The socio-economic shaping of minor tranquillizer use with particular reference to Australia [manuscript]

Vivien Colless  
University of Wollongong

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---------------------------
Vivien Colless
I sleep comfortably and I have never taken even one of our tranquillizers

Adolf W. Jann
Chairman & President, Roche
Business Week, 16 June 1975, p.51

I consider myself well-balanced and therefore do not need minor tranquillizers

Otto Nowotny
Roche executive
Bulletin, 1 September 1973, p.61

"I've told you many times, Miss Gordon", he said with a hint of impatience, "they are non-addictive and do a great deal to help you"

Doctor to Barbara Gordon
I'm Dancing As Fast As I Can, p.49
ACKNOWLEDGEMENTS

I wish to thank Ev Richards for her invaluable supervision during the progress of my work. Her generosity of time, enthusiasm and support gave me the intellectual challenges and confidence necessary to complete this project.

There are many others whose support and encouragement have been vital contributions to my work. They include: the late Ian Langham, whose inspired teaching stimulated my interest in science and technology studies, and whose guidance and support helped my transition from science into the study of science; Kaye Brock, who helped foster my initial interest in the social aspects of science; Katherine Ingram, who guided me through my political awakening; Barbara Sullivan, who suggested the topic of research; and Louise Pople, who lightened my load of day-to-day responsibilities and in many other ways gave me the support I needed throughout this project.
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14c
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<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>AANA</td>
<td>Australian Association of National Advertisers</td>
</tr>
<tr>
<td>ACA</td>
<td>Australian Consumers' Association</td>
</tr>
<tr>
<td>ADEC</td>
<td>Australian Drug Evaluation Committee</td>
</tr>
<tr>
<td>AIDC</td>
<td>Australian Industry Development Corporation</td>
</tr>
<tr>
<td>AMA</td>
<td>Australian Medical Association</td>
</tr>
<tr>
<td>APMA</td>
<td>Australian Pharmaceutical Manufacturers' Association</td>
</tr>
<tr>
<td>BMA</td>
<td>British Medical Association</td>
</tr>
<tr>
<td>CHF</td>
<td>Consumer Health Forum</td>
</tr>
<tr>
<td>CSL</td>
<td>Commonwealth Serum Laboratories</td>
</tr>
<tr>
<td>DHSS</td>
<td>Department of Health &amp; Social Security</td>
</tr>
<tr>
<td>EEC</td>
<td>European Economic Community</td>
</tr>
<tr>
<td>FDA</td>
<td>Food and Drug Administration</td>
</tr>
<tr>
<td>IAC</td>
<td>Industries Assistance Commission</td>
</tr>
<tr>
<td>NBSL</td>
<td>National Biological Standards Laboratory</td>
</tr>
<tr>
<td>NCADA</td>
<td>National Campaign Against Drug Abuse</td>
</tr>
<tr>
<td>NHS</td>
<td>National Health Scheme</td>
</tr>
<tr>
<td>PBAC</td>
<td>Pharmaceutical Benefits Advisory Committee</td>
</tr>
<tr>
<td>PBPA</td>
<td>Pharmaceutical Benefits Pricing Authority</td>
</tr>
<tr>
<td>PBPP</td>
<td>Pharmaceutical Benefits Pricing Bureau</td>
</tr>
<tr>
<td>PBS</td>
<td>Pharmaceutical Benefits Scheme</td>
</tr>
<tr>
<td>R &amp; D</td>
<td>Research and Development</td>
</tr>
<tr>
<td>SMH</td>
<td>Sydney Morning Herald</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
</tbody>
</table>
This study analyzes the economic, political and social forces which shape minor tranquillizer use in contemporary Western industrialised societies, with particular reference to Australia.

It exposes fundamental contradictions and weaknesses in medical knowledge and practice and the unresolved conflicts revolving around the medical profession's strong attachment to a biomedical model and its neglect of the socio-economic dimensions of illness. These and other factors are discussed which continually challenge, as well as support, the power of the medical profession and the nature of the doctor-patient relationship. It is argued that the patient, or health consumer, whose health is directly affected by this technology, has a vital role to play in its control, especially in the valuable contribution made by the women's movement.

The difficulties in confronting and curbing the excess profits and global power of the drug industry in maintaining tranquillizer sales, are outlined. Finally, some examples are given of how state intervention in Britain and Australia has shaped the increasing bureaucratization of medicine and the drug industry, and played an important role in a shifting balance of power between the interested groups.
The prototype benzodiazepines, chlordiazepoxide (Librium) and diazepam (Valium), were introduced and marketed in the early 1960s by the Swiss-based transnational pharmaceutical company, Hoffmann-La Roche. They were hailed as a significant technological innovation within the group of pharmaceutical drugs known as 'minor' tranquillizers and were promoted as 'wonder drugs' of remarkable safety and efficacy, able to "make even fierce wildcats turn as tame and playful as kittens" when tested at the zoo.

Since then the benzodiazepines have had a chequered history. Their widespread and uncritical promotion and acceptance peaked during the 1970s when Valium became the single most-prescribed drug in the United States (closely followed by Librium). In Australia, Valium was the most prescribed single item under the Pharmaceutical Benefits Scheme (PBS) in the first half of the 1970s, dropping to second place in 1976-1977. Meanwhile, Roche's inflationary and transfer-pricing tactics in relation to these two best-sellers (considered to be the most profitable pharmaceuticals ever produced) were exposed by a number of international enquiries. At the same time, concern mounted over their over-prescribing and addiction potential (even at normal dosage levels), and their efficacy in relieving anxiety was called into question. Valium was targeted by various consumer action and women's movement groups, and a concerted campaign was mounted against its use (especially by women, who have been consistently shown to be the major consumers of benzodiazepines).

In the 1980s, its increasing notoriety has led to a decline in Valium sales, but benzodiazepine sales have continued to escalate. Surveys and prescription audits have demonstrated that although Valium
is no longer the drug of choice, a plethora of other 'me too' benzodiazepines are taking its place. In Australia, benzodiazepines now lead the cases of reported drug poisonings, with double the number of mentions compared with alcohol.

This study is an attempt to explain the phenomenon of the benzodiazepines through an examination of their promotion and use in the context of the economic, social and political forces located in the interactions between the four major interested parties: the medical profession, the consumers, the drug industry, and the state.

Chapter 1 presents a brief history of the development of benzodiazepines and describes their pharmacological action and relationship with other tranquilizers and mood-changing drugs. By reference to the two major methods of data collection, surveys and prescription audits, the changing patterns of benzodiazepine use are presented.

Chapter 2 summarizes the debate in the medical-scientific literature over the efficacy and safety of benzodiazepines. The range of medical opinion on their recommended use is summarized. Conflict over their efficacy has centred on their alleged anti-anxiety activity. This has been exacerbated by problems surrounding the medical definition and measurement of anxiety, which is outlined. The long-held claim of a low mortality rate for the benzodiazepines is the first safety issue examined, followed by depression of the central nervous system (an expected side-effect associated with tranquilizers) and the debate on other unwanted effects on the foetus, the newborn and the elderly. The primary area of conflict over safety of the benzodiazepines is their addiction potential. An outline is given of medicine's efforts to define addiction and the withdrawal symptoms of benzodiazepine
addiction. This includes a summary of the debate on dosage, length of
time of use and different pharmacokinetic properties of benzodiazepines
as well as psychological and other non-technological factors. The
debate on addiction concludes with an examination of methods used for
detecting benzodiazepine addiction. The chapter ends with a brief
reference to other safety issues.

The next two chapters (3 and 4) examine the intersections amongst
the four major interested parties. Chapter 3 focuses on the medical
profession and the health consumer; whereas Chapter 4 examines the drug
industry and the state. This has been done for ease of analysis rather
than to imply any separation of effects between the four groups.

Chapter 3 develops the analysis of the medical-scientific debate
in the previous chapter. The conflict over benzodiazepine safety and
efficacy serves to identify medicine's difficulties with its biomedical
model of illness and this is exacerbated in the area of addiction. A
comprehensive description is then provided of the major consumers of
minor tranquillizers according to gender, age, health status and
institutional environment. This concentrates on women's greater use of
benzodiazepines and includes an analysis of the five most commonly used
explanatory models. The role of the doctor in prescribing
benzodiazepines is then examined, with reference to the influential
factors of medical education and the professionalization process. The
chapter ends with a description of the important role of the consumer
health movement in shaping tranquillizer use.

Chapter 4 introduces the drug industry, with an overview of its
global nature and high profitability. Both domestic and international
factors important to the outstanding financial performance of the drug
industry and its manufacture of the benzodiazepines are then outlined,
and include patent protection, research and development and promotion of their products. This is followed by an outline of the role of the state in enforcing controls over the drug industry on drug safety and efficacy, and the resultant effect of drug lag as well as some important issues concerning generics. Finally, two case studies are presented to illustrate the preceding discussions. Both are historical accounts concerning the benzodiazepines. The first outlines the British attempt to introduce a limited drug list in 1985 which highlights the various economic and political forces shaping the availability of benzodiazepines in that country. The second case study describes Roche's controversial use of transfer pricing strategies to increase its already unprecedented financial returns from the benzodiazepines and the largely ineffectual attempt by the British state to regulate the company's activities in the 1970s. Some theoretical implications of the relationship between the drug industry and the state are discussed in the conclusion.

Chapter 5 is an historical outline of socio-economic factors important to minor tranquillizer use in Australia and builds on the analysis developed in the previous chapters. The chapter opens with details of early post-war initiatives by the state which later were crucial to benzodiazepine use, including the establishment and development of the Prescription Benefits Scheme (PBS), as well as the introduction and strengthening of other important state controls on drug sales in Australia. The outstanding sales record of Valium following its release and listing on the PBS in 1972 is described, followed by the attempt by the Whitlam government to curb the drug industry in Australia. The conflict between the state and Roche (and the rest of the drug industry) is detailed, especially during 1973. The
changing pattern of benzodiazepine sales during the late 1970s is then described, followed by an outline of the Ralph Report's investigation into the Australian drug industry and the important role of the PBS. Various developments in the early 1980s are listed, including the continuing development of benzodiazepines by the drug industry and their changing patterns of use in the community, the drug industry's continuing call for state support and the consumer movement's campaign against drug advertising.

The Hawke government's response to the Australian drug industry is described, beginning with its efforts to curb the rising state drug bill. The other strategy of the Hawke government is then examined - the National Campaign Against Drug Abuse - a small part of which has been directed against women's use of minor tranquillizers. The erosion of doctors' professional power, both within the state and the community, is next discussed, followed by an account of the strengthening health consumer movement (especially the contribution of the women's movement) and the implications of these developments for minor tranquillizer use. The final section summarises the shifting power balance in Australia between the state, the drug industry, the medical profession and the consumer interest groups and their relevance to minor tranquillizer use. Some important contemporary critiques of the medical profession and the role of the state in health and medicine relevant to minor tranquillizer use, are then discussed.

Chapter 6 reviews and summarises the key economic, social, and political elements discussed in this study which have contributed to the changing pattern of benzodiazepine use, both in Australia and internationally. It concludes with some suggested strategies for change and emphasizes the crucial importance of gender issues.
FOOTNOTE:
1 BENZODIAZEPINES: A DESCRIPTION AND HISTORY OF THEIR USE

1.1 Historical Introduction

The use of tranquillizers as a treatment for anxiety has a long history; alcohol is, perhaps, the best known and most widely used in the Western world. Table 1.1 lists examples of commonly used mood-changing drugs, including the tranquillizers. During the first half of this century, medical intervention in the treatment of anxiety consisted mainly of prescribing sedatives such as bromides and barbiturates. The first barbiturate was introduced in about 1902 (barbitone, marketed as Veronal by Fischer and von Mering) and other barbiturates began to compete on the market in the following years: for example, phenobarbitone (Luminal) in 1912 and amylobarbitone (Amytal) in 1923. As the dangers of overdose and dependence associated with barbiturates became more widely recognised, alternative pharmacological treatments were sought such as the propanediols introduced in the 1950s, the best known being meprobamate (Miltown).

The first commercially available benzodiazepine was chlordiazepoxide (Librium) which was approved for marketing in 1960 in the United States by the Food and Drug Administration (FDA). Originally known as methaminodiazepoxide (or Ro 5-0690), chlordiazepoxide was first synthesised in 1955 by the chemist, Leo H. Sternbach, and his associates at the Roche laboratories. However, because it had been mistakenly assumed to be inert, its development by Roche was delayed until 1957 when their pharmacologist, Lowell O. Randall, found it had sedative and anti-convulsant activity in animals. According to Randall, chlordiazepoxide was:

2 to 10 times more potent than meprobamate ... Unlike meprobamate, it is more effective by the oral than by the subcutaneous route. An outstanding feature of the behavioral action of (chlordiazepoxide) is the wide dose
<table>
<thead>
<tr>
<th>Group</th>
<th>Generic Name</th>
<th>Example of Brand Name</th>
</tr>
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<tbody>
<tr>
<td>1. &quot;Major&quot; Tranquillizers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a) Substituted Phenothiazines</td>
<td>chlorpromazine</td>
<td>Largactil</td>
</tr>
<tr>
<td></td>
<td>trifluoperazine</td>
<td>Stelazine</td>
</tr>
<tr>
<td></td>
<td>perphenazine</td>
<td>Trilafon</td>
</tr>
<tr>
<td></td>
<td>fluphenazine</td>
<td>Anatensol</td>
</tr>
<tr>
<td></td>
<td>thioridazine</td>
<td>Mellaril</td>
</tr>
<tr>
<td>(b) Butyrophenones</td>
<td>haloperidol</td>
<td>Serenace</td>
</tr>
<tr>
<td></td>
<td>pimozide</td>
<td>Orap</td>
</tr>
<tr>
<td>2. &quot;Minor&quot; Tranquillizers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a) Barbiturates</td>
<td>thiopentone</td>
<td>Pentothal</td>
</tr>
<tr>
<td></td>
<td>amylobarbitone</td>
<td>Amytal</td>
</tr>
<tr>
<td></td>
<td>butobarbitone</td>
<td>Soneryl</td>
</tr>
<tr>
<td></td>
<td>cyclobarbitone</td>
<td>Placyl</td>
</tr>
<tr>
<td></td>
<td>pentobarbitone</td>
<td>Nembutal</td>
</tr>
<tr>
<td></td>
<td>quinalbarbitone</td>
<td>Seconal</td>
</tr>
<tr>
<td></td>
<td>phenobarbitone</td>
<td>Luminal</td>
</tr>
<tr>
<td>(b) Benzodiazepines</td>
<td>chlordiazepoxide</td>
<td>Librium</td>
</tr>
<tr>
<td></td>
<td>diazepam</td>
<td>Valium</td>
</tr>
<tr>
<td></td>
<td>nitrazepam</td>
<td>Mogadon</td>
</tr>
<tr>
<td></td>
<td>oxazepam</td>
<td>Serepax</td>
</tr>
<tr>
<td>(c) Miscellaneous</td>
<td>chloral hydrate</td>
<td>Noctec</td>
</tr>
<tr>
<td></td>
<td>methaqualone</td>
<td>Mandrax</td>
</tr>
<tr>
<td></td>
<td>L-tryptophan</td>
<td>Trypto-Sleep (prescription not necessary)</td>
</tr>
<tr>
<td>3. Anti-Depressants</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a) &quot;Tricyclics&quot;</td>
<td>imipramine</td>
<td>Tofranil</td>
</tr>
<tr>
<td></td>
<td>desipramine</td>
<td>Pertofran</td>
</tr>
<tr>
<td></td>
<td>amitriptyline</td>
<td>Tryptanol</td>
</tr>
<tr>
<td></td>
<td>nortriptyline</td>
<td>Nortab</td>
</tr>
<tr>
<td></td>
<td>doxepin</td>
<td>Sinequan</td>
</tr>
<tr>
<td>(b) Monoamine oxidase inhibitors (MAOI)</td>
<td>iproniazid</td>
<td>Marsilid</td>
</tr>
<tr>
<td></td>
<td>isocarboxazid</td>
<td>Marplan</td>
</tr>
<tr>
<td></td>
<td>phenelzine</td>
<td>Nardil</td>
</tr>
<tr>
<td></td>
<td>tranylcypromine</td>
<td>Parnate</td>
</tr>
</tbody>
</table>

range over which it is effective without producing ataxia or other side effects. After screening hundreds of other benzodiazepines, diazepam (synthesised in 1959) was marketed by Roche in 1963. In tests published the following year, diazepam was said to be more effective than chlordiazepoxide, and since then diazepam has become probably the most commonly used drug in the Western world. Other benzodiazepines soon came on the market from different pharmaceutical manufacturers: for example, oxazepam (Serax/Serapax) in 1965 by Wyeth Pharmaceuticals and clorazepate dipotassium (Tranxene) in 1972 by Abbott Laboratories.

During the 1970s many more benzodiazepines became available. There was an increase in the number both of new benzodiazepine derivatives and of similar generic compounds manufactured by different drug companies under their own brand names. The former may be categorized as 'me too' drugs as they are of similar structure and function to diazepam, although slightly modified to circumvent patenting restrictions held by Roche. The latter are identical drugs manufactured after a patent has expired or, sometimes, made under licence from the patent holder. By 1983 there were at least twenty-five different benzodiazepines marketed worldwide.

Roche enjoyed a monopoly on diazepam sales in Australia until 1978 (although in 1976 another brand (Ducene) was marketed by Sauter Laboratories, a subsidiary of Roche). All competitors were forced to wait until after the patent lapsed in December 1978. In Australia, there are currently fourteen benzodiazepines available, marketed under twenty-seven different brand names by twelve different pharmaceutical companies (Table 1.2). Roche manufactures the largest number of benzodiazepines (8), then Alphapharm (5), Wyeth (3) and Protea (2). Not
Table 1.2: Benzodiazepines available in Australia in July 1988

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Most Commonly Prescribed As</th>
<th>Brand Name</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>alprazolam</td>
<td>anti-anxiety</td>
<td>Xanax</td>
<td>Upjohn</td>
</tr>
<tr>
<td>bromazepam</td>
<td>anti-anxiety</td>
<td>Lexotan</td>
<td>Roche</td>
</tr>
<tr>
<td>clobazam</td>
<td>anti-anxiety</td>
<td>Frisium</td>
<td>Hoechst</td>
</tr>
<tr>
<td>clonazepam</td>
<td>anti-convulsant</td>
<td>Rivotril</td>
<td>Roche</td>
</tr>
<tr>
<td>clorazepate dipotassium</td>
<td>anti-anxiety</td>
<td>Tranxene</td>
<td>Glaxo</td>
</tr>
<tr>
<td>chlordiazepoxide</td>
<td>anti-anxiety</td>
<td>Librium</td>
<td>Roche</td>
</tr>
<tr>
<td>diazepam</td>
<td>anti-anxiety, muscle relaxant</td>
<td>Antenex, Diazepam (inj) Diazepam (inj) Ducene Pro-Pam Valium</td>
<td>Alphapharm Astra David Bull Sauter Protea Roche</td>
</tr>
<tr>
<td>flunitrazepam</td>
<td>sedative/hypnotic</td>
<td>Rohypnol, Hypnodorm</td>
<td>Roche Alphapharm</td>
</tr>
<tr>
<td>flurazepam</td>
<td>sedative/hypnotic</td>
<td>Dalmane</td>
<td>Roche</td>
</tr>
<tr>
<td>lorazepam</td>
<td>anti-anxiety,</td>
<td>Ativan</td>
<td>Wyeth</td>
</tr>
<tr>
<td>midazolam</td>
<td>sedative/hypnotic, anaesthesia, pre-op. med.</td>
<td>Hypnovel</td>
<td>Roche</td>
</tr>
<tr>
<td>nitrazepam</td>
<td>sedative/hypnotic</td>
<td>Alodorm, Dormicum Mogadon</td>
<td>Alphapharm Protea Roche</td>
</tr>
<tr>
<td>oxazepam</td>
<td>anti-anxiety</td>
<td>Alepam, Benzotran Murelax Serepax</td>
<td>Alphapharm Protea Ayerst Wyeth</td>
</tr>
<tr>
<td>temazepam</td>
<td>sedative/hypnotic</td>
<td>Euhypnos/Forte Normison Temaze</td>
<td>Sigma Wyeth Alphapharm</td>
</tr>
</tbody>
</table>

Source: Intercontinental Medical Statistics (Australasia) Pty Ltd, MIMS, 25, No.4, June/July 1988
all of these companies are independent of each other. As well as Sauter Laboratories being a subsidiary of Roche, Ayerst and Wyeth are subsidiaries of American Home Products.¹¹ Sixteen brands are available on both the Pharmaceutical Benefits Scheme (PBS) and the Repatriation Pharmaceutical Benefits Scheme (RPBS) whilst seven are available only on the RPBS and three are not subsidised by the state under either scheme. A comparison of the benzodiazepines available in Australia with those available in other countries shows that the number of different kinds of benzodiazepines is at a minimum in both Australia (14) and the United States (12), in contrast to Britain (20) or other countries such as Japan (21) (Table 1.3).

Because they were believed to be selective as anti-anxiety agents and sedatives without severe effects on the central nervous system, benzodiazepines were separated out as 'minor' tranquillizers, or sedatives, in contrast to the anti-psychotics, or 'major' tranquillizers (Table 1.1). A new term, 'anxiolytic', was coined in order to stress the selectivity of the minor tranquillizers.¹²

1.2 Pharmacological Description of Benzodiazepines

Benzodiazepines are chemically related compounds which can be generally characterised by their rate of elimination from the bloodstream: that is, whether they have a short, intermediate or long half-life (Table 1.4). Their differences become even less marked when their metabolic relationship, following ingestion, is examined, as many of them are broken down into the same metabolite (for example, desmethyldiazepam, which has a long half-life) (Figure 1.1).

Twenty-five years after their introduction on the market, the mechanism of action of the benzodiazepines is still not fully understood. During the 1970s they were found to affect almost every
Table 1.3: Benzodiazepines available in Australia and other selected industrialized countries (1984)

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Australia</th>
<th>USA</th>
<th>UK</th>
<th>Germany</th>
<th>Italy</th>
<th>Japan</th>
<th>France</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alprazolam</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>---</td>
<td>---</td>
<td>Yes</td>
</tr>
<tr>
<td>Bromazepam</td>
<td>Yes</td>
<td>---</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Camazepam</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>Yes</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Chlordiazepoxide</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Clorazepate</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Cloxazolam</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Delorazepam</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Diazepam</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Estazolam</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
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<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Ethyl loflazepate</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>Yes</td>
</tr>
<tr>
<td>Fludiazepam</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>Yes</td>
<td>---</td>
</tr>
<tr>
<td>Flunitrazepam</td>
<td>Yes</td>
<td>---</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Flurazepam</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Flutazolam</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Halazepam</td>
<td>---</td>
<td>Yes</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Haloxazolam</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Ketazolam</td>
<td>---</td>
<td>Yes</td>
<td>Yes</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Loprazolam</td>
<td>---</td>
<td>Yes</td>
<td>---</td>
<td>---</td>
<td>---</td>
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<td>---</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Lorbutazepam</td>
<td>---</td>
<td>---</td>
<td>Yes</td>
<td>Yes</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Medazepam</td>
<td>---</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Midazolam</td>
<td>---</td>
<td>Yes</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Nitrazepam</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>Yes</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Nordiazepam</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>Yes</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Oxazepam</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Oxazolam</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>Yes</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Pinazepam</td>
<td>---</td>
<td>---</td>
<td>---</td>
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<td>Yes</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Prazepam</td>
<td>---</td>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Temazepam</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Tetrazepam</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>Yes</td>
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<td>---</td>
</tr>
<tr>
<td>Tofisopam</td>
<td>---</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Triazolam</td>
<td>---</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

13 12 20 22 21 21 19

### Table 1.4: Elimination half-life of selected benzodiazepines

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Active Metabolite Formed</th>
<th>Elimination Half-Life</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>(long &gt; 50 hours)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(intermediate 10-50 hours)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(short &lt; 10 hours)</td>
</tr>
<tr>
<td>Chlordiazepoxide</td>
<td>Yes</td>
<td>Long</td>
</tr>
<tr>
<td>Diazepam</td>
<td>Yes</td>
<td>Long</td>
</tr>
<tr>
<td>Clorazepate</td>
<td>Yes</td>
<td>Long</td>
</tr>
<tr>
<td>Flurazepam</td>
<td>Yes</td>
<td>Long</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>No</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Clobazam</td>
<td>Yes</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Flunitrazepam</td>
<td>Yes</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Nitrazepam</td>
<td>Yes</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Bromazepam</td>
<td>Yes</td>
<td>Short-Intermediate</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>No</td>
<td>Short-Intermediate</td>
</tr>
<tr>
<td>Alprazolam</td>
<td>Yes</td>
<td>Short-Intermediate</td>
</tr>
<tr>
<td>Oxazepam</td>
<td>No</td>
<td>Short</td>
</tr>
<tr>
<td>Temazepam</td>
<td>No</td>
<td>Short</td>
</tr>
<tr>
<td>Midazolam</td>
<td>No</td>
<td>Ultra-Short</td>
</tr>
<tr>
<td>Triazolam</td>
<td></td>
<td>Ultra-Short</td>
</tr>
</tbody>
</table>

Figure 1.1: Metabolic relationship between some commonly-used benzodiazepines

chlordiazepoxide

↓

* desmethylchlordiazepoxide

* demoxepam

↓

clorazepate

diazepam

↓

* temazepam

* desmethyldiazepam

medazepam

* desmethyldiazepam

* oxazepam

glucuronic acid conjugate

elimination

* pharmacologically active metabolite

known neurotransmitter, including the catecholamines (acetylcholine, glycine and serotonin). More recently, medical opinion appears to favour the theory that benzodiazepines bind to specific receptor sites in the central nervous system, particularly in certain areas of the brain where they enhance the action of the inhibitory neurotransmitter, gamma-aminobutyric acid (GABA). The discovery in the late 1970s of specific binding sites in the brain, and other tissues, has led to the belief that there may be natural compounds made in the body similar to benzodiazepines, although these have not been identified.

The complexity of the human body and its emotional and physical interactions create problems in gaining an understanding of the mechanism of action of benzodiazepines. The widespread use of benzodiazepines without any clear understanding of how these drugs work, confirms the accepted practice which Chesher has pointed out:

despite the enormous number of potent drugs now available to the physician and in constant use, in only a few cases can it be said that we know how the drug is working.

1.3 Patterns of Benzodiazepine Use

The two common methods for measuring tranquillizer or benzodiazepine use focus either on the consumer (population surveys) or the prescription (prescription audits). As well as the usual methodological problems, care must be taken in analysing such data because of the confusing diversity in nomenclature of mood-changing drugs as well as the inclusion of both benzodiazepines and barbiturates within the minor tranquillizer group and the separate listing of benzodiazepines as tranquillizers or sedatives.
1.3.1 Surveys

American researchers carried out surveys in the early 1970s in Europe and the United States to find that between 10% and 17% of people reported using anti-anxiety and/or sedative drugs in the past year (12.5% to 21.5% women and 7% to 12% men) (Figure 1.2). In the European study, between 3.5% to 9% reported regular use (daily use for one month or more) and of these, 5% to 12% were women and 2% to 6.5% were men. When the American survey was repeated in 1979, reported minor tranquilizer use for the previous year had fallen from 15% to 11%. However, none of the data separated out benzodiazepines from other minor tranquilizers. Marks estimated that approximately 60% of the drugs were benzodiazepines in the earlier surveys compared with about 84% in the later American survey (that is, whilst reported use of minor tranquilizers had dropped, the proportion of benzodiazepines had increased - this was not measured).

Survey data collected in Australia during the 1970s give variable results and are also difficult to compare because of differences such as in methodology, survey population, class of drug examined, definition on rate of usage of drug. For example, a small survey carried out in 1971 by George in "a beach-side suburb of the North Shore of Sydney" found one-third of respondents reported having ever used tranquillizers and/or sedatives, whilst 5% said they used them daily. Her later 1973 survey carried out in a Western Suburb of Sydney gave a similar result as did the 1971 Canberra Mental Health Survey, which found 5% of women used tranquillizers daily. However, higher estimates have been found in other surveys. For example, a 1975 survey of Sydney members of a union found that 13% of women and 6% of men were daily users of tranquillizers or sedatives whilst a survey of Medicheck patients in Sydney in 1975
Figure 1.2: Comparison between men and women of use of anti-anxiety/sedative drug during previous year (used at least once)

found 19% of women and 7% of men were daily users of sedatives, tranquilizers or antidepressants. Both these were non-random population samples. A small-scale but random survey of Sydney women in 1976 found that 12% were daily users of tranquilizers and sedatives. The 1983 Australian Health Survey, using a larger sample but omitting populations in hospitals and other institutions, found that 7% of those surveyed reported taking a tranquilizer and/or sleeping pill in the previous two weeks (9% women and 5% men).

1.3.2 Prescription Audits

In 1972 in the United States, Valium was the most frequently prescribed drug whilst sales of all benzodiazepines peaked in 1975, with approximately 65 million prescriptions of Valium and 90 million prescriptions of all benzodiazepines. Benzodiazepine prescription sales in Europe (measured by the method preferred by the World Health Organisation which expresses drug sales in terms of 'defined daily dose') levelled out or fell slightly in the late 1970s. Similarly, an estimate of the number of NHS non-hospital prescriptions in England found only a slight decline of sedatives and tranquilizers (from approximately 20 million in 1976 to 18 million in 1982) whilst sedatives remained relatively static.

However, a Canadian prescription audit in Saskatchewan found a greater than 50% drop in Valium prescriptions between 1977 and 1982 (from 213,549 in 1977 to 96,372 in 1982) whilst sedative prescriptions of benzodiazepines, although less in quantity, had more than doubled (from 39,619 in 1977 to 96,473 in 1982) - due mainly to the marketing of a new drug, triazolam. Australian data support the Saskatchewan report.

It should firstly be noted that Australian prescription audit
figures all understate quantities, since they do not include prescriptions in hospitals nor Repatriation, defence and private (non-PBS) prescriptions. Furthermore, numbers of prescriptions do not specify quantities of the drug prescribed. For example, 2mg and 5mg diazepam tablets can be prescribed in lots of 50's on the PBS whereas 15mg and 30mg oxazepam tablets are available in 25's. Therefore, a prescription of 50 x 5mg Valium tablets, at a conservative dosage of 2.5mg three times per day with two repeats, gives about five months supply; a higher, but not unusual, dosage of 30mg per day yields just under one month's supply. On the other hand, a prescription of 25 x 30mg Serepax tablets, at a conservative dosage of 15mg three times per day with one repeat, gives about two weeks' supply; the maximum recommended dosage of 30mg four times per day yields just under one week's supply.32 Prescription regulations have been revised by the state from time to time so that prescription numbers do not represent equivalent dosage units from one year to another, nor do those made under the PBS represent a constant ratio of all prescriptions.33 Despite these qualifications to Australian prescription audits, a definite trend in benzodiazepine prescribing can be discerned.

Of the top fifty most prescribed items in Australia in 1984/85, there were four benzodiazepines. In descending order of prescription volume, they were: oxazepam, nitrazepam, diazepam and temazepam.34 Diazepam, prescribed mainly as an anti-anxiety agent, was the most prescribed single item in Australia under the Pharmaceutical Benefit Scheme from the year it was introduced on to the PBS in 1972/73 up to 1975/76. The following year it dropped to second place.35

Prescription sales for the 1970s of the minor tranquillizers available under the PBS in Australia have closely followed overseas
patterns, although the Australian sales volume was significantly lower than in the United States.\textsuperscript{36} The number of PBS prescriptions for minor tranquillizers (mainly diazepam and oxazepam) peaked in 1974/75 at almost 5 million prescriptions (approximately 4.5 million of these were for diazepam). However, sales of diazepam and oxazepam bottomed out around 1980 and, since then, have slowly increased to approximately 4 million in 1984/85.\textsuperscript{37} This has been due to the fact that, whilst prescriptions for diazepam dropped to 1.5 million in 1984/85, those for oxazepam increased from 0.98 million to 2.5 million, making oxazepam the seventh most prescribed PBS item for 1984/85 (Figure 1.3).\textsuperscript{38}

Nitrazepam, the second best selling benzodiazepine in Australia, is prescribed mainly as a sedative. PBS prescription sales for nitrazepam (listed on the PBS in December 1970)\textsuperscript{39} peaked in 1977/78 at just over 2 million, and have fallen since then to about 1.6 million in 1984/85. However, this has been offset by prescription sales of the new benzodiazepine, temazepam, also marketed as a sedative, which have rapidly increased since its introduction in Australia in 1980/81. As a result, total sales of benzodiazepines sold as sedatives have steadily continued to increase to just over 2.5 million prescriptions in 1984/85 (Figure 1.4).

