of the total population. However they make up 41% of people taking medications and a much higher proportion of those taking the more expensive types of drugs (Table 3).

Table 3 Distribution of medication use by age, 1995, %

	45-64	65 and over	45 and over
Medication for diabetes	34.5	46.1	80.6
Medication for arthritis	39.0	50.5	89.5
Stomach medications	32.6	35.5	68.1
Fluid tablets/diuretics	26.4	67.8	94.1
Medications for heart problems/blood pressure	37.7	55.4	93.1
Medications to lower cholesterol/triglycerides	48.7	44.2	92.9
Sleeping medications	29.0	44.5	73.5
Medications for anxiety, nervous tension, depression	36.7	25.5	62.2
Total	24.4	17.3	41.7

Source: ABS 1999, Table 1.

More recently, the Department of Treasury (2007) has published figures on the cost of pharmaceutical benefits by age as part of its *Intergenerational Report* for 2007. While those in the age group 45-54 have spending on pharmaceutical benefits close to the average for all people and younger age groups spend much less, spending in older age groups rises strongly from 55 onwards (Table 4).

Table 4 Index of the age profile of spending on pharmaceutical benefits, 2005-06 Per person, compared to average for all persons = 1.00

Age group	0-4	5-14	15-24	25-34	35-44	45-54	55-64	65-74	75-84	85+	All
Index	.07	.08	.17	.32	.52	.91	1.81	3.47	4.50	3.87	1.00

Source: Department of the Treasury, 2007, p102.

2.2 Pharmacists

Under legislation enacted by State and Territory Governments, only pharmacists and hospitals are able to dispense prescription medicines in Australia. According to the 2006 Census (ABS 2006) there were 15,300 pharmacists in Australia in mid-2006 and about 85% (13,001) of these worked in some 4,951 community (ie retail, shop-front) pharmacies (DoHA 2006b), 11% (1,716) were employed in hospitals and clinics and the remaining 4% (583) worked as industrial pharmacists. Total employment in pharmacies was 46,506 with a turnover of about $11.5 billion in 2004-05 (Pharmacy Guild 2007).

Pharmacies sell a range of products aside from prescription medicines and pharmacy-only medicines, including other over-the-counter (OTC) drugs, vitamins,

minerals, complementary medicines, beauty products, toiletries, optician services and film development. According to a submission by National Pharmacies to the Review of Friendly Society Dispensaries by the Australian Competition and Consumer Commission (ACCC 2002), the share of various types of products in pharmacy sales is as shown in Table 5. Prescription medicines account for about 65% of sales, while other pharmacy-only medicines make up another 10%. The value of subsidised PBS and RPBS (Repatriation PBS) medicines is known and can be used to calculate the value of sales in the other categories. Table 5 shows these estimated sales values for 2001-02 and 2002-03.

Table 5 Pharmacy sales by category

	Share	Value $b	
	%	2001-02	2002-03
Subsidised PBS and RPBS prescription medicines	48.1	5.37	5.87
Unsubsidised PBS and RPBS prescription medicines[2]	13.1	1.46	1.60
Private prescription medicines	3.9	0.44	0.48
Non-prescription medicines only available through pharmacies	10.0	1.12	1.22
Other products	24.9	2.78	3.04
Total	100.0	11.16	12.20

Source: ACCC 2002.

Over time, the sales of dispensed drugs have become more important for pharmacies as they have lost market share in the sale of non-pharmacy only medicines, and other products to supermarkets, specialty beauty product and health product stores, and other retailers.

Through the Pharmaceutical Benefits Pricing Authority (PBPA), the Department of Health and Ageing sets the prices that pharmacists can charge for PBS and RPBS medicines. Under the Community Pharmacy Agreements negotiated between the Commonwealth Government and the Pharmacy Guild, the PBS also sets both the maximum price paid by the pharmacist to the supplier, and the pharmacist's retail mark-up (10% on most drugs) and dispensing fee ($5.15 on most drugs).

According to the ACCC (2002), approximately half of the community pharmacy sector complies with a pricing schedule for private prescription medicines issued by the pharmaceutical supplier, Arrow Pharmaceuticals, specifying a maximum dispensed price for the private prescription medicines they provide. Arrow Pharmaceuticals merged with Sigma Company Limited in December 2005 to form Sigma Pharmaceuticals Limited. The prices of non-prescription medicines sold only in pharmacies as well as other OTC medicines and other pharmacy products are not controlled.

State and Territory legislation by and large restricts the ownership of pharmacies to pharmacists (or friendly societies) and imposes a limit on the number of pharmacies in which a pharmacist may have a proprietary interest. In Victoria, for instance, the maximum is 3 pharmacies. These restrictions on ownership have prevented pharmaceutical wholesalers and distributors, as well as supermarkets from entering the pharmacy market. Changes to these restrictions have been assessed by the Council of Australian Governments (COAG) but the Fourth Community Pharmacy Agreement will continue the restrictions on pharmacies locating within supermarkets.

[2] This category is those medicines consumed by general patients which available under the PBS and RPBS at a price below the general co-payment level, currently $30.70. The prices of these drugs are set by the PBS, but the general patient pays the full price.

Further restrictions are placed on the operations of pharmacies by the PBS which must approve new pharmacies selling PBS medicines and any changes in location of pharmacies.

Despite these restrictions on ownership, pharmacies join together in a number of ways. Banner groups are groups of pharmacies operating under the same marketing banner. According to the ACCC, the banner group provides common advertising and promotional support to members of the group as well as advice on store layout and business practices. In some instances, the banner group provides goods branded with the name of the group, although this is necessarily restricted to off-patent medicines. In return pharmacies pay an annual subscription to the banner group.

About 54% of pharmacies are in banner groups and 51% of pharmacies belong to a banner group controlled by one of the 3 major wholesalers – API, Sigma and Symbion Health (IBISWorld 2006c). These banner groups are listed in Table 6. In addition some pharmacies join together in buying groups to obtain cheaper prices from wholesalers and/or manufacturers. Chemplus is an example of such a group.

Although pharmacies may be a member of a banner group this does not mean they are obligated to buy all their supplies through this channel. In its annual report for 2005-06 for instance Sigma says that pharmacies associated with its Amcal banner group buy 67.2% of their supplies through the group. For its Guardian pharmacies the proportion is 77.9% (Sigma 2006).

Table 6 Pharmacy banner groups

Wholesaler	Affiliated Pharmacies	Banner Groups
API	153	Chemworld
	290	Independent Pharmacies Australia
	60	Pharmacist Advice
	208	Soul Pattinson
Symbion Health	220	Chemmart
	110	Terry White
Sigma	371	Amcal
	235	Guardian
Independent	56	National Pharmacies
	47	MyChemist
	50	Chemplus

The successful operation of the PBS and RPBS requires the cooperation of community pharmacies and the terms and conditions under which pharmacies participate in these programs is set out in the Fourth Community Pharmacy Agreement. The Commonwealth Government has entered into agreements with the dominant pharmacist industry association (now called the Pharmacy Guild of Australia) from time to time since the two schemes began[3] but this was put onto a more formal basis in 1990 when the first of the five year Community Pharmacy Agreement was signed. The fourth of these agreements commenced on 1 December 2005 and expires on 30 June 2010 (DoHA 2005a, 2005b)

The agreement sets out the basis for remuneration of pharmacists under the PBS (and by extension the RPBS) by specifying the relationship between the price paid by the pharmacist and the dispensed price of a medicine charged by the pharmacist. A formula describes both the mark-up that will apply and the dispensing fee(s) to be added to the marked-up price. A key feature of the dispensing fee is that it is regularly adjusted for inflation to maintain its value in real terms.

[3] The history of agreements prior to 1990 is described in Sloan (1995).

Other topics covered by the agreement include rules about location of pharmacies and funding for professional programs and services. Although wholesalers and manufacturers are not parties to the agreement, there are also provisions governing the mark-up by wholesalers of the manufacturer's price and a fund to encourage wholesalers to supply the full range of PBS medicines.

In summary, the pharmacy sector is highly regulated through legislation and agreements which determine the ownership structure of the sector, the number of pharmacies that can operate, the conditions under which they operate, and the prices they can charge for most of the products they supply.

One of the few areas of opportunity open to pharmacists has been the discount offered by suppliers on the listed wholesale price determined by the PBS. Large discounts on the wholesale price of popular medicines have typically been offered by generic suppliers trying to take market share from originator brands.

Policy changes announced by the Minister for Health and Ageing in November 2006 include a requirement for suppliers of new brands of some PBS medicines to disclose the actual price paid by pharmacists and for the listed price to be adjusted to this actual price (DoHA 2006a, 2007). Although there is a provision for a fund to compensate pharmacists for the reduction in income associated with this policy, this will expire at the end of the Fourth Community Pharmacy Agreement. The requirement to reveal actual prices paid by pharmacists will provide an insight into the extent and size of discounts offered to pharmacists by suppliers when the policy takes effect in August 2009.

2.3 Wholesalers/Distributors

Although the wholesaling of pharmaceuticals in Australia is dominated by three companies – API, Sigma, and Symbion Health – which between them account for over 90% of the market the relative market shares and ownership of these companies has become increasingly uncertain and the long term structure of the sector remains to be settled. The description of the sector given here draws on IBISWorld (2006b), company reports and information current in mid-2007.

Prescription drugs make up approximately 75% of the sales of pharmaceutical wholesalers a proportion that has been increasing over time because, as retail pharmacies have lost market share in OTC medicines to supermarkets and other retailers, these organisations have utilised their own wholesaling and distribution operations. Pharmacy-only products represent 15% of sales and OTC products the remaining 10%.

Aside from the 3 full-line wholesalers, there are a number of other short-line wholesalers supplying particular segments of the market, and these account for 5% of drugs supplied to pharmacies. In addition, manufacturers supplying directly to pharmacies account for about 7% of drugs bought by pharmacists. Chief among these is AstraZeneca, although many of the major companies such as GlaxoSmithKline, Merck, Roche, Bayer, BMSA, Pfizer, Aventis and Wyeth also supply directly to pharmacies. Direct supply from manufacturers is responsible for 30-40% of hospital purchases of drugs and wholesalers are increasingly targeting this market for expansion.

The relative importance of the various operations of API, Sigma and Symbion Health are shown in Table 7 based on the annual reports of the companies for 2005-06.

Assuming that the three companies represent 90% of pharmaceutical wholesaling in Australia, the values in Table 8 imply the following market shares – Symbion Health 33.5%, API 29.4% and Sigma 27.1%. In terms of the measures of market concentration described in Section 3 below, these market shares mean that pharmaceutical wholesaling has an H index of at least 2721 and a CR_4 index of at least 90.0, signifying a high degree of oligopoly.

Table 7 Pharmaceutical wholesalers, revenue in 2005-06, $m

	Wholesaling	Manufacturing	Other	Total	Manufacturing sites
API	2,020.4	9.4	546.2	2,576.0	Auckland, NZ
Sigma	1,864.3	380.7	-	2,245.0	Clayton, Dandenong VIC Baulkham Hills NSW Tennyson QLD
Symbion Health	2,305.5	186.4	909.9	3,401.8	Virginia, QLD

Source: Company annual reports, 2005-06.

A proposed merger of Sigma and API in 2003 was refused by the ACCC and a more recent takeover attempt of API by Sigma was refused by API in December 2006. In November 2005 Mayne Group was split into Mayne Pharma and Symbion Health and Symbion Health is currently being acquired by private equity investors.

An insight into the extent to which PBS medicines are supplied directly to pharmacists by suppliers was provided by the change in the wholesaler margin arising from the Fourth Community Pharmacy Agreement. Up to July 2006, the price paid by the pharmacist was split 10% to the wholesaler and 90% to the manufacturer, a mark-up of 11.1% on the manufacturer's price. In July 2006 this was changed to a mark-up of 7.5%, implying a decrease in the price to the pharmacist of 3.2%.

Using information from the monthly dataset of information from the PBS Schedule maintained by CSES, the percentage change from June to July 2006 in the price to the pharmacist[4] for all listed combinations of item and manufacturer was calculated. If the price change was zero the combination was classified as "Manufacturer supplied", if the price change was in the range -3% to -3.5%, the combination was classified as "Wholesaler supplied", and as "Other" for any other value (which may or may not include a change due the change in mark-up). The cost to the PBS in 2005-06 for each combination was then allocated to the appropriate category.

Restricting the comparison to the two categories where the designation is certain, the percent of cost accounted for by both categories is shown in the Table 8. The table differentiates between Section 100 medicines (mainly those in the Highly Specialised Drugs Program) which are supplied directly by the manufacturer and all other PBS medicines. Over 90% of Section 100 medicines are supplied through hospital pharmacies rather than through community pharmacies.

Excluding the Section 100 medicines, the overwhelming majority of PBS drugs are supplied to pharmacists via wholesalers with only a small amount coming direct from the manufacturer. For the PBS as a whole, manufacturers supply 10% directly either to community pharmacists or to hospitals.

[4] The Commonwealth price to the pharmacist for the manufacturer's pack.

Table 8 Supply arrangements for PBS medicines, %

	Manufacturer supplied	Wholesaler supplied
General PBS	2.2	97.8
Section 100	100.0	0.0
Total	10.0	90.0

Source: CSES databases.

2.4 Manufacturers/Suppliers

The supply of pharmaceuticals to the Australian market is dominated by global companies, the 6 largest accounting for 50.5% of the market while the top 20 are responsible for 85.8%. Three Australian manufacturers – CSL, Mayne Pharma and Sigma – have a 4.8% share[5]. As noted earlier, the sale of pharmaceuticals through pharmacies is worth about $10 billion, with a further $1.1 billion in hospitals.

Of the global companies, one is principally a supplier of generic drugs (Alphapharm – previously an independent Australian company purchased by Merck KGAA in 2000), while 8 have manufacturing facilities in Australia (DITR 2002). The location of these manufacturing plants is given in Table 9.

Table 9 Pharmaceutical manufacturing sites, global companies

Company	Manufacturing sites
Alphapharm (Merck KGAA)	Carol Park QLD
AstraZeneca	North Ryde NSW
Bristol-Myers Squibb Australia (BMSA)	Noble Park VIC
GlaxoSmithKline Australia (GSKA)	Boronia, Port Fairy VIC, Latrobe TAS, Ermington NSW
Janssen-Cilag (Johnson & Johnson)	North Ryde, Eveleigh NSW, Westbury TAS
Merck, Sharp & Dohme (Australia) (MSDA)	Granville NSW
Pfizer	West Ryde, Caringbah NSW
Roche Products	Dee Why NSW
Schering-Plough	Baulkham Hills NSW

Source: Company web sites, IBISWorld (2006a).

GlaxoSmithKline Australia and Janssen-Cilag are both manufacturers of active ingredients derived from opium grown in Tasmania, while the Australian company IDT Technologies also supplies active ingredients to other manufacturers and researchers. All the companies listed in Table 9, with the exception of GlaxoSmithKline Australia and Janssen-Cilag, operate secondary manufacturing facilities, ie they combine active and other ingredients into various drug forms, and package and label them.

According to IBISWorld (2006c), there are about 150 pharmaceutical manufacturers in Australia with an estimated 15,700 employees and revenues of $6.8 billion in 2005-06. Domestic demand was satisfied by products manufactured within Australia worth $3.4 billion and by imports worth $7.8 billion. In addition to supplying the local market, manufacturers also exported some $3.4 billion, or about 50% of their total output.