Prescription sales of the four major-selling benzodiazepines (sold as both minor tranquillizers and sedatives) have increased gradually in the past ten years. After a drop in the late 1970s, prescription volumes in 1984/85 have returned to a level similar to that in 1975/76, at just over 6.5 million (Figure 1.5).

1.4 Conclusion

A cross-cultural gender bias in benzodiazepine use has been consistently found in the industrialized countries, with twice as many
Figure 1.3: PBS prescription volume of benzodiazepines commonly prescribed as sedative/hypnotics (nitrazepam and temazepam) in Australia from 1972-73 to 1984-85

Source: Commonwealth Department of Health (personal communication) (1986)
Figure 1.4: PBS prescription volume of benzodiazepines commonly prescribed as minor tranquillizers (diazepam and oxazepam) in Australia from 1972-73 to 1984-85

Source: Commonwealth Department of Health (personal communication) (1986)
Figure 1.5: PBS prescription volume of four most commonly prescribed benzodiazepines (diazepam, oxazepam, nitrazepam and temazepam) and expressed as a percentage of total PBS prescription volume in Australia from 1972-73 to 1984-85

Source: Commonwealth Department of Health (personal communication) (1986)
women as men reporting their use. Other trends in use, or prescribing patterns, are less consistent. Generally, tranquillizer sales soared in the early 1970s, mainly due to Roche's Valium but also to 'me too' products marketed by other companies. Australia ranks with the United States as having a relatively small number of benzodiazepines available, compared with other countries such as Britain and Japan. During the 1970s, about 15% of the population reported having used a minor tranquillizer in the preceding twelve months, whilst regular daily users averaged from 3.5% to 9%. Such averages conceal the gender-based differences, as women's use would be higher and men's use lower than these averages.

Many believe that as Valium sales declined later in the 1970s, benzodiazepine use generally decreased and is no longer a cause for concern. However, Australian figures (as elsewhere) show that whilst sales of diazepam (mainly Valium) under the Prescription Benefits Scheme (PBS) dropped sharply from the mid-1970s, sales of other benzodiazepines have increased significantly so that, overall, benzodiazepine prescriptions have increased steadily since the mid-1970s (although remaining relatively constant with respect to the total prescription volume). Sales of benzodiazepines classified as sedatives have increased at a faster rate than for the minor tranquillizer category.

Some of the factors influencing the changing trends in benzodiazepine sales are discussed in the next section, which traces the shifting scientific-medical debate as it has informed doctors and influenced their prescribing habits.
A survey of the literature reveals that this is a conservative estimate, as there are at least forty different benzodiazepines available world-wide. See: Intercontinental Medical Statistics (Australasia) Pty Ltd, MIMS, 25 (4), June/July 1988; Charles Medawar and Social Audit, The Wrong Kind of Medicine?, (London, Consumers' Association and Hodder & Stoughton Ltd, 1984); T.A. Ban & R. Prakash, op cit, (note 1)


25. Ibid


27. Ingrid Waldron, "Increased Prescribing of Valium, Librium, and Other Drugs - An Example of the Influence of Economic and Social Factors on the Practice of Medicine", Internat J Health Services, 7 (1), p.38

29. John Marks, _op cit._ (note 19), p.82


32. Intercontinental Medical Statistics (Australasia) Pty Ltd, _op cit._ (note 9), p.61


35. Patricia Healy, "Patterns of Drug Use in Australia", _Aust J Alcohol Drug Dependence_, 6 (3), 1979, p.96

36. For example, peak Valium sales in 1975 in Australia, at approximately 4.5 million, were only 7% of American sales, which totalled about 65 million (population differences alone cannot explain the much larger American sales).


38. Commonwealth Department of Health, _op cit._ (note 34)

39. A. Mant, _op cit._ (note 33) p.26
2 MEDICAL-SCIENTIFIC DEBATE ON BENZODIAZEPINES

2.1 Introduction

Benzodiazepines have been a focus of conflicting knowledge claims amongst medical-scientific 'experts' over evidence of their efficacy and safety. A doctor's decision to prescribe a benzodiazepine draws on her or his interpretation of this knowledge. The following review of literature written largely by and for a medical audience captures the process of conflict arising from divided expert opinion. It describes the shift in consensus over almost thirty years from the early widespread acceptance and promotion of benzodiazepines to contemporary medical opinion that they are effective and safe, if prescribed cautiously. However, consensus is no longer so widely established and there are many who hold strongly opposing views.

2.2 Efficacy of Benzodiazepines

2.2.1 Recommended Uses of Benzodiazepines

Over the past few decades, benzodiazepines have been prescribed or recommended to be prescribed for: anxiety, phobic anxiety and panic attacks, insomnia, seizures, musculoskeletal disorders, alcohol withdrawal, anaesthesia and premedication for endoscopy and surgery, night terrors or somnambulism in children, pathologic anxiety and anxiety associated with medical disease, depression, insomnia not associated with medical or psychiatric disease, anxiety and agitation associated with musculoskeletal disorders, depression with associated anxiety, cerebral palsy, sleep disorders including somnambulism and enuresis, childbirth, tinnitus, dizziness, postoperative shock, backache, neck pain, recovery from influenza, sleep disturbances for the parent of a hyperactive child, death or illness of a family member, marriage or relationship problems, rape, incest, problems with parents,
stressful house moving, and disorders in the Third World, such as tetanus, cerebral malaria and eclampsia. On the other hand, benzodiazepine use has been questioned or specifically not recommended for the following: situational anxiety, low levels of anxiety and muscle tension, anxiety associated with depression, psychosomatic illnesses, tension headache, nocturnal enuresis, organic brain disease, dysmenorrhoea, behaviour disorders, cerebral palsy, psychotic diseases or depression, pregnancy, and labour.

Clearly, conflict surrounds the application of minor tranquillizer technology, and within the medical literature resolution of the controversy depends upon the standard model and methodological procedures of scientific medicine. Yet far from resolving it, these have served only to polarize the debate, from appeals to ban benzodiazepines because they are so dangerous, to calls for them to be available without prescription because they are so safe.

Lennane, a leading medical expert in Australia in the addiction area, has recommended benzodiazepines only for short-term treatment of extreme insomnia difficulties and for long-term treatment of epilepsy. She has proposed that personality characteristics associated with anxiety and insomnia problems are also strongly linked with dependence on benzodiazepines. Consequently, she has not recommended their use for anxiety. Most controversy surrounds the use of benzodiazepines for anxiety and other disorders of a non-physical nature; although their use for physical problems has been far less questioned, this is also problematic.

2.2.2 Anti-anxiety or Sedative?

The drug manufacturers categorize different benzodiazepines exclusively as either anti-anxiety agents or sedatives (except for a
small number listed as anti-convulsants, and, in Australia, diazepam is an exception as it is listed as an anti-anxiety agent, and for the relief of muscle spasm as well as an anti-convulsant). A recent issue of a commonly used Australian drug compendium designated the following as anti-anxiety agents: alprazolam, bromazepam, chlordiazepoxide, clobazam, clorazepate, diazepam, lorazepam, and oxazepam. For the treatment of muscular spasm, chlordiazepoxide and diazepam were recommended; as hypnotics, it recommended flunitrazepam, flurazepam and nitrazepam; and for epilepsy it recommended clonazepam or, for status epilepticus, parenteral diazepam (See also Table 1.2).  

Despite more recent medical criticism of the artificial nature of this differentiation, especially as many are metabolised to the same compounds, doctors continue to prescribe selectively. The contemporary view is that benzodiazepines with a longer half-life are more appropriate for anxiety whilst the shorter acting variants are more appropriate as sedatives as they cause less trouble with unwanted residual effects the following day. The nitrazepam were the early available alternative to diazepam as sedatives, and continue to be the most prescribed 'sedative' benzodiazepine although a considerable body of expert opinion favours the much shorter acting variants such as temazepam.

2.2.3 Anxiety

However, the key to understanding the forces behind arguments about the efficacy of benzodiazepines is found in their use for anxiety. Here, appeals to rigorously designed scientific study have not solved basic problems defined by the agenda set by scientific medicine of simply identifying and measuring anxiety.
(a) Definition of anxiety

Usdin has described difficulties experienced by the medical profession in clearly defining the term anxiety. He found three different definitions in one volume concerning anxiolytics and more than six different definitions from various sources.19

In the United States, Greenblatt and his colleagues have published extensively in the New England Journal of Medicine, strongly promoting the efficacy and safety of benzodiazepines. However, in their first review of the benzodiazepines in 1974, Greenblatt and Shader admitted:

Anxiety is an elusive clinical syndrome. It describes a psychophysiologic response resembling fear but inappropriate to the reality of the perceived threat. Manifestations can include psychic symptoms (irritability, tension, excessive worry, and inappropriate apprehension) somatic symptoms (palpitations, breathlessness, diaphoresis, urinary frequency, fatigue, restlessness, or disordered sleep), or combinations of both. Anxiety characteristically is a phasic or episodic disorder with multiple remissions and exacerbations.20

Ten years later, in their next major review, Greenblatt and his colleagues addressed the definitional problems of anxiety by subdividing anxiety into various categories: situational, pathologic, chronic, associated with physical diseases, mixed anxiety depression, and anticipatory anxiety associated with panic disorders.21 The difficulties they experienced are evident; for example, when they differentiate between situational and pathologic anxiety:

Situational anxiety that is not disproportionately intense may improve performance and stimulate adaptive and coping behaviour; such anxiety is generally non-pathologic and probably better left untreated. Pathologic anxiety, on the other hand, is maladaptive and impairs rather than improves functioning in occupation and family. ... When symptoms last more than one month and are not distinguished by a pattern of panic attacks and avoidance behavior on the one hand or of obsessive-compulsive thinking and ritualistic behavior on the other, or both, a diagnosis of generalised anxiety disorder is usually warranted.22
They concluded by appealing to an "individualised common-sense approach" and "individually tailored clinical judgement". Hence, value judgements rather than clearly identifiable symptoms, prevail in assessing the intensity of anxiety.

Not only the intensity of anxiety but also the time course is considered relevant in diagnosis. Two systems of classification of anxiety are in concurrent use: the World Health Organisation's International Classification of Disease, Ninth Revision (ICD-9), revised in 1977, and the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM-III), revised in 1980. The DSM-III uses a multi-axial diagnostic system to classify four different categories in which anxiety is listed as the primary feature, containing sixteen different disorders. A distinction is made between panic disorders and generalised anxiety disorder. They are classified as two separate disorders because of the observed time scale: generalised anxiety disorder being persistent; panic disorder being episodic.

The British psychiatrist, Tyrer, and his colleagues, who favour a more conservative approach to prescribing benzodiazepines, have recommended short-term use of benzodiazepines only for periods of acute stress and not for generalised anxiety disorders such as described in ICD-9 and DSM-III. Difficulties in defining anxiety have moved the American psychiatrists in recent years to revise the DSM-III, partly to emphasise externally apparent symptoms of anxiety associated with a disorder, rather than on assumed underlying psychological symptoms.

(b) Measurement of anxiety

Numerous attempts have been made to measure emotional states, such as anxiety. For example, the battery of tests used by Shapiro and his
colleagues included the: Hopkins Symptom Check List (HSCL-62), Psychiatric Outpatients Mood Scale (POMS), Minnesota Multiphasic Personality Inventory (MMPI), Hamilton Anxiety Scale (HAS), Hamilton Depressive Scale (HDS), a fifteen-item Diagnostic and Background Information Scale, and a seven-point Likert Scale for anxiety, depression, psychopathology, prognosis and the predominance of anxiety over depression. They pointed out, however, that there is a lack of correlation between individual types of tests for measurement of anxiety, levels of anxiety and depression vary between patients so that it is difficult to separately classify these conditions, and levels of anxiety and depression vary for each patient with time. As a result, they were forced to resort to additional measurements of anxiety using clinical evaluations by psychiatrists. They reported that this provided more statistically reliable measurement of anxiety and depression.

Thus, like Greenblatt and his colleagues, they found individualised value judgements necessary for the 'reliable' measure of anxiety.

Nevertheless, tests such as those listed above have been important legitimating tools for asserting the scientific accuracy of medical studies on anxiety. For example, Mellinger and his colleagues earlier analysed data collected from an American national household survey of approximately 2,500 adults, to conclude that psychotherapeutic drugs were used generally by respondents who needed them; that is, by those who reported suffering at least medium levels of 'psychic distress'. This conclusion means that the researchers assumed first, that because the majority of regular drug users report high psychic distress and or life crisis, the drug use was a result of their living difficulties (that is, a way of coping); secondly, and more importantly, that these difficulties - more likely for those who were women, or in lower
socioeconomic groups, black, male and never married, or female and married - are a medical problem; thirdly, because these problems are experienced as severe, that they are severe medical problems and not minor everyday problems of living; fourthly, these severe medical problems require a medical solution based on an:

objective account of [drug therapy's] costs, risks, and benefits relative to those of available options.  

Finally, they claimed objectivity for their analysis because they used the measuring devices such as the HSCL and this had long-term expert approval.

However, as we have seen, other researchers such as Shapiro have expressed a less naive faith in such objective tests of anxiety and have resorted to using subjective personal assessments.

2.2.4 Summary of Efficacy

The previous discussion points up some of the difficulties in determining the efficacy of benzodiazepines. Most conflict has surrounded their use for the treatment of anxiety. Whilst their use for physical disorders such as muscular tension has not been so controversial, there is similar potential for doubts over their efficacy in this area. Scientific medicine has classified anxiety as an illness, or disease, and has encouraged a technical fix for its treatment with benzodiazepines. However, medicine's ability to define and measure the disease state of anxiety and treat it appropriately has been shown to be problematic.

Despite considerable evidence casting doubt on the efficacy of benzodiazepines, particularly for the treatment of non-physiological problems, the general consensus of medical opinion appears to be that benzodiazepines are effective for the short-term treatment of acute
anxiety and insomnia, as well as treatment of muscle tension, convulsive disorders (such as epilepsy) neuromuscular disorders (such as spasticity) and for anaesthesia. With respect to anxiety and sleep disorders, there have been some concessions towards accommodating alternative therapies which may even be non-medical, such as psychotherapy, occupational therapy, relaxation methods or community care. However, these are usually seen as adjuncts to drug therapy, thereby maintaining the role of the doctor in the treatment program.  

2.3 Safety of Benzodiazepines

2.3.1 Introduction

The alleged safety of benzodiazepines was another strong reason for the preference for the benzodiazepines over the barbiturates and meprobamate, as the minor tranquillizer of choice. It was widely believed that benzodiazepines had fewer and less severe unwanted effects, were much safer in overdosage, interacted very little with other drugs and were less addictive. Strong doubt has been cast on all four of these safety aspects and some, such as the addiction potential and withdrawal effects of benzodiazepines at clinically prescribed doses, have become highly controversial. Like the efficacy issue, the medical-scientific debate has become polarised between those who advocate cautious use (such as the British psychiatrists, Lader, Petursson, Tyrer, Catalan and Gath) and those who continue to voice the long-held views on their extreme safety (such as the American doctors, Greenblatt and Shader):

Probably the least controversial aspect of the pharmacology of benzodiazepines is their tremendous index of safety. The replacement of barbiturates by benzodiazepines as the primary agents for the treatment of anxiety and insomnia has greatly reduced the morbidity and mortality associated with overdosage of sedative-hypnotic drugs.
The major issues in the safety debate are summarized as follows.

2.3.2 Low Mortality Rate

The low mortality rate associated with overdose of benzodiazepines, compared with the barbiturates, is often referred to in the literature as a strong rationale for their use. Marks (a doctor who had previously worked for Roche during the development and marketing of the benzodiazepines) has summarised a number of studies which found only two deaths directly attributable to benzodiazepines alone, out of a total of 9,500 drug overdose cases and 1,500 drug fatalities examined.

Nevertheless, it is well accepted that benzodiazepines are dangerous if taken with alcohol, or other CNS depressants. Australian mortality data reveal the extent of problems from these drug combinations. Accidental drug related deaths reported by the Coroners Courts for New South Wales show that, of a total of 127 deaths in 1984, two deaths involved benzodiazepines alone while twenty-five deaths were associated with a mixture of benzodiazepines and one or more other drug (including alcohol) and can be compared with ninety-one deaths associated with heroin on its own or associated with other drugs. A Melbourne study of road deaths found that two-thirds of the victims had drugs other than alcohol in their blood and 46% of the drugs were prescribed by doctors. Altogether, of those who were in any way responsible for the fatalities, 82% had used alcohol or other drugs at the time of the accident. Although some have acknowledged that alcohol consumption is high throughout society, problems with accurately assessing a patient's alcohol consumption are conspicuously absent from the medical-scientific debate. Morbidity data also reveal benzodiazepines have become a problem. In Australia, they now lead the cases of reported drug poisonings, with double the number of mentions.
compared with alcohol. Occasional reports are found of deaths linked with benzodiazepine use, other than overdosage. A recent case was the death of a healthy volunteer medical student who was participating in British clinical trials of a new preparation of the benzodiazepine, midazolam. Although evidence at the inquest supported the view that the drug possibly contributed to his death from aplastic anaemia, an open verdict was returned so that the manufacturers, Roche, were able to pay compensation to the family without admitting negligence. The Australian drug compendia provide information on life-threatening disorders such as blood discrasias and liver abnormalities, which are listed as possible adverse reactions.

2.3.3 Depression of the Central Nervous System

Because of their sedative effects, the most common unwanted effect of benzodiazepines is excessive depression of the central nervous system (CNS). This can be manifested, even at low doses, as: drowsiness, impaired memory and recall, reduced co-ordination, fatigue, muscle weakness, impaired speech, loss of concentration and speech defects.

Disadvantages in collecting information on unwanted effects are that they may be considered too trivial to report, voluntary reporting systems are not heavily supported, and reports in the literature are often drawn from test conditions quite removed from every-day situations and from observations of people who would not be characteristically prescribed benzodiazepine medication. For example, healthy young adults may be recruited or simulated driving experiments carried out in a laboratory setting.

It can be argued that more relevant data could be collected from large-scale epidemiological studies. However, the problems are
considerable. For example, the first attempt to study the effects of benzodiazepine use on traffic accidents in natural conditions, carried out in Britain by Skegg and his colleagues, was criticised because the design of the study did not allow measurement of the contribution of alcohol consumption. It is also difficult to distinguish between contributory effects of the medication and the condition for which it is being treated. Greenblatt has also criticised this study, stating that:

such studies suggest but certainly do not prove that benzodiazepines cause automobile accidents.

Besides implying that benzodiazepines were not as effective as he had stated elsewhere, in that he questioned the emotional state of the drivers taking tranquillizers, Greenblatt opportunistically adopted a simplistic model of science's ability to prove any drug as a causative agent. Contemporary practice, drawing on epidemiological methods, is to examine the association of drug use with particular events, where the contribution of the drug(s) is part of a continuum of the effect, ranging from probably insignificant to highly probable that it is a contributory agent. 'Proof' is rarely obtained yet it is certainly possible to draw conclusions concerning strongly linked factors. For example, Drew in the Commonwealth Department of Health has estimated that tobacco is involved in the largest number of drug-related deaths. This data was calculated from 'death indices' associated with particular drugs derived from a study of Australian and international literature.

2.3.4 Effects on the foetus, newborn and elderly

Considering the delay in discovering the hidden dangers of another sedative, thalidomide, also prescribed in the early 1960s, surprisingly little attention has been given to the possible dangers of teratogenic
and other effects on the foetus by benzodiazepines. About fifteen years after their introduction, epidemiological studies in the United States and Finland found a link between birth defects and benzodiazepines when taken during the first trimester of pregnancy. However, conflicting evidence published at the same time, possibly together with the fact that the birth defects (cleft lip and/or cleft palate) were not as severe as in the thalidomide case, has resulted in this safety aspect being pursued no further. Occasional warnings are given, such as by the British Committee on the Review of Medicines in their revised guidelines for data sheets of benzodiazepines which stated:

-do not use during pregnancy, especially during the first and last trimesters, unless there are compelling reasons.

In addition, warnings provided by the drug companies are inconsistent. In Australia, the MIMS bi-monthly drug compendium mentioned benzodiazepine use during pregnancy fifteen times as requiring special precautions, four times as contraindicated whilst for eight different benzodiazepines there was no reference at all to use during pregnancy. For full information supplied by the drug companies, the MIMS Annual for the preceding year included entries for five different benzodiazepines which referred to possible foetal effects whilst the majority made general warnings on drug use during pregnancy. The variety of instructions for the six different brands of diazepam are of interest:

* Antenex: no information

* Astra Pharmaceuticals Diazepam Injection:

Diazepam should not be administered during pregnancy unless the expected benefits outweigh any potential risks. Placental transfer of diazepam does occur.

* David Bull Diazepam Injection:

Diazepam readily passes the placental barrier, with the concentration of the drug in the fetal
circulation approaching or similar to that in the maternal circulation. Epidemiological studies have shown an association between diazepam use during pregnancy and cleft palate in the offspring. Diazepam is therefore not recommended during the first trimester of pregnancy.57

* Ducene:

The established practice of not prescribing drugs in early pregnancy unless absolutely necessary should be adhered to.58

* Pro-Pam: no information

* Valium:

The established practice of not prescribing drugs in early pregnancy unless absolutely necessary should be adhered to.59

Contemporary reviews of the benzodiazepines generally refer to the studies on possible foetal effects as well as repeating general warnings on drug use in pregnancy.60 However, these and any other warnings concerning use in pregnancy were completely omitted in Greenblatt's updated 1983 review of the benzodiazepines.61

As well as being possibly dangerous in the early stages of pregnancy, it is now accepted that benzodiazepines can harm the newborn. A number of reports since 1972 have pointed out that high doses (30mg or more) of diazepam given to the mother during labour can cause in the newborn, multiple breathing difficulties, low temperature, poor sucking and "floppiness".62 These potential dangers were recognised by the British Committee on the Review of Medicines in their 1980 guidelines for data sheets.63 Nevertheless, a British survey found that obstetricians favoured use of benzodiazepines in treatment of pre-eclamptic toxaemia.64

Whilst British medical opinion had turned against the use of benzodiazepines during labour by 1980, in Australia they were still
being promoted to doctors for use in labour as late as 1984. Moreover, they were promoted quite clearly more for the doctor's convenience than for the patient, when suggested for:

the facilitation of labour, [as] 'Valium' Roche renders the parturient more calm and cooperative.65

Despite the known dangers to the foetus, for use during pregnancy it was recommended that "treatment must be continued consistently until the foetus reaches maturity".66

It is commonly accepted that the elderly are more sensitive to minor tranquillizers and recommended dosages are usually half those for adults,67 although the special requirements of the elderly are often ignored in the literature.68

2.3.5 Addiction and Withdrawal

The question of addiction to, or dependence on, benzodiazepines is the most emotive issue surrounding their use. For approximately twenty years the general consensus of medical opinion has been that normal dosages of benzodiazepines were relatively free of problems of addiction. Withdrawal reactions had been noted from the time of their introduction.69

However, there have been two waves of concern over benzodiazepine dependence in the medical-scientific debate. The first wave peaked in the late 1960s and early 1970s,70 when it was resolved that their addiction potential was low. Large-scale population surveys such as the Boston Collaborative Drug Surveillance Program of the early 1970s could detect no signs of benzodiazepine dependence.71 When found, benzodiazepine dependence at normal dosage was established to occur after three to four months continual use.72 Reports in the literature declined, despite use increasing to a maximum, until the second wave in
the late 1970s when addiction again became an issue but this time prompting stronger calls for more cautious use of benzodiazepines.73

Greenblatt and his colleagues provide excellent examples of the conservative medical reaction to the second wave of concern over addiction to benzodiazepines. Moral arguments were used to minimise the addiction effects, such as accusing the "lay media" of "sensationalistic and terrifying depictions of benzodiazepine abuse and addiction", and to exonerate the doctor's role at the expense of "substance-abusing populations".74 Appeals to a more rational scientific knowledge base were also used:

whenever this problem has been evaluated in systematic scientific studies, the results have not confirmed the implications of journalistic reports.75

Nevertheless, a considerable body of contemporary medical opinion has become more concerned about benzodiazepine addiction. The addiction controversy has centred on the following issues: the definition of dependence and of benzodiazepine withdrawal symptoms; the dose and length of time of benzodiazepine use; the different pharmacokinetic properties of the benzodiazepines; and design of research and the data used.

(a) Definition of addiction and benzodiazepine withdrawal symptoms

Drug dependence, or addiction, has been interpreted in a variety of ways. Indeed, definitional confusion has resulted in confusion with terminology.

Although there has been, and is, no commonly accepted definition of addiction, the World Health Organisation's (WHO) struggle with this concept reflects the continuing conflict of differing views of the medical-scientific community and in the public mind generally. In 1957,
the WHO Expert Committee on Addiction-Producing Drugs gave the following definition:

Drug addiction is a state of periodic or chronic intoxication produced by repeated consumption of a drug (natural or synthetic). Its characteristics include: (1) an overpowering desire or need (compulsion) to continue taking the drug and to obtain it by any means; (2) a tendency to increase the dose; (3) a psychic (psychological) and generally a physical dependence on the effects of the drug; (4) detrimental effect on the individual and society.76

This view of the drug having addictive properties was replaced in their 1964 definition, when they also replaced the term "drug addiction" with "drug dependence" in order to shift the focus on to the behavioural aspects. The current definition of drug dependence most commonly referred to is that put forward by the WHO in 1974, where drug dependence was defined as:

A state, psychic and sometimes also physical, resulting from the interaction between a living organism and a drug, characterized by behavioral and other responses that always include a compulsion to take the drug on a continuous or periodic basis in order to experience its psychic effects and sometimes to avoid the discomfort of its absence.77

Drug dependence is divided between physical and emotional effects. For example, the WHO described the two different states of dependence as:

Physical dependence. An adaptive state that manifests itself by intense physical disturbances when the administration of the drug is suspended.

Psychic dependence. A condition in which a drug produces a feeling of satisfaction and a psychic drive that requires periodic or continuous administration of the drug to produce pleasure or to avoid discomfort.78

The medical-scientific debate contains many examples of doctors maintaining the 'addictive drug' concept and the stereotyped picture of tranquillizer addiction based on barbiturates (tolerance, with subsequent escalation of dosage and gross drug seeking behaviour). The
competing picture of benzodiazepine addiction, on the other hand, is much more subtle, behaviourally-based and can include neither drug seeking behaviour nor tolerance.

The British contribution to the medical-scientific debate was to establish a benzodiazepine withdrawal syndrome. Some of the barriers to this discovery were revealed in an editorial in the *Lancet* in 1979 which stated that:

> many of the mild withdrawal symptoms are indistinguishable from the symptoms of anxiety states ... the condition should be suspect when a patient repeatedly tries to wean himself from a benzodiazepine and restarts ... because of headache ... or symptoms unrelated to the initial anxiety syndrome.

The dilemma had been revealed, if not resolved. If it was difficult to identify and measure anxiety states in order to determine whether to prescribe benzodiazepines (let alone determine their efficacy), how much more difficult was it to be certain that anxiety which occurred after withdrawal was due to re-emergence of the original 'syndrome' and not a withdrawal effect of the drug? Contradictory views of anxiety were further expressed in the *Lancet* editorial, which referred to anxiety as a "mild withdrawal symptom" but also considered it a serious illness suitable for treatment with benzodiazepines.

As a result, there are continuing attempts within the medical-scientific debate to differentiate anxiety states. It is generally accepted that a differential diagnosis can be done according to the time sequence of appearance of anxiety after withdrawal. The original anxiety symptoms are believed to appear more slowly and plateau out about two to three weeks after withdrawal whereas anxiety associated with withdrawal is said to appear two to three days after the drug is withdrawn, and to peak after about seven to eight days. However, some
withdrawal symptoms have been reported four to six months after medication has stopped.\(^82\)

(b) Dose and length of time of benzodiazepine use and method of withdrawal

The consensus of opinion within the medical-scientific debate is that the higher the dose and the longer the length of time of benzodiazepine use, the more likely is dependence. However, the second wave of debate about dependence from the late 1970s has produced divergent views on dosage and recommended time of use as well as method of withdrawal from benzodiazepines.

Withdrawal effects have been documented since the time of introduction of benzodiazepines. The best-known early study is one by Hollister and his colleagues which detailed unwanted effects observed in psychiatric in-patients given massive doses of Librium (300-600 mg. Librium per day - that is, six to forty times more than usual therapeutic dosages), and then abruptly withdrawn after five to six months of use.\(^83\) Occasional case reports of withdrawal effects from normal dosages of benzodiazepines also appeared at that time.

Despite the extreme nature of Hollister's study, it did appear to raise some general concern against benzodiazepines. Roche reacted by supporting staff members from their American laboratories to publish a literature review of clinical studies on Librium published from 1960 to 1966 in the United States.\(^84\) To support their arguments on the safety of benzodiazepines, they pointed to only twelve reported cases of withdrawal effects, ten of which were from the study by Hollister and his associates using extraordinarily large doses. Another literature survey on diazepam dependence up to 1965 also found few reports on withdrawal but these authors were critical of the inadequate
Experimental methodology.

The first wave of debate over dependence culminated in 1973 with a report on the first controlled study of withdrawal effects after normal dosages (actually at the top of the range of recommended dosages, at 45mg per day). It was stated that withdrawal effects could be avoided for up to a maximum of four months of benzodiazepine use. There has been widespread acceptance of this finding despite problems in the design of their study.

In the second wave of the debate, Tyrer's group examined dependence in long-term moderate users of benzodiazepines who were suddenly withdrawn in a double blind study. They found between 27% and 45% of the people who completed the study had withdrawal symptoms. There were also methodological problems with this study, relating to non-completing participants, which would have significantly reduced the estimate of withdrawal incidence. Another British study carried out at about the same time by Petursson and Lader found a 100% withdrawal reaction rate following normal doses of long-term benzodiazepine use. The methodology of this study has been criticised because of the small sample of self-selected participants.

(c) Different pharmacokinetic properties of benzodiazepines

In the late 1970's Kales and his colleagues described their discovery of 'rebound insomnia', consisting of:

- a marked worsening of sleep following the abrupt withdrawal of certain benzodiazepine drugs administered in only single doses nightly for short periods.

Rebound insomnia was linked with withdrawal from the shorter acting benzodiazepines (such as triazolam, flunitrazepam and nitrazepam) but not with flurazepam and diazepam which have metabolites with longer half-
lives. The short-acting benzodiazepines were also implicated in an analogous syndrome of 'rebound anxiety'.

In 1981, the British team led by Tyrer reported on withdrawal studies after long-term use of diazepam (which breaks down to a metabolite with a long half-life) and lorazepam (which has a much shorter half-life and tends not to accumulate in the body, mostly being eliminated after each dose). They found that the shorter acting benzodiazepine produced a more severe withdrawal reaction. They therefore recommended that withdrawal from benzodiazepines should commence with a withdrawal regime on a longer acting benzodiazepine, such as diazepam, with a gradual reduction in the dosage to follow.

However, others have revealed that it may be too simplistic to assume a direct link between rate of elimination from the bloodstream and withdrawal symptoms. Drugs with comparable half-lives do not produce similar effects and possible complicating factors could be the speed of absorption of benzodiazepines, such as its effects (or of a metabolite) in the free state versus bound to protein, or differences in levels in blood versus brain and other sites of the body.