As part of its review of the Pharmaceutical Industry Investment Program, the Productivity Commission (2003) surveyed the industry and estimated the extent of domestic content in pharmaceuticals sold in 2001-02. Parry and Thwaites (1988)

[5] Based on sales to Australian pharmacies and hospitals in 2002-03 (IMS Health 2004).

reported similar estimates for 1983. As can be seen in Table 10, based on data from these sources, twenty years ago the market was predominantly supplied by local manufacture, and that local manufacture had a greater degree of upstream processing, i.e. manufacture of active ingredients and their formulation. In recent years, packaging and formulation of brought-in ingredients has predominated.

Table 10 Pharmaceutical supply by degree of manufacturing, %

	1983		2001-02	
Fully imported products	13.0		43.6	
Manufactured in Australia	87.0		56.4	
Products imported fully finished in bulk and packaged locally		10.3		32.1
Products formulated and packaged locally from brought-in active ingredients		74.7		59.6
Other, incl actives manufacture, formulation and packaging		14.9		8.3
Total	100.0	100.0	100.0	100.0

Source: Productivity Commission (2003), Parry and Thwaites (1988).

The three major Australian pharmaceutical manufacturers have been active in acquiring additional capacity in recent years.

CSL is an Australian biopharmaceutical company that specialises in the extraction of plasma products from blood, and the production of vaccines and antivenoms. It distributes vaccines, antibiotics and other drugs on behalf of other manufacturers, including Merck, Schering, GSKA, and Pasteur Merrieux (Aventis). The company has manufacturing operations in Australia (Parkville in Victoria), Europe and the USA. International sales make up about 80% of revenue. Its pharmaceutical sales in 2005-06 were $212 million, while plasma products sales were $2,637 million.

Mayne Pharma has manufacturing operations based in Australia, North America and Europe. It focuses on the research, development, manufacture and sale of specialty pharmaceuticals with a particular emphasis on generic, injectable oncology treatments (anti-cancer drugs – primarily cytotoxic agents) and related therapeutic areas. The pharmaceuticals business has an increasing presence in branded generics and proprietary products which are marketed to specialists such as oncologists, urologists and anaesthetists. Revenue in 2005-06 was $788.9 million of which 75% was outside the Asia-Pacific region.

Sigma Pharmaceuticals has a history of acquiring manufacturing facilities in Australia from other companies principally from SmithKline Beecham (now part of GlaxoSmithKline Australia – GSKA) in 1999, and from Aventis Pharma in 2000. It acquired Australian manufacturers Herron Pharmaceuticals in 2003 and Arrow Pharmaceuticals in 2006. The company constructed plants to manufacture penicillin in Clayton and South Dandenong in 1990 and 1996 respectively. Traditionally Sigma has manufactured to supply its own branded prescription and OTC brands, but contract manufacturing for Australian and global companies such as GSKA, Aventis Pharma, Kyowa Hakko Kogyo in Japan, Roche Products, Johnson & Johnson, Wyeth Australia, and Abbott Australasia now accounts for 28% of sales (Sigma Pharmaceuticals 2006, IBISWorld 2006a).

2.5 Research and development

According to the ABS, R&D expenditure by business enterprises on Human Pharmaceutical Products was $456.4 million (ABS 2006). Using both published and

unpublished data from ABS, Medicines Australia shows that this R&D expenditure has increased strongly from $210 million in 2001-02, an average annual growth rate of 32% (Medicines Australia 2007).

Although direct figures are not available, at least 80% of the R&D spending supports the conduct of clinical trials, the remainder being for discovery and pre-clinical research. In Australia clinical trials cannot commence until the trial has been notified to the TGA, predominantly through the Clinical Trials Notification (CTN) Scheme. Institutions or organisations wishing to undertake a trial must obtain approval from their Human Research Ethics Committee prior to a notification to the TGA. The number of such notifications will be higher than the actual number of trials being undertaken because multiple sites and organisations may be involved in trialling a new medicine.

Table 11 shows the number of trials and CTNs conducted in Australia since 1991-92 based on a number of sources (Department of Human Services 2003, Medicines Australia 2003, Rankin et al 2006, Rankin 2007). The average annual growth rate for CTNs between 1994-95 and 2004-05 was 13.3% indicating a sustained increase in the amount of this type of medical research being carried out in Australia.

Table 11 Clinical trial applications, Australia

	CTNs	Trials
1991-92	400	
1992-93	650	
1993-94	727	
1994-95	794	
1995-96	1109	
1996-97	1247	
1997-98	1597	491
1998-99	1908	462
1999-00	1710	541
2000-01	1989	347
2001-02	2235	
2002-03	2374	
2003-04	2378	
2004-05	2776	739

Sources: Department of Human Services 2003, Medicines Australia 2003, Rankin et al 2006, Rankin 2007.

Rankin et al 2006 provides some insight into the nature of the trials conducted in 2004-05 both in terms of the therapeutic target and the trial phase. Over a third of all trials are for medicines to treat cancer (Neoplastic disorders) which combined with the next two therapeutic areas – cardiovascular system and central nervous system – make up over half of all trials conducted in Australia. Predominantly these trials are in Phase 2 and Phase 3 of the drug development process (Table 12).

A report to the Victorian Department of Human Services on *Advancing Clinical Trial Research in Victoria* (2003) shows that clinical trial activity by pharmaceutical companies and contract research organisations (ie for drug candidates from overseas) is more weighted to Phase 3 trials while that undertaken by biotechnology companies (which are usually Australian based) are more likely to be in phase 1 and 2.

Table 12 Clinical trial applications, Australia Therapeutic area and phase

	Trials	%
By therapeutic area		
Neoplastic disorders	252	34.1
Cardiovascular system	78	10.6
Central nervous system	71	9.6
Immunology	64	8.7
Endocrine and metabolic disorders	60	8.1
Other	214	29.0
By phase		
Phase 1	87	11.8
Phase 2	259	35.0
Phase 3	277	37.5
Phase 4	53	7.2
Other	63	8.5
Total	739	100.0

Source: Adapted from Rankin et al 2006.

2.6 Australian biomedical industry

The Australian biomedical industry is dominated by 3 companies – CSL, Resmed and Cochlear (aside from the companies already discussed above – ATI, Mayne Pharma, Sigma, and Symbion Health), and these three had a collective market capitalisation of about $19.9 billion at the end of December 2006 (Blake Industry and Market Analysis 2007).

As noted earlier, most of CSL's activities relates to plasma and blood products, although they have an active biopharmaceutical operation making vaccines and other therapeutic products. CSL has major R&D projects on improved influenza vaccines and plasma products as well as early stage projects on recombinant antibody treatments for acute myeloid leukaemia, rheumatoid arthritis and asthma. Resmed develops and manufactures equipment to treat sleep apnoea, while Cochlear has developed cochlear implants for people with severe hearing loss.

In its newsletter *Bioshares*, Blake Industry and Market Analysis Pty Ltd (2007) report on a number of Australian share market indexes covering listed companies in the Australian biomedical sector. The largest 6 companies (CSL, Resmed, Sigma, Cochlear, Mayne Pharma, Symbion Health and API) had a collective capitalisation of $34.1 billion. The other 121 listed biomedical companies had a total capitalisation of $8.1 billion or a mean of $67 million and a median of $29 million. Of these 121 companies only 25 had a capitalisation of $100 million or more. The Australian biotechnology sector therefore is dominated by companies that are very small by international standards.

In their annual review of biotechnology in Australia, Hopper and Thorburn (2007) report that employment in the sector was estimated to be 12,100 in November 2006 based on a survey of 427 Australian core biotechnology companies[6] and 85% of these jobs were within human therapeutics or diagnostics companies.

[6] Core biotechnology companies excludes medical device companies, such as Resmed, brewing companies and IT-based companies selling into the biotechnology market.

3. Market concentration and specialisation

3.1 Measures of market concentration and specialisation

The description of the pharmaceutical supply chain given above shows that the degree of market concentration varies significantly among the different sectors of the industry in Australia. While purchasing decisions are made by millions of individual patients on the advice of doctors, the fact that most prescription medicines are purchased under the PBS or RPBS combined with the control exercised by the PBS on pricing and listing of medicines ensures a high degree of oligopsony at the final consumer end of the supply chain. The public hospital pharmaceutical market is also governed by centralised purchasing guidelines and tendering arrangements controlled by the State and Territory Governments, and can also therefore be regarded as oligopsonistic.

Because the retail pharmacy segment is highly fragmented in terms of ownership the degree of competition in this sector could be regarded as high. This is to some extent offset however by the rules governing the location and operations of pharmacies within the Community Pharmacy Agreements and the PBS, and the supply arrangements between pharmacies and wholesalers, especially for those pharmacies that are members of banner groups. The wholesale segment is highly oligopolistic, being dominated by 3 companies, but the degree of market concentration among manufacturers and other suppliers is more difficult to assess and depends crucially on how pharmaceutical markets are defined.

The literature on industrial organisation (eg Shughart 1990, Tirole 1993) has developed a number of ways to measure the extent of concentration (and by extension competition) within markets, although three of these, the concentration ratio, the Herfindahl-Hirschman index and the entropy index, are the most commonly used.

The *n-firm concentration ratio* (CR) measures the share of sales α_i accounted for by the n (out of m) largest firms, namely

$$CR_n = \sum_{i=1}^{n} \alpha_i \qquad (3.1)$$

where firms are ranked by size and $\alpha_1 \geq \alpha_2 \geq ... \geq \alpha_n \geq ...\alpha_m$ are measured as percentages.

The 4-firm version of this ratio (CR_4) is used most often but there is no agreed interpretation of this ratio. Baldwin (1995) in his study of Canadian manufacturing citing earlier studies uses the following classification for the value of CR_4

Highly concentrated oligopoly	75 to100
Moderately concentrated oligopoly	50 to 75
Slightly concentrated oligopoly	25 to 50
Atomism	0 to 25

However, the CR_4 does not provide any information about the relative sizes of the top four firms. For instance a CR_4 with a value of 80 does not distinguish between the case where 1 company has 50% of the market and the other 3 have 10% each and the case where all four companies have 20% of the market each.

The *Herfindahl-Hirschman (H) index* is defined as

$$H = \sum_{i=1}^{m} \alpha_i^2 \tag{3.2}$$

and hence uses information on the shares of all m companies in the market. The index can be regarded as a weighted average of shares where the weight is just the share itself. By using the square of market share, it gives the companies with larger shares an added importance in the index.

The H index can be decomposed as

$$H = \frac{1}{m} + mV$$

where $V = \frac{\sum_{i=1}^{m} \left(\alpha_i - \frac{1}{m} \right)^2}{m}$ is the variance of shares.

This formulation shows firstly that if all shares are equal and hence the variance is zero, the H index will be equal to $\frac{1}{m}$ and concentration will fall as m increases. Secondly, the index increases with increasing variance of the shares, ie as the distribution of shares becomes more skewed.

The highest value of the H index is 10,000[7] where there is a perfect monopoly with one company having 100% of the market. The US Department of Justice use the H index in its assessment of the effects of mergers on competition and regards a value of 1,800 or higher as "highly concentrated" and a cause for concern. Where five companies have equal 20% shares of the market the H index has a value of 2000[8]. By contrast the Department characterises markets with H index values less than 1000 as "unconcentrated", as would be the case with 10 companies holding equal 10% shares, while an index between 1000 and 1800 is described as "moderately concentrated" (U.S. Department of Justice and the Federal Trade Commission 1992, Section 1.5.1).

The entropy index is defined[9] as

$$\ln(E) = \sum_{i=1}^{m} \alpha_i \ln(\alpha_i) \tag{3.3}$$

[7] The range can be normalised to lie between 0 and 100 or between 0 and 1 if preferred.

[8] More generally $\frac{10000}{H}$ represents the number of equally sized firms in the market that would result in the value of *H.*

[9] Shughart (1990) prefers a more complicated but equivalent formulation namely, $\ln(E) = -\sum_{i=1}^{m} \alpha_i \ln(\frac{1}{\alpha_i})$

An axiomatic derivation of concentration indexes shows that there is a family of concentration indexes

$$I = \sum_{i=1}^{m} \alpha_i h(\alpha_i)$$

which satisfies a reasonable set of conditions, where h is an arbitrary nondecreasing function such that $\alpha h(\alpha)$ is convex. The H index and the entropy index are members of this family and the n-firm concentration index satisfies the conditions without being a member of the family (Tirole 1993).

A casual inspection of the sales and product portfolios of pharmaceutical companies reveals that there is a wide disparity in their size, the number of medicines they market and the number of therapeutic areas in which they are active. While the larger suppliers such as GlaxoSmithKline, Merck, Pfizer and Sanofi-Aventis, have diverse product portfolios and a presence in most therapeutic areas, there are many smaller firms specialising in the supply of a handful of medicines within particular market segments. The degree of specialisation among companies can be measured by looking at how far the distribution of their products differs from the overall distribution.

The literature on specialisation in international trade has developed a number of ways of measuring specialisation which can be also be used to analyse pharmaceutical markets. The following index is adapted from Krugman (1993)[10] and is the sum of the absolute difference between the importance of market i in the sales of company *m* and the importance of market i overall.

$$S_m = \frac{\sum_{i=1}^{k} \left(\left| s_i^m - s_i^* \right| \right)}{2} \qquad (3.4)$$

where $s_i^m = \frac{v_i^m}{\sum_{i=1}^{k} v_i^m}$ is the importance of sales in market i v_i^m for company m as measured by its share in company m's total sales. s_i^* is the share of market i in the overall market. If the distribution of the sales of company m is identical to the average, the value of the index is zero while the further the distribution is from the average the closer the index will be to 1.

3.2 Market concentration in the PBS

The CSES has assembled a number of pharmaceutical-related datasets. The analysis in this section draws upon annual financial year data for the period 1991-92 to 2005-06 covering PBS expenditure and scripts for each combination of PBS item and manufacturer code. This data is cross-classified using the scheme developed by the WHO Collaborating Centre for Drug Statistics Methodology (WHO 2006, 2007). Each medicine has a unique 7-digit code but medicines are also classified at higher levels. These higher level codes can be used to define pharmaceutical treatment markets consisting of medicines used to treat a particular disease and this process is described more fully in Appendix 1.

[10] The index shown is Krugman's index divided by 2 to so that it ranges from 0 to 1.

Using the PBS dataset H, E and CR_4 indexes were calculated for the PBS as a whole over the period 1991-92 to 2005-06, as well as for markets defined by ATC codes at the ATC1, ATC3, ATC4, and ATC5 levels. For the purpose of these calculations, the manufacturer code in a particular year is redefined to include the company and its subsidiaries as they were in that year. This enables the effect of mergers and acquisitions to be reflected in the concentration measures. The results of these concentration index calculations are reported in Tables 13 to 17 and Figures 3 to 7 in Appendix 2 of this paper.

Table 13 shows that the level of concentration for the PBS considered as a single market is moderate there being some 86 suppliers in 2005-06 with the top 4 accounting for 37.9% of the market. In that year the H index was 588.8, and the entropy index was 0.0412. Somewhat surprisingly the level of concentration has increased over time according to all 3 measures even though, as shown by some of the tables in Sweeny (2007b) , the size of the PBS market increased four-fold, the number of medicines listed on the PBS grew from 543 to 687, and the number of suppliers rose steadily after 1999-00.

Figure 3 plots the three indexes standardised so that each has a value of 1 in 1991-92 and shows that they all follow broadly similar paths and agree on most of the turning points during the period. Periods of declining concentration are punctuated by periods in which concentration increases sharply to be followed by periods of decline again, with most of the increase in concentration occurring in the years from 1999-00 to 2003-04.

The simultaneous increase in the number of suppliers and in market concentration points to the importance of mergers and acquisitions among the larger established companies within the PBS and the relatively small proportion of the market accounted for by new entrants after 2000-01. The principal mergers that occurred during the period, and which coincide with increases in the concentration measures, were those that created Glaxo Wellcome in 1996-97, Aventis in 2000-01, AstraZeneca in 2001-02, and GlaxoSmithKline in 2002-03 and the acquisition of Pharmacia by Pfizer in 2003-04. Other mergers such as that between Sanofi Synthelabo and Aventis have occurred since 2005-06. A complete list of company changes as they affect consideration of the PBS market is given in Table 18.

Although the PBS as a whole shows an increase in concentration a somewhat different picture emerges when concentration within particular PBS markets is considered. It is argued in Appendix 1 that medicines have only a limited range of uses and that treatment markets comprise only selected substitutable medicines. These treatment markets can be defined using the ATC classification and concentration measures can be calculated using this classification.

Tables 14 to 17 show concentration measures calculated at the ATC1, ATC3, ATC4 and ATC5 levels respectively. At each level the concentration measure is calculated for each code and both weighted and unweighted averages of these codes are presented. The weighted averages are displayed graphically in Figures 4 to 7, again standardised so that 1991-92 = 1. They are calculated using the proportion of PBS sales in that year as the weight.

It is clear that the average concentration within the PBS increases as markets are defined at progressively more disaggregated levels. In 2005-06 for instance the H index is 588.8 for the PBS as a whole which indicates quite low market concentration, while it increases to 1400.2 at the ATC1 level which is “moderately concentrated” according to the Department of Justice guidelines, to 2599.8 at the

ATC3 level, 3348.8 at the ATC4 level and 4583.1 at the ATC5 level all of which are above the Department's "highly concentrated" level of 1800.

Table 18 Significant mergers and acquisitions among pharmaceutical companies

Year*	Company changes
1995-96	Pharmacia acquires Upjohn to form Pharmacia and Upjohn
	Pharmacia acquires Farmitalia Carlo Erba
	Hoechst merged with Marion Merrill Dow to form Hoechst Marion Roussel
1996-97	Glaxo and Burroughs Wellcome form Glaxo Wellcome
	Roche acquires Syntex
	Wyeth acquires Lederle
	Rhone Poulenc Rorer acquires Fisons
1997-98	Novartis formed from Ciba-Geigy and Sandoz
1998-99	Roche acquires Boehringer Mannheim
1999-00	Pharmacia and Upjohn acquires Monsanto/Searle
2000-01	Aventis formed by the merger of Rhone Poulenc Rorer and Hoechst Marion Roussel
2001-02	Astra and Zeneca form Astrazeneca
	Pfizer acquires Warner Lambert
2002-03	Glaxo Wellcome and SmithKline Beecham form GlaxoSmithKline
	Mayne acquires Fauldings
	Abbott acquires Knoll
	Baxter acquires ASTA
2003-04	Pfizer acquires Pharmacia
2005-06	Novartis acquires Hexal

* year in which change affects PBS

Sources: Company web sites, CSES database, DoHA 2007, Royal Pharmaceutical Society of Great Britain 2006.

The change in concentration over time also varies with ATC level. Whereas the H index for the overall PBS market indicates increasing concentration, although from a low base, as the ATC level becomes more disaggregated, the average level of concentration decreases more sharply over time. At the ATC 3, 4 and 5 levels the concentration profile steadily falls, experiences a one-off increase in 2000-01 and resumes falling thereafter. At the ATC1 level the increase continues to 2003-04 before falling.

As the markets become more disaggregated, the H index and the entropy index increasingly agree on the course of concentration displaying very similar profiles over time, but the CR4 index loses explanatory power. Beyond a certain level of concentration, values of 1 predominate in the calculation of this index making it less able to distinguish degrees of concentration at higher levels.

The profiles of the H index at the ATC4 and ATC5 levels are very similar – both record a 27% fall in the concentration index between 1991-92 and 2005-06, while the fall for the ATC3 level index is also quite close at 23%.

The contrast between an increasing degree of concentration when the PBS is considered as a single market and decreasing concentration (although at higher absolute levels) when considered as a collection of more narrowly defined treatment markets is probably due to the way mergers and acquisitions impact on the number of suppliers of medicines within these treatment markets. Mergers among pharmaceutical companies occur for a number of reasons. Partly there is a desire by companies to exploit economies of scale and scope in both research and development and in sales and distribution.

Henderson and Cockburn (1996), Cockburn and Henderson (2001) and Nightingale (2000) have identified the economies of scale and scope that can arise in research and development. Danzon, Epstein and Nicholson (2007) have shown that, for large

companies, mergers are a response to excess capacity of fixed marketing resources due to anticipated patent expirations and gaps in a company's product pipeline[11].

Mergers therefore might be expected to involve the acquisition by the dominant company of medicines that are complementary to rather than competing with its existing or anticipated product portfolio. Competition regulators in any case would examine carefully the effects on competition of any merger and would be likely to require an acquiring company to divest any products that might be seen as reducing competition.

If mergers are largely complementary in nature this means that they are unlikely to reduce the number of suppliers or change their market shares within a particular treatment market. For instance if company X has products in markets A, B and C and acquires company Y with products in markets D and E, the merger will leave the number of suppliers and their shares in markets A, B and C unchanged and the principal effect will be to change the name of the supplier within markets D and E. If the market is considered to encompass all five markets however then company X will increase its market share following the acquisition and there will be one less independent company, so concentration will rise.

Although the degree of concentration increases when calculated at higher ATC levels, there is still a large degree of variability of concentration from market to market. Table 19 shows the H index for the PBS in 2005-06 for the ATC1, ATC3, ATC4 and ATC5 levels as well as the range within each level and the number of markets that comprise each ATC level. Also included is the number of monopoly markets with an H index of 10000 at each level.

At the ATC1 level the H index ranges from an unconcentrated low of 705.1 (*L - Antineoplastic and immunomodulating agents*) to a concentrated 3399.6 (*R - Respiratory system*). The ranges for the H index given in Table 19 are quite large at each of the ATC levels. Although there are ATC codes at ATC1, ATC3, ATC4 and ATC5 levels which have only a single supplier, even at ATC5 there are still some markets that show only moderate concentration. Nonetheless, the percentage of markets with single suppliers increases as the ATC level increases, so that at ATC5 over 35% are monopolies. It should be noted however that the size of these markets at any particular ATC level varies enormously. At ATC4 for instance it ranges from *C10A – Statins* with an H index of 3343.0 and which was worth $1,112.3 million in 2005-06 to say *C04A – Peripheral vasodilators* with an H index of 10000 and a worth of $1.4 million.

Table 19 H index for the PBS at different ATC levels, 2005-06

	ATC1	ATC3	ATC4	ATC5
Average	1400.2	2599.8	3348.8	4583.1
Lowest	705.0	1181.1	1373.8	1554.7
Highest	3399.6	10000.0	10000.0	10000.0
Number in level	14	71	149	313
Number =10000	0	10	27	110

[11] The actual value of mergers in terms of the performance of the new entities is unclear. Danzon, Epstein and Nicholson (2007) find their performance similar to companies that did not merge while Ornaghi (2007) finds that on average their performance is worse.

Aside from mergers and acquisitions, there are a number of other factors that are likely to have an influence on the degree of market concentration within PBS treatment markets. As demonstrated in Sweeny (2007b), the PBS adds around 20 new medicines each year to its formulary but new codes at the ATC4 and ATC3 levels are rare. This means that new medicines typically add to the stock of medicines within an ATC3 or ATC4 code and will therefore tend to increase the number of suppliers within that code. The result is that increasing the number of medicines on the PBS will tend to reduce the amount of concentration, and this effect will be more marked at ATC3 and ATC4 levels.

Between 1991-92 and 2005-06 PBS expenditure grew by 398% and the amount of medicines consumed by patients has shown similar growth. This expansion in the PBS has provided more incentive for new suppliers to enter the market even though the initial market share they gain may be small. This opportunity extends to both the suppliers of new medicines similar to those already on the market (ie follow-on medicines) and for new and existing generic suppliers when large selling popular medicines lose patent protection. Concentration is therefore likely to fall both as the market expands and the proportion of medicines off-patent increases.

The importance and interrelationship among these factors was assessed and quantified using econometric techniques to estimate the coefficients of two equations. The first equation uses the H index as the concentration measure for the dependent variable and the number of suppliers within each treatment market as the principal explanatory variable. Both linear and logarithmic versions of the equation are estimated and aside from the number of suppliers, other explanatory variables considered are a time trend and dummy variables for ATC markets.

The second equation explains the number of suppliers by the number of molecules in the market and the size of the market measured in terms of the total expenditure within that market. In addition two other explanatory variables are considered – the number of molecules in the market that are off-patent and the size of the market for these off-patent molecules. These latter variables were used both in original form and as proportions, namely the proportion of molecules that are off-patent and the proportion of the size of the overall market accounted for by off-patent molecules. Again both linear and log-linear forms are estimated.

The sets of two equations were estimated using data for markets defined at the ATC1, ATC3, ATC4 and ATC5 levels.

The two equations are then

$$h_{at} = f(nsup_{at}, year_t, d_a) \tag{3.5}$$

and

$$nsup_{at} = g(mol_{at}, size_{at}, molop_{at}, sizeop_{at}, year_t, d_a) \tag{3.6}$$

with the variables defined as follows

constant	Constant
d_a	Dummy variable with value 1 for ATC code a, 0 otherwise
h_{at}	H index for ATC code a in year t
mol_{at}	Number of molecules in ATC code a in year t
$molop_{at}$	Number of off-patent molecules in ATC code a in year t

$nsup_{at}$	Number of companies supplying medicines within ATC code a in year t
$prsizeop_{at}$	Proportion of PBS expenditure in ATC code a in year t due to off-patent molecules
$prmolop_{at}$	Proportion of molecules off-patent within ATC code a in year t
$size_{at}$	PBS expenditure in ATC code a in year t
$sizeop_{at}$	PBS expenditure on off-patent medicines in ATC code a in year t
$year_t$	Time trend, with value 1 in 1991-92 to 15 in 2005-06

Tables 20 and 21 (in Appendix 3) report the results of the linear and logarithmic regressions with the H index as dependent variable and estimated using Ordinary Least Squares (OLS). In all results, the number of suppliers is the chief factor explaining the degree of concentration. The addition of dummy variables for each ATC code increases the explanatory power of the equation and although the coefficients of these dummy variables are not shown, most are significant. Although the time trend is significant at the ATC1 level it becomes insignificant at other ATC levels and in any case makes only a small contribution to the equation. The fit of the equation is best when estimated at the ATC4 level, although there is not much difference from that for the ATC5 level. In all cases the values of the adjusted coefficient of determination and the Durbin-Watson statistic indicate that the equation is well specified with no autocorrelation.

The logarithmic specification performs somewhat better in terms of explanatory power and again the number of suppliers is the chief explanatory variable. However the time trend is now significant at all ATC levels and points to decreasing concentration over time.

The equation for the ATC4 level with ATC dummy variables indicates that the concentration measure falls by 431 points for each additional supplier that enters the market. The logarithmic version suggests that an increase from 4 to 5 suppliers will reduce the concentration measure by about 524 points.

The equations for explaining the number of suppliers at each ATC level give more varied results, the best of which are shown in Tables 22 to 25 (in Appendix 3) for both a linear and a logarithmic specification. At ATC3, ATC4, and ATC5 levels there are a number of markets where either all or none of the molecules in the market are off-patent. This means that it is not possible to include the logarithms for the number of off-patent molecules or the size of the off-patent market in the logarithmic specification for regressions at these levels. Instead the actual proportion of off-patent molecules or the proportion of the market accounted for by these molecules is used instead.

In all cases the number of molecules within an ATC code is a strong predictor for the number of suppliers present within that code. Again the values of the adjusted coefficient of determination and the Durbin-Watson statistic indicate that the equation is well specified with no autocorrelation. An examination of correlation coefficients among the explanatory variables indicates fairly strong correlation between the mol_{at} and $molop_{at}$ and between $cost_{at}$ and $costop_{at}$ and this may have affected the standard errors of estimates of the coefficients of these variables and hence the t-statistic but not the coefficient itself.

At the ATC1 level the best predictors for the linear specification are the size of the off-patent market, and the proportion of molecules within the market that are off-patent. Adding ATC dummy variables for each ATC code causes the size of the off-patent market to become insignificant. The logarithmic version on the other hand identifies separate effects for the size of the market, the proportion of molecules off-

patent and the proportion of the market accounted for by these off-patent molecules. Adding ATC dummy variables reduces the significance of both these latter variables. At the ATC1 level there is a distinct negative trend over time in the number of suppliers which offsets the influence of the other factors.

At the ATC3 level the time trend is much weaker and the other significant variables are the size of the market and the proportion of off-patent molecules, although the importance of these variables is reduced by the addition of ATC dummy variables. The logarithmic version gives similar results although including the proportion of the market accounted for by off-patent molecules gives a better result when ATC dummy variables are added.

The overall fits for equations become noticeably poorer when estimated at ATC4 and ATC5 levels, particularly in the latter case. On the other hand all four variables are significant at the ATC4 level even with the addition of the ATC dummy variables. This indicates that the number of molecules both on and off-patent, and the size of the overall market and the market for off-patent molecules have separate effects on the number of suppliers. At this level the logarithmic version does not perform as well as the linear version although the proportion of the market accounted for by off-patent molecules is still significant, along with the overall size of the market. At the ATC5 level the results are similar although the overall fit is worse.

Concentrating on the results at the ATC4 level, the linear equation with ATC dummy variables implies that the number of suppliers will increase by one for each additional two molecules that enter the market, and for each additional three to four molecules that become off-patent. On the other hand increases of $360 million and $90 million respectively in the sizes of the overall market and the market for off-patent molecules within an ATC4 code will also attract an additional supplier on average.

3.3 Concentration in Australian, Japanese and US pharmaceutical markets

The concentration measures reported above can be compared with those calculated on a somewhat different basis for a range of pharmaceutical markets in Australia, Japan and the USA. H indexes for the following 12 markets are based on IMS Health data for each year from 1998 to 2003. Four firm concentration ratios are reported in Sweeny (2004)

Australian Hospitals
Australian Pharmacies
Japanese Hospitals
Japanese Pharmacies
US Clinics
US Federal Hospitals
US Foodstores
US HMO
US Long Term Care
US Mail Order
US Non-Federal Hospitals
US Pharmacies

An important difference between H indexes calculated using IMS data is that IMS Health retrospectively allocates sales to the merged entity when mergers occur. The effect of this is to increase artificially the measures of concentration in years prior to the merger.