(d) Psychological and other factors

Most of the medical-scientific debate on benzodiazepine addiction has emphasised the technical aspects of the drug use (dosage, length of time of use and method of withdrawal). Psychological aspects have received less attention and usually in terms of predisposing personality disorders. Often, a judgemental attitude serves to place blame on the person addicted to benzodiazepines. For example, Greenblatt has split those who are addicted into two groups. On the one hand, there are those who are willing to place themselves under medical supervision and are rewarded by being cared for by a responsible and knowledgeable
doctor. On the other hand, there is the deviant group who are
denigrated as "substance-abusing populations".95

Tyrer's group has stated that personality is an important factor in benzodiazepine dependence and that "patients with passive and dependent personality characteristics are more liable to develop symptoms".96 They concluded that this "explains why almost all the reports of pharmacological dependence have come from patients being treated with benzodiazepines for psychiatric reasons".97 However, an alternative explanation is that doctors would be less likely to look for dependence in people with 'normal personalities' who are using benzodiazepines for physical conditions such as spasticity. Other evidence contradicts their findings. For example, although working with only a small sample, Ashton recently found only two patients with psychiatric problems out of twelve referred to her by their general practitioners for help in withdrawal from long-term benzodiazepine use.98 More importantly, Tyrer has not distinguished between prospective and retrospective studies: the majority of dependence studies are of the latter type and could not differentiate between personality disorders resulting from drug use and pre-existing conditions.

(e) Methods for detection of benzodiazepine dependence

The early literature review by the Roche workers can be criticized as methodologically weak, as they did not state how many of the 287 clinical studies surveyed, covering 17,935 patients, even attempted to investigate withdrawal effects, let alone discontinued use of the drug, except for the Hollister study.99

The literature review published by Marks about ten years later has often been used to support the view that the incidence of benzodiazepine
dependence was insignificant. Marks found only twenty-eight cases of dependence recorded in Britain over the period 1960 to mid-1977, giving a risk of dependence from normal therapeutic dosages of one case per fifty million patient-months. He concluded that there were fewer than five hundred cases of dependence world-wide. However, this can be contrasted with a much higher incidence of benzodiazepine dependence found over a three-year period (1977-1980) in only one clinic in Gottingen than Marks had found in his literature survey covering 18 years for the entire Federal Republic of Germany. A more recent estimate (only five years after Marks' literature survey) using evidence from clinical studies, has suggested that benzodiazepine dependence may affect two to three million people worldwide.

The Drug Abuse Warning Network (DAWN) in the United States has also been criticised for its poor data collection methods.

2.3.6 Other Safety Issues

Apart from excessive depression of the CNS (causing oversedation, reduced physical coordination and impaired memory), other unwanted effects from benzodiazepines are considered to be rare and include 'paradoxical' aggression, brain scan abnormalities, respiratory problems, rashes and other skin problems, and blood dyscrasias such as aplastic anemia.

2.3.7 Summary of Safety

Safety issues concerning the benzodiazepine minor tranquillizers have been focussed on addiction problems, where two distinct waves of opinion have prevailed: the first came to a peak in the early 1970s when prescribing of benzodiazepines was also reaching a maximum, and the second became prominent about ten years later when a much more cautious attitude became prevalent. The debate over addiction problems has
centred around problems of definition of addiction and solutions which are largely technical such as altering the prescribed dose or the length of time of use. Safety issues concerning foetal effects and effects on the newborn and elderly have emerged from time to time but have not engendered the same controversy.

2.4 Conclusion

The early enthusiastic optimism for benzodiazepines can be seen as a reaction against the high death rates from barbiturate overdoses. The contemporary reaction against benzodiazepines has shifted focus to morbidity rather than mortality issues, that is quality rather than quantity of life. The different American and British attitudes possibly reveal cultural influences within the debate.

The medical-scientific debate has played a part in shaping the meaning of minor tranquilliser technology. An examination of the debate has captured the problematic nature of the positivist claims of medicine's scientific knowledge base. These mirror fundamental problems within the model of scientific medicine which promotes a mind-body split reflected in the physical and mental separation of disease states, an essentialist view of disease favouring the concept of specific etiology, and the overarching Cartesian influence of the body viewed as a machine.

The contemporary medical-scientific debate has, above all, sought to define problems with tranquilizer use in technical terms which have, nevertheless, failed to yield satisfactory solutions. Minor tranquillizers continue to be used at very high levels. Technical solutions continue to be sought. Already, alternative drugs such as propanolol, low doses of major tranquillizers and anti-depressants are being promoted. Behind the technical barriers lie the social forces which have shaped the course of the debate and the use of minor
tranquillizers. A more rational use of benzodiazepines must start with the extension of the debate into the social context, which continues in the next chapter dealing with factors influencing prescribing and consumption patterns.
FOOTNOTES:


11. Committee on the Review of Medicines, op cit, (note 2)


15. Shapiro and his colleagues have cast doubt on the two most common uses of benzodiazepines: one of which rests on a firm belief in their muscle relaxing effects; the other being for anxiety.

A.K. Shapiro et al, op cit, (note 9), p.51


18. Ibid; G.D. Burrows et al, op cit, (note 1);


22. Ibid

23. Ibid


27. A.K. Shapiro et al, op cit, (note 9), p.52

28. Ibid


30. Ibid, p.1052

31. Ibid

32. J. Marks, op cit, (note 7), pp.61-67


34. For example, see: Ibid; Peter Tyrer and Siobhan Murphy, op cit, (note 25); and J. Catalan & D.H. Gath, "Benzodiazepines In general practice: time for a decision", Brit Med J, 290, 1985, pp.1374-1376

36. J. Marks, *op cit*, (note 7), pp.68-70

37. Ibid

38. For example, see the introductory remarks at the beginning of the 'Antianxiety' section of the June/July issue of MIMS.

   Intercontinental Medical Statistics (Australasia) Pty Ltd, *op cit*, (note 16) p.58


44. Intercontinental Medical Statistics (Australasia) Pty Ltd, *op cit*, (note 16), p.62


46. R. Cooperstock & J. Hill, *op cit*, (note 45), p.25


51. Ibid


without cleft palate and prenatal exposure to diazepam", The Lancet, 1975, pp.478-480


57. Ibid, p.4-210

58. Ibid, pp.4-210,4-211

59. Ibid, p.4-216


64. R.J. Rowlatt, op cit, (note 62)

65. Intercontinental Medical Statistics, op cit, (note 56), p.171

66. Ibid


The similar positions of the two author groups are reflected in the heavy reliance by the Australian authors on Greenblatt's interpretations

69. Leo Hollister, Francis P. Motzenbecker and Roger O. Degan, "Withdrawal Reactions from Chlordiazepoxide ("Librium")", Psychopharmacologia, 2, pp.63-68

70. Malcolm Lader and Hannes Petursson, op cit, (note 33), pp.207-208

71. Ibid

72. L. Covi, R.S. Lipman, J.H. Pattison, L.R. Derogatis & E.H.
Uhlenhuth, "Length of treatment with anxiolytic sedatives and response to their sudden withdrawal", *Acta psychiat scand*, 49, pp.51-64


75. *Ibid*


78. *Ibid*


81. J. Marks, *op cit*, (note 7), p.36

82. C. Heather Ashton, "Benzodiazepine overdose: are specific antagonists useful?", *Brit Med J*, 290, 1985, p.1139

83. Leo E. Hollister et al, *op cit*, (note 69), pp.63-68


86. L. Covi et al, *op cit*, (note 72)


89. R.T. Owen & P. Tyrer, *op cit*, (note 73), p.393


91. *Ibid*, p.1040

92. P. Tyrer et al, *op cit*, (note 87)

93. J. Marks, *op cit*, (note 7), p.46
94. Peter J. Tyrer & Nicholas Sievewright, "Identification and Management of Benzodiazepine Dependence", *Postgrad Med J*, 60 (Suppl.2), 1984, p.44


97. P.J. Tyrer and N. Seivewright, *op cit*, (note 94)


100. M. Lader & Petursson, *op cit*, (note 33), pp.208-209


102. P.J. Tyrer et al, *op cit*, (note 92)


106. "Death of a volunteer", *op cit*, (note 43), pp.1369-1370

3 THE MEDICAL PROFESSION AND CONSUMERS

3.1 Introduction

The previous chapter demonstrated that the debate over efficacy and safety of minor tranquillizers in the medical literature has been largely structured in terms of scientific and technological problems and solutions. Despite the positive role of stress as an aid in adaptation to, or protection from, the environment, anxiety and other stress-related problems often have been interpreted as discrete medical diseases amenable to technological solutions such as a prescription. People who consult doctors often expect a technological cure (prescription) for their ills, although it seems that doctors may reinforce these expectations. Similarly, solutions to the addictive potential of the minor tranquillizers have been sought in terms of a technologically deterministic and futile pursuit of the non-addictive minor tranquillizer, or in an anti-technological stance such as advocating total withdrawal of the benzodiazepines from the market.

This chapter opens with a discussion of the inadequacy of the biomedical model of disease in light of the social forces which shape health and illness. These are examined with respect to the prescribing of benzodiazepines for the four groups most at risk: women, the elderly, the chronically ill and the institutionalized. The influence of the medical profession and the health consumer movement on the application of this particular drug technology is examined.

3.2 Illness - More Than a Technological Problem

3.2.1 The Limits of the Biomedical Model

The search for better and safer tranquillizers has been based on an ideology of scientific and technological progress. This ideology has been crucial to the legitimation of medical science. For example,
improvements in the health of industrial societies were interpreted as the result of the medical control of infectious agents, such as vaccines and the sulphonamides and antibiotics introduced earlier this century. More recently, the work of McKeown and other have shown instead that improved nutrition, housing, hygiene and general public health measures (often fought against by doctors themselves) were the major factors responsible for the marked decline in mortality in Britain after industrialisation in the 19th century. Nevertheless, this myth of medical and scientific progress continues to underpin the contemporary drug industry and medical prescribing practices which support the widespread manufacture and use of minor tranquillizers and other drugs.

Social attitudes to health and illness and the conflicts between and within medical and general community definitions of health are important to this analysis. For example, health can be viewed negatively or positively, functionally or as an ideal, such as: "freedom from disease or ailment"; "not the mere absence of disease, but total physical, mental and social well-being"; and "a state of optimum capacity for the effective performance of valued tasks". The latter two definitions acknowledge the social component surrounding judgements on 'well-being', 'optimum capacity', 'effective performance' and 'valued tasks'.

Western medicine has been criticised for its mechanistic and reductionist view of illness as a mechanical failure obeying scientific principles. It implies a deviation from the 'normal' state of a perfectly functioning machine; that is, a state of health which can be objectively assessed, or measured, and differentiated from other disease states. Kennedy, for example, has stated:
Illness, a central concept of medicine, is not a matter of objective scientific fact. Instead, it is a term used to describe deviation from a notional norm. So, a choice exists whether to call someone ill. The choice depends upon the norm chosen and this is a matter of social and political judgement.6

As an example of the social meaning behind the medical judgement of normal health, Kennedy has pointed out that when a doctor decides a woman is anxious or depressed because she is not coping with an unfulfilling and stressful lifestyle as a housewife, the doctor has made a judgement that not being able to cope (that is, being anxious) is an abnormal state requiring medication with tranquillizers or anti-depressants.7

The previous chapter showed the difficulties for the medical profession in establishing a norm for measuring anxiety using a medical model which assumes that there is a normal anxiety-free state of health. In Western medicine, the mind-body split and the subdivision of medicine into specialities has established that there are abnormal diseases of the mind which can be objectively assessed and treated medically such as within psychiatry. Efforts to explore the social meaning of illness have been hampered by the acceptance of medical definitions of illness within the social sciences. For example, sociological texts commonly distinguish between disease, illness and sickness, accepting a positivist definition of disease such as "organic malfunctioning, to objectively measurable disorders".8 The distinction between mental and physical illness is contradicted by other sociological reports on the holistic manner in which people tend to report illness.9

The contemporary critique of Western medicine has shown how the medicalization of common social problems rests on assumptions about 'normal' emotional health and what Dubos has called a 'mirage of
Numerous sociological studies have confirmed the pervasive nature of illness generally as well as problems such as anxiety which could be classed as mental disorders. Other studies have explored the social processes in establishing a norm for psychiatric diagnosis, such as Temerlin's classic experiment. An actor portraying 'normal' behavior was diagnosed as normal by only 50% of one group of psychiatrists and clinical psychologists whilst for two other groups diagnoses were polarised between a unanimous decision or a minority opinion that he was normal, depending on an accompanying expert opinion on the absence or presence of mental illness respectively.

Some critics such as Szasz, have chosen to reject the concept of mental illness. Others have sought to more firmly establish medical psychiatry, such as Engel, an American professor of psychiatric medicine, who has proposed the expansion of the biomedical model of disease to that of a 'biopsychosocial' model, in order to incorporate 'disease' states such as grief. Engel's call for educational reforms of the medical profession "soundly based on scientific principles" and his assertion that:

it is the doctor's, not the patient's, responsibility to establish the nature of the problem and to decide whether or not it is best handled in a medical framework,

expose his goal of reinforcing the power of a scientific medical elite by expanding its jurisdiction over both body and mind into a wider social arena. Within the social sciences, an alternative to Engels' biopsychosocial model has been an ethnomedical model, based more on the Parsonian concept of disease in terms of social functioning and set within a cultural context.

The ascendancy of the scientific psychomedical expert as arbiter
of health-related decisions has been linked with the exclusion of women from the healing professions, a long-term process which some historians trace back to the elimination of female lay healers during the time of the European witch hunts. By the beginning of this century the medical expert had become male, white and a member of the upper socio-economic class, unlike the majority of his patients. This imbalance has been identified as a major force in the use of minor tranquillizers and is explored later in this chapter.

3.2.2 Addiction

The limits of the dominant biomedical model of disease are vividly illustrated in the area of addiction which has emerged as a major safety issue with respect to the benzodiazepines. An historical outline was given in Chapter 2 of changes to WHO definitions of addiction over the past thirty years. By the 1970s the term 'dependence' had been put forward to replace 'addiction', as its use had been limited to describe a purely physiological process and primarily focussed on the opiates. This model of addiction has been described by Moss and Nicholson as:

a model that included the inherent overpowering nature of the drugs .... the two key indicators of addiction became the development of physical tolerance to the drug and the appearance of physical withdrawal symptoms once the drug was removed from the person's system.

Within a space of only twenty years since the formation of its Expert Committee on Addiction-Producing Drugs, the interpretation by WHO has undergone considerable change; from one which attached addictive properties to certain drugs, with the primary effect being physical addiction, to a more recent emphasis on addictive behaviour, in which physical effects may or may not be present. This shift toward a behavioural view of drug addiction reflects a contemporary view that
physical effects are not a necessary part of drug dependence. However, the WHO definition is still problematic in that it perpetuates a dichotomy between the mind and body. We are still viewing two sides of the same coin; our attention is merely being focused on to the other side of that same coin. Nevertheless, contemporary debate on benzodiazepines reveals that some medical 'experts' continue to hold the view that the danger is in the drug. For example, Marks recently differentiated between a "psychoactive substance" (one which "influences mental processes") and a "psychotropic substance" (which "influences mental processes and on which dependence occurs").

Furthermore, the term 'addiction' has not been wholly replaced by the term 'dependence'; both coexist amongst health professionals and in popular usage. There are a growing number of health professionals, other than doctors, working in the field of addiction. During the 1970's, the concept of addiction as a behavioural phenomenon had broadened beyond the use of drugs. For example, changed community attitudes were reflected in the concept of addiction put forward in 1975 by the American social psychologist, Stanton Peele, in terms of any object, including relationships between people. Soon after, he proposed the following definition:

addiction is any compulsive activity or involvement which decreases a person's ability to deal with other aspects of his life to the point where that activity or involvement comprises the dominant source of emotional reinforcement and identity for the person.

Nicholson and Moss have proposed that this contemporary view of addiction corresponds to that which was widely held prior to the Industrial Revolution. Industrialisation was accompanied by a sense of personal powerlessness at the widespread and fundamental changes in the
structure of society. Alcohol and, later, opiates and other drugs were seen to be able to take control of the individual. This view of the 'dangerous drug' profited the medical profession, who could appoint themselves to the control of such substances, thereby enhancing their power as well as medicalizing problems that people encountered with drugs.  

Levine has traced the history of the emergence of the disease concept of alcoholism (loss of control over drinking behaviour, curable only by abstinence). He states that around the turn of the 19th century a new paradigm, or model, was created which:

defined addiction as a central problem in drug use and diagnosed it as a disease, or disease-like. ... During the 17th century, and for most of the 18th, the assumption was that people drank and got drunk because they wanted to, and not because they 'had' to. ... alcohol did not permanently disable the will; it was not addicting, and habitual drunkenness was not regarded as a disease.  

Levine depicts the emergence of the disease concept of addiction at that time as a paradigm shift from the Old World view, where a person's behaviour was believed to be based on choice (not compulsion), to a New World view, which embraced:

Locke's argument that it is possible to differentiate between 'Desire' and 'Will'. This distinction is ... at the heart of the concept of addiction.  

The two paradigms can be represented by two conflicting views of individual behaviour: 'voluntary' (active choice) and involuntary (loss of control). Despite its apparent attempts to move away from some of the aspects of the disease theory of addiction, through replacement of terms such as 'alcoholism' with 'alcohol dependence syndrome', the WHO clearly still uses an "involuntary" model, for example when they
recently described alcohol dependence syndrome as:

characterised by behavioural and other responses that always include a compulsion to take alcohol.\textsuperscript{28}

The contemporary re-emergence of the 'voluntary' model of addiction has accompanied a rejection of use of terminology such as the 'disease' of addiction, which was so long associated with the 'involuntary' model.\textsuperscript{29} In her review of contemporary views of addiction, Krivanek captures the prevailing sentiment amongst health workers in the field of addiction when she rejects a disease model, preferring to describe addiction as the extreme of a 'drug misuse-addiction continuum'. Like others, she resists rejecting the term 'addiction'; instead, it has been redefined in behavioural terms, describing drug addiction as:

a behaviour pattern characterised by an ongoing and overwhelming preoccupation with the use of a drug and the securing of its supply.\textsuperscript{30}

The challenges to the concept of addiction within different health professions mirror a corresponding tension within community concepts of disease. A 'voluntary' model of disease, coming out of 'marketplace' psychology is competing for acceptance.\textsuperscript{31} Some medical practitioners have also adopted these new concepts.\textsuperscript{32} The struggle over concepts and terminology concerning addiction hinge on the role of different health professions and their struggle for legitimacy with respect to the medical profession. Moss and Nicholson point out the crucial role of the medical profession in the last century in promoting the 'involuntary' concept and, thus, that addiction was a disease.\textsuperscript{33}
3.3 The Consumers of Tranquillizers

It was shown in Chapter 1 that women are twice as likely as men to be prescribed benzodiazepines. Cooperstock and Hill\textsuperscript{34} have identified three other groups at risk: the elderly, chronically ill and the institutionalized. Because these groups are not mutually exclusive, elderly women are most at risk. Another study on elderly women's high use of psychoactive drugs has described the phenomenon as the medicalization of poverty.\textsuperscript{35} Whilst relevant, this view does not recognize sufficiently that the medicalization process also includes being female and aged.

A Canadian study has examined high consumers of mood-changing drugs, including minor tranquillizers (that is, those more likely to be addicted to these drugs). High consumers were found to: be women; be in the older age groups; report relatively poor health and a higher degree of unhappiness; have difficulty defining their problems to their doctors; have a low level of education; be married; be unemployed outside the home; and more likely to be heavy smokers yet abstain from alcohol.\textsuperscript{36} By contrast, men are more likely to be high consumers of alcohol and less likely to visit the doctor for help with emotional and other life-style problems.\textsuperscript{37} An American survey found that women who are long-term users of minor tranquillizers and/or sedatives are more likely to be poorly educated and of lower socio-economic status\textsuperscript{38}. In Australia, it was found that the highest users of prescribed mood-changing drugs were pensioners or housewives.\textsuperscript{39}

Gender-based differences in tranquillizer use have been most extensively examined, undoubtedly as a direct result of the strong resurgence of interest in women's health issues coming out of the second wave of feminism.\textsuperscript{40} Class-based differences in tranquillizer use have
been more difficult to identify and reflect the problematic relationship between illness and class as well as gender and class. Differences based on ethnicity or aboriginality have received minimal attention in Australia, as elsewhere.

3.3.1 Women

There is a marked gender imbalance between doctors and patients: in Western societies about 80% to 90% of doctors are male (in Australia the figure is about 85%) whereas twice as many women as men are prescribed benzodiazepines. Clarke's review of gender and illness should be borne in mind with respect to medical and sociological research on gender-based illness presented in this section.

The following five models summarise the reasons most often used to explain prescribing patterns of benzodiazepines: they are the morbidity, consulting, reporting, stereotyping and social control models.

(a) Morbidity Model

According to this model, more women than men suffer from psychiatric and other emotional illness.

This can be a biologically determinist argument claiming innate differences between men and women in susceptibility to mental or emotional disturbances (such as hormonal influences) and draws on medical definitions of disease as discussed above. Medical evidence is usually sought by attempts to "measure" psychiatric illness, using information obtained either in the clinical situation, from the patient or the doctor, or from health surveys, as shown in Chapter 2. Under the guise of 'scientific' questionnaires, these are basically either self-reports or 'expert' judgements masked by the subsequent conversion to numerical data useful for statistical analysis and a positivist belief
in a value-free science. It was shown in Chapter 2 that such data are restricted by the limits of the measuring device, which make it impossible to measure psychiatric illness free from bias of the observer or the observed, and thus social and political norms.

Alternatively, women's higher morbidity can be linked with their different social roles. Common reasons put forward include women's social roles being more stressful, the sick role being more compatible with other role responsibilities, or women's over-socialisation and adoption of a feminine role. For example, married women in Britain and the United States are more likely than single women to be treated for depression and anxiety, whilst for married men the reverse is true. Women in paid work outside the home have been reported to use fewer benzodiazepines and to be less liable to depression compared with women who stay at home. Often these 'social role' arguments are placed within a social control model. A positivist attitude towards identification and measurement of anxiety and other social problems is also important to this model.

(b) Consulting Model

There is a general consensus that women consult doctors more often than men. However, gender differences are relatively minor. For example, the 1983 Australian Health Survey found 57% of people who reported consulting a doctor were women. And a recent survey in Perth found no significant gender differences in use of health services, including consulting a doctor. These results may be confounded by factors discussed in the reporting model.

There are two common explanations of the consulting model. One is medical dominance over women's fertility cycle (contraception, pregnancy, child-birth, menopause). For example, in the field of
surgery medical dominance over women's fertility resulted in hysterectomy becoming the most frequent operation in the United States by 1980, replacing the tonsillectomy and the appendectomy. The other is that social structures assign greater responsibility to women for childcare so that children are brought to the doctor more often by women, who may therefore also consult the doctor. Moreover, data collection often does not allow for variations in the ratio of men to women in a population, especially amongst the aged who more often consult a doctor and are more often women.55

(c) Reporting Model

Surveys both in Australia and other Western industrialised societies agree that women, more often than men, report illness as well as emotional difficulties such as stress and depression. A Canadian study of long-term use of tranquillizers reported that men were less able than women to express emotions generally.57

Surveys can be criticised for using medical definitions of disease. For example, illness groupings in the Australian Health Surveys place "nerves, tension and depression" within the "mental disorders" category whilst migraine, hypertension, asthma, diarrhea and other stomach disorders, skin rashes, allergies, insomnia, breathing difficulties, chest pain, heartburn, dizziness, and headaches are grouped under other categories according to the international code number of medically defined diseases. Yet all of these complaints would be likely to have a stress-related component; whilst the medical model has split the mental from the physical and then into various categories consonant with specialisation within the profession, the common lay interpretation of stress-related illness could include many of the above.
Another problem lies with the exclusion of illness groupings. For example, in the Australian Health Surveys, whilst "hangover" is a category included, the frequency of drinking is not, and withdrawal from tranquillizers or other prescribed drugs was not included yet frequency of use of prescribed drugs was included. Similarly, cigarette smoking is not included in these health surveys despite the high incidence of tobacco use in drug-induced deaths (81% in 1984)\textsuperscript{59} and therefore morbidity. Alcohol and tobacco use have, instead, been segregated as "drug problems" rather than "health problems". Mechanic has described alcohol and tobacco use as "acting out" behavioral symptoms of stress-related illness, more likely to be expressed by men and, moreover, he has extended the symptoms to include violent crimes. That is, gender differences in reporting are not due to numerical differences in symptoms but rather to differences in the type of symptoms.\textsuperscript{60}

The gender of the person to whom a woman is reporting is also important. Cooperstock has found that women alter the content of their reporting when a man is present to agree more with the male view.\textsuperscript{61} The gender of the doctor also influences the doctor's attitudes. Male doctors have been reported to complain that female patients report vague emotional complaints which are trivial.\textsuperscript{62} This can also be considered within the stereotyping model.

(d) Stereotyping Model

According to this model, doctors are more prone to look for, and therefore diagnose, neurotic disorders in women because this is seen to be normal for women. The etymological roots of hysteria as a disease of the womb and the history of medicine's change of view of hysteria from a physical to a mental disorder have been described by Ehrenreich and English\textsuperscript{63}. This stereotypical view of women as emotionally unbalanced
and ruled by her biology permeates our society and is reinforced in medical education and by drug advertising as well as by women themselves who are not immune to social pressures.

Although there is no doubt that female stereotypes are used in describing patterns of illness in educational texts and in drug advertisements promoting minor tranquillizers for women, it is difficult to directly assess the effects on the doctor. However, the power of drug promotion is indirectly confirmed by the drug industry's continuing high expenditure on promotion, and by doctors' changing prescribing habits away from generics towards brand name products when moving from hospital practice to general practice.

Doctors' consistent reports of 'trivial' complaints from patients may also be gender biased when a male norm for health is chosen by the doctor and when a female patient is unable to describe her symptoms in terms clear to the doctor (that is, consistent with the medical model). Mant and her colleagues have proposed that doctors do not so much over-diagnose psychiatric disease for their female patients as that they under-diagnose among men.

(e) Social Control Model

Many criticisms of Western medicine and technology have viewed medicine as an agent of social control, a concept first suggested in 1951 by Parsons. Feminists have used this model with respect to the social control of women. Women's high rate of benzodiazepine use has been explained in terms of this model although a wave of publications on this subject in the mid-1980s have adopted an individualistic approach aimed more at the psychological problems of tranquillizer addiction and methods of self-help for withdrawal.
3.3.2 The Elderly

The extent of prescribing of minor tranquillizers to the elderly is under-stated. The elderly comprise a significant proportion of patients in general hospitals, veterans' hospitals, nursing homes and other institutions, and yet these same institutions are usually not included in data collections (for example, Australian figures on prescription sales and the Federal Government Health Surveys of 1978-79 and 1983). Nevertheless, surveys repeatedly show that elderly women are prescribed more psychoactive drugs than any other group according to age and sex.

An American survey done in 1970/71 found that minor tranquillizers and hypnotics were taken in the previous year by 33% women and 18% men, of the population surveyed aged 60-74. In Canada, it has been reported that twice the number of prescriptions for psychotropics are given to the elderly as for younger people. The 1983 Australian Health Survey found that the incidence of use of tranquillizers and sleeping pills for people 65 years and over (24%) was almost double that of those between 45 and 64 years of age (14%)—similar to the Canadian findings. However, methodological differences make it difficult to compare the various surveys.

Poly-drug use is another frequent problem for the elderly, creating iatrogenic illnesses. An English study has found that 75% of people over 75 years of age receive a drug and that two-thirds of these receive up to three drugs simultaneously. A Canadian study found that the average number of prescriptions dispensed in 1978-79 to those aged 65 and over in a regional drug benefit plan was 16 prescriptions per person per annum. This is particularly disturbing in view of the generally-held medical opinion that the elderly have less ability to metabolise
and eliminate drugs.\textsuperscript{74} Reasons put forward for the disproportionately high use of psychotropics by elderly people include the following. The morbidity and consulting models point to elderly people's poorer health and more frequent contact with doctors. For example, the 1983 Australian Health Survey found that the highest incidence of consultation with a doctor in the two weeks prior to the survey was for people aged 65 years and over (approximately 28\% followed by children under 5 years (22\% and then in decreasing order from 64 years down).\textsuperscript{75} By contrast, the consulting and social control models have also been applied to the high rate of prescribing of benzodiazepines to elderly people in terms of medicalization of social and other problems which are more often presented to the doctor.\textsuperscript{76}

3.3.3 The Chronically Ill

Chronic, rather than acute, disease has become increasingly important in Western medicine. Australian estimates of chronic health problems vary between 14\% and 45\% of the population, with the ten most often reported conditions being arthritis, hay fever, hypertensive disease, eczema and dermatitis, migraine, bronchitis, asthma, deafness, varicose veins and heart disease.\textsuperscript{77} Although many of these could be interpreted as strongly social in origin, they are commonly viewed as part of the changing pattern of modern disease within a medical framework. For example, Cooperstock has adopted this concept within a biopsychosocial model of illness but has criticized the widespread prescribing of mood-changing drugs such as the benzodiazepines to the chronically ill (such as for acute myocardial infarction, migraine and gastrointestinal disorders).\textsuperscript{78} An American study in the early 1970s found that 70\% of cases in which diazepam was prescribed were for
conditions other than "mental disorders"; they included musculoskeletal, circulatory, medical/surgical aftercare, gastrointestinal and other mainly physiological disorders (as well as "senility and geriatric care"). This has been confirmed elsewhere. The usual medical purpose stated for prescribing tranquillizers to the chronically ill is to either 'protect' the person from stress which could exacerbate their illness or from emotional reactions to the illness itself although this could also be expressed in terms of a social control model.

3.3.4 The Institutionalized

Information is much more difficult to gather concerning institutionalized people. Institutions such as hospitals, nursing homes and prisons appear to have considerable autonomy and to not be required to participate in government organised data collection on patterns of drug use. This is also true for Australia.

However, there is some evidence that these populations may be those most prescribed psychotropics. An American survey of mainly nursing homes in the early 1970s concluded that their high rate of use of tranquillizers indicated that benzodiazepines were also used as a tool for institutional control. Cultural or social differences in rates of use do exist, however. It was recently reported by a Sydney behavioural scientist that a nursing home he visited in Holland was supplying drugs to only two of the 240 people in the home, whereas the reverse trend is common in Australia.

3.4 The Medical Profession

Two important factors concerning the medical profession which have shaped benzodiazepine prescribing are medical education and the professionalization of medicine (a third - drug promotion - is discussed
3.4.1 Medical Education

The biomedical model of disease has dominated contemporary Western medical education. For example, a British medical student in the late 1960s, commenting on medical education, stated:

It is ridiculous that the study of venereal disease is compulsory when the study of sexual relations is ignored.83

A considerable body of evidence on sexism within medical education has been documented.84 A common belief amongst doctors is that most women are neurotic and it has been proposed that this has arisen from a conjunction of medicine's ideological emphasis on the physical over the psychological with the belief in the inferiority of women. Examples are given of ignorance or misinformation concerning female sexuality in American and British gynaecology textbooks as well as trivializing physiological problems such as menstrual disorders, vaginal infections and pain during labour.

It is only in recent years that medical education has begun to change a long-term practice of excluding women, from the early European university-trained physicians of the Middle Ages through to the establishment of obstetrics and gynaecology with the exclusion of midwives in America a little more than fifty years ago.85 Whilst women are increasingly studying medicine (and graduating more successfully than men), in Australia they are practising in lower status fields such as community medicine or specialised areas such as psychiatry. This trend has been blamed on educational constraints linked with the sexual division of domestic labour (female doctors carry most of the burden of domestic work). Medicine and obstetrics and gynaecology are perceived to have higher social status which is reinforced by rigorous
postgraduate education requirements. This effectively excludes women, whereas in psychiatry it is possible to qualify more quickly. Similar patterns have also been observed overseas. The high prevalence of a traditional sexual division of domestic labour amongst male and female doctors also strongly indicates that medical education has done little to correct (and may even reinforce) sexist stereotypes and these must flow on to affect attitudes to patients and prescribing patterns.