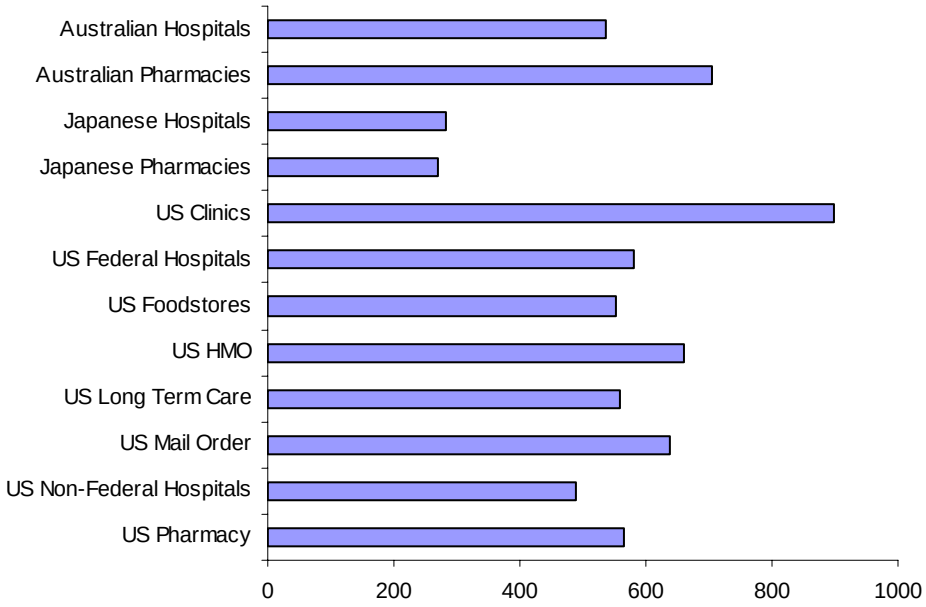
Table 26 shows the H index for the 12 markets over the 6-year period, as well as total sales in US dollars for 2003 as an indication of overall market size. Figure 8 compares the H index for these markets in 2003. In general all markets are

unconcentrated using the US Department of Justice criteria for the H index. The Japanese markets are the least concentrated with H ranging from 270 to 280.

Table 26 H Index for 12 pharmaceutical markets, 1998 to 2003

	1998	1999	2000	2001	2002	2003	Sales in 2003 US$ billion
Australian Hospitals	587.4	598.1	587.2	580.3	542.4	535.6	0.6
Australian Pharmacies	711.5	702.0	695.1	777.8	738.1	703.8	2.7
Japanese Hospitals	271.5	272.7	274.7	275.6	278.9	280.6	18.4
Japanese Pharmacies	250.7	251.7	252.5	258.7	262.9	269.4	24.3
US Clinics	770.8	758.3	731.8	708.5	774.5	896.5	16.7
US Federal Hospitals	569.9	567.5	567.6	585.5	619.8	582.3	3.2
US Foodstores	542.0	574.0	573.9	568.7	565.8	551.0	19.2
US HMO	580.8	573.0	638.8	682.9	718.1	658.9	1.4
US Long Term Care	536.4	573.1	590.3	588.2	576.1	558.4	7.0
US Mail Order	705.0	709.5	725.8	717.9	684.2	638.9	26.0
US Non-Federal Hospitals	524.8	505.6	486.0	482.2	487.5	489.6	19.9
US Pharmacies	540.0	591.1	604.4	595.6	586.1	565.9	104.9

Figure 8 H Index for 12 pharmaceutical markets, 2003



The Australian pharmacy market shows more concentration than does the Australia hospital market, which is in turn similar to most of the institutional markets in the US. Both Australian markets have a tendency to reduced concentration over time the H index falling from 587.4 to 535.6 for hospitals and from 711.5 to 703.8 for pharmacies.

The H index for the whole of the PBS reported in Table 13 has a value of 569.3 in 2002-03 which is significantly less than the 703.8 for the Australian pharmacy market in 2003 given in Table 26. This may reflect a lesser degree of concentration in the non-PBS prescription medicines and non-prescription medicines part of the Australian pharmacy market.

The US markets show surprising variability (H ranging from 490 to 900) given the size of their markets, with all markets except Non-Federal Hospitals having higher H indexes than does the Australian Hospital market.

Taking all the markets together however, there is virtually no relationship between market size as measured by total sales in 2003 and concentration (r = -0.0972).

To understand how the level of market concentration changes at different levels of differentiation among treatments, H indexes were calculated for each ATC level for each market for the year 2003. The results are presented in Table 27.

Table 27 H index for 12 pharmaceutical markets, by ATC levels, 2003

	Total	ATC1	ATC2	ATC3	ATC4	ATC5
Australian Hospitals	536	1,344	2,946	4,225	5,012	8,411
Australian Pharmacies	704	1,631	2,816	3,743	4,159	8,398
Japanese Hospitals	281	595	1,746	2,988	3,686	8,093
Japanese Pharmacies	269	794	1,893	2,942	3,475	7,884
US Clinics	897	1,424	3,752	4,986	5,803	8,104
US Federal Hospitals	582	1,295	2,743	4,096	5,009	8,547
US Foodstores	551	1,181	2,160	3,367	3,815	8,294
US HMO	659	1,665	3,094	4,330	5,067	8,644
US Long Term Care	558	1,235	2,615	3,515	3,970	8,641
US Mail Order	639	1,516	2,718	3,762	4,384	8,778
US Non-Federal Hospitals	490	1,090	2,607	4,098	4,975	8,162
US Pharmacies	566	1,209	2,219	3,415	3,891	8,339

Not surprisingly, the level of market concentration increases steadily as the treatment markets become more specific and there are fewer drugs at each ATC level. Roughly speaking, the H index at ATC2 is double the index at ATC1 which is double that for the whole market. At ATC2, the index is well above the Department of Justice level of concern, while at ATC3 and ATC4 all markets show high degrees of concentration. The very high values at ATC5 show the dominance of single supplier patent-holders for a large number of individual drugs.

The lowest concentration levels are in Japanese markets at all ATC levels, while Australian concentration ratios are among the highest, for both hospitals and pharmacies. The amount of variation in the H index among markets reduces with increasing ATC levels – while there is considerable variation at the whole of market level and at ATC1, there is very little difference at ATC5.

It might be expected that there would be less concentration at the ATC5 level in the US given the higher market share enjoyed by generic suppliers, but this is not borne out by the data. The H index at both ATC4 and ATC5 levels are very similar for both Australian and US pharmacies.

3.4 Market specialisation in the PBS

As with measures of market concentration, the specialisation index can be calculated for markets defined at the ATC1, ATC3, ATC4 and ATC5 levels. For each of the 144 suppliers to the PBS over the period 1991-92 to 2005-06, the distribution of its PBS sales across the ATC markets is compared to the overall distribution of PBS sales across markets using equation (3.5) defined earlier. A specialisation index for each

company is thus obtained for each of the years 1991-92 to 2005-06. For instance in 2005-06 the largest supplier, Pfizer, was present in all 14 of the ATC1 markets and had a specialisation index of 0.360, while Merck, Sharpe & Dohme (Australia) was in 9 of these market and had an index of 0.589. In the same year Pfizer was present in 56 ATC4 markets with an index of 0.572 while Merck, Sharpe & Dohme (Australia) was present in 22 ATC4 markets with an index of 0.723.

As this example shows, the specialisation index increases when markets are defined more narrowly at higher ATC levels.

Table 28 (in Appendix 2) reports the results of calculating market specialisation indexes for each suppliers and then averaging these across all suppliers. Both weighted and unweighted averages are shown, where the weights are the proportion of PBS sales accounted for by the company in that year. The unweighted averages show that specialisation is relatively high among PBS suppliers even when markets are defined at the ATC1 level. These average levels of specialisation remain largely the same over time indicating either that suppliers remain within the markets that they initially enter or that there is a steady stream of new entrants which start out by specialising in just a few markets. Once account is taken of the size of the supplier, average specialisation is significantly lower and declines over time, however the markets are defined. The reason for this is that as companies grow organically or by acquisition they will supply more a more representative set of markets. As noted earlier the principal effect of mergers is to extend the reach of the acquiring company into different markets. Pfizer for instance was in 7 ATC4 markets in 1992-92 with an index of 0.913 and in 56 ATC4 markets with an index of 0.572 in 2005-06.

As was the case when examining concentration measures in Section 3.2 above, the relationship between the degree of market specialisation and explanatory variables can be quantified using econometric techniques. Specialisation is assumed to be a function of the number of ATC markets in which the company is present and the size of the company as measured by its PBS sales. A time trend is also used to account for any systematic trends in specialisation.

$$s_{at} = f(markets_{at}, size_{at}, year_t) \tag{3.7}$$

where the variables are defined as follows

constant	
d_c	Dummy variable with value 1 for company c, 0 otherwise
$markets_{ct}$	Number of PBS ATC markets for company c in year t
s_{at}	Specialisation index for company c in year t
$size_{ct}$	PBS expenditure on medicines from company c in year t, $ billion
$year_t$	Time trend, with value 1 in 1991-92 increasing to 15 in 2005-06

Results are presented in Tables 29 and 30 (in Appendix 3) for equations in linear and logarithmic form and including and excluding company dummy variables. Again there are equations based on data for each of the four different ATC levels

In general equations have coefficients on variables with the expected signs and the dominant explanatory influence comes from the number of markets in which the company has a presence rather than the size of the company. The inclusion of company dummy variables results in better fit statistics indicating the influence on specialisation of factors peculiar to particular companies. The size of the markets is more strongly influential at ATC4 and ATC5 levels in the linear specification while the time trend is only sometimes significant. For the logarithmic specification on the other

hand the time trend is significant in all cases while the size of the market is generally insignificant.

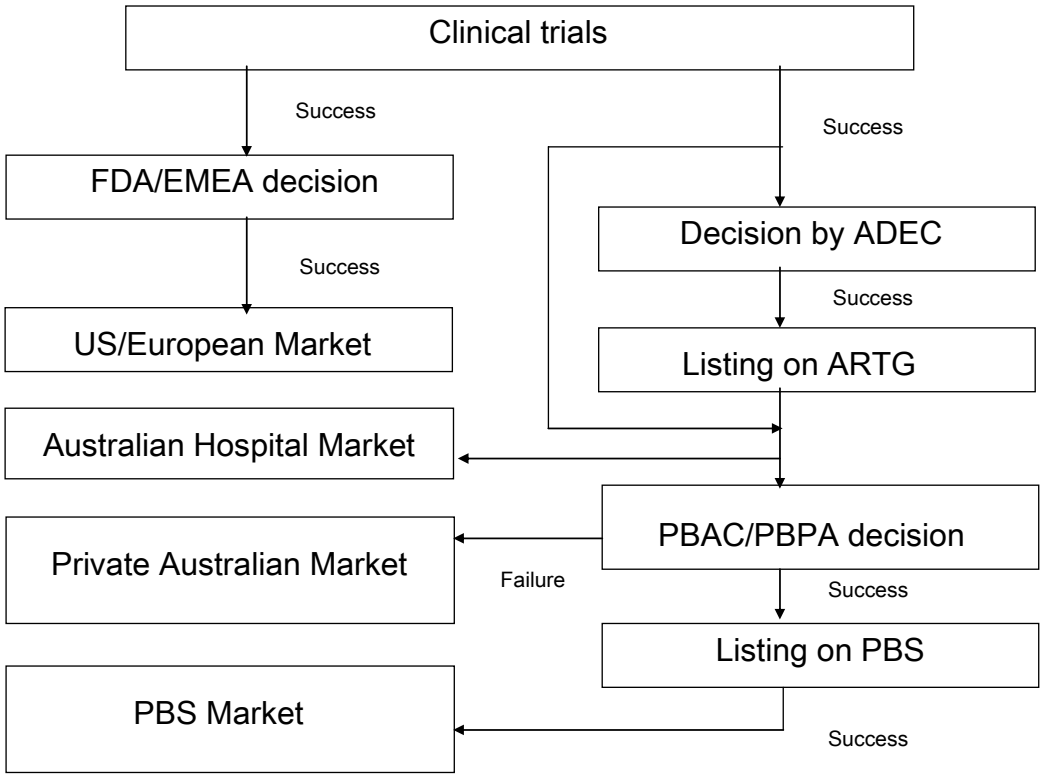
Comparing equations which include the company dummy variables indicates that the linear outperforms the logarithmic specification and the best fit for the linear equation is at the ATC4 level. Here all coefficients on variables are significant with the expected signs. This equation implies that if a company can increase the number of ATC4 markets in which it is present by 20 this will reduce its specialisation index by 0.112. By contrast it would require an increase in sales of $986 million to achieve the same reduction.

4. Regulatory approval and lags

4.1 Regulatory approvals process

The process for discovering and developing a new medicine is a lengthy process and the probabilities of failure at each stage. If a medicine successfully completes Phase III in the opinion of the company developing the medicine, the next step is to apply for regulatory approval. In Australia companies will usually also seek to obtain listing on the PBS. The process of obtaining these approvals and bringing the medicine to market is illustrated in Figure 11.

Figure 11 The approvals process from phase III to PBS



Because of the size of the markets involved, most companies will seek to obtain approval for sale from the Food and Drug Administration (FDA) in the USA and from the European Medicines Agency (EMEA) in Europe. Since 1995, the approval of medicines in Europe has been carried out under the auspices of the EMEA, which makes use of national regulatory agencies for this purpose. Medicines applying for approval under the EMEA must include evidence of relative performance against a

comparator medicine while in the USA the comparison may be made against a placebo only.

In Australia, companies wishing to market a medicine must apply to the Therapeutic Goods Administration (TGA, a unit of the Department of Health and Ageing) to have their product listed on the Australian Register of Therapeutic Goods (ARTG). Although medicines have been regulated in Australia by the Commonwealth Government in a systematic way since 1956, the current regulatory framework was established under the *Therapeutic Goods Act 1989* which created both the TGA (replacing the National Biological Standards Laboratory) and the ARTG from February 1991. McEwen (2007) provides a useful history of therapeutic goods regulation in Australia.

The TGA requirements for data from companies making applications are based on the European Union (EU) requirements and the TGA accepts data packages (or dossiers) in the European Union format (TGA 2007b). The guidelines for submissions are also very similar to those of the EU. For high priority medicines for important and serious illnesses, which often include medicines to treat cancers, sponsors may, by prior agreement, submit the US dossier. In general however the TGA follows the EMEA approvals process quite closely.

The documentation submitted by the company seeking registration on the ARTG provides evidence on the chemistry and quality control aspects of the manufacture of the medicine so assessment can be made on the quality of the medicine, its pharmacological and toxicological properties to assess safety, and evidence from clinical trials to assess both safety and efficacy. Each of these aspects is assessed by the relevant section within the TGA and their findings and recommendations are referred to the Australian Drug Evaluation Committee (ADEC), which makes final recommendations to the TGA. ADEC is a committee of experts established in July 1963 which assesses all applications for new chemical entities, as well as for products which have already been approved but are seeking to have their indications varied.

The TGA has a system of priority evaluation for products that meet certain criteria. These are that 'the product should be a new chemical entity, that it is not otherwise available on the market as an approved product, and that the product is for the treatment of a serious, life-threatening illness for which other therapies are either ineffective or not available (that is, that the product should offer a significant therapeutic advance)' (TGA 2007b). Unfortunately the TGA does not indicate whether an approved medicine has been given a priority evaluation. The average evaluation time for a new chemical entity is about 300 working days or about 420 elapsed days (TGA 2007c).