Current medical education in Australia appears to promote conservative attitudes to prescription of benzodiazepines. It has also been stated that Australian medical students are encouraged to prescribe generically during their hospital training. However, this practice changes dramatically once they enter private practice and appears to be strongly influenced by drug industry promotional activities (see Chapter 4).

For the specialisation of psychiatry, several studies in the late 1960s and early 1970s exposed differences in psychiatric diagnoses between and within Britain and the United States which could be traced to educational differences. London psychiatrists were ten times more likely to diagnose 'manic-depressive psychosis' than their New York colleagues who tended to diagnose 'schizophrenia' more often. British psychiatrists generally diagnosed mental illness less often although regional differences within Britain indicated that those trained at Glasgow more often diagnosed 'affective illnesses' (such as manic-depressive psychosis) than 'schizophrenia', while those trained at Maudsley Hospital in London diagnosed mental illness less often (as also did younger compared with older psychiatrists).

### 3.4.2 Professionalization

Turner has described the important role of professionalization as
a strategy of occupational control by doctors. He has identified three key factors in the process of professionalization: the production and maintenance of 'esoteric' knowledge, the cultivation and maintenance of a large base of clients, and the maintenance of autonomy and the relationship with the clients. In addition, for the medical profession he has stressed the importance of medical dominance over other health-related occupations such as midwifery (subordination), optometry (limitation) and chiropractic (exclusion) as described by Willis.91

Medical education and professionalization are strongly interdependent. The hospital has been identified as the primary influence on medical professional power.92 For example, the introduction of the British National Health Scheme (NHS) perpetuated the control of the teaching hospital sector by the specialists. Teaching hospitals operated with government funding whilst the specialists determined priorities for research and education within them. At the same time, the specialists also benefited financially from consultancy fees and from private practice.93 In America, the alliance of medicine with science and the accompanying educational changes introduced with the Flexner Report in the early twentieth century all consolidated power within a medical elite and facilitated greater professional controls over the practice of medicine, which has been categorized as activist, heroic and masculinist.94

Willis95 has provided a Marxist analysis of the power relations of the medical profession in Western industrialised societies. In tracing the history of the rise of medical power in Australia, he has stressed the importance of professionalization in his analysis of the division of labour in health care. He has shown that the social relations of class and gender have shaped "which technology is used, how and when it is
used and who controls its use within a hierarchically organized health care system where the medical profession is in the most powerful position. The significance of the medical profession in shaping minor tranquillizer use is illustrated in a Canadian survey which found that nurse practitioners prescribed far less use of tranquillizers and sedatives than doctors. Freidson and Johnson have been acknowledged as key figures in the development of structuralist theories on professionalism around issues of power: Freidson in emphasising a profession's organised autonomy over control of its own work, permitting it to form a monopoly unlike many other occupations; Johnson for rejecting trait theory and functionalist interpretations of professions in favour of a theory of different institutionalized forms of professional control, whether collegiate, by patronage or state mediation.

By examining the division of labour in health care, Willis has concluded that state patronage underpins medical dominance and its reproduction of class structure, but he goes further to stress the importance of the ideology of professionalism in legitimating autonomy of doctors and therefore strengthening their position of power through self-regulation. Willis also attempts to incorporate the effects of gender, race and other factors in his discussions on power relations within medicine. When he examines gender issues within the division of labour, mainly through a section dealing with the subordination of midwifery, he concedes that: "in this instance gender struggle takes precedence (over class)" and "in some historical instances, such as the subordination of midwives ... the gender of the historical actions must also be considered". However, with respect to the other two sections on optometry and chiropractic within the division of labour
(both male dominated fields), he has concluded that gender is not important to the history of medical dominance. His assertion denies the historical antecedents to the exclusion of women from optometry and chiropractic and, above all, from medicine itself (for example, the emergence of male medical dominance in the United States arising from the early conflict between the irregular and regular doctors).104

Many writers on the power of the medical profession, such as those discussed above, omit to include the importance of medical prescribing power. This has been important in maintaining medical dominance such as over the profession of pharmacy and with respect to drug industry sales where two distinct markets have been created: 'ethical' and 'over-the-counter' (OTC) drugs. American pharmacists, for example, have been given a greater role in prescribing since the early 1970s with the repeal of the anti-substitution laws.105 Pressures to introduce similar practices in Australia have been unsuccessful so far. Medical dominance with respect to other health practitioners has also reinforced high prescribing rates since non-medical practitioners are excluded from the Medicare system, or not permitted to prescribe drugs, or practice non-drug therapies (such as counselling, meditation, acupuncture, and massage). The medical profession zealously guards its 'freedom to prescribe' and generally resists state auditing or regulation of this.106

Most importantly, the Marxist focus on the division of labour in medicine has led writers such as Willis to neglect the power relations in the doctor-patient relationship and therefore to virtually deny the important role of the patient. This has been addressed by Freidson in his discussion of the ways in which bureaucratic or professional medicine treat the client as an object.107 This has important
implications for prescribing practices, in that the objectification of
the patient linked with the profit motive, has shaped the structure of
medical practice so that consultations are brief and pressures increase
on the doctor to prescribe in order to be seen to be effective. It has
been estimated that 75% of consultations with a general practitioner,
family practitioner or internist result in the use of at least one
drug.108

However, prescribing patterns of benzodiazepines are not constant
within the medical profession and indicate marked divisions between
different sections of the profession. Psychiatrists and neurologists
have accounted for only 17% of prescriptions for mood-changing drugs and
even less for the two major benzodiazepines, diazepam and
chlordiazepoxide. By contrast, general practitioners produce 40% of
prescriptions for mood-changing drugs.109 Drug promotion is often
blamed for high prescribing rates but it is clear that an important
factor is also the doctor's susceptibility to the drug industry message.
This would be shaped by educational differences which, in turn, depend
on the professional organization and strength of the different medical
groups and the way they determine their own educational processes.
Postgraduate education has the potential to educate doctors in a more
conservative approach to drug therapy. As psychiatrists would tend to
see people with severe anxiety or other emotional problems, they may
tend to prescribe major rather than minor tranquillizers (although in
Chapter 2, evidence was cited for benzodiazepine efficacy only against
medium to high levels of anxiety). This tendency has not been evaluated
in the literature. Most importantly, the retreat from professional
unity by specialisation within the medical profession has diluted
medical political power.110
The economic and political benefits enjoyed by doctors closely involved in drug and other health-related industries have been described as contributing to a medical-industrial complex. These can arise from doctors' entrepreneurial activities in profit-making health care industries, such as private hospitals or non-hospital based diagnostic laboratories or from their position as employees within the drug industry. In the latter case, doctors are attempting to improve their image and legitimate their activities within the process of professionalization. In the 1970s a new medical specialty - pharmaceutical medicine - was created and reinforced by promotion of appropriate certification and publication of specific textbooks.

3.5 Health Consumer Movement

Health consumers have played a crucial role in changing attitudes to tranquilizers. In the late 1970s and early 1980s, critical reports of benzodiazepines - mainly Valium - became widespread. In the United States, the public attack against Valium intensified with the release in 1979 of Barbara Gordon's autobiography, *I'm Dancing As Fast As I Can*, detailing her addiction to Valium and which underwent eleven printings in 1979 (its year of release) and was serialized in the *Ladies' Home Journal*. Most importantly, political pressure from Ralph Nader's consumer group - the Public Citizen Health Research Group - provoked a strong public and industry response with the release in 1982 of their book, *Stopping Valium* (publication coincided with the release of the film version of *I'm Dancing As Fast As I Can*). Roche reacted to the adverse publicity surrounding their best-selling product, vital to their profitability, by initiating legal proceedings against the book's allegedly inappropriate use of a trade name and demanding the pulping of all copies.
The groundswell of change in public attitudes to minor tranquillizers in the United States during the 1970s, led by women's groups as well as other health and consumer organizations, forced the government to respond in 1979 with an enquiry by the House Select Committee on Narcotics Abuse and Control on the use of these drugs amongst women. The drug industry responded by intensifying the focus of their advertisements on other markets, such as old people (that is, by medicalizing a normal process of aging into a disease state) and people having difficulties coping with physical illness. After repeated warnings from the Food and Drug Administration (FDA) to the drug industry to improve its self regulation with respect to promoting unnecessary use of tranquillizers, in 1980 the FDA itself finally imposed tighter regulations on advertising of benzodiazepines, by requiring the following warning in the product labelling:

(name of anxiolytic) is indicated for the management of anxiety disorders or for the short term relief of the symptoms of anxiety. Anxiety or tension associated with the stress of everyday life usually does not require treatment with an anxiolytic.117

Concurrently, the FDA tried to enforce compulsory inclusion of drug information for the consumer whenever a prescription for a benzodiazepine was filled. But, after a year of lobbying by the drug industry, trade groups and the AMA, the government suspended the regulation.118

The second wave of increased debate within the medical community over benzodiazepine safety, outlined in Chapter 2, which began in the late 1970s is clearly a reaction to the consumer movement's actions over benzodiazepine addiction. Whilst the debate still flourishes within the medical-scientific literature and in the community at large, prescribing
practices have only been slightly modified in that prescription rates have not continued to increase (see Chapter 1). A substantial number of these prescriptions may represent users who have become addicted to benzodiazepines. An unknown quantity of these prescriptions may never be filled or, once filled, not used completely. Whilst difficult to measure as well as carried out on an individualistic basis, non-compliance also represents consumer action against benzodiazepines and cannot be ignored. Patient non-compliance was estimated in 1980 to cost more than 300 million pounds per year.\textsuperscript{119}

Consumer power is also exercised through the litigation process. Recent legal actions over health related problems have been initiated by consumers overseas\textsuperscript{120} and in Australia\textsuperscript{121} against the giant tobacco companies (one case had cost the industry about $25 million in legal defence costs).\textsuperscript{122} Doctors' prescribing of benzodiazepines in Australia may be curtailed by fear of legal and economic costs, following the first successful prosecution in 1986 of a West Australian psychiatrist by a former patient who had become addicted to Lexotan.\textsuperscript{123}

The current strengthening of conservative forces within Western industrialized societies threatens the continued effectiveness of movements for social change, such as the health consumer and women's movements. The dangers of neo-Romanticism to the women's movement\textsuperscript{124} and the professionalization of consumer representatives on official organising bodies dealing with health issues\textsuperscript{125} are just some of the potential traps. Nevertheless, the political power of the health consumer movement continues to challenge medical dominance and, in Australia, has undergone remarkable growth in the past few years (see Chapter 5).
3.6 Conclusion

The changing meaning of benzodiazepine use has been explained in terms of changing concepts of health and illness. The biomedical model of scientific medicine is being challenged by medicine's extension into the social sphere. The disease concept of addiction was used to explore some of the conflicting forces in the struggle for a dominant paradigm within medicine. The social forces shaping the use of benzodiazepines were firstly elaborated by turning to the major users of minor tranquilizer (women, the elderly, the chronically ill and the institutionalized) and examining five different models commonly used to explain their behaviour. The role of the medical profession was then examined for their direct effects on the consumer (structure of the consultation process, sexist stereotypes) and indirectly through education and continuing education (including drug industry advertising) and the professionalization process of the doctor.
FOOTNOTES

1. It has been found that only 30% to 50% of patients want a prescription whereas 80% to 90% of doctors think the patient wants them.


3. The Macquarie Dictionary, (McMahon's Point, Sydney, Macquarie Library Pty Ltd, 1982)


7. I. Kennedy, op cit, (note 4), pp.11-12


15. Ibid, p.133

17. Barbara Ehrenreich and Deirdre English, For Her Own Good. 150 Years of the Experts' Advice to Women, (London, Pluto Press, pp.29-61)


24. S. Peele, op cit, (note 19), p.103


27. Ibid, pp.149,150


30. Ibid, p.83

31. For example: Louise Hay, Metaphysical Causations for Physical Illness, (Concord NSW, Specialist Publications, 1982)

32. John Harrison, Love Your Disease. It's Keeping You Healthy, (Sydney, Angus & Robertson, 1984)


A great deal of work on minor tranquillizer use has been done by Canadian researchers, of whom Cooperstock is most prominent.


These findings have been supported by Australian studies, such as the Adelaide study in the late 1970s which found women who used high quantities of benzodiazepines tended to be either pensioners or housewives. Warwick Heine and Andrea Mant (1979), "Drug Use in Adelaide 1978", in Royal Commission into the Non-Medical Use of Drugs, South Australia, *Three Studies in Drug Use*, (Adelaide, Royal Commission into the Non-Medical Use of Drugs, 1979), p.82


38. Hugh J. Parry et al, "National Patterns of Psychotherapeutic Drug Use", *Arch Gen Psychiatry, 28*, pp.778-790

39. W. Heine & A. Mant, *op cit*, (note 36), p.82


41. L. Rogers, *op cit*, (note 1), pp.73-74


44. Lesley Rogers, *op cit*, (note 1), p.71

45. A. Mant et al, *op cit*, (note 40), p.191

46. J. Clarke, *op cit*, (note 9)

47. Andrea Mant et al, (note 40), pp.185-192

48. Hilary Standing, "'Sickness is a Woman's Business?' Reflections on the Attribution of Illness", in The Brighton Women & Science Group,


50. R. Cooperstock & J. Hill, op cit, (note 34), p. 11

51. L. Rogers, op cit, (note 1), p. 72


53. This figure approximates other data obtained from surveys of general practitioners in Australia. See A. Mant et al, op cit, (note 40) p. 188

54. Juanne N. Clarke, op cit, (note 9), p. 65

55. Ibid, p. 75


57. R. Cooperstock & H. L. Lennard, op cit, (note 40), p. 335


60. Juanne N. Clarke, op cit, (note 9), p. 73

61. R. Cooperstock & H.C. Lennard, op cit, (note 40), p. 335


63. B. Ehrenreich & D. English, op cit, (note 17), pp. 120-126

Their results contradicted most other evidence on the high rate of prescribing of minor tranquillizers for women and may be explained by methodological problems such as the small number of doctors in the sample.

Peter Conrad, "Types of medical social control", Sociology of Health and Illness, 1 (1), 1979, p.1

For example, Phyllis Chesler, Women & Madness, (NY, Avon Books, 1973); B. Ehrenreich & D. English, op cit, (note 17); L. Doyal, op cit, (note 40)

L. Rogers, op cit, (note 1); J. Harding, op cit, (note 35).

Celia Haddon, Women and Tranquillisers, (London, Sheldon Press, 1984); Joy Melville, The Tranquillizer Trap and How to Get Out of It, (Fontana, 1984); Valerie Curran & Susan Golombok, op cit, (note 49)

R. Cooperstock & J. Hill, op cit, (note 34), p.14

L. Rogers, op cit, (note 1), p.73

R. Cooperstock & J. Hill, op cit, (note 34), p.14

Ibid


L. Rogers, op cit, (note 1); J. Harding, op cit, (note 35)

E. Bates & S. Linder-Pelz, op cit, (note 52), pp.57-58

R. Cooperstock & J. Hill, op cit, (note 34), pp.15-16


R. Cooperstock & H.L. Lennard, 1979, op cit, (note 40), p.342


I. Zola, "In the Name of Health and Illness", in I.K. Zola, Socio-Medical Inquiries. Recollections, Reflections, and

84. L. Doyal with I. Pennell, op cit, (note 40), pp.221-226; Diana Wyndham, "He was her medical man, but he done her wrong", New Doctor, Sept-Oct 1983, p.30

85. B. Ehrenreich & D. English, op cit, (note 17), pp.33-88


87. L. Doyal with I. Pennell, op cit, (note 40), pp.201-203

88. A. Britton, L. Forcier & D. McKissock, Phase I Report of the NSW Medical Education Project: Alcohol and Other Drugs, (Sydney, NSW Medical Education Project: Alcohol and Other Drugs, 1986), p.245


91. Evan Willis, Medical Dominance. The Division of Labour in Australian Health Care, (Sydney, George Allen & Unwin, 1983)

92. B.S. Turner, op cit, (note 42), p.158

93. L. Doyal with I. Pennell, op cit, (note 40), pp.180-182

94. B. Ehrenreich & D. English, op cit, (note 17), pp.74-88

95. Evan Willis, op cit, (note 91), pp.12,13

96. Ibid, p.201

97. Diana Wyndham, op cit, (note 40), p.23


100. Evan Willis, op cit, (note 91), p.11

101. Ibid, pp.8, 204

102. Ibid, p.123

103. Ibid, p.205

104. B. Ehrenreich & D. English, op cit, (note 17)

106. For further discussion, see Chapter 4

107. Eliot Freidson, Professional Dominance, op cit, (note 98)

108. Ingrid Waldron, "Increased Prescribing of Valium, Librium, and Other Drugs - An Example of the Influence of Economic and Social Factors on the Practice of Medicine", Intern J Health Services, 7 (1), 1977, p.53

109. Ibid, p.39

110. B.S. Turner, op cit, (note 42), p.192

111. B.S. Turner, op cit, (note 42), p.188


116. Ibid

117. E. Bargmann et al, op cit, (note 64), p.118

118. Ibid, p.41

119. B.S. Turner, op cit, (note 42), p.50

120. Frances Gibb, "UK smoker sues over sickness", The Australian, 21 August 1986

121. Prue Innes, "Woman says she was told: too young for lung cancer", The Age, 19 August 1986

122. Frances Gibb, op cit, (note 120)

123. "$19,000 for addiction to tranquilliser", SMH, 13 May 1986; "Tranquilliser case a landmark for doctors", SMH, 14 May 1986

4 THE DRUG INDUSTRY AND REGULATION BY THE STATE

4.1 Introduction

The economic successes and political and ethical problems experienced by the drug industry have attracted considerable attention from both Marxist and other analysts. This work, as for many others, makes use of Silverman's extensive research of the industry, in both the United States and the developing countries, gained from his background as a trained scientist, academic and science writer with many years' experience in the United States as a consultant to the state on health issues.¹

Whilst including the important role of the medical profession and consumer, this chapter concentrates on the drug industry and its interactions with the state. Firstly, factors significant to the development and marketing of minor tranquilizers and other ethical drugs are discussed, including industry profits, patent protection and its importance to profitability, different avenues for research and development, the complexity of drug promotion, and interventions by the state on drug safety and efficacy. Secondly, two case studies conclude the chapter: one describing the British attempt to curb the numbers of benzodiazepines available on the NHS and at the same time to introduce a limited drug formulary, and the other describing the confrontation between the British state and Roche over the company's transfer pricing policies with respect to Valium and Librium. Both studies provide valuable insight into past attempts at and potential future state controls on the drug industry in Australia, which will be examined in Chapter 5.

The chapter concludes with a discussion of various neo-Marxist analyses of the state and medicine and their application to the minor
tranquillizer drug industry. Whilst none of these theoretical approaches has been adopted, a broad summary has been provided of the economic, political and social forces shaping minor tranquillizer use through the drug industry and the state.

4.2 Profitability of the Drug Industry

The pharmaceutical drug industry has the reputation of being the most powerful and profitable in the world. It is dominated by a small number of transnational companies established in Germany, Switzerland, France, Britain and the United States but with subsidiaries world-wide, as shown in Table 4.1 (which lists the top fifty drug companies in 1977 ranked by value of pharmaceutical sales).

In Australia, there are about 140 companies which manufacture and/or supply pharmaceutical drugs, and about 110 of these supply items for the Pharmaceutical Benefits Scheme (PBS). In 1985 the largest market shares (in descending order of market share) were held by five subsidiaries of overseas transnationals: Merck, Sharp and Dohme; Ciba-Geigy; Wellcome Australia; Roche; and Glaxo. The top four companies held about 40% of the PBS market and about 20% of the overall drug market. Only a small number of drug companies supplying the Australian market manufacture locally and most of these established facilities in Australia during the 1950s and 1960s, when profits were high and Australia was attractive as a regional base for exporting to the South-East Asian region.

There are about ten thousand drug manufacturers around the world. Of these, only about one hundred operate at an international level, accounting for about 90% of world shipments of all drugs for human use (valued at $(US)50 billion in 1976) whilst the top fifty drug companies account for two-thirds of this total. Australia's small contribution to
Table 4.1: Top Fifty Transnational Pharmaceutical Companies, 1977

<table>
<thead>
<tr>
<th>Rank</th>
<th>Company</th>
<th>Domicile</th>
<th>Pharmaceutical sales $(US)</th>
<th>Proportion of pharmaceutical sales to total sales (%)</th>
<th>Product Lines included in pharmaceutical sales^a</th>
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85a
Table 4.1 (continued)

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<th>Rank</th>
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<td>69</td>
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</tr>
<tr>
<td>44</td>
<td>A.H. Robins</td>
<td>USA</td>
<td>212</td>
<td>69</td>
<td>1, 2, 4, &amp; 5</td>
</tr>
<tr>
<td>45</td>
<td>BASF</td>
<td>FRG</td>
<td>210</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>46</td>
<td>Meiji Seika</td>
<td>JPN</td>
<td>175</td>
<td>32</td>
<td>1</td>
</tr>
<tr>
<td>47</td>
<td>CM Industries</td>
<td>FRA</td>
<td>165</td>
<td>62</td>
<td>1, 2, 3</td>
</tr>
<tr>
<td>48</td>
<td>Altana (Varta)</td>
<td>FRG</td>
<td>158</td>
<td>47</td>
<td>1</td>
</tr>
<tr>
<td>49</td>
<td>Miles Laboratories</td>
<td>USA</td>
<td>158</td>
<td>33</td>
<td>1, 7</td>
</tr>
<tr>
<td>50</td>
<td>Tanabe Seiyaku</td>
<td>JPN</td>
<td>154</td>
<td>51</td>
<td>1, 5</td>
</tr>
</tbody>
</table>


world sales is shown in a 1986 geographic breakdown of world sales (by value): European Economic Community (EEC) 25%; USA 20%; Eastern Europe 15%; Japan 15%; Australia 2%; Other 23%.^  

The level of 'foreign' sales of the top fifty drug companies varies widely, from a low of 7% (or less) of output for the Japanese companies (which manufacture mainly for a large domestic market) to a high of more than 90% for the Swiss companies. Only three countries (the United States, the Federal Republic of Germany and Japan) produce half of the world's output of pharmaceutical products.5 Table 4.2 illustrates how Australia (and Canada) is in a similar position to Third World and developing nations in its low level of support of a domestic pharmaceutical drug industry, and its corresponding reliance on imports from overseas-based transnationals.

Profits in the pharmaceutical industry generally far exceed those for other manufacturing industries.6 World-wide sales (human and veterinary products, dosage and bulk forms) of American drug companies from 1950 to 1960 approximately doubled in value, and in the subsequent decade improved even further by almost trebling in value (from $1.4 billion in 1950 to $6.8 billion in 1970). The profitability of the drug industry was estimated to generally average about double the rest of manufacturing industry. Net profits (as a percentage of sales) for the American drug industry averaged 9% from 1960 to 1972, with some companies showing profits far above this average (for example, in 1972 profits of the twenty-six major drug companies in the United States varied from 2.1% to 21.9% of sales; at other times, net profits have been reported of up to 54% and even during the depression years of 1930 to 1935, Upjohn reported minimum profits of 30%). In contrast, profits on sales for all other American manufacturing industry have usually been
<table>
<thead>
<tr>
<th>Country</th>
<th>Domestic Share (%)</th>
<th>Foreign Share (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saudi Arabia</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Nigeria</td>
<td>3</td>
<td>97</td>
</tr>
<tr>
<td>Belgium</td>
<td>10</td>
<td>90</td>
</tr>
<tr>
<td>Venezuela</td>
<td>12</td>
<td>88</td>
</tr>
<tr>
<td>Canada</td>
<td>15</td>
<td>85</td>
</tr>
<tr>
<td>Australia</td>
<td>15</td>
<td>85</td>
</tr>
<tr>
<td>Brazil</td>
<td>15</td>
<td>85</td>
</tr>
<tr>
<td>Indonesia</td>
<td>15</td>
<td>85</td>
</tr>
<tr>
<td>Mexico</td>
<td>18</td>
<td>82</td>
</tr>
<tr>
<td>India</td>
<td>25</td>
<td>75</td>
</tr>
<tr>
<td>Iran</td>
<td>25</td>
<td>75</td>
</tr>
<tr>
<td>Argentina</td>
<td>30</td>
<td>70</td>
</tr>
<tr>
<td>Philippines</td>
<td>35</td>
<td>65</td>
</tr>
<tr>
<td>Italy</td>
<td>40</td>
<td>60</td>
</tr>
<tr>
<td>Netherlands</td>
<td>40</td>
<td>60</td>
</tr>
<tr>
<td>South Africa</td>
<td>40</td>
<td>60</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>40</td>
<td>60</td>
</tr>
<tr>
<td>Sweden</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>France</td>
<td>55</td>
<td>45</td>
</tr>
<tr>
<td>Spain</td>
<td>55</td>
<td>45</td>
</tr>
<tr>
<td>Germany, Federal Republic of</td>
<td>65</td>
<td>35</td>
</tr>
<tr>
<td>Switzerland</td>
<td>72</td>
<td>28</td>
</tr>
<tr>
<td>United States</td>
<td>85</td>
<td>15</td>
</tr>
<tr>
<td>Japan</td>
<td>87</td>
<td>13</td>
</tr>
<tr>
<td>USSR</td>
<td>100</td>
<td>0</td>
</tr>
</tbody>
</table>

a The home country of at least one of the major pharmaceutical transnational corporations

around 6%. Similarly, annual after-tax profits based on investment averaged 18% in contrast with only 11% for all major American manufacturing industry. Profits on prescription drugs would be even higher, since these figures include other pharmaceutical products, subject to much greater price competition. A similar pattern of high profitability compared with the manufacturing sector as a whole has been demonstrated in the British drug industry.

Table 4.3 illustrates the differential effects on profits by various manufacturing items in the drug industry. Because profits are so much more sensitive to price changes compared with sales volume, drug companies will set prices as high as the market will bear and will defend those prices, sometimes at great cost in the short term, with a view to protecting their profits over the longer term.

4.3 Patents

Patents have been crucial to the ability of drug companies to monopolise an innovative drug treatment and therefore to charge high prices. In the case of Roche's Valium and Librium, this has been clearly documented in Section 4.9.2. Historically, the patented medicine business was an important forerunner of the modern drug industry. The high profits possible from patented drugs were realised at an early date and examples can be found dating back to at least seventeenth century Britain.

Contemporary drug companies tend to specialize in a restricted range of patented products (for example, ICI's heart pills, Beecham's antibiotics and Roche's tranquillizers), effectively concentrating research, production and marketing around non-competing specialities. Up until the 1960s, large numbers of combination products were marketed containing drugs whose patents had expired but which could be repatented.
### Table 4.3: The Effect of Various Manufacturing Items on Profit in the Pharmaceutical Industry

<table>
<thead>
<tr>
<th>Factor</th>
<th>Increase or Decrease</th>
<th>Increase in Profit before Tax</th>
</tr>
</thead>
<tbody>
<tr>
<td>Price</td>
<td>10% increase</td>
<td>33%</td>
</tr>
<tr>
<td>Sales volume</td>
<td>10% increase</td>
<td>20%</td>
</tr>
<tr>
<td>Manufacturing costs</td>
<td>10% decrease</td>
<td>13%</td>
</tr>
<tr>
<td>Marketing expenditure</td>
<td>10% decrease</td>
<td>5%</td>
</tr>
<tr>
<td>Research expenditure</td>
<td>10% decrease</td>
<td>3%</td>
</tr>
<tr>
<td>General and administrative expenditure</td>
<td>10% decrease</td>
<td>2%</td>
</tr>
</tbody>
</table>

**Source:** Arabella Melville & Colin Johnson, *Cured to Death. The Effects of Prescription Drugs*, (Sevenoaks, Kent, New English Library, 1983), p.49
in combination with another drug. The combined effect of patent protection and the profit motive in drug research and development has contributed to the large number of drugs available. Market leaders stimulate other companies to imitate their success with 'me too' drugs, producing similar compounds which have been modified sufficiently to be patentable and with less associated risk and lower research and development costs. As a result, the market for branded prescription drugs has been described as "product-competitive" rather than "price-competitive".\textsuperscript{10}

Whilst some countries, such as the Communist bloc and Italy, do not provide patent protection, other countries which do, such as Britain, Canada and Sweden, can enforce compulsory licensing arrangements which grant a limited period of exclusive rights to the patent holder, after which the company must grant a licence in return for royalties from other companies for the remainder of the patent period.\textsuperscript{11} Some of the economic and political ramifications of licensing of patented drugs have been illustrated in the case study of Valium and Librium in Britain, set out in Section 4.9.2.

4.4 Drug Research and Development

Most drug companies spend about 10\% of their turnover on research and development (R & D).\textsuperscript{12} The drug industry defends its high profits with the argument that it is a high risk industry, especially in research and development. However, data on market share instability and equity capital investments for the drug industry show that the high risks are more than offset by much higher profits.\textsuperscript{13}

Industrial drug research has changed dramatically since its beginnings last century as a side-line for European dye-manufacturers. It now follows the highly successful American example of large teams of
researchers working in expensively equipped laboratories (for example, Upjohn employed approximately four hundred scientists in 1970 compared with only twelve in 1938).