Companies wishing to have their medicines listed on the PBS must make an application to the Pharmaceutical Benefits Advisory Committee (PBAC) in the Department of Health and Ageing, a process described in detail in Sweeny (2007a). Although a company seeking to have a medicine listed must provide with its application to the PBAC a copy of the letter from the TGA approving the entry of the product in the Australian Register of Therapeutic Goods, in practice companies make parallel submissions to the TGA and PBAC. If a positive recommendation is made by the PBAC, the conditions of listing are negotiated between the sponsoring company, the Pharmaceutical Benefits Pricing Authority (PBPA) and the Department.

Once regulatory approval has been granted, medicines may be sold within the jurisdiction of the regulatory authority. In Australia and many other countries in

Europe and elsewhere, where a government insurance scheme dominates the market, there is likely to be further delay in the process of bringing the medicine to market company as companies seek inclusion in the scheme's formulary.

In the USA, once FDA approval is granted, market entry is quite quick, although the increasing scrutiny of third party payers and their agents, such as Prescription Benefit Managers (PBM), means that the situation in that country is becoming increasingly similar to that in Australia or Europe.

If a medicine is unsuccessful in obtaining a listing on the PBS, it can still be sold on the private market although this is often not a commercial proposition in Australia. Non-PBS medicines used in hospitals are not assessed by the PBAC.

In terms of the pipeline from Phase III to PBS listing therefore, there are a number of distinct stages and by understanding the time taken within each stage, it is possible to get an idea of how long it will take for a medicine to be listed on the PBS if it is successful in traversing each stage.

FDA and EMEA

Companies seeking to test medicine candidates on humans in the USA are required to submit an Investigational New Drug Application (IND) and obtain approval from the Food and Drug Administration (FDA). Once the trials in humans have been completed, the company then submits a New Drug Application (NDA) which can have three outcomes – (i) an approval letter allowing commercial marketing of the product, (ii) an 'approvable' letter which lists minor issues to be resolved before approval can be given, and (iii) a 'non-approvable' letter describing important deficiencies that preclude approval unless corrected. Suppliers of bioequivalent medicines (generics) prepare a simpler submission called an Abbreviated New Drug Application (ANDA) (FDA 2004). The FDA posts information about approvals on its web site but does not give any information about 'approvable' or non-approved medicines. Approval can be withdrawn for a medicine if new evidence about its safety becomes available.

Although the FDA does not provide information on NDAs, 'approvables', or non-approvals, companies often announce this as part of their disclosure requirements and this information is incorporated in commercial and other databases that track medicine approvals, such as Drugs.com (2007).

Medicines which offer a significant improvement compared to existing products are given a 'Priority' review by the FDA (about 40% of new medicines over the past 5 years), while medicines which appear to have therapeutic qualities similar to existing medicines are given a 'Standard' review. About 80-85% of Priority medicines are approved with an average approval time of 8-10 months. On the other hand, about 65-70% of Standard medicines are approved with an average approval time of about 15-20 months. Median approval times for Priority and Standard new medicines have been 8.2 and 21.1 months over the past 5 years (FDA 2006).

Most medicine approvals in Europe now occur through the European Medicines Agency (EMEA) which was established in 1995. Applications for new medicines are reviewed by the Agency through the Committee for Medicinal Products for Human Use (CHMP). The Committee assesses the quality, safety and efficacy of a medicine and, based on an overall balance of the benefits and risks of the medicine, gives its

opinion on whether or not the European Commission should grant a Community-wide marketing authorisation (EMEA 2007b).

In 2005, the EMEA approved 24 new medicines with a mean approval time of 359 days.

4.2 Regulatory approval and PBS listing times

The majority of medicines listed on the PBS have been developed in the USA or Europe. Because the USA is responsible for about 45% of global pharmaceutical sales, companies usually concentrate on obtaining FDA approval, although this does not usually exclude the parallel pursuit of listing in Europe and other countries such as Australia. To estimate the extent of any lags between approval by the FDA or the EMEA, and TGA approval and PBS listing, information on approval dates was obtained from the relevant agencies.

The TGA maintains an interactive database of all medicines on the ARTG on its web site (TGA 2007c), but the information available is limited to the medicine's brand name, chemical name, name of supplier, strength and form. It does not provide date of approval or listing or indication. However, upon request, the TGA has supplied CSES with a list of all medicines registered on the ARTG since the beginning of 1991, which is the earliest date for which electronic records are available. This list consists of a description of the medicine, its brand name, chemical name, strength and form, ARTG code, product code, sponsor name, indications and date of listing. The most recent information is to October 2006.

The information from the ARTG listing was supplemented where necessary by data extracted from the minutes of the bi-monthly ADEC meetings from February 1998 onwards which are posted on the TGA web site (TGA 2007a). These minutes list those medicines that ADEC has recommended for registration on the ARTG. In most circumstances the lag between ADEC recommendation and ARTG listing is quite short.

FDA approvals data was obtained from downloadable database at the *drugs@FDA* web site (FDA 2007). This contains information on all approvals by the FDA over a considerable period of time and includes chemical name, brand name, sponsor, date of approval, and other information.

EMEA data was obtained from two sources. The EMEA itself publishes cumulative lists of approvals from time to time (EMEA 2007a) and each year's approvals are listed in the annual report of the agency (EMEA 2007b). These can be supplemented by monthly reports from the Committee for Medicinal Products for Human Use (EMEA 2007c). The second source is the database called the *Community Register of Medicinal Products* maintained by the European Commission (2007).

PBS listing dates are taken as the date on which the medicine first appears in the electronic version of the PBS Schedule. As the PBS Schedule in electronic form is only available from August 1991, only medicines newly listed from that date can be given a first listing date in this way.

(i) FDA and EMEA approval and PBS listing

There were some 385 new medicines listed on the PBS between August 1991 and October 2006. To this might be added a further 63 medicines listed only on the RPBS over the same period. Of these, FDA approval dates were obtained for 288 PBS

medicines and 23 RPBS medicines. Only new chemical entities or new combinations were considered.

Among these medicines there was considerable variation in the time between FDA approval and PBS listing. At one extreme, there were 30 medicines listed on the PBS before receiving FDA approval. On the other hand there were 51 medicines where the lag was 6 years or more before PBS listing. This wide variation means that the average lag of 48.4 months (median lag 23.4 months) is not a good indicator of how long it typically takes from FDA approval to PBS listing. Figure 12 charts the distribution of medicines in 6-monthly intervals and shows that the typical lag is about 12-24 months. If the average is taken of medicines with lags from –12 months to 72 months the average is 24.6 months, with a median lag of 19.3 months.

The average lag has shown some tendency to increase over recent years (Table 31) although the small numbers of medicines in each year means that these averages should be treated with caution.

EMEA approval dates were found for 87 medicines listed on the PBS from August 1996 onwards. The later starting date was used because the EMEA only began listing medicines from October 1995. The results of comparing the approval dates for EMEA and PBS are less affected by extremes than comparing the FDA and PBS. There were 6 medicines with an earlier listing on the PBS and 11 medicines which were listed on the PBS 3 years or more after being approved by the EMEA. The average lag was 18.2 months with a median of 11.4 months. Table 32 shows the distribution of the average lag by year, while Figure 13 shows the distribution in six-monthly intervals.

(ii) TGA approval and PBS listing

Of the 377 PBS medicines newly listed from December 1991 to December 2006, 337 were matched with an entry on the ARTG list provided to CSES. Some of the PBS products are not medicines while some of the PBS medicines may have been approved before 1991. In addition there have been a few medicines listed on the PBS which have been withdrawn for safety reasons from the ARTG. Of those medicines with an ARTG listing date, there were 18 with a PBS date earlier than the ARTG date. Some of these medicines may have been listed under the Special Access Program within the PBS but for most the reason is likely to be that the medicine was listed on the ARTG prior to 1991. These medicines were excluded when comparing the lag between ARTG and PBS listing.

For the remaining 319 medicines, the average lag was 17.4 months with a median lag of 8.8 months. Figure 14 shows that for most medicines the lag is between 3 and 12 months. As Table 33 indicates, there has been some tendency for the average lag to increase over the past few years, although there is significant variation from year to year.

In summary, the lag between the availability of medicines in the USA and their listing on the PBS is around 18 to 24 months on average although there is considerable variation among medicines. The lag between availability in Europe and the PBS is between 12 to 18 months while the time taken from approval by the TGA to PBS listing is 9 to 12 months. In general all these lags have shown a tendency to increase over time, especially over the last few years.

Table 31 Lag from FDA approval to PBS listing

Year of PBS listing	Average lag*	Number
1991-92	37.0	17
1992-93	79.7	14
1993-94	71.4	14
1994-95	22.4	20
1995-96	34.6	14
1996-97	57.0	30
1997-98	23.2	29
1998-99	30.4	15
1999-00	46.4	25
2000-01	57.6	23
2001-02	33.0	13
2002-03	39.4	19
2003-04	48.5	17
2004-05	48.7	20
2005-06	125.3	13
2006-07	64.8	5
1991-92 to 2006-07	48.4	288

* Average (mean) time in months from FDA approval to PBS Schedule listing.

Figure 12 Distribution of lag from FDA approval to PBS listing

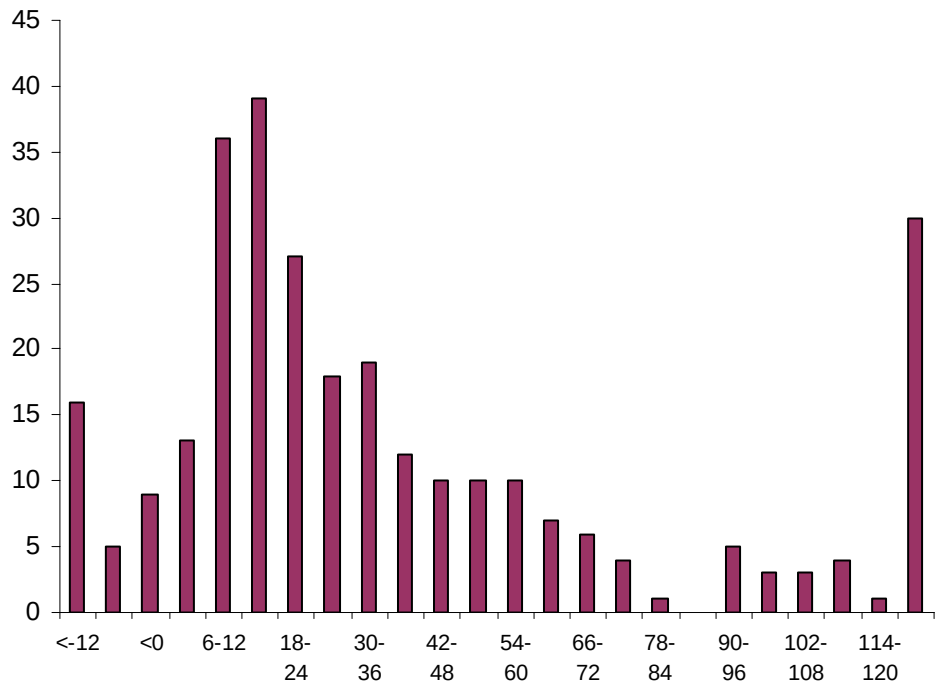


Table 32 Lag from EMEA approval and PBS listing

Year of PBS listing	Average lag*	Number
1996-97	3.9	8
1997-98	13.5	10
1998-99	14.2	5
1999-00	7.6	10
2000-01	3.9	5
2001-02	8.9	7
2002-03	12.9	8
2003-04	38.9	12
2004-05	18.9	12
2005-06	21.2	5
2006-07	57.7	5
1996-97 to 2006-07	18.2	87

* Average (mean) time in months from EMEA approval to PBS Schedule listing.

Figure 13 Distribution of lag from EMEA approval to PBS listing

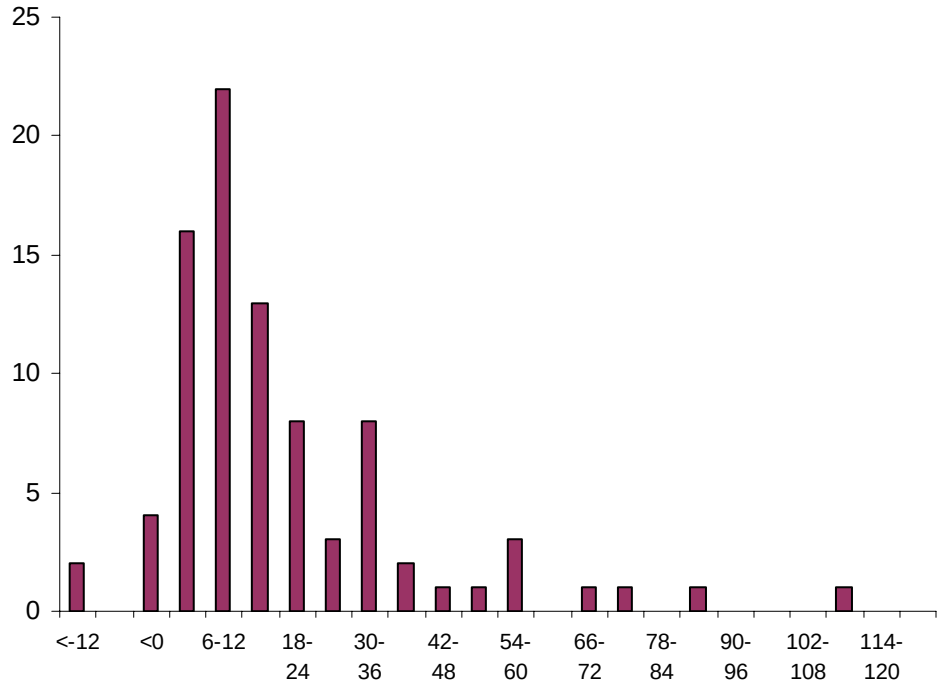
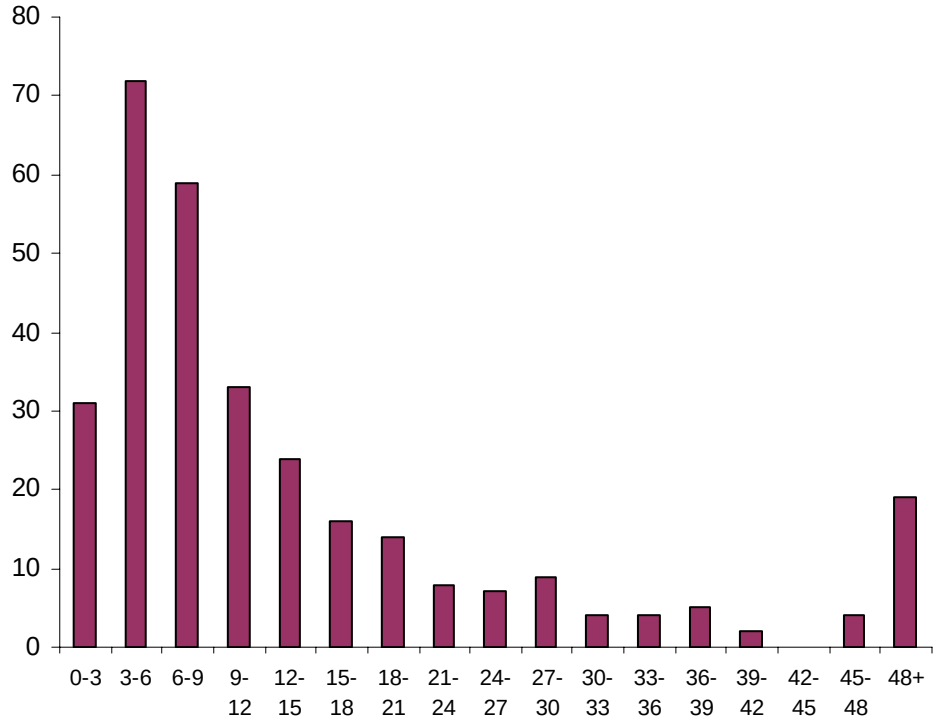


Table 33 Lag from ARTG listing to PBS listing

Year of PBS listing	Average lag*	Number
1991-92	4.5	8
1992-93	11.4	15
1993-94	10.1	13
1994-95	13.7	21
1995-96	19.1	15
1996-97	18.9	35
1997-98	10.3	31
1998-99	17.7	18
1999-00	8.9	23
2000-01	16.9	25
2001-02	15.9	17
2002-03	12.0	20
2003-04	29.3	21
2004-05	19.7	22
2005-06	36.6	19
2006-07	28.1	16
1991-92 to 2006-07		
Total	17.4	319

* Average (mean) time in months from ARTG listing to PBS Schedule listing.

Figure 14 Distribution of lag from ARTG listing to PBS listing



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Appendix 1 Defining pharmaceutical treatment markets

When a pharmaceutical company develops a new drug it is usually aiming to treat a single disease or condition or at least a very narrowly defined range of diseases and conditions. Before being able to market a new drug, the supplier needs permission from the regulatory authority to do so, and this authority will stipulate which diseases can be treated with the drug and under what conditions. Companies seeking to have other conditions treated by the drug will need to go through the regulatory process again to obtain approval. Intermediaries, such as the PBS, may further restrict the range of diseases that the drug can be used to treat and put additional conditions on their use.

There are some instances where a particular drug will be able to treat more than one condition – painkillers and antibiotics are examples – but in most cases a drug will be effective (or at least the first choice) only for a single disease or condition. This means that of the 680 drugs available through the PBS, for instance, only a handful will be effective against a particular disease and only this group of medicines can be regarded as competing with each other as the preferred treatment for that disease.

The limited extent of substitutability among medicines means that pharmaceutical companies can be regarded as competing within a large number of narrowly defined disease or treatment markets.

There are a number of ways in which these treatment markets can be defined. There is an increasing trend by medical practitioner groups, government agencies, insurers, and other organisations concerned with health to develop and promulgate therapeutic guidelines based on systematic reviews of the evidence available on suitable treatments for specific disease or groups of diseases. The Cochrane Collaboration founded in 1993 and responsible for the Cochrane Database of Systematic Reviews is probably the best known of these efforts to "explore the evidence for and against the effectiveness and appropriateness of treatments (medications, surgery, education, etc) in specific circumstances" (Cochrane Collaboration 2007).

In particular areas of medicine, specialist associations are often responsible for undertaking these reviews. In the field of mental disorders, for instance the American Psychiatry Association has produced the well known "Diagnostic and statistical manual of mental disorders" currently in its fourth edition (American Psychiatry Association 1994). The equivalent professional associations in Australia and the United Kingdom have released similar guidelines for mental health practitioners (RANZCP 2004 and Anderson et al 2000).

In Australia this campaign is carried out under the title of "Quality Use of Medicine" and has lead to the establishment of agencies such as the National Prescribing Service which promotes the findings to doctors and others responsible for treating ill health. Standard reference works for doctors incorporate these recommendations as do stand alone databases such as that provided by Therapeutic Guidelines Limited (2007).

One of the most widely used ways of classifying medicines in terms of their use is the Anatomical Therapeutic Classification (ATC), a classification scheme maintained by the WHO Collaborating Centre for Drug Statistics Methodology in Oslo, under which medicines are "divided into different groups according to the organ or system on which they act and their chemical, pharmacological and therapeutic properties". (WHO 2006)

The table below gives the names for the five levels of classification within the ATC system as well the number of codes at each level at January 2007.

Level	Title	Number	Code*
1st	Anatomical main group	14	ATC1
2nd	Therapeutic subgroup	94	ATC3
3rd	Pharmacological subgroup	265	ATC4
4th	Chemical subgroup	854	ATC5
5th	Chemical substance	4123	ATC7

*The code ATCn is the author's and refers to the length (n) of the ATC code at that level.

The highest level – Anatomical main group – is a list of 14 bodily systems, such as the cardiovascular system, respiratory system, musculo-skeletal system and the nervous system. The fifth level, at the other extreme, is the particular drug listed using its chemical name. Some of the medicines in the ATC system are listed with more than one ATC7 code because they can treat multiple conditions. There are some 252 medicines with 2 ATC7 codes, 67 with 3 codes and 53 with 4 or more codes.

To illustrate how the ATC scheme works an example of its application for PBS medicines to treat depression is given in Table A1 at the end of this section.

The *anatomical main group* (ATC1), "N – Nervous system", is made up of 7 *therapeutic subgroups* (ATC3) all of which contain medicines that act on various parts of the nervous system, namely

N01	Anaesthetics – for blocking pain and other sensations
N02	Analgesics – painkillers
N03	Antiepileptics – for treating epilepsy
N04	Anti-Parkinson drugs – for treating Parkinson's disease
N05	Psycholeptics – for treating psychosis and anxiety and for sedation
N06	Psychoanaleptics – for treating depression, stimulants, dementia
N07	Other nervous system drugs – for addiction, vertigo, Alzheimer's disease etc

Each therapeutic group is distinct and different in the types of illnesses that are treated by the medicines contained in the group. Analgesics (N02), antiepileptics (N03) and anti-Parkinson drugs (N04), for instance, are never used to treat depression.

Depression is sometimes accompanied by other nervous system conditions such as anxiety and psycholeptics (N05) could be co-prescribed in that case. One PBS drug listed for depression, lithium carbonate (N05AN01) is classified within the N05 therapeutic subgroup.

The therapeutic subgroup psychoanaleptics (N06) is made up of 4 *pharmacological sub-groups* (ATC4)

N06A	Antidepressants
N06B	Psychostimulants, agents used for ADHD and nootropics
N06C	Psycholeptics and psychoanaleptics in combination
N06D	Anti-dementia drugs

Psychostimulants (N06B) are used to treat conditions such as attention deficit hyperactivity disorder and narcolepsy and anti-dementia drugs (N06D) are used for

dementia – in both cases these are nervous conditions quite different from depression. The pharmacological sub-group N06C consists of two antidepressants – amitriptyline and melitracen in combination with a psycholeptic but these combinations have never been available in Australia.

Within the Antidepressant pharmacological sub-group (N06A) there are 5 *chemical sub-groups* (ATC5) which are principally differentiated by their mode of action within the nervous system, in particular which chemical pathways they attempt to modify.

ATC code	ATC name	Mode of action
N06AA	Non-selective monoamine reuptake inhibitors (tricyclic antidepressants)	Nonselective uptake inhibitors of noradrenaline and serotonin
N06AB	Selective serotonin reuptake inhibitors	Selective inhibitors of serotonin uptake
N06AF	Monoamine oxidase inhibitors, non-selective	Irreversibly inhibit the enzymes MAO-A and MAO-B
N06AG	Monoamine oxidase type A inhibitors	Reversibly inhibit monoamine oxidase type A (MAO-A)
N06AX	Other antidepressants	
	Nefazodone	Selective postsynaptic serotonin 5HT2A antagonist
	Mianserin Mirtazapine	Block alpha$_2$-autoreceptors which prevents the receptor inhibitory effects on the release of 5HT and noradrenaline
	Venlafaxine	Serotonin reuptake inhibitor, and noradrenaline reuptake inhibitor
	Reboxetine	Selective noradrenaline reuptake inhibitor

Within each of these chemical sub-groups the efficacy and side effect profiles of the individual medicines (ATC7) are quite similar. One of the drawbacks of the ATC system however is the inclusion of "residual" categories such as *N06AX – Other antidepressants* which include a more heterogeneous collection of medicines with somewhat different modes of action. Often medicines in these residual categories form the basis of new chemical sub-groups on subsequent consideration by the WHO Centre.

The market for pharmacological treatments of depression using the ATC system therefore can only be considered as consisting of those medicines within the pharmacological sub-group N06A with the possible inclusion of lithium carbonate from N05A – a total of 23 PBS medicines at January 2007. However as Table A1 shows, this only represents about 40% of the 58 antidepressants within the ATC system.

At the beginning of 2007, only two of the listed PBS antidepressants – venlafaxine and reboxetine – were still protected by patents and the off-patent medicines had attracted varying number of suppliers. The most popular antidepressants, the selective serotonin reuptake inhibitors, had the most suppliers along with moclobemide. On the other hand some of the older medicines had more suppliers in previous years, for instance amitriptyline which currently has only one supplier has had al least 3 others over the past 15 years.

In total there were 29 suppliers of medicines within the pharmacological sub-group N06A – antidepressants.

The example of the antidepressants suggest that markets for medicines can only be considered at their broadest at the ATC4 level and the degree of substitutability increases when moving from ATC4 to ATC5 and ATC7. At the ATC4 level the market consists of medicines that are suitable for treating a particular condition but vary significantly in their modes of action and side effect profiles. At the ATC5 level the medicines are quite similar in their action and chemical composition and usually their side effect profiles. At this level some medicines will be patent protected and some will be off-patent. Those off-patent will vary in the number of companies willing to supply that medicine. At the ATC7 level the market is for supply of the same chemical entity and products are only differentiated by their brand name, if the medicine is off-patent. Patent-protected medicines are monopolies by definition.

The ATC system is commonly used to classify medicines and is widely used in research on pharmaceutical markets. The largest supplier of data on pharmaceutical markets world-wide, IMS Health, for instance uses a modified version of the ATC system at the pharmacological sub-group level (ATC4) as a category for classifying medicines in its databases.

Despite this, the ATC system is not wholly definitive in terms of the degree of substitutability of medicines. The evidence presented by companies when seeking to list medicines on the PBS is used by the Department of Health and Ageing as the basis for determining Reference Pricing Groups (RPG) which consist of medicines listed on a cost-minimisation basis and having a high degree of substitutability. More detail on listing procedures and RPGs are provided in Sweeny (2007a).

In the case of antidepressants there are four such RPGs as shown in Table A1, the most important of which is N06(3) consisting of all the SSRIs (N06AB) plus moclobemide from N06AG and three medicines from the residual category N06AX. Reference Pricing Groups could therefore be used as an alternative way of classifying medicines in defining markets for treatments. The chief drawback however is that many medicines on the PBS have not been classified to an RPG.

Markets defined at the ATC5 level will vary in terms of the practical substitutability of medicines within that market. Although all the antidepressants have similar efficacy and side effect profiles, patients vary in their response to the different types of antidepressants and sometimes a doctor may have to try a number before a suitable one is found for a particular patient. Guidelines have been developed to advise doctors on how to undertake this experimentation to ensure patient safety and this in practice limits the degree of substitutability among antidepressants. On the other hand doctors freely switch between different versions of proton pump inhibitors (A02BC) a popular type of treatment for peptic ulcers, because there are no adverse consequences from doing so. Marketing efforts by pharmaceutical companies tend to be concentrated on markets like these where patients and doctors are largely indifferent to the range of medicines available and switching between medicines is common.

There were 151 different ATC4 codes, 315 different ATC5 codes and 634 individual ATC7 codes on the PBS at January 2007.

Table A1 Types of antidepressants listed on PBS classified by ATC and RPG

	PBS total	RPG group	ATC code	ATC name	PBS suppliers at Jan 2007
532	115		**N**	**Nervous system**	
96	28		**N06**	**Psychoanaleptics**	
58	22		**N06A**	**Antidepressants**	**29**
21	8		**N06AA**	**Non-selective monoamine reuptake inhibitors**	**9**
			N06AA01	DESIPRAMINE HYDROCHLORIDE*	
		N06(1)	N06AA02	IMIPRAMINE HYDROCHLORIDE	2
			N06AA04	CLOMIPRAMINE HYDROCHLORIDE	5
			N06AA06	TRIMIPRAMINE MALEATE*	
		N06(1)	N06AA09	AMITRIPTYLINE HYDROCHLORIDE	1
			N06AA10	NORTRIPTYLINE HYDROCHLORIDE	1
		N06(2)	N06AA12	DOXEPIN HYDROCHLORIDE	2
		N06(2)	N06AA16	DOTHIEPIN HYDROCHLORIDE	2
9	6		**N06AB**	**Selective serotonin reuptake inhibitors**	**18**
		N06(3)	N06AB03	FLUOXETINE HYDROCHLORIDE	10
		N06(3)	N06AB04	CITALOPRAM HYDROBROMIDE	9
		N06(3)	N06AB05	PAROXETINE HYDROCHLORIDE	8
		N06(3)	N06AB06	SERTRALINE HYDROCHLORIDE	9
		N06(3)	N06AB08	FLUVOXAMINE MALEATE	5
		N06(3)	N06AB10	ESCITALOPRAM OXALATE	2
6	2		**N06AF**	**Monoamine oxidase inhibitors, non-selective**	**2**
			N06AF03	PHENELZINE SULFATE	1
			N06AF04	TRANYLCYPROMINE SULFATE	1
2	1		**N06AG**	**Monoamine oxidase type A inhibitors**	**9**
		N06(3)	N06AG02	MOCLOBEMIDE	9
20	5		**N06AX**	**Other antidepressants**	**7**
			N06AX03	MIANSERIN HYDROCHLORIDE	2
		N06(3)	N06AX06	NEFAZODONE HYDROCHLORIDE*	
		N06(3)	N06AX11	MIRTAZAPINE	5
			N06AX16	VENLAFAXINE HYDROCHLORIDE	1
		N06(3)	N06AX18	REBOXETINE MESILATE	1

* No longer listed on the PBS – trimipramine since November 1999, desipramine since February 2002 and nefazodone since May 2004.