In the early 1970s, the American drug industry was spending about $700 million per year on drug research and had introduced several dozen major new drugs (as well as over one hundred 'me too' types of drug) during the preceding decade. Additionally, about $100 million per year was spent by the American government to produce about one dozen major new drugs. Even within the state, however, expenditure on drug R & D is not easily accountable. For example, of about $1.5 billion spent within the medical research budget of the National Institutes of Health (NIH), it has been estimated that a not inconsiderable portion would have included basic research of potential long-term benefit for the development of new drugs for both government and private industry.\textsuperscript{14}

The drug industry also funds researchers outside their organizations such as in academic institutions. Results from benzodiazepine research funded in this way have sometimes been the opposite of corporate expectations, and this was illustrated by two of the studies discussed in Chapter 2. Tyrer and Owen were partly funded by the British drug company Bristol-Myers for their study, which found no evidence that short-term diazepam use was effective in the treatment of anxiety by general practitioners.\textsuperscript{15} The work by Shapiro and his colleagues, which found no evidence that long-term use of diazepam was effective against anxiety, was initially funded by Roche. However, the authors noted that this funding did not extend to most of the data analysis, which gave results unfavourable to Roche's major selling product.\textsuperscript{16}

Clinical trials of new drugs are also an important part of the
contemporary drug industry research program. These are usually carried out by consultant doctors not employed by the drug industry but, nevertheless, paid a substantial fee. Criticisms have been levelled at the methodological shortcomings in the conduct of drug trials. Also, standard short-term clinical trials cannot detect a variety of unwanted effects which may appear years later, and negligence or even outright fraud are difficult to detect. This was shown in a large-scale WHO study of clofibrate, an anti-cholesterol drug, which had been on the market for many years yet was found in this study not to be effective and perhaps even a danger to health.\(^{17}\)

In Australia, it has been estimated that limitations set by the state on clinical trials for marketing approval of a drug have produced a situation in which:

the product may have been studied in fewer than 100 subjects to establish efficacy and only up to 2000-3000 for assessing safety. Furthermore, it is uncommon to have data on long-term safety (>1 year) in more than 500 patients.\(^{18}\)

4.5 Drug Promotion

Estimates vary widely on how much the drug industry spends on drug promotion. Nevertheless, it is widely accepted that promotion attracts about double the funding of R & D within the drug industry. An estimated 22% of sales income (totalling about $1.8 billion) was spent on drug promotion in 1975 in the United States. The majority was spent on detailing and sampling whilst about 15% went to advertising in professional journals. British figures are at the lower end of the range of estimated promotional costs. For example, promotion has been estimated at only 14% of sales (about 32 million pounds in 1973). However, there is considerable variation within this estimate, ranging from less than 10% up to about 40% of sales (see Table 4.4). For
Table 4.4: Costs of promotion as a percentage of sales by size of company for the UK drug industry in 1969

<table>
<thead>
<tr>
<th>Sales of prescription drugs (in UK million pounds)</th>
<th>No of companies</th>
<th>Ave % of sales spent on promotion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over 8</td>
<td>4</td>
<td>9.6</td>
</tr>
<tr>
<td>5 to 8</td>
<td>4</td>
<td>10.0</td>
</tr>
<tr>
<td>3 to 5</td>
<td>9</td>
<td>12.1</td>
</tr>
<tr>
<td>2 to 3</td>
<td>9</td>
<td>16.9</td>
</tr>
<tr>
<td>1 to 2</td>
<td>6</td>
<td>23.2</td>
</tr>
<tr>
<td>0.5 to 1</td>
<td>14</td>
<td>24.3</td>
</tr>
<tr>
<td>below 0.5</td>
<td>52</td>
<td>40.0</td>
</tr>
</tbody>
</table>

example, a large company such as Roche, with sales of 9 million pounds, would spend less than 10% of sales income to employ about 66 detailers whereas Berk, a much smaller company with sales of only 2-3 million pounds, would have had to spend almost double the proportion of its sales income in order to maintain an equally large team of detailers.19

An increase in prescription volume has been linked with a drug detailer's increased visits to a doctor, although this may not be causative as detailers have been known to select high prescribers in preference, if they can gain access to this information.20 The high promotional expenditure on drug detailing has given unprecedented direct sales contact with doctors. Estimates of drug detailer:doctor ratios vary from 1:20 in Britain to 1:10 for the United States and only 1:3 for some developing countries (Mexico, Guatemala, Brazil).21

Promotional techniques tolerated for other products have been seen as unethical when offered by detailer to doctor. Examples range from free drug samples and preprinted prescriptions to more extravagant incentives such as colour television sets and travel.22 Recent controversy in Australia surrounded the Searle drug company's promotion of Lomotil, an anti-diarrhoeal, when they staged a competition with an overseas trip as first prize. About six thousand doctors saw no ethical problems in the promotion, when they sent in their entry coupons which included the following statement:

I am a Lomotil prescriber (we'll take your world for it) and would like to enter your Lomotil Summer Olympics' competition.23

Not so well publicized was the promotion in Australia of Capoten, an anti-hypertensive from Squibb, offering doctors loan of a computer, free of charge, in return for supplying medical data on at least five
patients using the drug. The drug company and the doctor benefited from this arrangement at the expense of the state. As Capoten is an expensive drug and for long-term use, it represented a large cost to the state ($79.30 per prescription) compared with the patient contribution of $10.24 Many large and reputable drug companies have been criticized for over-selling drugs, some of which have other potentially dangerous effects (for example, Parke-Davis' Chloromycetin (chloramphenicol) which causes aplastic anaemia and other blood disorders, Merk's Indocin (indomethacin) which can cause peptic ulcers, and Searle's oral contraceptive which was found to cause dangerous and even fatal blood clots).25

Claims of safety and efficacy in promotional literature rely on scientific authority by referencing scientific literature which, on closer examination, may have little or no relevance to the specific industry claims.26 Examples continue to surface indicating that the drug industry has difficulty conforming to state requirements, not only with its written claims of scientific support but also in the overall design of promotional material. For example, an employee of one British drug company was reported to comment on requirements imposed by the Department of Health and Social Security (DHSS):

As an art director you try to hide all this away ... We have to incorporate all this stuff without letting it dominate the ad or interfere with what we are trying to do ... We are actually more restricted in what we can say than what we can show.27

Doctors are exposed to drug advertising in most of their professional literature. In the United States the only medical publication free of drug company advertising is The Medical Letter28 (an equivalent situation exists in Australia with the Australian
By the early 1970s, advertising of the benzodiazepines was coming under increasing criticism. Gaylord Nelson, the American Senator who successfully challenged the drug industry, attacked Sandoz for advertising its minor tranquillizer Serentil in medical journals as useful for the relief of everyday tensions and anxiety-provoking situations such as "the newcomer in town who can't make friends" and "the woman who can't get along with her new daughter-in-law".29

Others have criticized the sexist advertising of minor tranquillizers (already mentioned in Chapter 3). Advertisements of benzodiazepines in medical journals have been seen to reinforce stereotypical sex roles. Doctors have been cast as the mediators when they prescribe long-term benzodiazepine therapy for many women expressing anxiety from unsuccessful attempts to conform to unrealistic social roles. Drug companies target stereotyped attitudes within the medical profession with advertisements which present the young housewife whose "symptoms reflect a sense of inadequacy and isolation", the female student whose "newly stimulated intellectual curiosity may make her more sensitive to and apprehensive about unstable national and world conditions", or the married female graduate "currently centered around home and children, with too little time to pursue a vocation for which she has spent many years in training".30

Promotional texts and accompanying illustrations dominate the greater part of advertisements; side effects are presented in smaller and harder to read type. A useful example of promotional methods was an advertisement for Valium in a 1983 Australian edition of MIMS.31 The dominant text appealed to a doctor's professional power of prescribing and a male doctor was pictured as the authority and expert in the decision-making process. Side effects were listed on the other side of
the page in small type together with other product information. An appeal to facts rather than feelings attempted to cast criticism of Valium and other benzodiazepines as irrational and unscientific. Finally, references to the scientific literature were used to support the use of diazepam in withdrawal from dependence on short-acting benzodiazepines and to deny the addiction potential of Valium.

The *Journal of the American Medical Association* earns at least $7 million per year from drug advertising. Its strengthening links with the drug industry, particularly its increasing economic dependence on advertising revenue from the mid-1950s on, have raised questions about its editorial independence (for example, its turn around on the subject of generic prescribing in 1955). The *Medical Journal of Australia* can similarly be seen to be in a compromising position with respect to its inclusion of drug advertising.

Advertising in American journals is subject to stringent regulatory controls by the state in contrast to the British drug industry's self-regulation. American controls have progressively increased since the Kefauver-Harris amendments and are reflected in the greater space given to side effects and contraindications in the advertisements.

The standard prescription drug reference journals, controlled by the drug industry and widely available to the medical profession, are also influential promotional tools. Entries in the American *PDR* and British *MIMS* (also in Australia) are listed alphabetically according to the brand name. To find information in order to prescribe a benzodiazepine, the American doctor needs to know the brand name and the drug company name whereas the British (and Australian) doctor can refer to the alternate section divided according to the drug's designated
action (for benzodiazepines these are listed in MIMS under "antianxiety agents", "sedatives, hypnotics" and "anticonvulsants"). These publications promote brand name loyalty and are selective about the inclusion of products (for example, generics) and warnings of unwanted effects (for example, MIMS publications in different countries), and even within a country the product information for the different benzodiazepines has been found to vary more widely than expected for a basically similar family of drugs.

Other literature put out by the drug industry is often disguised as unbiased scientific information. For example, a large 'newsletter' format report on an international symposium on hypnotics was recently distributed to Australian doctors. The publishing company was funded by Wyeth International Limited, manufacturers of Normison brand temazepam, one of the newer short-acting benzodiazepines. The majority of articles detailed positive comments on temazepam and on its superiority compared with nitrazepam (the established market leader in hypnotics but not marketed by Wyeth), and the remainder of the articles generally confirmed the safety and efficacy of benzodiazepines. Numerous medical-scientific experts were pictured and quoted, including Professor Karl Rickels who is a prominent advocate of benzodiazepines, stating that "psychotropic drugs are conservatively used and possibly even underused". Rickels has even gone as far as to suggest:

(From the public health point of view as well as from a cost/benefit point of view, wouldn't it be more sensible to try a psychotherapeutic drug first before entering into more expensive, time-consuming and not necessarily more effective non-drug treatments?)

4.6 Drug Safety and Efficacy and Controls by the State

Britain was the first Western industrialized nation to introduce
state controls on the purity of manufactured food and drugs in 1872.\textsuperscript{38} The main British regulatory body is the Committee on Safety of Medicines (CSM), first established as the Committee on Safety of Drugs in 1964. From its terms of reference, it is clear that its role is an advisory one which emphasises drug safety. Proof of drug efficacy appears to require only that a drug can be shown to be better than placebo rather than being better than drugs already available. The CSM structure has been criticized because of its secrecy and lack of cohesion. In 1978 it was reported to rely on advice from 587 people (mainly academics and doctors), on thirty-two sub-committees and two ad hoc consultative groups with one joint sub-committee and one working party, as well as bureaucratic staff support. Allegations of secrecy have been levelled at the CSM on the grounds that the Committee refused to pass information on to the American Food and Drug Administration (FDA) because of fear that the American Freedom of Information Act would allow public access to it.\textsuperscript{39}

The American regulatory agency is the FDA, part of the Department of Health and Human Services (DHHS). Pharmaceutical drugs are covered by the Bureau of Drugs, within which exist numerous subdivisions (Division of Drug Experience, New Drug Evaluation, Division of Scientific Investigations, Division of Drug Advertising), each headed by a Director and with their own specialist staff. These subdivisions also invite experts from outside the FDA to join advisory committees. The FDA has been praised for its more effective role compared with the British CSM, especially with respect to its lack of secrecy and its greater powers to enforce compliance. On the other hand, the FDA's system of drug approval has been criticized because it depends on evidence provided by drug manufacturers rather that carrying out drug
In the United States, proof of drug safety was first required in 1938 following the introduction of the Food, Drug and Cosmetic Act. This legislation was introduced following strong public reaction to the tragic deaths of 107 people, most of them children, who had tried a new sulphur drug in liquid form, containing di-ethylene glycol which attacks the liver and kidneys. Another death, not so well publicised, was that of the drug company's chief chemist, who committed suicide.

Although the Americans appear to have been slow initially in introducing state controls on drug production and distribution, they have now become world leaders in this respect despite their cultural stereotype of being free-market adherents. From 1962, proof of drug efficacy in addition to drug safety was mandatory, following the Kefauver-Harris Senate Bill.

The thalidomide tragedy also induced the FDA to establish a national registry of adverse drug reactions. More recently, state controls were considerably strengthened when it became compulsory in the United States for doctors and drug companies to report suspected adverse drug reactions to the Bureau of Drugs.

Nevertheless, other barriers to safe benzodiazepine use still exist. The doctor or other health professional must be able to recognize a possible adverse drug reaction (in the case of prescribing benzodiazepines for anxiety, Chapter 2 has already shown the problems in differentiating the emergence of anxiety as a withdrawal symptom from the re-emergence of the original anxiety).

Secondly, time and effort have to be invested in making a report to the relevant state authority. It has been estimated that perhaps only 1% of adverse reactions are reported. An American estimate for
1974 was that 55,000 life-threatening adverse reactions, resulting in 30,000 deaths, occurred from the misuse of antibiotics in American hospitals. A more conservative American estimate in 1978 was 100,000 adverse reactions over eleven years. An Australian study suggested that there are about one million cases each year of all types of adverse drug reactions but that only a very small number are considered sufficiently serious to report to the relevant authorities.

Thirdly, there are the social and political problems in the process of risk assessment and state controls on a drug with suspected adverse actions. For example, in Australia, the Adverse Drug Reactions Advisory Committee appears to apply conflicting estimates of risk to women's health, as shown in the following two statements taken from their 1976-77 report:

Oral contraceptive preparations were the subject of a number of reports suggesting that their use was associated with increased risks of myocardial infarction. This possibility was studied carefully and, while there was some evidence of increased risk, the Committee felt the evidence needed strengthening before regulatory action was justified.

As a result of initial investigations into the risk of abortion or the possibility of congenital abnormalities being induced in the babies of pregnant women exposed to anaesthetic gases, a warning statement was issued to hospitals. Although the studies were inconclusive, it was felt prudent to assume that exposure to these gases and vapours, particularly in operating theatres and anaesthetic rooms, could constitute a risk in pregnancy.

On the one hand, the Committee chose not to act on "some evidence of increased risk" whilst, on the other, it chose to act on "studies (which) were inconclusive".

In Australia, despite some favourable reports, the state continues to rely on a voluntary system similar to the British for detecting adverse drug reactions. Declining participation in this
scheme forced the Australian Department of Health to institute 'educational' measures, such as: providing quarterly reports to the drug industry on adverse drug reactions; supporting the department's publication Australian Prescriber (established in 1975 and containing articles on adverse effects of new drugs, notification forms of adverse drug reactions, etc.) as well as submitting articles in the Medical Journal of Australia; and two direct mail approaches to all Australian doctors in mid-1982. The Health Department has even resorted to using drug company representatives (detailers) to collect information on adverse drug reactions: drug companies were required to supply reporting forms to doctors under a scheme which aimed to speed up the introduction of new drugs on to Australian markets.

A summary of the regulation process prior to marketing a new drug in Australia is summarized in Table 4.5 (some changes have occurred more recently, such as with the reorganization of the Health Department in 1984-85). The marketing of a drug, such as a benzodiazepine, is determined by the Australian Drug Evaluation Committee (ADEC), whilst the Pharmaceutical Benefits Advisory Committee (PBAC) decides whether it is to be listed under the PBS. Both of these committees are dominated by medical-scientific 'experts', and the PBAC has been criticized by the drug industry for giving medical considerations precedence over pricing issues. Prices of drugs under the PBS are determined by the Pharmaceutical Benefits Pricing Authority (PBPA), comprising equal representation by the Department of Community Services and Health, and the Department of Industry, Technology and Commerce, as well as by the drug industry and health consumers.
Table 4.5: Process of drug regulation in Australia

Application to market a new drug, new formulation, extend currently approved indications or change dosage regimens (supporting data provided by sponsor)

Australian Department of Health

Chemistry, formulation, quality control

Animal pharmacology and toxicology

Human clinical trial data

National Biological Standards Laboratory

Drug Evaluation Section

Australian Drug Evaluation Committee (ADEC)

Subcommittees:
Adverse Drug Reactions Advisory
Congenital Abnormalities
Endocrinology
Parenteral Nutrition
Anti-Cancer
Radiopharmaceuticals
National Drug Information Advisory
Vaccines

Recommendation to Minister for Health

4.7 Drug Lag

The strengthening of American state controls has lengthened the time for marketing new drugs (to about five years) compared with Europe, although still comparable with Canada and Japan. In Australia, it was recently estimated that the average length of time for marketing a new drug from overseas and for it to then become widely available on the PBS was about 9-1/2 years. A comparison between Australia and eleven major countries of time differences in granting approval to market drugs between 1970 and 1983 has shown that Australia has a longer average lag time (about 3-1/2 years) compared with, say, Britain (about 1-3/4 years) and the United States (about 2-3/4 years). However, there is a lack of agreement on drug lag estimates because of methodological differences, such as choice of numbers and types of drugs. For example, other evidence has been presented which has suggested that most countries take longer than Australia to approve marketing of new drugs.

The increase in drug lag in the United States, following the 1962 Kefauver-Harris amendments to the Food, Drug and Cosmetic Act, has been repeatedly criticized by the drug industry and its supporters. A common criticism and one raised by the American economist, Milton Friedman, and an American drug researcher, William Wardell, is that the FDA is preventing more people from getting help from, possibly, life-saving drugs which could have been available earlier.

In his 1973 article in the widely-read Newsweek magazine, Friedman applied a cost-accounting analysis in accordance with his free-market philosophy to urge the repeal of the Kefauver-Harris amendments (as well as the abolition of the FDA) because "the cost of delaying a beneficial innovation is something like ten to 100 times the value of avoiding a thalidomide-type mistake". For evidence, Friedman largely relied on "a
brilliant paper" given by another economist at a conference in which the
author:

uses highly imaginative techniques to assign dollar values to
the benefit from suppressing harmful drugs and to the harm
from suppressing or postponing the introduction of useful new
drugs. His methods are too complex to describe here.58

However, cost-accounting approaches can only attempt to deal with
economic problems and certainly cannot come to grips with the full
meaning and value of life and the effects of drugs on it. Moreover,
Henry E. Simmons, the Director of the FDA's Bureau of Drugs, effectively
challenged Friedman's argument by questioning his interpretation of data
showing a fall in approval of new chemical entities. Simmons agreed
that there had been a drop in the number of new drugs introduced on to
the market but that this had occurred in the six years before the
passing of the Kefauver-Harris amendment. Most importantly, the number
of new drugs, compared with recombinations or reformulations ('me too'
drugs), had remained stable since about 1950 at about five to seven per
year.59

4.8 Generics

The escalating cost of their drug bill has been seen as a serious
problem for many nations since World War II. In the late 1960s,
following the introduction of the Medicare and Medicaid schemes, the
American government initiated inquiries into the high cost of
prescription drugs (the Nelson hearings and the (HEW) Task Force on
Prescription Drugs).60

Generic drugs became a focus of attention in heated discussions of
drug cost with respect to quality. Greater use of generics was made
possible in the United States by the repeal of anti-substitution laws in
the early 1970s, so that the dispensing pharmacist could substitute a
cheaper generic for a more expensive brand name drug prescribed by a
doctor. This was an important move in challenging the doctors'
previously powerful position as the sole decision-makers in prescribing.
However, economic benefits to the state were more long-term as,
initially, about 75% of drugs were still patented and there were no
equivalent generics.61

4.9 Case Studies

4.9.1 Limited drug lists - the British experience

Generics continue to be important world-wide, especially with
respect to prescription drug controls by the state. In 1985 in Britain,
Thatcher's Conservative government aroused considerable hostility from
both the pharmaceutical industry and medical practitioners when it
announced a cost-cutting scheme involving generics, in an attempt to
revise their pharmaceutical pricing policy in the National Health Scheme
(NHS). The sequence of events over the ensuing five months provides an
examplar of a political power struggle over control of pharmaceuticals,
especially with respect to benzodiazepines, in an industrialised Western
country.

(a) The proposed plan and the final outcome

The British government's campaign to promote the limited drug list
was spearheaded by publicity over its intention to restrict minor
tranquillizers.62 The preliminary list proposed by the DHSS contained
three benzodiazepines only - diazepam, nitrazepam and temazepam63 - and
may be favourably compared with only one benzodiazepine listed as an
essential psychotherapeutic drug by a WHO Expert Committee.64 However,
the final list presented to Parliament contained seven different
benzodiazepines in twenty-five different forms (see Table 4.6).

The government's initial proposal contained a total of only thirty
Table 4.6: Benzodiazepine Sedatives and Tranquillisers included in limited drug list approved by UK House of Commons, March 1985

<table>
<thead>
<tr>
<th>Drug</th>
<th>Form</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>chlordiazepoxide</td>
<td>caps</td>
<td>5, 10 mg</td>
</tr>
<tr>
<td>chlordiazepoxide</td>
<td>tabs</td>
<td>5, 10, 25 mg</td>
</tr>
<tr>
<td>chlordiazepoxide hydrochloride</td>
<td>tabs</td>
<td>5, 10, 25 mg</td>
</tr>
<tr>
<td>diazepam</td>
<td>elixir</td>
<td>2 mg in 5 ml</td>
</tr>
<tr>
<td>diazepam</td>
<td>tabs</td>
<td>2, 5, 10 mg</td>
</tr>
<tr>
<td>lorazepam</td>
<td>tabs</td>
<td>1, 2.5 mg</td>
</tr>
<tr>
<td>nitrazepam</td>
<td>mix</td>
<td>2.5 mg in 5 ml</td>
</tr>
<tr>
<td>nitrazepam</td>
<td>tabs</td>
<td>5, 10 mg</td>
</tr>
<tr>
<td>oxazepam</td>
<td>tabs</td>
<td>10, 15, 30 mg</td>
</tr>
<tr>
<td>temazepam</td>
<td>caps</td>
<td>10, 20 mg</td>
</tr>
<tr>
<td>temazepam</td>
<td>elixir</td>
<td>10 mg in 5 ml</td>
</tr>
<tr>
<td>triazolam</td>
<td>tabs</td>
<td>0.125, 0.25 mg</td>
</tr>
</tbody>
</table>

Note: also still available were all benzodiazepines prepared for parenteral or rectal administration and those licensed only as anticonvulsants (e.g., clonazepam - 'Rivotril'). Clobazam was still available by special arrangement for patients with epilepsy only.

listed drugs whereas there were 108 drugs included on the limited list approved in March 1985 by the House of Commons. The government achieved its primary economic objective of a reduction in the NHS drug bill for the state, although its intention to restrict minor tranquillizers failed due to concessions granted to the medical and drug industry lobby.

(b) The doctors' response

The strong reaction from British doctors against a limited list of NHS drugs was not so much against the government's proposal to introduce generic compounds, as it was to protect their professional power, expressed in their 'freedom to prescribe'. A preliminary short list of drugs prepared by the DHSS provoked 650 letters from the medical profession.

Scientific journals were an important medium for political expression by doctors presenting their case against the proposals. During the controversy, the two major medical-scientific journals, The British Medical Journal and The Lancet, carried editorials, letters and articles supporting the existing systems of voluntary limited formularies (under investigation or already introduced into individual general practice and hospitals). These voluntaristic policies were, of course, directly under the control of the medical profession rather than the state.

Other tactics adopted by the medical profession included the distribution of a letter written from the British Medical Association (BMA) to all general practitioners in Britain; a move which brought censure on the BMA by government Ministers.

(c) Response by the drug industry

The drug industry's campaign against the British restricted drug
list included the following appeals to both the medical profession and the consumer: Roche Products Ltd. sent a circular letter to general practitioners which needed only to be endorsed with the surgery stamp and signed before posting to the local MP (a stamped envelope was also supplied); and full-page newspaper advertisements were placed by the drug industry "showing the happy pensioner who can afford her drugs and the sad one who will not be able to".70

The state achieved a cut about 5%, or 74 million pounds, from the NHS drug bill in contrast to the preliminary target of 100 million pounds,71 which indicates that its concessions for a considerably expanded drug list did not represent a proportionate economic loss. Overall, however, state savings on the NHS were quite conservative compared with the magnitude of profits (1325 million pounds) anticipated by the British drug industry for that year.

(d) The contradictory role of the state

The state failed to significantly challenge the power of the drug industry interests. Despite having imposed some limits on the number of drugs available on the NHS, British drug pricing policy is still seriously hampered by structural difficulties,72 arising from conflicts within the state. The Pharmaceutical Price Regulation Scheme (PPRS), introduced in 1978, gave the state two essentially conflicting roles: firstly, to ensure safety and efficacy of NHS drugs and, secondly, to enable the DHSS to promote R & D in the British drug industry. As a result, drug safety and efficacy must be compromised when a regulatory body of the state is intimately bound up with promoting the corporate interests of the drug industry, whilst at the same time monitoring drug safety and efficacy which the industry views as threatening to corporate profits.
The PPRS is basically a limited system of financial control: the small secretariat of fourteen staff in 1985 employed only three accountants and no doctors. It is a voluntary scheme based on a 'gentlemen's agreement' which allows the state to request certain information and actions from the drug industry. It arose initially from a Voluntary Price Regulation Scheme proposed by the Association of British Pharmaceutical Industries and set up by the British government in 1957. The PPRS, for example, allows the DHSS to ask the drug companies to aim for profit levels set by the state. It can also ask for annual financial statements of all large-selling British drug companies for the purpose of setting limits on the industry's expenditure on promotion and on their profits. The DHSS has authority to then determine the profits of drug companies from their calculated capital expenditure and offsetting costs.

As a result, a company's sales of drugs to the NHS are crucial for calculating their allowable profit. The importance of sales figures to the calculations of state-determined profits has been exploited by transnational corporations based outside Britain, which have understated capital expenditure and other items. Under the PPRS, manufacturing costs (the largest of drug industry costs) are open to distortion by company transfer pricing arrangements although the state was satisfied this was no longer a problem after the much publicised Roche affair in the 1970s (see Section 4.9.2). Whilst R & D costs in the British drug industry rose from 82 million pounds (12% of NHS sales) in 1978 to 247 million pounds (18% of sales) in 1983, the PPRS has not enabled the state to check how much of this was innovative R & D compared with developing 'me too' or other slightly modified chemical compounds, or drugs for sale overseas, over the counter or to the private sector.
rather than drugs for the NHS. Instead, the state has used the PPRS to focus on drug industry profits which they reduced from 25% in 1982-83 to 15%. However, this is a notional figure open to political manipulation, representing an average for the whole industry which can vary from only 4% of sales for Hoechst in 1984-85 to 33% for Fisons.74

Furthermore, the action to curb drug industry profits arose only after disclosures made by the Commons Public Account Committee in 1983. Inadequate resources provided by the state (such as the DHSS having only one full time accountant to counter the combined expertise of sixty-five of the biggest transnationals in the world) had allowed about 200 million pounds per year to disappear in transnational transfer pricing arrangements by multinationals, and excess profits of about 33 million pounds to be siphoned off from the NHS by nine drug companies over two years.75

4.9.2 Transfer Pricing & Roche

(a) Background history of Roche

The Swiss-based company, F. Hoffman-La Roche & Co. (Roche), initiator of the minor tranquillizers, has been perhaps the most profitable drug company of all. Founded in Basle in 1896 by Fritz Hoffman with the aim of using scientific research to produce brand name pharmaceutical products for the world market, Roche was soon successful in marketing a variety of drugs including a cough syrup (Sirolin), a heart remedy (Digalen), and a painkiller containing all the alkaloids of natural opium (Pantopon) (which was still on the market in 1971).76 Its marketing of opium products implicated the company in the illegal drug trade. Between the two major world wars, it has been alleged that Roche (and other drug companies) was heavily involved in trafficking of morphine and heroin with illegal drug dealers in underworld centres.
including China. These activities led Sir John Campbell, chairman of the British delegation to the League of Nations Opium Advisory Committee meeting of 1927, to comment that "Hoffman La Roche and Company was not a firm to which a licence to deal with drugs should be given". Its success between the wars with vitamin production, especially vitamins C and A, marked Roche's transition to synthesis of new pharmaceutical products. This, in turn, led to its marketing of Librium and Valium in the early 1960s. Dr. Adolf W. Jann, a law graduate and ex-banker who joined Roche in 1957 and has been its President and Chairman of the Board since 1965, has directed Roche's course since the time that Librium was the best-selling prescription drug in the early 1960s in the United States (until 1969 when Valium pushed it back to second place).

(b) Profitability of Roche

As with other drug companies, accurate financial information on Roche's activities is extremely difficult to obtain. In addition, the protection offered to Swiss-based drug companies, together with its not being a publicly listed company, has supported Roche's policy of secrecy and enabled it to generally understate its true financial position (for example, its earnings for 1970 have been estimated to be more than eight times its reported figure). In the late 1960s, Roche's sales worldwide were estimated to be increasing by approximately 15%, with total revenues for 1970 estimated at $(US)1.2 billion (almost double those of Merck, its nearest competitor) largely from sales of only one type of drug: the benzodiazepines (Librium and Valium). They accounted for about one half of world sales of all tranquillizers.

Roche's financial success is epitomized by its unusual corporate position of being able to finance all its investments from earnings, in part derived from cash reserves. However, its code of secrecy began to
break down in the early 1970s when Roche's obvious success with Valium sales attracted world-wide attention to the company's financial returns, fuelled by the wide-spread judgement that profit margins for prescription drugs, generally, were excessive.\(^81\)

(c) The benzodiazepines

Librium and Valium profited Roche enormously because of their patent protection, being the first and best-known brand names of benzodiazepines. This is clearly illustrated in Table 4.7 which compares prices of Valium and Librium world-wide at a time when British prices were reaching a peak.

Table 4.7 also illustrates the effect of political forces through the widely differing state controls on drug prices: the British had been hardening their attitude to their already relatively stringent policy of setting prices in accordance with a state-defined predetermined profit to the companies; high American prices were subject to minimal intervention by the state;\(^82\) Italy did not recognise patent protection (hence, lower prices) and negotiated prices based simply on costs of raw materials and production (thus easing the downward pressure on prices for those companies able to convince the state of their high production costs); New Zealand used legal measures for pressuring manufacturers to lower prices (the lowest prices surveyed); and, in Australia, Valium escaped state scrutiny of its price until after it was included in the PBS scheme in December 1972, when it was taken off the restricted list.\(^83\)

(d) Preliminary action by the state in Britain

Although British prices were lower than in many other countries, the state had been involved in a long-running battle with Roche to lower its prices even further and to break its monopoly. From 1964 to 1971
<table>
<thead>
<tr>
<th>Country</th>
<th>Librium&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Valium&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Price of Librium&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Price of Valium&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>United Kingdom</td>
<td>2.40</td>
<td>2.88</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>United States</td>
<td>6.40</td>
<td>8.03</td>
<td>267</td>
<td>279</td>
</tr>
<tr>
<td>Australia&lt;sup&gt;d&lt;/sup&gt;</td>
<td>3.74</td>
<td>3.74</td>
<td>159</td>
<td>130</td>
</tr>
<tr>
<td>Brazil</td>
<td>2.40</td>
<td>3.62</td>
<td>100</td>
<td>126</td>
</tr>
<tr>
<td>Canada</td>
<td>5.45</td>
<td>6.01</td>
<td>227</td>
<td>209</td>
</tr>
<tr>
<td>Ireland</td>
<td>2.05</td>
<td>2.46</td>
<td>85</td>
<td>85</td>
</tr>
<tr>
<td>Italy</td>
<td>3.55</td>
<td>3.42</td>
<td>148</td>
<td>119</td>
</tr>
<tr>
<td>New Zealand</td>
<td>1.83</td>
<td>2.72</td>
<td>76</td>
<td>94</td>
</tr>
<tr>
<td>Sweden</td>
<td>3.11</td>
<td>3.71</td>
<td>130</td>
<td>129</td>
</tr>
</tbody>
</table>

<sup>a</sup>For 100 x 10-mg capsules  
<sup>b</sup>For 100 x 5-mg tablets  
<sup>c</sup>As percentages of UK price  
<sup>d</sup>Valium was not included in the Prescription Benefit Scheme (PBS) at this time  

Roche refused nine different applications for voluntary licences to manufacture their minor tranquillizers in Britain;\textsuperscript{84} Japan had been the only country Roche issued with new product licenses.\textsuperscript{85} It was only in 1968 that the state broke this monopoly when Roche was ordered to grant a compulsory licence to DDSA Pharmaceuticals to manufacture chlordiazepoxide (Librium) and its intermediates, and to DDSA and Berk Pharmaceuticals in 1971 to manufacture diazepoxide (Valium). Royalties payable to Roche were set, based not on sales but rather on the amount of drug produced, at a generous rate of 140 pounds/kg and 465 pounds/kg.

Roche fought back strongly to prevent its competitors from gaining access to its own established market. As profits in the drug industry are most sensitive to price variation, Roche had continuously and strongly resisted lowering its prices. However, in order to maintain its monopoly Roche defended its market by immediately reducing its tranquillizer prices by about one-third (but keeping them still slightly higher than those of its competitor). When Berk was invited by the state to tender for a contract to supply NHS hospitals and the armed forces with its diazepam product (Atensine) in 1972, the company lost the contract to Roche who tendered a price equivalent to 480-530 pounds/kg, only slightly above Berk's royalty fees payable to Roche and therefore clearly below the profitable range of its only competitor.\textsuperscript{86} Other tactics Roche used were to supply Librium and Valium free of charge to British hospitals for a limited period (from July 1969 and July 1971 respectively to June 1972).\textsuperscript{87}

Roche was forced to repay excess profits to the state, but it was allowed to maintain its high prices. Total repayments for excess profits in the two and a half years up to December 1969 were 1.6 million pounds.\textsuperscript{88} This compromise by the state meant that Britain played an
important contributory role in maintaining high prices of Librium and Valium world-wide, as a drop in British drug prices could have been an effective bargaining tool for other countries to enforce a price reduction.\textsuperscript{89}

As well as profit refund deals such as these with Roche, Britain has caused concern for regulatory bodies such as the WHO and the European Committee for Proprietary Medicinal Products because of similar voluntary and private negotiations over drug safety between the state and British drug companies. The British Committee on Safety of Medicines can privately request drug companies to voluntarily withdraw drugs from sale (for example, practolol, marketed as Eraldin by ICI, and released in 1970, was sold to approximately 100,000 people in Britain before being voluntarily withdrawn in 1975 by ICI because of severe adverse affects).\textsuperscript{90} Because the government has not had to exercise a regulatory decision, legal requirements to report withdrawal of a drug to other regulatory bodies have not applied. Other countries do not, therefore, benefit from the British experiences. This has entrenched the individualistic approach (at a national level), preventing a truly international effort at networking and establishing uniformly consistent regulatory codes. It is interesting that Australia is one of the countries cooperating with WHO in setting limited standards for new drug applications.\textsuperscript{91}

\textbf{(e) The British Monopolies Commission Inquiry into Librium and Valium}

The state's procrastination in taking action against Roche finally came to an end, apparently when it was discovered the state had lost considerably more than that first calculated, despite the large compensation payments made by Roche. According to the DHSS, in 1965 they first suspected that Roche's transfer pricing policy was fixing the
price of imported base ingredients from the parent company about 20% higher than would be reasonably expected from costs involved. However, when they discovered that this figure was more likely to be about 80% too high, and Roche was still refusing to reduce tranquillizer prices to the NHS (whilst having supplied hospitals free of charge), they called on the Department of Trade and Industry to refer the matter to the Monopolies Commission in 1971. In its report released in 1973, the Commission recommended that Roche reduce its price of Librium by at least 60% and Valium by at least 75% of the 1970 prices. The government ordered Roche to reduce prices by 40% and 60% respectively.