Appendix 2 Tables and Figures for Concentration and Specialisation Indexes

Table 13 Concentration indexes for the PBS, 1991-92 to 2005-06

	H index	E index	CR_4 index	Number of suppliers
1991-92	478.1	0.03237	34.2	73
1992-93	452.6	0.03155	33.7	75
1993-94	439.1	0.03064	32.8	78
1994-95	420.3	0.02964	31.5	77
1995-96	429.4	0.03143	31.5	75
1996-97	482.1	0.03455	34.6	74
1997-98	481.4	0.03583	33.4	73
1998-99	448.0	0.03474	30.8	74
1999-00	430.0	0.03382	28.9	75
2000-01	489.1	0.03775	31.4	75
2001-02	551.7	0.04074	35.7	79
2002-03	569.3	0.04164	37.4	81
2003-04	662.8	0.04506	41.8	80
2004-05	625.1	0.04266	39.2	84
2005-06	588.8	0.04123	37.9	86

Figure 3 Concentration indexes for the PBS, 1991-92 to 2005-06

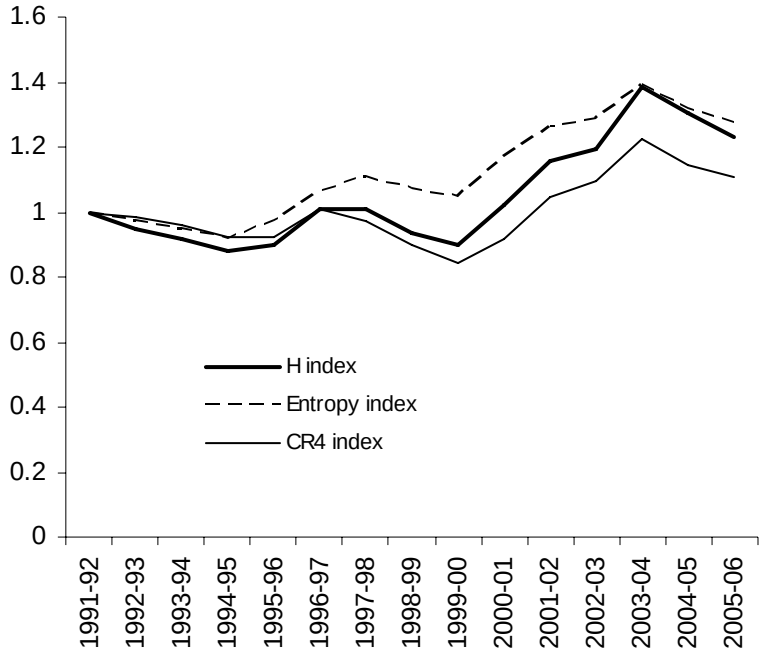


Table 14 Concentration indexes for the PBS, 1991-92 to 2005-06 ATC1 level

	H index		Entropy		CR4	
	Weighted	Unweighted	Weighted	Unweighted	Weighted	Unweighted
1991-92	1667.9	2245.8	0.1091	0.1456	64.7	71.7
1992-93	1566.5	1999.3	0.1075	0.1371	65.9	72.7
1993-94	1474.4	1886.7	0.1014	0.1300	65.0	71.7
1994-95	1393.3	1843.7	0.0969	0.1262	63.2	70.8
1995-96	1385.4	1811.8	0.0981	0.1275	63.8	71.7
1996-97	1352.9	1768.1	0.0962	0.1247	61.7	69.9
1997-98	1329.3	1830.3	0.0953	0.1304	59.4	70.0
1998-99	1289.2	1757.9	0.0923	0.1263	58.4	68.8
1999-00	1263.5	1708.6	0.0911	0.1239	58.6	69.1
2000-01	1537.6	1882.4	0.1067	0.1356	62.4	70.8
2001-02	1574.0	1848.9	0.1105	0.1354	64.3	71.3
2002-03	1619.9	1903.8	0.1126	0.1392	65.7	73.0
2003-04	1594.3	1903.0	0.1119	0.1399	65.9	73.7
2004-05	1479.5	1827.1	0.1046	0.1354	64.2	72.9
2005-06	1400.2	1776.6	0.0992	0.1319	61.0	71.3

Figure 4 Concentration indexes for the PBS, 1991-92 to 2005-06 ATC1 level

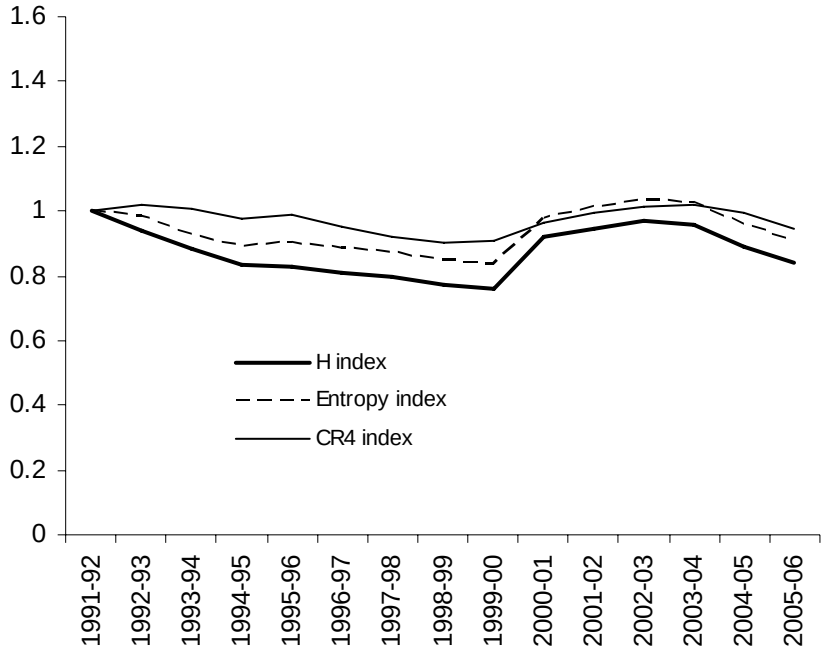


Table 15 Concentration indexes for the PBS, 1991-92 to 2005-06 ATC3 level

	H index		Entropy		CR4	
	Weighted	Unweighted	Weighted	Unweighted	Weighted	Unweighted
1991-92	3367.7	5419.6	0.2657	0.4748	87.0	94.5
1992-93	3284.1	5308.4	0.2582	0.4583	87.3	94.7
1993-94	3165.5	5266.4	0.2449	0.4508	86.6	94.6
1994-95	3025.0	5155.0	0.2354	0.4383	85.6	94.0
1995-96	2955.7	5177.4	0.2300	0.4409	85.4	94.1
1996-97	2828.6	4981.1	0.2202	0.4289	84.5	93.5
1997-98	2753.7	4912.0	0.2137	0.4264	82.7	93.3
1998-99	2664.9	4873.5	0.2066	0.4256	81.9	92.5
1999-00	2629.3	4855.3	0.2030	0.4294	82.1	92.2
2000-01	3028.0	4990.5	0.2297	0.4359	83.8	93.1
2001-02	2871.4	4849.6	0.2197	0.4206	83.7	92.6
2002-03	2830.1	4707.3	0.2182	0.4121	84.1	92.9
2003-04	2789.3	4938.0	0.2173	0.4356	84.1	92.7
2004-05	2692.9	4903.5	0.2075	0.4312	83.6	92.4
2005-06	2599.8	4812.2	0.1950	0.4199	82.3	91.9

Figure 5 Concentration indexes for the PBS, 1991-92 to 2005-06 ATC3 level

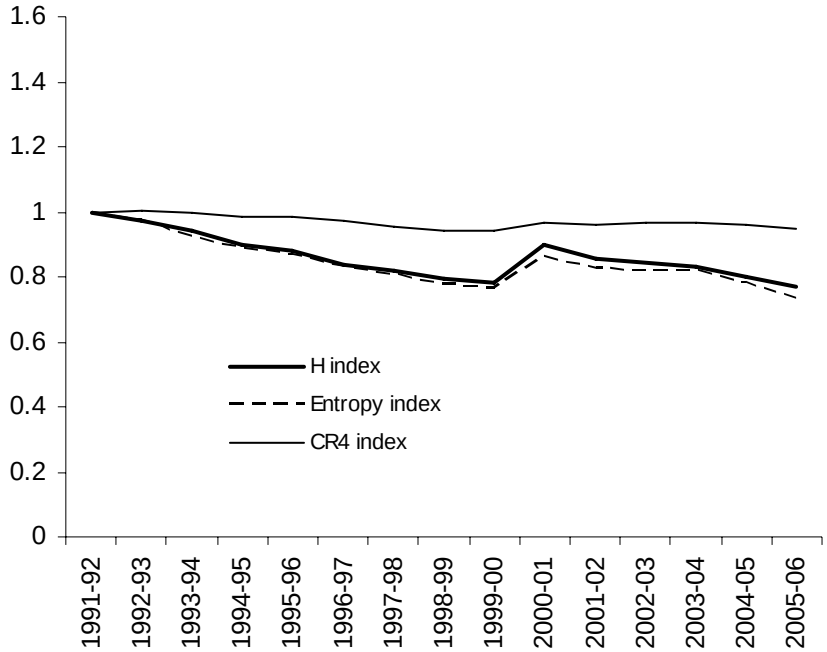


Table 16 Concentration indexes for the PBS, 1991-92 to 2005-06 ATC4 level

	H index		Entropy		CR4	
	Weighted	Unweighted	Weighted	Unweighted	Weighted	Unweighted
1991-92	4576.1	6283.5	0.3935	0.5710	95.6	97.9
1992-93	4465.3	6263.1	0.3764	0.5653	95.5	98.0
1993-94	4279.8	6219.3	0.3542	0.5576	94.7	97.9
1994-95	4075.5	6094.6	0.3374	0.5465	93.6	97.5
1995-96	3911.2	6112.1	0.3233	0.5476	93.0	97.6
1996-97	3676.4	5948.9	0.3027	0.5335	91.4	97.2
1997-98	3519.4	5845.4	0.2900	0.5302	89.3	97.0
1998-99	3374.4	5872.0	0.2785	0.5332	88.7	96.8
1999-00	3358.1	5877.3	0.2745	0.5348	88.7	96.6
2000-01	3767.0	5918.2	0.3027	0.5370	90.3	96.9
2001-02	3632.4	5796.6	0.2936	0.5242	90.4	96.7
2002-03	3563.4	5753.2	0.2886	0.5213	90.6	96.7
2003-04	3523.6	5874.7	0.2855	0.5347	90.5	96.6
2004-05	3437.1	5896.6	0.2755	0.5353	89.9	96.4
2005-06	3348.8	5806.0	0.2622	0.5248	88.5	96.2

Figure 6 Concentration indexes for the PBS, 1991-92 to 2005-06 ATC4 level

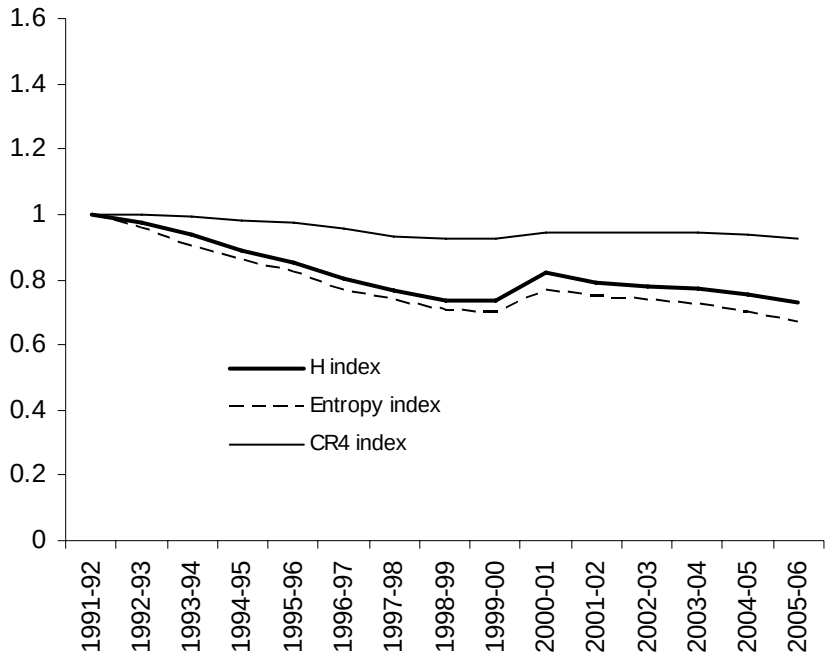


Table 17 Concentration indexes for the PBS, 1991-92 to 2005-06 ATC5 level

	H index		Entropy		CR4	
	Weighted	Unweighted	Weighted	Unweighted	Weighted	Unweighted
1991-92	6238.2	7898.0	0.5689	0.7524	99.2	99.6
1992-93	6091.5	7923.0	0.5521	0.7546	98.7	99.6
1993-94	5977.2	7821.2	0.5372	0.7442	98.0	99.6
1994-95	5729.8	7627.7	0.5109	0.7245	97.4	99.5
1995-96	5600.0	7627.4	0.4960	0.7217	96.9	99.5
1996-97	5334.6	7366.1	0.4682	0.6906	96.2	99.5
1997-98	5069.6	7322.9	0.4415	0.6905	95.1	99.4
1998-99	4823.6	7232.6	0.4240	0.6821	95.1	99.3
1999-00	4738.7	7191.3	0.4136	0.6777	95.2	99.2
2000-01	5085.7	7208.1	0.4479	0.6805	96.6	99.3
2001-02	4828.1	7069.0	0.4276	0.6651	96.4	99.2
2002-03	4751.5	7167.5	0.4177	0.6738	96.1	99.0
2003-04	4704.6	7214.9	0.4090	0.6783	95.9	99.0
2004-05	4635.2	7272.8	0.3967	0.6832	95.7	98.9
2005-06	4583.1	7215.2	0.3865	0.6784	94.3	98.7

Figure 7 Concentration indexes for the PBS, 1991-92 to 2005-06 ATC5 level

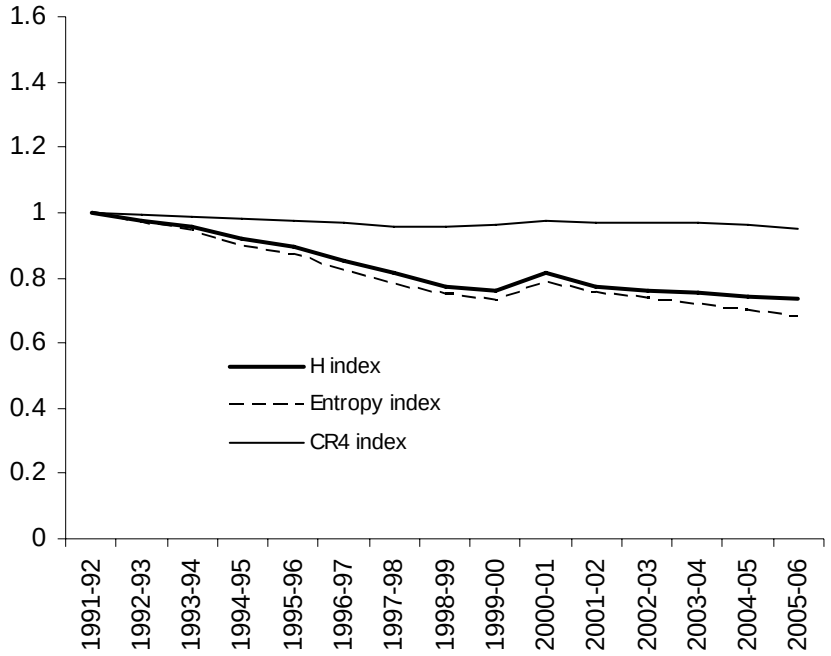


Table 28 Specialisation indexes for the PBS, 1991-92 to 2005-06

	Weighted				Unweighted			
	ATC1	ATC3	ATC4	ATC5	ATC1	ATC3	ATC4	ATC5
1991-92	0.595	0.783	0.842	0.890	0.744	0.902	0.931	0.974
1992-93	0.605	0.782	0.836	0.884	0.770	0.917	0.929	0.987
1993-94	0.602	0.776	0.828	0.878	0.743	0.885	0.928	0.954
1994-95	0.595	0.774	0.823	0.876	0.738	0.880	0.922	0.950
1995-96	0.580	0.765	0.811	0.868	0.739	0.881	0.918	0.946
1996-97	0.545	0.736	0.780	0.848	0.734	0.873	0.908	0.941
1997-98	0.527	0.714	0.759	0.834	0.721	0.863	0.896	0.933
1998-99	0.530	0.719	0.765	0.839	0.724	0.863	0.894	0.935
1999-00	0.537	0.725	0.773	0.839	0.735	0.869	0.899	0.935
2000-01	0.534	0.720	0.769	0.836	0.743	0.876	0.907	0.942
2001-02	0.522	0.704	0.754	0.817	0.751	0.880	0.910	0.943
2002-03	0.527	0.701	0.751	0.812	0.764	0.887	0.916	0.946
2003-04	0.491	0.677	0.724	0.785	0.756	0.886	0.913	0.944
2004-05	0.491	0.681	0.728	0.790	0.754	0.886	0.913	0.943
2005-06	0.488	0.669	0.719	0.779	0.759	0.885	0.911	0.939