The Commission reviewed data on sales, costs and profits provided by Roche to confirm enormously inflated transfer prices (compared with prices of active ingredients set by Italian manufacturers who do not recognise patent protection) and inflated overheads and research costs (using alternative data supplied by Roche). They estimated that Roche had grossly understated its profits: for only one year (1970) profit on Librium had been 405 pounds/kg, not 1 pound/kg as stated by Roche; and on Valium it was 1,210 pounds/kg rather than 191 pounds/kg. As a result, the Commission calculated that the apparently large amount Roche had repaid to the DHSS since 1966 represented only a small part of the total 24 million pounds owing solely on Librium and Valium. Roche's understated profits from its transfer pricing policy also served to reduce its tax burden in foreign markets such as Britain, since the company paid only 40% profits tax in Switzerland in contrast with other countries such as 50% tax in Britain, Germany and America and 78% tax in India.

(f) Roche's response

Undaunted, Roche played for time by launching an appeal through
the House of Lords, which effectively deferred its final response until November 1975, when Roche made an out-of-court settlement to pay 3.75 million pounds to Britain. This was light penalty indeed, since the state had initially sought from Roche 12 million pounds in excess profits from 1970 to 1973. It now agreed to repay 8.25 million pounds to Roche in compensation for inflation and devaluation effects on prices of Valium and Librium, frozen in 1973.

In the year that Roche was negotiating a compromise solution, the effects of the price freeze relative to world-wide prices of Valium and Librium were as shown in Table 4.8. By this time, however, Roche knew that its monopoly on the tranquillizers was coming to an end. The patent on Librium had already expired and was soon to end for Valium (December, 1976).96 The settlement also saved the state further embarrassment arising from Roche's subsequent allegations of excessive transfer pricing arrangements by British drug companies (Beecham, a British company, and Bristol-Myers, its American subsidiary, had been overcharging for antibiotics in the United States).97

(g) Other attempts to regulate Roche's activities

Roche's success with protracted litigation in Britain was repeated in West Germany, where the state had followed the British lead and ordered Roche to reduce prices by 35% (Librium) and 40% (Valium) in late 1974.98 In this instance, Roche was permitted to continue charging its usual prices during the drawn-out legal battle which was finally resolved six years later in the West German Supreme Court, well after the patents had expired (Librium in 1977 and Valium in 1978). Similar victories won in Denmark in 1977 and Holland in 1979 meant that Roche has never been successfully prosecuted for over-pricing its tranquillizers.99
Table 4.8: Relative Wholesale Prices of Librium and Valium, 1975 (in US dollars)

<table>
<thead>
<tr>
<th>Country</th>
<th>Librium^</th>
<th>Valium^</th>
<th>Price of Librium^</th>
<th>Price of Valium^</th>
</tr>
</thead>
<tbody>
<tr>
<td>United Kingdom</td>
<td>0.83</td>
<td>0.63</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>United States</td>
<td>5.80</td>
<td>6.89</td>
<td>699</td>
<td>1,093</td>
</tr>
<tr>
<td>Germany, Federal Republic</td>
<td>4.38</td>
<td>5.35</td>
<td>528</td>
<td>849</td>
</tr>
<tr>
<td>Switzerland</td>
<td>4.75</td>
<td>5.44</td>
<td>572</td>
<td>908</td>
</tr>
<tr>
<td>Mexico^</td>
<td>4.42</td>
<td>6.03</td>
<td>532</td>
<td>957</td>
</tr>
<tr>
<td>Costa Rica^</td>
<td>7.03</td>
<td>9.13</td>
<td>847</td>
<td>1,449</td>
</tr>
</tbody>
</table>

^ For 100 x 10-mg capsules
^ For 100 x 5-mg tablets
^ As percentages of the UK price
^ Data are for 1976

Moreover, Roche emerged virtually unscathed from legal action taken against it during this time by the EEC for abusing its dominant position in the vitamin market. Roche was found guilty in 1976 of limiting competition by giving "loyalty discounts" to its twenty-two largest customers of its vitamins. Roche's appeal ended in the European Court of Justice in February 1979, which confirmed the company's guilt but reduced the fine. This relatively minor setback for Roche involved far greater hardship for Stanley Adams who had played an important role in the EEC's initial inquiries when, in February 1973, he passed on information gained while working for Roche.

After leaving Roche later that year to set up his own pig-farming business in Italy, Adams' anonymity was broken leading to his imprisonment for three months in Switzerland (an event which precipitated his wife's suicide). Adams was subsequently found guilty of "persistent economic espionage" and "persistently betraying trade secrets" and sentenced to twelve months' suspended imprisonment, ordered to pay costs and forfeit bail and banished from Switzerland for five years.

Adams' trial highlighted the strong links between corporate and state interests in Switzerland forged by the economic successes of the Swiss-based transnational drug companies, acting in concert to criminalise Adams' deed as an act of treason whilst condoning Roche's illegal activities which Adams had exposed. Roche's political strength in the internal affairs of governments other than the Swiss is evidenced in the EEC's reticence to play the full strength of its hand in its negotiations with the Swiss government and in the company's apparent influence with the Italian government in exacerbating Adams' difficulties.
High profits and their dependency on only a small number of products are certainly powerful inducements for companies such as Roche to fight hard to maintain their position as leaders in the drug industry. It is easy to believe Adams when he states:

[Roche's] history over the last twenty years shows clearly the lengths to which they were prepared to go in order to suppress competition and ensure that their profits remained high, even at the expense of the individual. 102

4.10 Conclusion

The drug industry is an excellent example of the monopoly sector of capitalism in that it is organised at an international and national level, is not price competitive because of its highly organised sales markets which have been assisted by patent protection, and production is capital intensive. 103 Its development and marketing of minor tranquillizers are also a clear example of the industry's pattern of concentration of resources on marketing in preference to R & D, and within R & D on 'me too' products in preference to innovative drugs (refer to Chapter 1).

In Chapter 3 it was shown that health is not a finite and quantifiable entity which can be objectively assessed and cannot therefore be easily incorporated into long-range economic planning by the state. Decisions on medical care must be based on rationing of available resources according to health priorities which are set by the state. Increasing state intervention in Western industrial societies and economic crises of capitalism have recently favoured monetarist policies such as 'Thatcherism' and 'Reaginism' which have sought to restrict social welfare spending, such as on health.

The concentration of capital in large transnational corporations, such as in the drug industry, and corporate interactions with the state
have formed the basis of renewed debate on and interest in Marxist theoretical approaches. The evidence presented in this chapter on the relationship between the drug industry and the state supports the view that the state is deeply involved in the contradictions of capitalism. Following Habermas,104 the crises of late monopoly capitalism can be seen as the result of contradictory functions of the state which support, on the one hand, capital accumulation (directly for the drug industry, and indirectly for the national economy) and, on the other hand, legitimation of its social welfare role (the state must show it can fulfil its function of supplying basic health needs).105

In the health area, the fiscal crisis with the British NHS drug bill prompted the British government to introduce a limited drug list in an attempt to cut back on costs by appealing to its legitimation role in health welfare. Here, the growing public awareness of addiction problems within society and, in particular, the dangers of addiction associated with benzodiazepines were useful ideological tools for proposing to cut back on unnecessary and potentially dangerous drugs. Whilst this was useful for one section of the national economy, the state was also bound by its contradictory commitment to support the British drug industry and its continued research and development program. The final political decision capitulated to the drug industry's market requirements of a greatly expanded NHS drug list. This ensured that the national economy continued to benefit from revenues obtained from the industry as well as obtaining greater legitimacy for the state in its relations with industry. The role of the medical profession in protecting its professional power was another important factor in the policy change.

Doyal has complained of the state's reluctance to nationalise the
British drug industry as a logical extension of its earlier nationalisation of health in the formation of the NHS. However, the difficulties are considerable when compared with the struggle outlined above between the state and only one drug company - Roche - in Britain: a less ambitious, yet unsuccessful, attempt by the state to gain access to knowledge of corporate (transfer) pricing policies and to increase state control over the drug industry. The problems were reflected in the delay in establishing the Monopolies Commission examination of Valium and Librium pricing and, subsequently, in enforcing its findings to obtain financial compensation from Roche. The legislative tactics used by Roche in Britain, and successfully repeated in Europe, enabled it to maximise profits during the final years of patent protection on their two best-selling minor tranquillizers. The antagonism between the state and Roche in Britain was not assisted by the British state's refusal to punish its own domestic drug industry for transfer pricing deals with subsidiaries in other countries. Similarly, Roche has enjoyed strong protection from the state in Switzerland, its country of origin, and from other national and international bodies (such as the Italian state and the EEC), due to their mutual political and economic interests meshing with that of Roche.

Turner has summarised some problems with Marxist critiques of health and medicine, such as their failure to identify different types of capitalism, and to identify different patterns of illness and health care and their expression within different forms of capitalism, and to deny the positive role of welfare systems. Doyal's political economy analysis of medicine, whilst well-researched as well as being moderately gender and culture inclusive, illustrates some of these failings. For example, she has strongly emphasised the repressive role of the state in
reproducing existing capitalist relations whereas others, such as Frankel, have shown how the contradictory role of the state allows it to become an important "emancipatory force". Doyal also has inadequately explained why the British health system was nationalised and not the American, except to state:

the absence of a militant labour movement in the USA must be seen as a major reason for the failure to develop an American state health service.

Whilst the absence of a strong radical political movement and unionisation in the United States is a likely component, Doyal's interpretation denies the importance of other social movements, such as the health consumer movement, in shaping American state policy. It also denies the comparatively stronger controls with respect to drug safety and efficacy exerted on the drug industry by the American state compared with those in Britain. Her analysis shows a tendency to be culture bound within the British Marxist tradition. Additional explanations for the different American health system point to the constitutional separation of powers and the consequent absence of centralised state activity, and to ideological causes based on American individualism.

Further analyses of the drug industry and the state will be developed in Chapter 5, which examines the socio-economic forces shaping the Australian drug industry in an historical context.
FOOTNOTES:


3. Australian Pharmaceutical Manufacturers' Association, Submission to Industries Assistance Commission Inquiry into the Pharmaceutical Products Industry, January 1985, p.31


12. Ibid, p.29.

13. J. Braithwaite, op cit., (note 6), p.161. An exception was the merger of Parke-Davis with Warner-Lambert after Parke-Davis' profits suffered from overdependence on chloramphenicol (later found to have serious side effects) and from insufficient investment in research. M. Silverman & P.R. Lee, op cit, (note 7), p.32


17. A. Melville & C. Johnson, *op cit*, (note 9), p.121


20. J. Braithwaite, *op cit*, (note 6), pp.213,214


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43. M. Silverman & P.R. Lee, op cit, (note 7), pp.110-134

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5 THE SOCIO-ECONOMIC SHAPING OF MINOR TRANQUILLIZER USE IN AUSTRALIA

5.1 Introduction

An historical outline is presented of major factors important to the use of minor tranquillizers in Australia. Important state initiatives in medicine are described, including the setting up and operation of the Prescription Benefits Scheme (PBS), and various committees which review drug prices and evaluate new drugs for marketing as well as monitoring continuing drug use.

The attempt by the Whitlam government to exert increased state controls on benzodiazepine sales, and the overall drug industry, is outlined. The drug industry's continuing call for greater financial assistance from the state has been met by a number of inquiries, and two of these are discussed in detail: the Ralph Inquiry (in the late 1970s) and the IAC Inquiry (in the mid-1980s). The Hawke government's approach to the drug industry has been more conciliatory, and evidence is given of its attempts to encourage a greater research and development effort and to give the industry input into decision-making on PBS drug prices. At the same time, equal representation was granted to the health consumer movement and an outline of events within the past two years show it has entered a period of strong growth.

A summary is presented of the erosion of medical power within some sectors of the state, whilst the profession retains an important role as medical-scientific 'experts' in an advisory capacity. The profession's significant role in prescribing minor tranquillizers has not been addressed in a systematic manner nor have any effective controls been instituted. Whilst there have been minor attempts to correct problems of minor tranquillizer use by reaching the consumer and addressing problems of addiction, as well as preliminary research on doctors'
training and attitudes to minor tranquillizer use, no concerted action in state control of professional prescribing power has been initiated.

5.2 The Prescription Benefits Scheme and the Escalating Drug Bill

In common with the post-war trend in developed countries around the world, there has been increasing state intervention in medicine in Australia. For prescription drugs such as the benzodiazepines, an important arena of struggle has been the PBS, which has had a politically contentious history since the Labor government's first attempts to introduce a universal drug benefit scheme in 1944. A limited scheme was introduced in 1950 to provide 139 drugs free to the general population and in 1951 the range of drugs was extended for pensioners and their dependents.\(^1\) The scheme's brief was widened by the National Health Act of 1959 introduced in 1960.\(^2\) In 1953 the Pharmaceutical Benefits Advisory Committee (PBAC) was set up as a Ministerial committee of medical-scientific experts, whose identity was kept secret until 1970 when the Senate forced their disclosure.\(^3\)

By the early 1960s, the Menzies government was under heated attack by the Labor Party over high drug prices. Only ten years after the PBS had been set up, the national drug bill was climbing at an annual rate of 20\% to 30\%.\(^4\) In 1963, following world-wide publicity of the discovery of the dangerous effects of thalidomide and the lead of other countries, and under continuing attack from its political opposition,\(^5\) the government initiated greater state controls over both drug prices and drug evaluation.

The Australian Drug Evaluation Committee (ADEC) was established to assess the safety of new drugs from overseas for approval for marketing in Australia. ADEC's range of activities was later widened to include drug efficacy and, subsequently, advisory subcommittees were set up.\(^6\)
The Pharmaceutical Benefits Pricing Bureau (PBPB) was established to assist the Department of Health in setting prices for PBS items. A voluntary scheme was first instituted in 1964 for doctors, chemists, dentists and other health professionals to report adverse drug reactions. When the PBPB negotiated a number of cuts in drug prices, the drug industry argued that higher charges were necessary in Australia because of additional costs of transport charges, higher wages and a greater ratio of investment in plant and equipment to the size of the population covered.

Amidst increasing pressure from the opposition, including calls for a Royal Commission into the Australian drug industry, drug prices for 1962-63 rose by 9%. The government appeared to adopt a tough bargaining stance when Menzies publicly warned the industry that tougher controls would be enforced. The then Minister for Health, Senator H.W. Wade, disclosed that drugs sold in Australia were up to three times more expensive than in Britain and that six of the most frequently prescribed drugs in Australia were also the most expensive. Nevertheless, the drug bill increase was not insignificant and the government statements may be interpreted more as political posturing to satisfy public concern about drug prices, whilst the drug industry's agreement to moderate price increases helped it to avoid public scrutiny of its finances.

However, criticism continued into the late 1960s of the high cost of drugs in Australia, with further calls for a Royal Commission into the drug industry and reports from health officials that "Australia had become one of the world's most lucrative areas of operation for international drug concerns .... Australia is the laughing stock of the medical health authorities in Canada and the United States". Although
the average cost of drugs had fallen since 1963, the rising prescription volume meant the total cost of drugs on the PBS had continued to rise. A Senate committee on drugs was established and further regulatory controls were initiated. Since 1959, when it had been set up, the National Biological Standards Laboratory (NBSL) had imposed standards on new drugs in Australia similar to British standards. New standards specific to Australia were set in the Therapeutic Goods Act (1966) covering labelling, packaging and container requirements. The Code of Good Manufacturing Practice was also established in cooperation with the States to promote drug quality.

Despite the increased state controls, the Australian drug industry continued to maintain high drug prices. For example, in the early 1970s prices for benzodiazepines were generally higher than in Britain and New Zealand, although lower than in the United States (refer to Chapter 4, Table 4.7). Nevertheless, in 1972 the industry launched a major indirect cost-cutting exercise when the largest manufacturer, the US-owned Merck Sharp and Dohme, reduced wholesalers' margins from 20% to 15% of the selling price. Most of the major drug companies followed suit within six months. Some companies, such as Burroughs Wellcome, and Squibb, accused the government of being partly responsible because of the Health Department's more stringent pricing policy for the PBS, and other state controls affecting their profitability. However, these reductions merely brought the Australian wholesaling process more into line with the majority of overseas countries, especially Britain and the United States, where the industry had already established margins of about 15%. Moreover, the 20% margin had clearly been excessive as many wholesalers had been able to offer rebates to chemists of up to 7.5%. (Wholesale margins were reported to have been revised downwards again in
1987, to 10% of the price charged to pharmacies.\textsuperscript{22}

5.3 The Whitlam Government Initiatives

Despite growing concern about the safety of psychotropic drugs,\textsuperscript{23} Roche's Valium was approved for listing under the PBS on 1 December 1972.\textsuperscript{24} On 2 December 1972 the Whitlam Labor government was elected.\textsuperscript{25} Within one month, prescriptions of Valium had soared to more than most other drugs for the entire six months ended 31 December 1972. This was a dramatic improvement on an already strong market performance for the year ended June 1972, prior to its PBS listing, when it had ranked fourth.\textsuperscript{26} The economic value of PBS listing to Roche was indicated by its agreement to a 13% price reduction and the imposition of limits on the number of tablets prescribed (a reduction by half to fifty tablets and only one repeat).\textsuperscript{27} Prescriptions, however, continued to climb, almost doubling in three months (Table 5.1).

Health services became highly politicised during the 1970s, especially with the Whitlam government's initiatives in health insurance (Medibank) and in hospital and other health services.\textsuperscript{28} The medical profession's political activity became more visible as it came under attack, and the sovereignty of the Australian Medical Association (AMA) was challenged by conflict within the profession between groups such as the militant right-wing General Practitioners' Society of Australia (GPSA), and the left-wing Doctors' Reform Group.\textsuperscript{29} In line with a more open style of government, the new Minister for Health, Doug Everingham, reversed a long-term policy of keeping secret details of market shares by the different drug companies in Australia. In March 1973 the Health Department released a list of the top ten most prescribed drugs in Australia: Valium was in fourth place, just edging out Amytal, a barbiturate sedative.\textsuperscript{30}
Table 5.1 Number of prescriptions for Valium dispensed under the PBS for the three months January to March, 1973

<table>
<thead>
<tr>
<th>Valium dosage</th>
<th>Month</th>
<th>No prescriptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>2mg</td>
<td>January</td>
<td>86,152</td>
</tr>
<tr>
<td></td>
<td>February</td>
<td>118,810</td>
</tr>
<tr>
<td></td>
<td>March</td>
<td>143,707</td>
</tr>
<tr>
<td>5mg</td>
<td>January</td>
<td>102,419</td>
</tr>
<tr>
<td></td>
<td>February</td>
<td>148,338</td>
</tr>
<tr>
<td></td>
<td>March</td>
<td>189,478</td>
</tr>
</tbody>
</table>

The drug industry reacted with alarm when in February 1973 the Minister for Social Security, Bill Hayden, launched further state controls to curb drug prices. No doubt spurred on by the British Monopolies Commission inquiry into Valium and Librium (see Chapter 4), Hayden publicly criticised the high profits of the drug industry. He estimated a ratio for profits to funds employed within the Australian drug industry of over 20% compared with 13% for all Australian industries (the APMA reported this had dropped to about 16% by the end of the 1973 financial year).  

Hayden announced an investigation into the setting up of a state-owned drug manufacturing company in addition to, or in conjunction with, the Commonwealth Serum Laboratories (CSL) - which manufactured mainly biological pharmaceutical products such as vaccines, especially Australian-specific items. In reply Gibbs, the executive director of the APMA, quoted alternative figures on the industry's profits to sales ratio of 12.8% before tax and 6.7% after tax, although no comparison was made for the rest of Australian industry. The APMA press conference provided a platform for the industry to launch an emotive attack against the government for its 'socialist' aims and allegations that public money would be lost on this new government venture just as for CSL which had recorded a loss in the previous year because 'all socialist industries are inefficient'. The mutually beneficial goals of both the Liberal Party and the APMA against the Labor Party proposals were no doubt assisted by Gibbs' links with the Liberal Party as a former Liberal MP.  

One month later Everingham announced that the Australian Industry Development Corporation (AIDC), the state-owned bank established in 1974 to finance Australian-owned industrial development, had been asked to
finance the purchase of a drug company which would be linked with CSL and that at least five different companies were interested in negotiating with the government.34

Less than one month after that, in mid-April, the Australian press gave wide coverage to the British Monopolies Commission report and the high price of Valium in Australia compared with the British prices. Following the 40% reduction in British prices in 1972 for diazepam, the Health Department had tried to negotiate a similar price reduction with Roche in Australia, achieving reductions of only 13.3% (2mg tablets) and 11.5% (5mg tablets). Australian wholesale prices for Valium were a little more than twice those in Britain.35

Everingham reported that the Attorney-General, Lionel Murphy, was investigating the feasibility of breaking the patent monopoly held by drug companies in Australia, especially for Valium which was the most expensive item on the state's drug bill. Three possible options were considered: shorter patent lifetimes, compulsory patent licences granted to other companies, and price restrictions on drugs under patent.36 Everingham was reported to favour patent lengths of only one year, and that companies with a monopoly on a particular drug under patent should be subject to compulsory licence laws.

The drug industry and the state were in open, angry confrontation. Everingham accused the drug industry of being a "mercenary, money-grabbing bunch". The APMA's Gibbs continued the attack on the inefficiency of state enterprises when he retorted:

Dr Everingham does not know what he is talking about. His comments are a load of pure, unadulterated rubbish. If he wants to run a government company at a loss to taxpayers, let him.37

A report by the AIDC on the feasibility of expanding CSL's
activities into non-biological drugs and on variation of patent rights was submitted to the government in early May. At that time, Everingham stated that an important role for the state's entry into drug manufacture was as a means to gain access to information on production costs, in order to expose hidden profits in the industry. He criticised the industry's assertion that high profits were justified in order to cover long-term research costs, arguing that: "investigation shows that only 6% of their prices is spent on research with 25% going into dividends and 25% into promotion", with much of research concentrating on developing 'me too' products. In other comments, Everingham revealed possible difficulties with some of the alternative options considered by the government. He rejected the Italian example, imposed by Mussolini, of virtually abolishing drug patents, conceding that this would impose undue hardship on the Australian drug industry. However, he maintained his determination to shorten lengths of drug patents, although this might involve the state in lengthy legal proceedings in the High Court. He also rejected the New Zealand system of fixing a flat rate for similar drugs under pharmaceutical benefits, with the user paying any differences. Overall, he favoured proceeding with a state venture into manufacture of non-biological drugs.

A Cabinet decision was finally announced in May 1973 to set up an "Australian pharmaceutical commission" which would own and operate one or more drug companies, although no decision had been made on CSL's involvement.

The Australian drug industry blamed Roche and its recalcitrant attitude towards the British government for the Australian government's new policies on tighter controls of drug prices, stating in its trade journal:
[Roche] last month unwittingly handed the Australian Federal Government the public relations weapon it needs to enforce restrictive drug patent laws and depress drug prices ... Australian prices, not only of Valium but also of many other drugs, are sure to come down in the near future. For manufacturers, it means that their public relations battle with the new Government over drug prices and changes to patent laws is already lost. The only weapons they have left are the ultimate threats of curtailment of some Australian manufacturing and research activities, or even total withdrawal from the Australian market.42

Twelve years later, some transnational drug companies decided that Australian operations were no longer sufficiently profitable and ceased operations here.43

The Whitlam government continued to maintain its pressure on the drug industry in other ways. A Joint Parliamentary Sub-Committee heard evidence in June 1973 from the Health Department criticizing Roche and other drug companies for maintaining their prices despite an upward revaluation of the Australian dollar, thereby increasing their profits on imported products and ingredients.44 At that time, Roche had declared that about half of Valium's total production, including its basic ingredients, was manufactured at its Dee Why plant in Australia. Despite their stated aims of increasing this to total production, this could well have been a temporary move to keep up with the surge in demand until the 'plateau' anticipated by Roche.45 In June 1973 Roche's Basle headquarters sent Otto Nowotny to present its case to Everingham. Nowotny had also been assigned to convince the Swedish government to reject the British Monopolies Commission findings. The Australian negotiations were interrupted when Nowotny was sent back to Basle for more precise financial information, especially on contributions of capital, overheads and research costs to the cost of Valium.46

Nowotny's return to Australia six weeks later in July signalled a
hardening of Roche's refusal to negotiate price reductions for Valium in Australia. The company's resolve, however, was challenged by reports at that time of its attempt to maintain a monopoly of the New Guinea market by drastically reducing Valium prices to the New Guinea Department of Health. In response to New Guinea's decision to purchase a relatively small amount of diazepam from Hungary (where no patent protection applied), at a reduced cost totalling about $8,000, Roche had offered to sell Valium to the New Guinea government at prices up to one-third lower than Australian prices, and to replace the Hungarian shipment with Valium free of charge, provided most of the Hungarian diazepam was destroyed. A small amount of the Hungarian diazepam was to be released to Roche for testing, effectively preventing any challenge to Roche's allegations concerning the poor quality of its competitor's product.  

July and August 1973 were decisive months in the tranquillizer stakes, with unexpected long-term repercussions, when Roche's monopoly of the minor tranquillizer market was broken. In July the lower priced benzodiazepine, Serepax, was added to the PBS. Roche's Nowotny again visited Australia at the end of August to continue negotiations with Everingham on Valium prices. As political leverage, Roche appealed to Labor's policy of encouraging research by announcing the establishment of a $4 million research unit into marine pharmacology at their Dee Why plant, costing an estimated $1 million per year.

Nevertheless, Roche received a setback in 1974 when the state imposed a price freeze on Valium. A year later, further state controls were imposed on the drug industry in Australia. After a delay of two years, proposed amendments to the National Health Bill were introduced into Parliament, to increase the power of the Health Department to obtain cost and other financial information from the
manufacturers of PBS drugs. The Health Department's strongest bargaining lever in price negotiations with the drug industry was the threat of de-listing a drug from the PBS.51

In June 1974, the government also announced its purchase of the Fawnmac group of companies, comprising manufacturing and marketing divisions for its own and other overseas companies' products, for a sum later disclosed in Parliament as $8.7 million.52 The purchase was completed in September, 1975.53 Fawnmac Industries was chosen from nine other drug companies investigated by the AIDC.54 About one month after completion of the purchase of the Fawnmac group, Everingham was able to inform Parliament of the company's high record of profits of around 25% to 30% of annual turnover.55

The financial secrecy of the Australian drug industry was broken at last. Everingham announced that the new state-owned drug company would function separately from CSL and he anticipated that both state-owned companies would set the pace for drug prices.56 These state initiatives were short-lived. Two months after the Whitlam government was defeated at the polls in December 1975, the new Fraser government decided it would sell the Fawnmac group of companies.57

5.4 Valium - the Falling Star

The last half of the 1970s saw a continuing increase in sales of prescribed drugs in Australia: total drug sales in pharmacies and hospitals increased by 70% from 1975 to 1979. However, prescription sales in pharmacies rose most slowly (see Table 5.2).

In 1976, under the new Fraser government, the Health Department responded to recommendations by the PBAC to restrict the availability of benzodiazepines because of their addiction potential. As a result, the Department removed 10mg Valium tablets from the PBS list, abolished
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<tbody>
<tr>
<td>Ethical drugs ($m)</td>
<td>188.4</td>
<td>195.0</td>
<td>215.6</td>
<td>228.4</td>
<td>255.7</td>
</tr>
<tr>
<td>Index of per capita usage</td>
<td>100</td>
<td>102</td>
<td>112</td>
<td>117</td>
<td>130</td>
</tr>
<tr>
<td>Proprietary drug(s) ($m)</td>
<td>56.6</td>
<td>63.5</td>
<td>73.4</td>
<td>81.0</td>
<td>90.5</td>
</tr>
<tr>
<td>Index of per capita usage</td>
<td>100</td>
<td>111</td>
<td>127</td>
<td>138</td>
<td>153</td>
</tr>
<tr>
<td>Drugs from hospitals ($m)</td>
<td>36.9</td>
<td>45.0</td>
<td>51.0</td>
<td>54.3</td>
<td>58.7</td>
</tr>
<tr>
<td>Index of per capita usage</td>
<td>100</td>
<td>121</td>
<td>136</td>
<td>142</td>
<td>152</td>
</tr>
<tr>
<td>Total drugs ($m)</td>
<td>281.9</td>
<td>303.5</td>
<td>340.0</td>
<td>363.7</td>
<td>404.9</td>
</tr>
<tr>
<td>Index of per capita usage</td>
<td>100</td>
<td>107</td>
<td>118</td>
<td>125</td>
<td>137</td>
</tr>
</tbody>
</table>

**Source:** Bureau of Industry Economics, Research report 17, *Retail Pharmacy in Australia - An economic appraisal*, p.87
repeats for the 5mg and 2mg tablets, and abolished special provisions for three months' supplies of the three benzodiazepines available at the time (Valium, Ducene and Serepax). In effect, a person would get only three weeks' supply of benzodiazepines with one prescription. As well as reducing the addiction potential for consumers of the drugs, it was estimated that the government would benefit financially by saving approximately 10% of its drugs bill. The chemists also reaped financial rewards at the consumers' expense, as it was estimated that at least 20% of sales of the benzodiazepines were subsequently at the private retail price, which gave calculated profits of between 187% and 281% for Valium.

By 1978, Valium's popularity was well on its down-hill slide. Sales of Valium had fallen by one-third from their peak in 1972 of $6 million (226 million 5mg tablets) to $2.3 million (112 million 5mg tablets) in 1978. Roche failed to recapture the market with a new brand of diazepam: Ducene, marketed in 1974 by a subsidiary company, Sauter. Diazepam had fallen out of favour well before the Valium (and Mogadon) patent had expired in December 1976. Nevertheless, Roche had intensified its marketing strategies competing against its own subsidiary by supplying Valium and Mogadon free to chemists, requesting payment only at the end of the month on stock sold, and had begun direct trading with chemists to avoid wholesalers' marked-up prices.

Two new brand names appeared on the Australian market in 1978: Hoechst's Lorinon (withdrawn several years later) and Protea's Pro-Pam. None were able to repeat Valium's past performance. Whilst Valium's notoriety had spread to any diazepam, other benzodiazepines were ready to step in and fill the gap in the 'anti-anxiety' market. In Australia, ironically, this role was taken up by oxazepam, the
tranquillizer introduced by the Whitlam government to break the Roche monopoly and cut the country's drug bill. By the end of the 1970s, sales of Valium had been overtaken by Serepax (oxazepam), marketed by the US-owned company Wyeth (see Chapter 1). Roche's other best-seller, Mogadon, was challenged by another nitrazepam, Protea's Dormicum, when the patent expired. However, in the same year, Roche attempted to recapture the benzodiazepine sedative/hypnotic market with a 'me too' product when it introduced Dalmane (flurazepam).65

By diversifying its interests, Roche had no cause for great concern over the growing uncertainties of the benzodiazepine market. In Australia in 1978 its highest turnover was in agrochemicals ($30 million) and sales were increasing steadily (no doubt assisted by its takeover of the agricultural company, Lane Ltd.), whilst ethicals were in second place ($15 million) and static. Although recording losses in 1977 ($2.2 million) and 1978 ($4.8 million), Roche had still been able to make its usual research contributions to its parent company in Basle ($2.8 million in 1978). However, at that time the money was re-directed to Australia for its Research Institute of Marine Pharmacology in Dee Why, then employing sixty-two staff,66 as the research centre continued to be a useful political tool for Roche.

5.5 The Ralph Inquiry

Since 1970, a number of inquiries and other studies at both Federal and State level have examined the drug industry and the use of prescription drugs in Australia (Table 5.3). The first of the most recent inquiries directly investigating the drug industry in Australia is discussed below.

Following intense lobbying by the drug industry,67 the Inquiry into the Pharmaceutical Manufacturing Industry was appointed by the
Liberal government in September, 1978 and was chaired by J. T. Ralph, the mining industrialist and Executive Director of Conzinc Riotinto of Aust Ltd. In contradiction of the drug industry's calls for greater state assistance, the inquiry's report, tabled in Parliament in September 1979, recommended less state regulation and more competition within the drug industry. In response to its terms of reference seeking ways of encouraging an Australian-based drug industry, the Ralph Inquiry found no case for any special treatment over and above for manufacturing industry, in general, and that the dominance of existing large transnational drug companies precluded Australia becoming a major exporter of pharmaceuticals.

Instead, the Inquiry turned its attention to PBS pricing policies and the role of patents, drug lag and use of generics. The APMA had proposed that patent life on drugs be extended from sixteen to twenty years. The Association complained that drug lag gave less patent protection because of the shorter time of the drug on the market and referred to the British precedent set in 1977 when patent life was extended to twenty years. The Ralph Inquiry did not agree that the drug industry warranted special consideration over patents.

In response to the drug industry's complaints that they were forced to set low prices in Australia, the Inquiry found that the state was able to negotiate with drug manufacturers to lower drug prices in Australia if there were competitors able to supply cheaper generic versions of drugs on the PBS. However, because the state also did not permit significant price differentials between competing brands of the same drug, and because of the subsidised standard rate of payment for drugs on the PBS by the consumers, drug manufacturers of brand name drugs were cushioned from suffering adverse competition from generics.
As a result, prices of out of patent major selling drugs sold under the PBS in Australia were significantly higher than in Britain. Moreover, this enabled brand name drugs to continue to be predominantly prescribed in Australia after patent expiry. This became increasingly important with the drop in the proportion of patented to out-of-patent drugs. Patented drugs fell from 55% to 30% of the market between 1972 and 1978 for the fifty most prescribed PBS drugs. On the other hand, manufacturers of generics were protected also, as their listing on the PBS provided evidence of drug quality, ensuring sales to hospitals and central purchasing houses (often made by tender at lower prices). Nevertheless, average hospital prices were only slightly lower than the PBS price to wholesalers, although price reductions to hospitals were possible for some benzodiazepines, and in some cases these were significantly discounted. Hospital prices for diazepam and oxazepam were an average of 16% and 5%, respectively, less than the PBS price to the wholesaler. However, drug companies were able to selectively reduce prices much further. For example, the lowest price recorded for diazepam was 34% lower than the PBS price (2mg diazepam), and for oxazepam it was 13% (15mg oxazepam).

As a result, the Inquiry recommended that the state set a maximum purchase price and that any additional costs be borne by the consumer (a scheme similar to that in New Zealand). It also recommended that monitoring of prices and profits should come under the jurisdiction of the Prices Justification Tribunal.

The APMA's submission to the Ralph Inquiry included the proposal to introduce a pharmaceutical profit monitoring scheme, similar to the British PPRS (see Chapter 4). The Inquiry rejected this proposal because it represented special assistance to the drug industry, stating:
The scheme offers scope for a guarantee of industry-wide and individual company profitability, a privilege not enjoyed by any other industry.\textsuperscript{74}

The Inquiry acknowledged that reported profitability of the drug industry in Australia had fallen significantly during the 1970s from just over 14\% to around 3\% or 4\% (see Table 5.4). Nevertheless, despite a 70\% to 80\% drop in reported profitability, drug companies had been increasing their already very high outlays on promotion to almost 20\% of sales in the PBS.\textsuperscript{75} Manufacturing costs had also increased, more than half being in the biggest item (imported raw materials from overseas) accounting for more than one third of all costs (see Table 5.5). This strongly suggests that the Australian drug industry was continuing to adjust profits with artificially high transfer pricing strategies. However, the Inquiry did not confront the drug industry in its financial reporting, merely noting that:

\begin{quote}
transfer prices can be set in such a way as to lower the profitability of the local subsidiary without affecting its contribution to corporate profitability or its viability.\textsuperscript{76}
\end{quote}

Instead, a price rise of 4.4\% was recommended to restore profits to a level consistent with the rest of Australian manufacturing industry. It should be noted that Ralph, who chaired the Inquiry, headed Conzinc Riotinto, a subsidiary of Rio-Tinto Zinc, which had been named in a British study as one of twenty large industrial companies which avoided taxes by transfer pricing adjustments between countries.\textsuperscript{77}

Neither the drug industry nor the government were happy with the Ralph Inquiry's recommendations. The APMA responded by calling for a 10\% price rise whilst the government made a preliminary decision to increase drug prices by 3.5\% (plus 10 cents per prescription at 'price to chemist' level for the PBS maximum quantity), effective from November
Table 5.4: Profits (as percentage of sales) reported by drug companies in Australia in the PBS Pharmaceuticals Sector

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant group of companies (coverage: 30 (84%) companies surveyed)</td>
<td>14.4</td>
<td>12.7</td>
<td>9.7</td>
<td>6.1</td>
<td>3.8</td>
<td>4.0</td>
<td>2.9</td>
</tr>
<tr>
<td>Maximum number of companies surveyed (coverage: No. of companies Percentage)</td>
<td>14.4</td>
<td>13.0</td>
<td>10.3</td>
<td>6.7</td>
<td>4.6</td>
<td>4.7</td>
<td>3.9</td>
</tr>
</tbody>
</table>

Table 5.5: Costs (as percentage of sales) reported by drug companies in Australia in the PBS Pharmaceuticals Sector (1972 to 1978)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Variable Manufacturing Costs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Materials from overseas affiliates</td>
<td>32.8</td>
<td>31.7</td>
<td>32.0</td>
<td>33.1</td>
<td>34.3</td>
<td>34.5</td>
<td>36.1</td>
</tr>
<tr>
<td>Other</td>
<td>13.2</td>
<td>13.9</td>
<td>14.1</td>
<td>16.2</td>
<td>16.6</td>
<td>17.1</td>
<td>16.9</td>
</tr>
<tr>
<td><strong>Fixed Manufacturing Costs</strong></td>
<td>5.4</td>
<td>5.6</td>
<td>5.1</td>
<td>6.7</td>
<td>6.9</td>
<td>7.7</td>
<td>7.7</td>
</tr>
<tr>
<td><strong>Total Cost of Goods Sold</strong></td>
<td>51.4</td>
<td>51.2</td>
<td>51.2</td>
<td>56.0</td>
<td>57.8</td>
<td>59.3</td>
<td>60.7</td>
</tr>
<tr>
<td><strong>Administration Costs</strong></td>
<td>6.9</td>
<td>7.3</td>
<td>7.1</td>
<td>6.4</td>
<td>6.6</td>
<td>6.3</td>
<td>6.1</td>
</tr>
<tr>
<td><strong>Distribution Costs</strong></td>
<td>2.8</td>
<td>3.2</td>
<td>3.7</td>
<td>4.2</td>
<td>4.1</td>
<td>4.0</td>
<td>3.8</td>
</tr>
<tr>
<td><strong>Selling, Marketing and Promotion Costs</strong></td>
<td>17.1</td>
<td>19.4</td>
<td>20.6</td>
<td>19.7</td>
<td>19.5</td>
<td>19.8</td>
<td>19.4</td>
</tr>
<tr>
<td><strong>Research and Medical Costs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overseas payments</td>
<td>0.6</td>
<td>0.6</td>
<td>0.6</td>
<td>0.6</td>
<td>0.6</td>
<td>0.6</td>
<td>0.7</td>
</tr>
<tr>
<td>Other</td>
<td>1.6</td>
<td>2.0</td>
<td>2.4</td>
<td>2.1</td>
<td>2.8</td>
<td>2.5</td>
<td>2.7</td>
</tr>
<tr>
<td><strong>Royalties and Service Costs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overseas payments</td>
<td>4.1</td>
<td>4.1</td>
<td>3.8</td>
<td>4.1</td>
<td>3.7</td>
<td>3.6</td>
<td>2.8</td>
</tr>
<tr>
<td>Other</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.4</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td><strong>Financial Costs (excluding interest)</strong></td>
<td>-0.4</td>
<td>-1.4</td>
<td>0.7</td>
<td>0.5</td>
<td>1.3</td>
<td>-0.1</td>
<td>0.4</td>
</tr>
<tr>
<td><strong>Total Non-Manufacturing Costs</strong></td>
<td>33.2</td>
<td>35.7</td>
<td>39.4</td>
<td>38.1</td>
<td>39.1</td>
<td>37.1</td>
<td>36.3</td>
</tr>
<tr>
<td><strong>Total Costs</strong></td>
<td>84.6</td>
<td>86.9</td>
<td>90.6</td>
<td>94.1</td>
<td>96.9</td>
<td>96.4</td>
<td>97.0</td>
</tr>
</tbody>
</table>

(Note: Information from 27 companies (73% of companies with sales in PBS pharmaceutical sector)

1981. This increase was estimated to cost the government $25 million (which was at variance with the Ralph Inquiry's estimate of only $8 million for a 4.4% increase). The APMA also criticised the Report's emphasis on enhancing competitiveness within the industry, pointing out that a majority (60%) of consumers under the PBS were subsidised pensioners, so that free market principles would apply to only 40% of the total market.

One year later, no significant action had been taken on the Ralph Inquiry proposals to alter existing PBS arrangements on drug prices. Aside from the political costs of increasing drug prices, two other issues had tested the state's ability to follow the recommendations. The first was that only two days after announcing its budget decision in favour of this recommendation, the government backed down on its decision to allow chemists to discount prices. Secondly, considerable concern arose from an independent study of the cost of the Ralph Inquiry's recommendations which calculated drug price increases of about 62% (patented drugs) and 55% (unpatented drugs) and a $94 million increase in the PBS bill, in contrast to an increase of only 1% per year since 1972 under the existing scheme.

5.6 The Early 1980s

In 1980 temazepam, a new benzodiazepine classified as a sedative/hypnotic, was added to the PBS. In the same year the import of a barbiturate sedative - Mandrax (methaqualone) - was banned. Mr. Justice Williams of the Australian Royal Commission into Drugs stated that Mandrax was the most abused prescribed drug in Australia and that "it had little therapeutic value", "was mainly abused by the people taking it medically", was habit-forming and often mixed with alcohol or other drugs. Although similar criticisms had been made of the
benzodiazepines, no such recommendation was made concerning their withdrawal.

Less than two years later, Jean Lennane, the well-known director of a leading Sydney drug and alcohol treatment unit, publicised a significant rise in clients addicted to sedatives (from 3% in the previous year to 10% in April 1982). The drug most likely to be misused was Serapax (oxazepam), which had produced severe withdrawal effects in a number of her clients. By December 1982, Lennane was reporting an incidence of 25% of clients addicted to benzodiazepines.

Meanwhile, the Australian Consumers' Association (ACA) was following the lead of similar consumer organisations overseas in publicising unethical actions by the Australian drug industry. In September 1982, the Australian-owned drug company, Nicholas Pty Ltd was accused of dumping its compound analgesic, Vinac (containing caffeine, aspirin and salicylamide) on Third World countries such as Malaysia and African countries, including Ethiopia. Vinac was not available in Australia because of strict government controls on compound analgesics here, but was manufactured and promoted in Malaysia where legal restrictions were not as severe.

Around the same time, the APMA was given some state encouragement when the Liberal Health Minister, Jim Carlton, announced his support for the Ralph Inquiry's recommendations which were in agreement with his free market philosophy. He asked the APMA to submit a proposal for a new pricing system after having rejected their previous submission made soon after the release of the Ralph Report. However, any further development of these plans was interrupted by the election of the Hawke government.

Lobbying of the new Hawke government became intense. In March
1984 the APMA released a report it had commissioned which was strongly critical of the PBS pricing system. Once again the drug industry was blaming PBS pricing for its low profits and cited, as examples, the CIBA-Geigy (Australia) Ltd closure of its plant at Smithfield in Sydney and the cancellation of Boehringer Ingelheim's research project into heart disease at St Vincents Hospital, Sydney, worth $350,000. This latter move had been a retaliatory reaction by Boehringer against a state decision to remove one of its drugs from the PBS because it had refused to lower the price to that of a competitor. By April 1985, Lilly Industries had closed one of its factories and announced that it would withdraw completely from local manufacture by July 1985, a loss of ninety-six jobs in total. The loss of eighty jobs from the closure of CIBA-Geigy's Smithfield plant in 1984, and of 180 jobs by Merck Sharpe and Dohme in 1983 added up to a total loss of just under 5% of the total of eight thousand jobs generated by the industry. The drug industry also blamed the devaluation of the Australian dollar for an increase in the cost of materials and, thus, for a fall in profits.

However, the Hawke government's desire to encourage Australian technology and industrial development, and specifically to support an Australian drug industry were in obvious conflict with its desire to curb health costs. In the continuing struggle between the state and the drug industry, Health Minister Neal Blewett introduced amendments to the National Health Act which would allow a drug to be included within the PBS even when agreement had not been reached on price. A maximum state-determined price would be set and the consumer pay the difference. This was approved in May 1985 together with an increase to the PBS general contribution rate from $4 to $5. Although presenting this legislation as being of benefit to the consumer who would otherwise be deprived of a
necessary drug, the state had nevertheless passed on to the consumer a charge which it had considered unreasonable.

Also in 1985, the ACA launched a public campaign critical of drug advertising and calling for greater state intervention. At that time, only State controls applied and these were limited to prohibiting misleading advertisements. The only federal controls were through a voluntary Code of Conduct for marketing and advertising prescription drugs set by the APMA. Despite a number of misleading advertisements having been identified by independent researchers, the APMA had never acted against a company for breaching its Code. In response to the ACA campaign, the National Therapeutic Goods Committee began to prepare guidelines, in consultation with consumer and other interested groups such as the Medical Lobby for Appropriate Marketing (MLAM) (an international organisation based in Adelaide). In 1986, the APMA revised its code of conduct to allow input from the scientific-medical community on an 'independent' advisory committee, with representation by pharmacologists and doctors. This recognised the doctor's role as consumer of the industry's promotional messages and reinforced the conjunction of interests between the medical profession and the industry. It also confirmed the industry's difficult relations with the health consumer movement, representing the consumer of the industry's product but not represented on the APMA committee.

More recently, the ACA's criticism of Searle for unethical promotion of Lomotil (see Chapter 4) which drew a great deal of publicity, brought a quick reaction from the APMA, which asked Searle to withdraw its advertisement as it was in breach of their voluntary code of conduct. The APMA later announced the formation of another committee to monitor prescription drug advertising on a regular basis as
well as retaining its former committee to deal with specific complaints.\textsuperscript{97} Their prompt action was no doubt influenced by the current two-year trial period granted to the industry to establish a self-regulation process considered effective by the state.\textsuperscript{98}

5.7 The IAC Inquiry

The final Report from this inquiry was handed to the government in April 1986. The drug industry continued to claim it was suffering from problems of low profitability with costing estimates that were essentially unchanged from those submitted to the Ralph Inquiry (see Table 5.6). Referring to the soaring drug bill (which had undergone a forty-fold increase in the thirty-five years since the introduction of the PBS – see Table 5.7), the IAC (Industries Assistance Commission) Inquiry repeated the Ralph Report's decision to focus on the PBS as the major concern for the drug industry,:

(although industry assistance considerations have played a small role in the introduction of these (government) regulations, the existing regulatory framework has a pervasive influence on the structure and operations of the pharmaceutical industry. Thus this report differs from many Commission reports in that its primary focus is not upon tariffs nor direct financial assistance to the industry. Rather, the focus is on the regulatory framework and its impact on the industry and the community generally.\textsuperscript{99}

The IAC Report's main recommendations were that the government should subsidise only the cost of the cheapest drug within any group of therapeutically substitutable drugs, and that a concession scheme be introduced to cover excess costs (essentially an insurance scheme by which the consumer would pay an appropriate sum for the privilege of paying for prescription drugs at a reduced price, which would become free after more than fifty scripts had been dispensed in one year). The scheme would permit generic substitution by the chemist dispensing the
### Table 5.6: Costs (as percentage of sales) reported by drug companies in Australia in the PBS Pharmaceutical Sector (1983)

<table>
<thead>
<tr>
<th></th>
<th>PBS</th>
<th>Total Human Use Pharmaceuticals</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Variable Manufacturing Costs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Material from overseas affiliates</td>
<td>35.1</td>
<td>24.4</td>
</tr>
<tr>
<td>Other</td>
<td>19.9</td>
<td>23.6</td>
</tr>
<tr>
<td><strong>Fixed Manufacturing Costs</strong></td>
<td>7.8</td>
<td>7.9</td>
</tr>
<tr>
<td><strong>Total Cost of Goods Sold</strong></td>
<td>62.8</td>
<td>55.9</td>
</tr>
<tr>
<td>Administration Costs</td>
<td>5.9</td>
<td>5.8</td>
</tr>
<tr>
<td>Distribution Costs</td>
<td>2.9</td>
<td>3.2</td>
</tr>
<tr>
<td><strong>Selling, Marketing and Promotion Costs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Advertising</td>
<td>3.9</td>
<td>5.7</td>
</tr>
<tr>
<td>Representatives</td>
<td>8.3</td>
<td>7.5</td>
</tr>
<tr>
<td>Other promotion</td>
<td>1.7</td>
<td>1.6</td>
</tr>
<tr>
<td>Marketing/Promotional managerial expenses</td>
<td>3.9</td>
<td>3.9</td>
</tr>
<tr>
<td>Other</td>
<td>0.5</td>
<td>0.7</td>
</tr>
<tr>
<td><strong>Research and Medical Costs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overseas payments</td>
<td>0.8</td>
<td>0.9</td>
</tr>
<tr>
<td>Other</td>
<td>2.3</td>
<td>2.0</td>
</tr>
<tr>
<td><strong>Royalties and Service Costs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overseas payments</td>
<td>1.5</td>
<td>1.5</td>
</tr>
<tr>
<td>Other</td>
<td>0.2</td>
<td>0.1</td>
</tr>
<tr>
<td><strong>Financial Costs (excluding interest)</strong></td>
<td>0.3</td>
<td>(0.1)</td>
</tr>
<tr>
<td><strong>Total Non Manufacturing Costs</strong></td>
<td>32.2</td>
<td>32.8</td>
</tr>
<tr>
<td><strong>Total Costs</strong></td>
<td>95.0</td>
<td>88.7</td>
</tr>
</tbody>
</table>

**Source:** Australian Pharmaceutical Manufacturers' Association: Submission to Industries Assistance Commission Inquiry into the Pharmaceutical Products Industry, (1985), p.34.
<table>
<thead>
<tr>
<th>Year</th>
<th>General users</th>
<th>Concessional</th>
<th>Pensioners</th>
<th>Total Govt expenditure</th>
<th>Index of Govt expenditure (1951-52 = 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patient expenditure</td>
<td>64.03</td>
<td>84.15</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1968-69</td>
<td>20.13</td>
<td>64.03</td>
<td>84.15</td>
<td>-</td>
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<tr>
<td>1969-70</td>
<td>21.94</td>
<td>73.23</td>
<td>95.17</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1970-71</td>
<td>24.38</td>
<td>88.18</td>
<td>112.56</td>
<td>-</td>
<td>-</td>
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<tr>
<td>1971-72</td>
<td>35.47</td>
<td>90.06</td>
<td>125.53</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1972-73</td>
<td>48.64</td>
<td>87.43</td>
<td>136.07</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1973-74</td>
<td>59.02</td>
<td>108.07</td>
<td>167.08</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1974-75</td>
<td>66.83</td>
<td>131.34</td>
<td>198.17</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1975-76</td>
<td>95.25</td>
<td>149.03</td>
<td>244.28</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1976-77</td>
<td>111.68</td>
<td>111.08</td>
<td>222.75</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1977-78</td>
<td>115.03</td>
<td>118.30</td>
<td>233.33</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1978-79</td>
<td>129.54</td>
<td>110.43</td>
<td>239.97</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1979-80</td>
<td>123.42</td>
<td>101.19</td>
<td>224.60</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1980-81</td>
<td>129.92</td>
<td>107.90</td>
<td>237.83</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1981-82</td>
<td>157.96</td>
<td>139.55</td>
<td>297.51</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1982-83</td>
<td>170.62</td>
<td>131.77</td>
<td>302.39</td>
<td>5.88</td>
<td>11.10</td>
</tr>
<tr>
<td>1983-84</td>
<td>166.04</td>
<td>114.64</td>
<td>280.68</td>
<td>19.98</td>
<td>39.28</td>
</tr>
<tr>
<td>1984-85</td>
<td>201.14</td>
<td>142.44</td>
<td>343.58</td>
<td>20.21</td>
<td>43.27</td>
</tr>
</tbody>
</table>

a Excludes payments for the provision of PBS pharmaceuticals to hospitals, bush nursing centres, the Royal Flying Doctor Service.

drug, as in the US. By this time, the majority of PBS drugs were no longer protected by patent (see Table 5.8). The Report also suggested cutting back on drug evaluation procedures by allowing drugs approved for marketing in other approved countries to be marketed in Australia immediately, with evaluation studies to follow.100

In order to combat what they viewed as excessive drug use by pensioners (and benzodiazepines are a significant component of these drugs), the IAC recommended that pensioners pay for all drugs at the concessional rate of $2 each up to a maximum of fifty scripts, and that a pension increase (of $50 per year) be paid in compensation. Essentially, it would cost pensioners $50 before they could qualify for free prescriptions. An alternative was to offer pensioners the 'choice' of foregoing the pension rise and obtaining free medication if they would accept the cheapest drug within a therapeutically substitutable category.101

In the mid-1980s it was estimated that the federal government would save nearly $150 million per year if it followed the IAC recommendation to remove subsidies on most prescription drugs.102 Instead, the 1986 budget raised the Medicare levy by 0.25 percent (saving $175 million that year and approximately $325 million in a full year), and the state continued to subsidise prescription drugs but at a reduced level. The maximum cost to the consumer was doubled to $10 per prescription drug (this was estimated to represent a saving to the government of $67 million).103 Thus, the general users' PBS contribution rate had increased over thirty-five years from zero to $10 per prescription (see Table 5.9). The IAC proposal for a concession scheme was rejected. However, the 1986 budget retained the concept of a limit beyond which prescription drugs would be available free (the
Table 5.8: Patent Status of the Australian Pharmaceutical Market (1983)

<table>
<thead>
<tr>
<th>% of Total Sales</th>
<th>Patented Products</th>
<th>Out-of-Patent Products</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>18</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>No other manufacturer sells the same presentation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Another manufacturer(s) sells the same presentation</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(Note: Information from APMA survey of pharmaceutical drug industry (41 companies) in Australia in October 1984.

Source: Australian Pharmaceutical Manufacturers' Association, Submission to Industries Assistance Commission Inquiry into the Pharmaceutical Products Industry, January 1985.)
Table 5.9: PBS Contribution Rate for General Users (1950-1985)

<table>
<thead>
<tr>
<th>Date</th>
<th>Contribution Rate $</th>
</tr>
</thead>
<tbody>
<tr>
<td>September 1950</td>
<td>Free</td>
</tr>
<tr>
<td>March 1960</td>
<td>0.50</td>
</tr>
<tr>
<td>November 1971</td>
<td>1.00</td>
</tr>
<tr>
<td>September 1975</td>
<td>1.50</td>
</tr>
<tr>
<td>March 1976</td>
<td>2.00</td>
</tr>
<tr>
<td>July 1978</td>
<td>2.50</td>
</tr>
<tr>
<td>September 1979</td>
<td>2.75</td>
</tr>
<tr>
<td>December 1981</td>
<td>3.20</td>
</tr>
<tr>
<td>January 1983</td>
<td>4.00</td>
</tr>
<tr>
<td>July 1985</td>
<td>5.00</td>
</tr>
<tr>
<td>November 1986</td>
<td>10.00</td>
</tr>
</tbody>
</table>

number of scripts being set at twenty-five in any one year), possibly in an attempt to appease consumer anger with the 100% price increase.

The 1986 budget also followed the usual recommendations made from time to time by the PBAC to remove from the pensioner free list some commonly used drugs available without prescription. These included analgesics (including some forms of aspirin), antihistamines, cough mixtures and some vitamins. This was estimated to save the government approximately $30 million. In response to pensioner reaction against this decision, the head of the PBAC referred to the Committee's charter which set out that the PBS scheme was set up to provide "life saving and disease preventing" drugs and they could not recommend a drug for the treatment of "minor or trivial" conditions. In the case of aspirin, this is clearly untenable: although analgesics are probably used for many minor or trivial conditions (and probably misused), they are nevertheless indispensable for relief of severe pain. It is notable that, in the case of benzodiazepines, which, like aspirin, can hardly be considered life saving drugs, the PBAC did not also recommend their removal from the free list for pensioners (nor the more economical step of providing only one generic benzodiazepine).

The state and the drug industry have been continually locked in battle over drug pricing policy. Using similar tactics to those against doctors' proposals to raise their fees beyond that which the state was prepared to support through Medicare, the state has refused to subsidise what it perceives as unreasonable drug price increases. For example, in mid-1986 when Parke Davis attempted to increase, by 25%, the cost of Dilantin (an anti-convulsive drug for which there was no other substitute drug), Blewett publicly criticised the company for its action. The drug companies complained, however, that they were being
forced to price their products too low in Australia.

In support of the proposed Dilantin price increase, the APMA released information on the cost of the top fifteen brand name drugs in Australia (Table 5.10). In a pre-budget newspaper article just before the government was to announce its response on the IAC Inquiry recommendations, the APMA complained about the cheap drug prices in Australia: according to industry information, our drugs were 38% cheaper than in Britain and 67% cheaper than in the United States. These figures were not comprehensively surveyed nor easily comparable.

The IAC Inquiry exposed the extreme difficulty in making price comparisons because of the considerable price variability between drugs within Australia and between Australia and overseas. For example, for nine of the ten most commonly prescribed drugs on the PBS in Australia, prices in Australia were 37% lower than in New Zealand. However, three of the ten most prescribed drugs in Australia were sold to New South Wales hospitals at 94% of the PBS price. This could perhaps be explained by the hospital tendering system for bulk items permitting some price discounting, although these same drugs were sold by a major drug supplier to countries in the South Pacific region at 24% of the Australian PBS price. Furthermore, of fourteen commonly used drugs it was found that 35% were cheaper in the South Pacific region than in NSW hospitals.

In their pre-budget lobbying, the APMA also blamed the lack of research in Australia by drug companies on the low Australian drug prices, claiming that "low prices have led to cancelled investments of $15 million, deferred investment of $40 million, the loss of 720 jobs, about $4 million that was not spent on research and $7.6 million not
Table 5.10: Cost of Top Fifteen Brand Name Drugs Sold in Australia Under the Prescription Benefit Scheme compared with other Countries as at July 1986

<table>
<thead>
<tr>
<th>Trade Name</th>
<th>Company</th>
<th>Price to Wholesaler</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Aust</td>
</tr>
<tr>
<td>1. Amoxil</td>
<td>Beecham Research Laboratories</td>
<td>2.68</td>
</tr>
<tr>
<td>2. Modiuretic</td>
<td>Merck Sharp &amp; Dohme (Aust)</td>
<td>1.85</td>
</tr>
<tr>
<td>3. Naprosyn</td>
<td>Syntex Aust</td>
<td>3.69</td>
</tr>
<tr>
<td>4. Septrim</td>
<td>Wellcome Aust Ltd</td>
<td>2.48</td>
</tr>
<tr>
<td>5. Ventolin</td>
<td>Glaxo Aust</td>
<td>2.52</td>
</tr>
<tr>
<td>6. Serapax</td>
<td>Wyeth Pharmaceuticals</td>
<td>1.50</td>
</tr>
<tr>
<td>7. Lasix</td>
<td>Hoechst Aust</td>
<td>2.13</td>
</tr>
<tr>
<td>8. Betaloc</td>
<td>Astra Pharmaceuticals</td>
<td>7.34</td>
</tr>
<tr>
<td>9. Clinoril</td>
<td>Charles E. Frosst (Aust)</td>
<td>3.72</td>
</tr>
<tr>
<td>10. Triphasil</td>
<td>Wyeth Pharmaceuticals</td>
<td>2.55</td>
</tr>
<tr>
<td>11. Mogadon</td>
<td>Roche Products</td>
<td>-</td>
</tr>
<tr>
<td>12. Tenormin*</td>
<td>ICI Aust</td>
<td>5.48</td>
</tr>
<tr>
<td>13. Aldomet</td>
<td>Merck Sharp &amp; Dohme (Aust)</td>
<td>5.91</td>
</tr>
<tr>
<td>14. Zyloprim</td>
<td>Wellcome Aust</td>
<td>3.30</td>
</tr>
<tr>
<td>15. Indocid</td>
<td>Merck Sharp &amp; Dohme (Aust)</td>
<td>2.42</td>
</tr>
</tbody>
</table>

* pre-March 1986 prices

spent on promotion" and that, consequently, "most research done here is limited to improving existing drugs".109

Complaints by the drug industry of being 'squeezed' by the state are not supported by the industry's continuing practice of importing most of its supplies in the unfinished state for formulation and packaging here (see Table 5.11). As a result, high transfer pricing could continue to support the industry's assertions of poor profits in Australia as a lever against the state pricing policies.

5.8 The New South Wales Women and Prescribed Drugs Campaign

Most recently, the Hawke government has turned to the consumer in an effort to improve controls on the use, or over-use, of drugs (both prescription and non-prescription). A major campaign across Australia was initiated on the use of alcohol and other drugs - the National Campaign Against Drugs and Alcohol (NCADA) - launched in April 1985 as a combined Federal-State project.110 A total of $100 million was committed over a three-year period. An additional $20 million of Federal funds was committed for the Drug Offensive media campaign ($5 million), research projects ($2 million), data collection ($1 million) and drug and alcohol services ($12 million).111 Both legal and illegal drug use was covered. A small component of that campaign was directed towards reducing the use of prescribed tranquillizers.

Political figures such as the Prime Minister, Bob Hawke, and the Premier of NSW, Barrie Unsworth, turned their own, or family, problems with drugs into favourable publicity for the parts they were playing in the NCADA. Political gains were sought overseas by Blewett at a world conference of Health Ministers when he spoke of the NCADA and described it as an aid for the state in reducing both the demand and supply of drugs.112 As well as gaining international recognition, the Hawke
Table 5.11: Composition of Human Use Pharmaceutical Sales in Australia (1983)

<table>
<thead>
<tr>
<th>Category</th>
<th>% of Total Sales Value (at dispensed price level)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Products imported in the fully finished and packaged form</td>
<td>13</td>
</tr>
<tr>
<td>Products imported fully finished in bulk then packaged in Australia</td>
<td>9</td>
</tr>
<tr>
<td>Active ingredients (or intermediates) imported which are then formulated as drugs and packaged in Australia</td>
<td>65</td>
</tr>
<tr>
<td>Drugs, formulated from active ingredients, manufactured in Australia then packaged in Australia</td>
<td>13</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
</tr>
</tbody>
</table>

government has also stood to gain much nationally, especially by promoting an image of social responsibility to the voting public through the Drug Offensive media campaign. The government took the risk of alienating voters who were also drug consumers unwilling to be 'educated' on responsible drug use (especially regarding alcohol and tobacco use which were included in the NCADA) but this was offset by focussing on illegal drug use (a small minority of drug users) and on improving the image of law enforcement agencies (appealing to the public's need to feel safe) as well as highlighting young people's drug use.