Figure 9 Average specialisation indexes for the PBS, 1991-92 to 2005-06 Unweighted

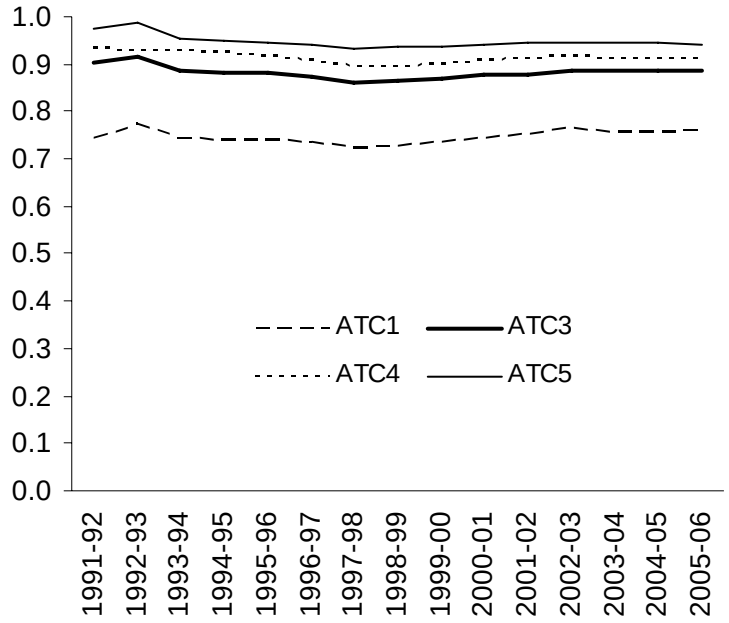
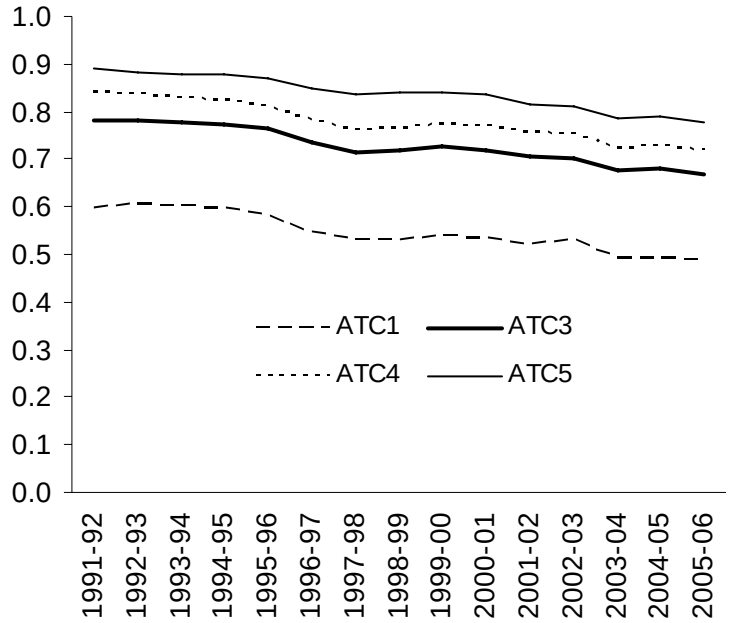


Figure 10 Average specialisation indexes for the PBS, 1991-92 to 2005-06 Weighted



Appendix 3 Regression Results for Concentration and Specialisation Indexes

Table 20 Regression results for H index, linear

a. with ATC dummy variables

ATC level	ATC1		ATC3		ATC4		ATC5	
	Coeff	t-stat	Coeff	t-stat	Coeff	t-stat	Coeff	t-stat
constant	3886.4	10.9	10329.6	31.8	10428.1	34.8	10791.1	21.3
year	-31.3	-3.5	-10.9	-1.2	0.3	0.0	-8.2	-1.9
nsup	-70.7	-5.3	-330.6	-16.4	-431.4	-24.7	-740.3	-45.4
Adjusted R^2	0.646		0.805		0.829		0.811	
D-W	0.478		0.579		0.669		0.645	
n	210		1111		2245		4620	

b. without ATC dummy variables

ATC level	ATC1		ATC3		ATC4		ATC5	
	Coeff	t-stat	Coeff	t-stat	Coeff	t-stat	Coeff	t-stat
constant	3638.0	22.7	7848.3	61.6	8560.6	92.7	9919.6	168.9
year	-29.7	-2.8	1.6	0.1	10.2	1.1	-2.6	-0.4
nsup	-64.4	-12.9	-373.1	-40.3	-553.1	-53.3	-884.3	-78.8
Adjusted R^2	0.442		0.596		0.559		0.577	
D-W	0.281		0.263		0.252		0.278	
Pedroni tests	3/11		10/11		10/11		11/11	

Table 21 Regression results for H index, logarithmic

a. with ATC dummy variables

ATC level	ATC1		ATC3		ATC4		ATC5	
	Coeff	t-stat	Coeff	t-stat	Coeff	t-stat	Coeff	t-stat
constant	10.332	25.2	9.435	164.6	9.382	179.6	92.65	119.3
year	-0.016	-4.1	-0.006	-4.2	-0.005	-4.6	-0.002	-3.6
lnsup	-0.841	-6.7	-0.513	-24.5	-0.420	-31.2	-0.437	-54.0
Adjusted R^2	0.751		0.870		0.850		0.828	
D-W	0.414		0.613		0.633		0.676	
n	210		1111		2245		4620	

b. without ATC dummy variables

ATC level	ATC1		ATC3		ATC4		ATC5	
	Coeff	t-stat	Coeff	t-stat	Coeff	t-stat	Coeff	t-stat
constant	10.407	56.9	9.368	368.8	9.288	620.8	9.229	1171.8
year	-0.017	-3.6	-0.005	-2.4	-0.003	-2.6	-0.001	-1.7
lnsup	-0.916	-16.5	-0.575	-55.7	-0.539	-74.7	-0.496	-101.5
Adjusted R^2	0.566		0.738		0.715		0.693	
D-W	0.229		0.295		0.337		0.368	
Pedroni tests	2/11		9/11		11/11		10/11	

Table 22 Regression results for number of suppliers, ATC1 level

a. linear specification

	Coeff	t-stat	Coeff	t-stat
constant	5.954	2.2	4.942	1.4
year	-0.435	-5.5	-0.326	-6.8
sizeop	0.015	4.4		
mol	0.252	12.3	0.357	12.6
prmolop	11.320	4.1	14.672	4.7
atc dummies	no		yes	
Adjusted R^2	0.777		0.948	
D-W	0.170		0.634	
Pedroni tests	7/11			
n	210		210	

b. logarithmic specification

	Coeff	t-stat	Coeff	t-stat
constant	1.725	21.7	-0.472	-1.1
year	-0.022	-6.3	-0.023	-7.6
lsize	0.171	8.0	0.126	4.2
lmol	0.255	6.9	0.491	8.2
lprsizeop	0.161	3.5	0.106	2.9
lprmolop	0.350	2.9	0.226	1.8
atc dummies	no		yes	
Adjusted R^2	0.755		0.943	
Pedroni tests	9/11			
D-W	0.185		0.700	

Table 23 Regression results for number of suppliers, ATC3 level

a. linear specification

	Coeff	t-stat	Coeff	t-stat
constant	3.638	19.5	0.874	2.4
year	-0.055	-2.8	-0.001	-0.1
mol	0.340	10.5	0.567	18.3
size	0.009	7.3	0.003	3.4
molop	0.095	2.4	0.181	3.3
sizeop	0.029	8.9		
atc dummies	no		yes	
Adjusted R^2	0.773		0.946	
Pedroni tests	9/11			
D-W	0.141		0.501	
n	1111		1111	

b. logarithmic specification

	Coeff	t-stat	Coeff	t-stat
constant	0.424	10.8	0.294	4.2
year	-0.005	-2.1	-0.001	-0.6
lmol	0.612	40.3	0.735	29.1
lsize	0.101	17.7	0.048	8.4
prsizeop	0.211	6.6	0.081	2.1
atc dummies	no		yes	
Adjusted R^2	0.842		0.946	
Pedroni tests	9/11			
D-W	0.191		0.536	

Table 24 Regression results for number of suppliers, ATC4 level

a. linear specification

	Coeff	t-stat	Coeff	t-stat
constant	1.523	14.8	0.461	1.5
year	0.005	0.5	0.036	6.1
mol	0.509	20.8	0.519	19.8
size	0.005	6.1	0.002	2.9
molop	0.253	8.1	0.318	6.8
sizeop	0.033	13.7	0.009	4.9
atc dummies	no		yes	
Adjusted R^2	0.717		0.915	
Pedroni tests	8/11			
D-W	0.174		0.512	
n	2245		2245	

b. logarithmic specification

	Coeff	t-stat	Coeff	t-stat
constant	0.241	6.2	0.269	3.7
year	-0.001	0.5	0.005	4.1
lmol	0.604	42.9	0.655	30.3
lsize	0.118	25.9	0.057	11.7
prmolop	0.134	1.9		
prsizeop	0.198	3.3	0.099	3.1
atc dummies	no		yes	
Adjusted R^2	0.717		0.912	
Pedroni tests	10/11			
D-W	0.180		0.551	

Table 25 Regression results for number of suppliers, ATC5 level

a. linear specification

	Coeff	t-stat	Coeff	t-stat
constant	0.471	8.6	0.097	0.2
year	0.021	4.2	0.039	11.9
mol	0.779	34.8	0.750	24.3
size			0.002	3.0
molop	0.299	11.4	0.236	5.7
sizeop	0.048	33.3	0.014	8.8
atc dummies	no		yes	
Adjusted R^2	0.574		0.842	
Pedroni tests	8/11			
D-W	0.207		0.435	
n	4620		4620	

b. logarithmic specification

	Coeff	t-stat	Coeff	t-stat
constant	0.071	3.5	0.114	0.9
lmol	0.700	51.3	0.757	41.4
lsize	0.102	35.3	0.042	11.8
prmolop	0.231	3.9	0.286	10.0
prsizeop	0.192	3.5		
atc dummies	no		yes	
Adjusted R^2	0.590		0.854	
Pedroni tests	9/11			
D-W	0.201		0.546	

Table 29 Regressions for specialisation index, linear

a. without company dummies

ATC level	ATC1		ATC3		ATC4		ATC5	
	Coeff	t-stat	Coeff	t-stat	Coeff	t-stat	Coeff	t-stat
constant	0.9744	92.6	0.9834	252.6	0.9791	282.9	0.9974	305.5
year	-0.0029	-3.1			0.0006	1.7		
size			-0.1692	-4.9	-0.2923	-15.6	-0.2942	-9.3
markets	-0.0475	-40.6	-0.0126	-27.7	-0.0060	-34.9	-0.0031	-13.4
Adjusted R^2	0.587		0.579		0.763		0.385	
D-W	0.165		0.206		0.167		0.210	

b. with company dummies

ATC level	ATC1		ATC3		ATC4		ATC5	
	Coeff	t-stat	Coeff	t-stat	Coeff	t-stat	Coeff	t-stat
constant	0.8842	27.8	0.9605	45.0	0.9738	66.2	0.9706	58.8
year	-0.0017	-3.3			-0.0009	-3.2		
size			-0.0676	-2.8	-0.1136	-6.3	-0.1725	-8.4
markets	-0.0332	-17.9	-0.0107	-19.9	-0.0056	-21.9	-0.0029	-12.2
Co dummies								
Adjusted R^2	0.920		0.921		0.926		0.914	
D-W	0.867		1.200		0.560		1.700	

Table 30 Regressions for specialisation index, logarithmic

a. without company dummies

ATC level	ATC1		ATC3		ATC4		ATC5	
	Coeff	t-stat	Coeff	t-stat	Coeff	t-stat	Coeff	t-stat
constant	-0.0323	-1.2	0.0611	8.4	0.0551	9.4	0.0269	2.5
year	-0.0063	-4.7	-0.0047	-7.1	-0.0043	-8.0	-0.0033	-6.3
lsize	-0.0050	-2.1					-0.0028	-3.0
lmarkets	-0.2649	-28.6	-0.1192	-48.0	-0.0796	-43.1	-0.0466	-18.0
Adjusted R^2	0.625		0.666		0.618		0.455	
D-W	0.185		0.182		0.159		0.126	

b. with company dummies

ATC level	ATC1		ATC3		ATC4		ATC5	
	Coeff	t-stat	Coeff	t-stat	Coeff	t-stat	Coeff	t-stat
constant	-0.1777	-3.1	-0.0173	-0.6	-0.0062	-0.3	-0.0056	-0.3
year	-0.0030	-3.3	-0.0025	-5.4	-0.0029	-7.4	-0.0020	-6.8
lsize	-0.0047	-1.9						
lmarkets	-0.2029	-14.5	-0.1113	-21.9	-0.0798	-20.5	-0.0517	-18.4
Co dummies								
Adjusted R^2	0.892		0.897		0.880		0.888	
D-W	0.631		0.639		0.555		0.671	

Acronyms

ABS	Australian Bureau of Statistics
ACCC	Australian Competition and Consumer Commission
ADEC	Australian Drug Evaluation Committee
ANDA	Abbreviated New Drug Application
ARTG	Australian Register of Therapeutic Goods
ATC	Anatomical Therapeutic Classification
BEACH	Bettering the Evaluation and Care of Health
CHMP	Committee for Medicinal Products for Human Use
COAG	Council of Australian Governments
CR	Concentration ratio
CRO	Clinical Research Organisation
CSES	Centre for Strategic Economic Studies
CTN	Clinical Trials Notification
DITR	Department of Industry, Tourism and Resources
DoHA	Department of Health and Ageing
EMEA	European Medicines Agency
EU	European Union
FDA	US Food and Drug Administration
IMS	IMS Health
IND	Investigational New Drug
NDA	New Drug Application
NHS	National Health Survey
OLS	Ordinary least squares
OTC	Over-the-counter
PBAC	Pharmaceutical Benefits Advisory Committee
PBPA	Pharmaceutical Benefits Pricing Authority
PBS	Pharmaceutical Benefits Scheme
PIP	Pharmaceutical Industry Project (CSES)
RANZCP	Royal Australian and New Zealand College of Psychiatrists
RPBS	Repatriation Pharmaceutical Benefits Scheme
RPG	Reference Pricing Groups
TGA	Therapeutic Goods Administration
WHO	World Health Organisation