Two of the first projects launched in New South Wales were specifically concerned with the use of minor tranquillizers. One was the St Vincent's Hospital Hypnosedative Project which produced a 'patient education program' of a video and literature for the general public. Although also promoted as being for health professionals, the main target of the project was clearly the drug user.\textsuperscript{113}

The second project was aimed at women's use of minor tranquillizers. (Other educational campaigns on minor tranquillizer use by women have since been carried out in South Australia and Victoria, and planning is under way for one in Western Australia in 1989.)\textsuperscript{114} The New South Wales Women and Prescribed Drugs campaign was coordinated by the Women's Coordination Unit of the Premier's Department and funded by a grant of $103,800 from the NSW Drug and Alcohol Authority.\textsuperscript{115} The campaign was launched in May 1986 to inform women of risks associated with benzodiazepine use and to help them obtain counselling and information (in English and ten other community languages), initially through a state-wide phone-in and with further opportunities for face-to-face counselling involving specially trained counsellors, again
catering for the eleven major languages.

The campaign adopted a 'community education' approach, using TV, radio and printed media including women's magazines and medical and health journals, as well as posters and a specially prepared pamphlet in eleven languages mailed out to women's refuges, hospitals, health centres, doctors and other health professionals. Again, the primary target was the user. Although general practitioners received a copy of the poster for their waiting rooms (enclosed with the May issue of the Medical Practice journal) and multiple copies of the specially prepared leaflet for their patients (by mail), the campaign did not directly challenge the doctors' - nor the drug companies - role in over-prescribing; on the contrary, women were urged to seek their doctors' advice.116

Secondly, long-term effects of this campaign were limited severely because of its 'one off' preliminary nature. TV and radio coverage as well as contact with doctors and other health professionals were for only a short period of time. However, treatment services were better equipped to help people suffering from minor tranquillizer addiction through special training of counselling staff. Nevertheless, education and prevention strategies were certainly not comprehensively addressed. The campaign did not receive extra funding for national coverage nor even for additional, follow-up coverage in NSW. It essentially became a tokenistic effort to placate those concerned about women's health and tranquiliser use. It did not address the pharmaceutical industry's role and its profits from benzodiazepine sales in Australia, nor did it challenge the powerful medical lobby in NSW.

Whilst a number of women and minor tranquillizer support groups and services have now been set up (for example, the Italian speaking
self-help group sponsored by a Sydney Italian community group, and the Louisa Lawson House Minor Tranquillizer Clinic), the state campaign may be seen more as a response to political pressure from the women's health movement. Well before the state initiative, the Leichhardt Women's Health Centre had initiated a public awareness campaign when, in 1983, it conducted a phone-in on tranquillizer use. The response to the phone-in triggered the setting up of a minor tranquillizer clinic at the Health Centre. Many women's health workers were active in assisting the New South Wales Women and Prescribed Drugs campaign, such as educating other health workers in the associated workshops.

5.9 Erosion of Power of Medical Profession

In Australia there has been an erosion of doctors' powers over drug regulation within the state. In 1987 four senior officers (all of whom were doctors) resigned from the drug evaluation section within the Health Department following a Public Service Board review of its functions. The position of one of them, as head of the section, was reclassified as an administrative position rather than a medical one. This loss of medical dominance within the administrative functions of the state is also reflected in the recent decision to allow the Commonwealth Director General of Health to no longer be medically qualified. The review of the drug evaluation section was triggered by allegations of administrative errors concerning generics of doubtful bioequivalence having been listed under the PBS, and that some drugs may have been mistakenly approved for PBS listing prior to marketing approval having been granted. Claims by one of the outgoing medical officers of inadequate staffing and facilities being made available by the Department can be added to criticisms by the drug industry that most delays in evaluation procedures for drugs rest with the Department
rather than with ADEC.124

As discussed in Chapter 3, the hospital has been a crucial site for testing medical professional power. The public image of the medical profession, which had suffered during the Medibank controversy of the Whitlam years, fell even further in the 1980s with the conflict between the procedural specialists and the state over control of services within public hospitals. Their falling public image was a major cause of dissatisfaction amongst doctors (especially general practitioners) in a 1983 survey.125 An important factor in the medical profession's loss of power was its fragmented political representation. Membership of the AMA has dropped significantly to about half of all doctors in Australia126 (more recently, significant variations were found between states, with New South Wales having one of the lowest rates of membership at 38% of all doctors compared with a maximum of 62% in Western Australia).127 Following a recent review of its organisation, the AMA decided to remove power from the different state branches and centralise it within the executive.128 The drop in AMA membership has been accompanied by the formation of alternative medical lobby groups such as the General Practitioners' Society of Australia (GPSA)129 and the Doctors' Reform Society (DRS) in the 1970s (see Section 5.3), and the National Council of Procedural Specialists, the Private Doctors' Association, the Public Hospital Staff for the Protection of Medicare, and Doctors for Patients),130 as well as the resignation from the AMA of the Australian College of Surgeons. Other factors contributing to the profession's loss of power in Australia are the popular challenges to the biomedical model and the rise of alternative medicine in the 1970s and the oversupply of doctors, especially in New South Wales.131
5.10 Strengthening of Health Consumer Movement

The health consumer movement in Australia has strengthened its voice during the Hawke government's term. Following lobbying by a coalition of consumer groups in 1985, the Consumer Health Forum (CHF) was established at the end of 1986. Partly funded by the Department of Community Services and Health (formerly the Health Department), it comprises sixteen community health groups representing interests of different consumers such as, women, ethnic communities, aboriginal communities, pensioners and aged people, youth, disabled people, and others.132

An important role of the CHF is to improve consumer representation within the state. The newly formed PBPA (see Chapter 4) includes a consumer representative selected by the CHF. Other state health bodies for which the CHF provides consumer representation include: various committees of the National Health & Medical Research Council (NH&MRC), Australian Institute of Health, HEAPS (a national database of health promotion programs and resources), and other committees examining dental health, organ transplants, and a publication on tuberculosis.133 It also provides a small grants program for research in the health field (70 grant applications, totalling $450,000, were received for an available amount of only $60,000).134

The CHF has recently put out a discussion paper on "rational" drug policy. Whilst acknowledging the role of the drug industry, doctor, consumer and the state and the political, rather than technical, nature of drug use the authors contradict themselves in their reliance on rationality and objectivity, apparently mediated by greater state intervention, which denies the political and irrational elements permeating the process of drug use. For example, they point to a "need
to identify drugs that are essential to meet therapeutic needs. In the light of the British experience with limited drug lists, outlined in Chapter 5, the political process for implementation of a technically rational policy cannot ensure the expected outcome. More attention is required to identify and modify the political processes involved in order to implement technically rational objectives.

Nevertheless, the contemporary health consumer movement is challenging the power of the drug industry and those it supports. The formation and organisation of the CHF has been bitterly attacked by the Australian Association of National Advertisers (AANA) as "a precedent which must be arrested, if government policy is to reflect the balanced views of competing interests within a free-enterprise system." The strength of the attack illustrates the advertising industry's fear of the consumer movement as well as the strong influence of the drug industry within the AANA.

As mentioned in Chapter 3, increased consumer representation within the state carries with it potential dangers that the consumer movement will become professionalized and adopt strategies which it has criticized in the medical profession (such as objectification of the client or patient). This warning by Freidson is relevant to the Australian health consumer movement which, under the present Labor government, has been strengthened nationally by state funding of the CHF, and which has gained greater access to advisory and decision-making bodies within the state. Consumer groups in Australia now have greater scope for activity but also run the risk of losing power through greater economic and political ties with the state.

Freidson has also proposed consumer power could be increased by providing greater choice of medical services for consumers and a system
of regularly monitoring consumer satisfaction which will effectively act in order to translate individual choice into political power.\textsuperscript{138} Although he did not outline how consumers could effect these changes, an excellent example comes from the women's health movement in Australia. In 1973 political pressure from the women's movement\textsuperscript{139} was favourably received by the Whitlam government and led to the establishment of the first women's health centre in Australia at Leichhardt in 1974. Other centres quickly appeared in Liverpool (Sydney), Newcastle, Melbourne, Brisbane, Adelaide and Perth. The centres were funded through the Community Health Program, a new initiative to expand community health services which also included the setting up of women's refuges and rape crisis centres.\textsuperscript{140} Although state policy intended funding over a limited period of ten years with services to then be integrated in general community health services, the increased political strength of women's services has ensured their continued separate existence.

A discussion paper on national policy on women's health under consideration by the Hawke government this year proposed to continue women's health services "to operate alongside and complement mainstream health services".\textsuperscript{141} Acceptance of this draft policy will consolidate the political strength of women's services. However, the advisory committee within the state (the Australian Health Ministers' Advisory Council Subcommittee on Women and Health) is dominated by state bureaucrats: six representing Federal health services and nine from State health services. Only two of these are members of the medical profession. There are three organisations representing women health consumers: the CHF, the Australian Women's Health Network, and the ACTU.\textsuperscript{142} Nevertheless, the strategy taken up by the committee of extensive consultation with women around Australia concerning the draft
policy represents a useful example of Freidson's suggested "method of monitoring consumer satisfaction", and should help overcome some of the difficulties of adequate representation of all women's interests, rather than a professional elite within the state.

5.11 Conclusion

For the Australian drug industry, development and marketing of drug technology, such as for the benzodiazepines, has been strongly dependent on the PBS which has been an important arena of conflict between the industry, the state, the medical profession and health consumers since the Labor government's first attempts in 1944 to introduce a universal drug benefit scheme.

The state has a special relationship with the drug industry, exercising control both as its major client and by imposing regulatory controls on the industry. The soaring cost of the PBS saw government cost-cutting projects intensify from the early 1970s, fuelling strong reaction from the drug industry, whose political lobbying for greater government support instigated a major inquiry into the Australian drug industry in the late 1970s (the Ralph Inquiry). When the resultant report neither favoured the drug industry nor the state, a further major inquiry was held in the mid-1980s (the IAC Inquiry). Again, the government was urged to take the electorally unfavourable step of passing on more of the PBS costs to the consumer (especially the pensioner component) as well as cutting costs by reducing drug regulatory controls.

Political conflict over the availability of prescribed drugs in Australia has exposed differences within the Australian Labor Party during its current and previous terms of government. For example, the Australian drug industry has benefited by the Hawke government's strong
support of industry generally, by special programs to support industrial
R & D, and by its reluctance to attack the industry directly on the
high sales volume and consequent cost of tranquillizers and other drugs.
Instead, it has acted indirectly at what Blewett has described as the
"demand" side, through treatment and prevention of drug addiction in the
consumer under the NCADA. This may be seen as a strong political
strategy to promote a socially responsible image for the government.
This approach contrasts strongly with that of the previous Labor
government under Whitlam, which assumed an aggressively anti-drug
industry stance. Initiatives important to minor tranquillizer sales in
Australia included: launching a concerted public campaign against
excessive profits in the drug industry; establishing a state-owned drug
company; proposing significant cuts in patent life of pharmaceutical
drugs; and initiating increased legislative powers of the state to
obtain financial information from drug companies.

Secondly, prescribed drug use has exposed inter- and intra-
departmental conflict within the state. On the one hand, the Department
of Community Services and Health attempts to balance its fiscal
responsibilities over minimizing the drug bill with its social
responsibilities for providing appropriate medication for all citizens;
on the other hand, the Department of Industry, Technology and Commerce
strives to encourage the drug industry for its national economic,
employment and technological benefits without granting special
concessions which would adversely affect the rest of Australian
manufacturing industry.

The Australian government's continuing difficulties with managing
the Australian PBS expose the economic, social and political forces
which may be seen to impose contradictory functions on the state of
supporting capital accumulation (directly, for the drug industry and, indirectly, for the national economy) and legitimation of its social welfare role (the state must show it can fulfil its function of supplying basic health needs). Both the Whitlam and Hawke strategies may be seen as political forces enabling the state to further support capitalism in response to the legitimation crisis of contemporary democracy brought on by a persistent economic crisis within capitalism. With an escalating drug bill and tighter restrictions on available funds for health care, the Hawke era has favoured the former function of the state whilst the Whitlam era favoured the latter. However, a dichotomy between capital accumulation and legitimation may be too simplistic a view and this is explored with respect to an analysis of the state and health care put forward by Navarro.

A dominant voice within the Marxist school has been Navarro who, in the mid-1970s, provided an in-depth political economy analysis of medicine, concentrating on the role of class relations and the state in health care. Because of the importance recently given by Turner to Navarro's theories on the negative and positive modes of state intervention in health care, these are explored using some of the evidence presented in Chapters 4 and 5.

An example of Navarro's proposed ideological negative selection mechanism of state intervention, which "systematically and continually excludes those strategies that conflict with the class nature of the capitalist society", could be applied to benzodiazepine use. Using Navarro's example of an individualistic ideology being bound up in capitalism, it could be stated that the state favours individualistic solutions for health problems involving anxiety or sleep difficulties, thereby attempting to 'cure' the problems by a prescription, through the
PBS scheme, in contrast to 'preventing' the problem by economic and legislative changes such as supporting greater childcare facilities, less stressful working conditions, more equitable access to education, etc. In addition, the Hawke government's excursion into direct preventative measures against the over-use of benzodiazepines may be seen as individualistic as it has supported an "education" program aimed at changing the behaviour of the individual user rather than restricting the role of doctors or the drug industry.

However, Navarro's assertion of the class basis of the individualistic ideology within capitalism masks his gender bias. The ideology of individualism could also be described as a male ideology. Women in the paid workforce within capitalism may well appear to conform to a similar ideology but this conflicts with the concrete reality of their other social responsibilities, involving their far greater participation in maintaining the family unit through the care of children and other family members, as well as their greater representation in 'caring' rather than 'competitive' professions. This strongly suggests that women's greater role in promoting social cooperation and cohesiveness would weaken the case for a 'dominant' ideology of individualism. Giddens has also questioned the key role claimed for legitimation in maintaining capitalist societies, stating that:

"both Left and Right have greatly exaggerated the degree to which there is an ideological consensus among the majority of people in different classes. ... It is particularly important to be cautious about the thesis that crises of legitimation are the main sources of tension which threaten the stability of Western capitalist societies. Such a view presumes - in company with Parsons and Althusser - that social order rests upon normative consensus."

Giddens' cautions could also be applied to assumptions of consensus
across differences such as gender and race.

Navarro's proposed negative selection mechanisms in decision making can be seen in the composition of state bodies such as the PBAC and the ADEC which are overwhelmingly dominated by doctors. They would undoubtedly belong to Navarro's "capitalist" class. However, once again, they are also predominantly male, white and Anglo-Saxon and this is not adequately dealt with. According to Navarro, decision-making mechanisms favour the corporate and upper-middle classes who are dominant on the decision-making state bodies to the detriment of lower-middle and working classes. However, his class analysis is too crude a measurement and fails to deal with the conflicts between different members of the upper-middle class. In Australia, examples are the loss of medical dominance within the drug evaluation section of the Department of Community Services and Health, but its retention in the ADEC as a committee of medical-scientific 'experts'.

Positive selection mechanisms, divided by Navarro according to Offe's theory of the capitalist state into allocative and productive intervention policies, are defined in terms of laws and regulations of the state controlling allocation of resources already produced (such as laws requiring doctors to notify contagious disease and regulations covering ADEC's role in the evaluation of new drugs for release on the market or voluntary notification of adverse drug reactions) and policies which allow the state to be directly involved in production (for example, nationalized drug industries, state-funded medical education and the public hospital system).

Navarro contends that there has been a post-War shift from allocative to productive policies. However, the Australian experience provides a number of exceptions to this trend. For example, the PBS
scheme is very much an allocative function of the state and has continued for nearly forty years; the Whitlam attempt to introduce a state-controlled drug corporation dealing in non-biological pharmaceuticals, in order to challenge the capital accumulation in that industry, was a productive intervention policy which failed; whilst the Hawke government has been satisfied to maintain allocative intervention policies favouring the Australian drug industry. This is offset by the change from an allocative policy in the early 1970s of voluntary health insurance to the productive intervention policy of Medibank and Medicare (although, these schemes have important differences regarding the amount of support they have offered to overall capital accumulation).

Navarro has concluded that capital accumulation becomes the primary goal for the state, so that it is therefore dependent on the successful development of capitalism and, thus, the capitalist class is dominant over the state. He defines the second characteristic of a capitalist state (such as in Australia) by the fact that most of the powerful members of the state belong to the capitalist class "either by origin, association, or the sharing of beliefs." Thirdly, the ideology of the state supports the private sector and, fourthly, the capitalist state is responsible for the implementation of policy and is separate from the elected government executive and legislature which decides and formulates policy. Navarro states that these four factors affect the health sector because state intervention reproduces: the class structure, ideology and alienation of capitalism.

Most importantly, a crucial problem with Navarro's analysis (as for other strongly Marxist analyses) is his adherence to the primacy of class structure and the reproduction of power of the dominant class, which forces him to deny the importance of other power structures such
as organized occupations (for example, professions) as well as, on a wider basis, those based on differences such as gender and race. In his early major work on medicine he makes tokenistic reference to gender and race but, despite his positivist assertion that his arguments are strongly based on evidence, this is clearly not so in his decision to impose prime importance on class hierarchies. This has been confirmed more recently, when he attacked the "new pluralist view" which gives more equal attention to class, race and gender issues of power:

"Medicine (is) the interplay of power conflicts that operate within a matrix of social power categories (class, race, gender, and others), of which class is the organizer of how those conflicts, including the professional-patient conflict, take place. ... Racism and sexism in medicine, for example, are functional to the reproduction of power of not only the white male professions but, far more important, of the dominant class"\(^\text{150}\)

Again, he provides no evidence to support his assertions on the primacy of class over other power conflicts.

The erosion of power held by the medical profession within the state illustrates Johnson's theoretical analysis of professional power and the mediative role of the state. Johnson has defined mediation as arising when:

the state attempts to remove from the producer or the consumer the authority to determine the content and subjects of practice.\(^\text{151}\)

In the case of the PBS, the state is increasingly intervening in the relationship between the doctor and the patient in determining which drugs are available and at what cost to the patient. Initially, the power of the medical profession may have appeared to have been maintained, with the location of doctors in positions of power within the state administrative hierarchies. However, this bureaucratization of the medical profession has proved to weaken medical dominance.
Doctors employed in administrative positions, such as those in the drug evaluation section of the Health Department, although in relatively powerful positions, have had their performance subject to review by those outside the medical profession and have seen their authority decline in recent years with the loss of the requirement of medical qualifications for key decision-making positions, even for the Director General of Health. Economic and managerial knowledge and skills have gained the ascendancy within the administrative bureaucracy of the state.

In Australia, medical dominance has been weakened also as a result of the medical profession's political fragmentation from the 1970s, together with the contemporary challenge to the biomedical model and the rise of alternative medicine. Nevertheless, the professional power of the doctor continues in the role of medical-scientific 'expert' - drug evaluations for marketing and inclusion under the PBS are still seen largely as 'medical' issues. Medical dominance continues to exert power over women's use of minor tranquillizers. In New South Wales, the effectiveness of the Women and Prescribed Drugs campaign was adversely affected by the decision not to directly challenge the doctors' role in over-prescribing; in fact, women were urged to seek their doctors' advice.

The political power of Australia health consumers has strengthened considerably in recent years. Through the ACA, health consumers have strengthened their voice nationally on such issues as unethical drug advertising and marketing by the pharmaceutical drug industry. State support of the CHF and the opening up of decision-making on health issues within the state have enabled consumers to participate more in decisions such as those on drug pricing and drug policy. Dangers
associated with these new developments include professionalization of the consumer movement and erosion of its representative role. The women's liberation movement has been important in the contemporary health consumer challenge to the power of the drug industry and to medical dominance. In Australia, this has been reflected in a strengthening of public awareness of women's use of minor tranquillizers, and in campaigns to reduce consumption and support women during their withdrawal. Nevertheless, these preliminary initiatives have comprised 'one off' campaigns run in individual Australian states: a national and continuing education campaign has not yet been realised.
FOOTNOTES:


2. "Pharmaceutical prices will rise this year", Aust Fin Rev, 10 April 1975, p.5


7. Industries Assistance Commission, op cit, (note 1), p.28


13. "Costs of drugs in most use", SMH, 28 September 1963, p.6


15. John O'Hara, "Govt. bid to reduce drug prices", SMH, 23 August 1967, p.1

16. "Drugs cheaper after Govt. stated concern", SMH, 12 April 1969, p.11

17. Industries Assistance Commission, op cit, (note 3), pp.30,31

18. "Drugs cheaper after Govt. stated concern", Ibid, (note 16)

19. Ibid, p.29


money or your life", Aust Fin Rev, 10 May 1972, p.3 and 11 May 1972, p.2

22. Steve Burrell, "Govt move may reduce pharmaceutical prices", SMH, 14 September 1987, p.5

23. In 1971-72, media reports centred on overuse of bromureide (Relaxa Tabs) sedatives - their availability over the counter was strongly criticised by the Senate Select Committee on drug trafficking and abuse and by the National Health and Medical Research Council (NH&MRC) - and on imipramine (Tofranol), an antidepressant on which the Department of Health issued warnings to 18,000 doctors by telegram on possible foetal effects, following a warning by Dr William McBride.

Marie Toshack, "The loneliness pill. An alarming report on drug abuse in the home", SMH Women's Section, 13 May 1971, p.2; John O'Hara, "NSW will resist ban on sedative", SMH, 24 June 1971, p.3; Editorial, "Delayed reaction", SMH, 7 March 1972, p.6


Soon after Valium was listed on the PBS, Roche held a promotional stunt by hiring a floating restaurant on Sydney Harbour for a celebratory lunch attended by "practically every psychiatrist in Sydney". Jeremy Webb, "The pill pushers", Bulletin, 29 July 1972, p.23

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CONCLUSION

This study has reviewed society's dependence on minor tranquilizers in terms of a shifting power struggle over control of drug technology, between four major groups: the consumer, doctor, drug industry and the state.

Whilst alcohol has long been used as a tranquillizer, Western scientific medicine has pursued the search for its own equivalent 'magic bullet'. Sontag has described the popularization of the military metaphor in medicine late last century, with the elaboration of the germ theory. Subsequent examples include Ehrlich's successful development of chemotherapy (the so-called 'magic bullet' treatment of syphilis with an arsenic derivative), contemporary descriptions of cancer, both the clinical course of the disease and society's attempts to treat and cure the disease, and the use of Eisenhower's term 'military-industrial complex' to refer to a 'medical-industrial complex', indirectly associating the medical profession with military organisation and indicating its close links with industry interests. Within these terms, the medicalization of the tranquilizer 'arms race' empowered doctors' 'front line' control of the technology, through their monopoly over the power of prescribing, backed by the state as 'general', in its regulatory role, and the pharmaceutical industry as the 'arms dealers' and 'stockpilers'. To continue the analogy to war, the consumers of tranquilizers may be compared to civilians caught in the cross-fire, becoming the major casualties in a battle waged by the 'medical-industrial complex' for their 'liberation'.

This study has summarized evidence showing benzodiazepines are a form of medical drug technology whose application has spread widely and rapidly throughout the world, although information on their use has been
collected predominantly in Western industrialized societies. The gender imbalance is the most pronounced aspect of benzodiazepine use, and in the early 1970s the emergent women's movement, together with the health consumer movement, in the United States placed benzodiazepines in sharp public focus and expanded the debate on minor tranquillizer use from a medically dominated perspective, to include socio-economic factors. This was complemented by a changing public awareness of addiction which served to stress the dangers of addiction associated with benzodiazepines. The resultant fall in Valium sales world-wide was heralded as a downward trend to more conservative benzodiazepine use. However, Australian data has been presented which indicates that upward pressures on benzodiazepine sales continue, primarily through marketing of 'me too' benzodiazepines, and that the medical profession and the state have made no significant progress in curbing the pharmaceutical industry's control over the development and application of drug technology.

The medical-scientific debate on benzodiazepine efficacy and safety has been shown to capture the dilemma facing contemporary medicine's attempts to identify and treat illnesses of the mind and to seek technical solutions in drug therapies, using a biomedical model based on a mind-body split and successfully developed from the treatment of various illnesses identified as being of a physical nature. The medical profession's conversion of anxiety from what may be seen as a natural result of, perhaps, socio-economic difficulties, or even as a positive force for implementing change, to a medical illness is best understood as an outcome of this process. This study has traced the uncovering of problems of benzodiazepine addiction (just as for the earlier tranquillizers) which led to initial confidence and enthusiasm
for the benzodiazepines eventually being replaced by caution and, in some cases, condemnation. The process has been shown to be marked by unresolved conflict, not an accumulation of disinterested knowledge of the risks of the benzodiazepines. That is to say, it does not lend itself to the conventional interpretation of the relentless progress of medical science. Within the context of the scientific and medical journals, the debate has become polarized between those who urge their colleagues to stop prescribing benzodiazepines altogether and those who argue that they should be freely available without prescription because they are safer than all other tranquillizers, especially alcohol.

From extensive studies of the doctor-patient interaction in the consultation process, a summary has been presented of the five most commonly presented models to describe doctors' prescribing of benzodiazepines mainly to women, who also predominate amongst the aged, the chronically ill and the institutionalized (the other categories of high users of benzodiazepines). Whilst some models are mutually exclusive, others can complement each other so that no one model predominates, lending understanding to the complexity of factors influencing benzodiazepine use. Added to this, the mediative role of the doctor has been also traced to medical education (sexism built into the education process, and afterwards in the division of labour with specialization of medical practice and influences on prescribing practices) and the professionalization of medicine. The medical-scientific debate over benzodiazepine efficacy and safety may be seen as vital to the maintenance of the medical profession's position of power. Whilst Johnson has emphasized the importance of indetermination of medical knowledge as a vital factor in sustaining the power relations of the medical profession, this study, instead, supports Turner's proposal
that it is more appropriate to consider the profession's dominance over interpretation of medical knowledge as important to maintenance of its power. The medical profession has zealously guarded its authority to evaluate the indications and effects of the benzodiazepines, and this has been crucial to the perpetuation of benzodiazepine use. Benzodiazepine use may be understood, also, as a consequence of various professional strategies such as doctors' insistence on retaining authority to prescribe, their monopolistic role as consumer with respect to drug advertising and their medical dominance over other health professionals. These are all crucial to a doctor's control over medical knowledge. That is to say, professionalization reinforces and maintains the cognitive authority of the medical profession.

The Australian experience illustrates the role of the state in maintaining medical dominance, by defining drug regulation processes (such as approval for marketing of new drugs from overseas and their listing under the PBS) as medical issues, to be decided upon by medical-scientific 'experts'. The open-ended nature of health and illness and the limitations on state health budgets have led to competition for the health dollar, and inevitably to conflict in decision-making within the state. With respect to fiscal responsibilities over a national drug bill, the state has been shown to apply opportunistic policies with no comprehensive plan for addressing major social problems, reflecting the contradictory nature of capitalism. State-subsidised schemes for the provision of benzodiazepines and other drugs have exposed fundamental conflicts within the state. A case study has been presented of the British attempt to implement a limited drug list, illustrating the intra-departmental conflict within the state because of the dual role of the DHSS in monitoring profits of the drug industry in order to curb the
state's rising drug bill and in promoting drug R & D and general profit-raising activities of the drug industry. In Australia, interdepartmental conflict over this dual role of the state has been described with respect to the current government's activities. This study has examined the Hawke government's efforts to change drug consumers' behaviour, where (like the British government's focus on benzodiazepines in promoting the limited drug list) it has discovered the usefulness of creating an image of socially responsible government confronting the dangers of addiction. The present government's conciliatory approach to the drug industry has also been contrasted with the previous Labor government's confrontation with the drug industry in the 1970s.

The industry's ruthless strategies, at great cost to the individual and to the nation, have been described in Roche's overall successful battle to extract the maximum economic rewards from its best-selling product, Valium, whilst holding patent monopoly control in Britain and other European countries, as well as Australia. This study has described the importance of patents and promotion to the drug industry and of their vital role in Roche's financial success story with Valium and Librium. Whilst the drug industry continually refers to the high cost of R & D as justification for high prices, this study of benzodiazepines has clearly illustrated that the initial high outlays on R & D have generated almost thirty years of enormous profits for the drug industry - in particular, for Roche, whose benzodiazepines have been one of only a few concentrated pharmaceutical products manufactured by the company.

World-wide, the drug industry has been the target of health consumer groups, which have been an important force in checking the
meteoric rise in benzodiazepine consumption. Consumer interest groups, in particular the women's health movement, have played a crucial role in changing public attitudes towards the benzodiazepines. Whilst this has severely damaged Valium sales, overall benzodiazepine use has not been adversely affected, reflecting the drug industry's remarkable resilience. Other modified versions of benzodiazepines - the 'me too' drugs - have filled the 'Valium gap', and there are many others waiting in line (for example, other types of mood-changing drugs, such as the major tranquillizers and anti-depressants, and possibly other classes of drugs, such as analgesics).

Consumers have also exercised their power through the litigation process, such as the Australian case successfully brought against a psychiatrist, but this has targeted the doctor rather than the drug industry. In Australia, it has been shown that the health consumer movement has strengthened its links with the state and made significant gains in recent years in gaining access to policy-making, such as in determining prices of PBS drugs. Moreover, a strong women's liberation movement in Australia has generated considerable interest in curbing benzodiazepine use.

Nevertheless, any long-term solution for reducing society's dependence on minor tranquillizers must address fundamental questions in a number of key areas. Firstly, ideological changes are necessary. For example, social and environmental parameters need to replace individualistic descriptions of illness; and the search for a technological solution - the 'quick fix' - could be replaced by a longer-term and broader 'holistic' view of the world in which nature is no longer subjugated to the intellect. Secondly, pressure groups of citizens from such areas as the consumer health and women's movements
need to be strengthened further. Whilst significant gains have been made in consumer participation within state decision-making, the health consumer movement must continue to strengthen its non-governmental links in order to avoid an overdeveloped reliance on state patronage, and the dangers of professionalization and bureaucratization. Furthermore, the health consumer movement needs to identify the limits of legislative controls and to question fundamental assumptions that consumers will necessarily be adequately protected by increased state intervention, such as in the call for patient package inserts and mandatory state controls over drug advertising. Thirdly, whilst drug efficacy and safety remain as high priorities, the excessive profits of the drug industry must be checked. For example, as public opinion turns against the benzodiazepines in the industrialised nations, new markets may be created for 'disorders in the Third World'. In Australia, which has a world-wide reputation for stringent drug regulation and where the state is the major customer and regulatory agent, state controls on drug prices, whilst strict, have not challenged the hidden profits of the drug industry. Finally, the power of the medical profession needs to be addressed, such as in its role as medical 'expert' in the drug regulation process. Doctors' prescribing habits also need to be changed, and this would require extensive changes in medical education and promotional activities by drug companies.

In conclusion, women's special role as the major consumers of benzodiazepines and other mood-modifying drugs has been shown to reflect how medical science, medical practice, the drug industry and the state all contribute to the medicalization of women's social problems, which are exacerbated by age, poverty and chronic ill-health. The wave of literature on women and minor tranquillizers, which has flowed on from
the initial work of the women's and consumer movements, has reinforced
general awareness of many of the issues but, unfortunately, often
focuses on the addiction problems and offers individualistic solutions
to what is better understood as a significant and widespread social
problem. Other analysts have given tokenistic attention to the gender
differences whilst accentuating the economic or technological problems.
This study has, instead, explained minor tranquillizer use in terms of a
complex struggle over control of this particular drug technology. The
nature of any effective long-term change in minor tranquillizer use must
be similarly complex.
FOOTNOTES


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