

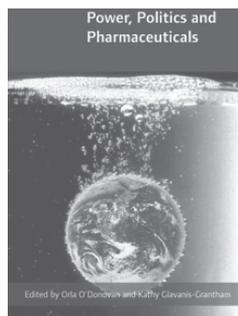
## Medicines policy and drug company investments: the Irish experience

*Power, politics and pharmaceuticals: drug regulation in Ireland in the global context*  
O'Donovan O, Glavanis-Grantham K, eds  
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**THIS BOOK IS ABOUT MANIFESTATIONS** of power in medicines and pharmaceutical industry policy. The main focus is on the Republic of Ireland but there are chapters also on drug regulation in Canada, Britain and Australia. The multinational pharma companies loom larger in Ireland than in most other countries; several chapters detail the implications for this small country of the presence of a major cluster of global drug companies.

Globalisation is the hallmark of the drug sector; innovation and production occur within international networks which are mirrored by interaction between regulatory agencies which operate similar systems of control and monitoring. Since the 1990s, many aspects of product safety regulation have been standardised across the developed countries through the International Conference on Harmonization (ICH) process, sponsored by the regulatory agencies and industry associations of the USA, the European Union and Japan. While orchestrating vast scientific, economic and technological resources, the big pharma companies participate as insiders in national policy processes, such as those described in this book. Firms typically affirm a commitment to the health and economic concerns of the local jurisdiction — however governments cannot help but be sensitive to their global reach and power to choose where to invest.

Globalisation is often said to have enhanced this type of structural power. Yet significant scope remains for nationally unique health policy arrangements and in drug reimbursement and pricing policy. Indeed, it may be that the very process of globalisation is eroding the advantages of big pharma vis-à-vis actors concerned with



health and social policy. Governments and other non-corporate actors have ready access to information about drug company activities everywhere, including safety and ethical controversies, and there is overlap and exchange in policy debates across

the globe. An obvious case in point is Australia's pioneering of cost-effectiveness analyses in the Pharmaceutical Benefits Scheme (PBS) listing process, a model which has attracted much international interest, and similar systems have been introduced or are under consideration in many countries. At times public health activists effectively challenge the power of the industry, as exemplified by the successful shaming of companies for access to HIV/AIDS medications in Africa. That there is a shift in drug policy dynamics is reflected in the centrality today of the notion of "partnerships". This theme is particularly conspicuous in Australia where it underpins the National Medicines Policy (NMP). Since its inception in the early 1990s, the very premise of the NMP is that all stakeholders, including consumers, should be able to exercise some influence.

It seems there is no similar framework for medicines policy in Ireland — several analyses in this book highlight the absence of effective constraints on industry power. This is explained as the outcome of economic policy which has created an unusual dependence on foreign multinationals, a development model described as inimical to economic diversity, domestic innovation and the quality of medicines regulation. (Indeed, presently Ireland is among the European countries most severely affected by the global economic crisis, which raises further doubts about this model.) It is not to be expected then

that the Irish perspective lends itself to an appreciation of the countervailing powers accrued by other policy actors in the pharmaceutical sector, in some national and international contexts, or of the problems and contradictions of the big pharma model itself, much discussed in the recent trade and academic literatures. Yet this excellent collection of essays is in itself testimony to the resourcefulness and intellectual depth of the international community of public health activists. The editors are members of Health Action International, and among the contributors are analysts based in Canada (Joel Lexchin), the UK (John Abraham and Andrew Herxheimer) and Australia (Agnes Vitry and Peter R Mansfield).

Several chapters explore tensions between public health and commercial interests through analyses of the incapacity or disinclination of regulatory agencies to appropriately and fearlessly assess medicinal products for safety and efficacy. The dependence of these agencies, including Australia's Therapeutic Goods Administration (TGA), on fees and charges paid by its "clients", that is, the pharmaceutical industry, and their general concern to retain close relations with the industry, is shown to give rise to bias in the regulatory process. John Abraham argues that institutional context and culture make scientists and others involved in drug testing and regulation unduly sensitive to commercial interests. This is illustrated by three cases studies: an analysis of the role of the sponsoring company in the production of scientific papers in support of marketing approval of a particular drug, a study of the way evidence is interpreted in the regulatory process, and an analysis of the production of international standards in the ICH process. Joel Lexchin assesses the Canadian system of so-called smart drug regulation, administered by the Therapeutic Products Directorate (TPD). This is an agency which, according to Lexchin, is strongly committed to a business-friendly environment even to the point of neglecting public health. In this context Lexchin identifies a shift in the regulatory philosophy of the TPD away from the precautionary principle, in favour of the risk management model. Risk management entails a

risk–cost–benefit approach said to be premised on an assumption of safety "unless there is information to the contrary and, therefore, in general, products should be allowed unfettered access to the market and once there largely left unattended" (p. 156). Lexchin details the high priority assigned in Canada to speeding up the drug approval process while making only inadequate resources available for post-marketing surveillance. This pattern applies across the major regulatory agencies; thus "in 1999, the FDA had 1,408 employees to review new drug applications, and 72 handling the post-marketing surveillance of nearly 50,000 medicines" (p. 168).

Additional evidence suggesting an unhealthy relationship between regulatory agencies and the drug industry is provided in Andrew Herxheimer's chapter on the story of shortcomings in the regulation of SSRI antidepressants in the UK. The sales of antidepressants in the UK expanded by 300% between 1990 and 2000 as paroxetine (Seroxat), fluoxetine (Prozac) and similar products entered the market. There were early warning signs that the new SSRIs could increase risks of suicidality and drug dependence. Herxheimer details the reluctance of regulators in the UK (and other countries) to take this possibility seriously. It took many years, several inquiries, and recurrent media attention, for these risks to be accepted as real and for consumer reports of adverse events to be accepted as valid inputs to the post-marketing surveillance system. In the UK, this experience "led to the discovery of serious deficiencies in the regulatory system, both in its legal basis and in the way in which the regulations are applied" (p. 181).

A similar story is told in the chapter by Agnes Vitry and co-authors on the case of COX-2 inhibitors, titled "Is Australia's National Medicines Policy Failing?". The TGA approved the marketing of celecoxib (Celebrex) and rofecoxib (Vioxx) in 1999. These drugs were subsequently listed on the PBS as restricted benefits for specific conditions but heavily promoted "in ways that implied superior safety and efficacy over other [non-steroidal anti-inflammatory drugs], despite the fact that studies had not shown any overall

safety and efficacy advantages” (p. 188). A 2003 study showed that a large proportion of prescriptions of both products were in breach of these restrictions. Vioxx was voluntarily withdrawn worldwide by Merck in 2004 after evidence of an association with increased risks of heart attacks and strokes had become incontrovertible. Celebrex was not withdrawn, but the TGA advised in 2004 that “all drugs in the class of Cox 2 inhibitors should be regarded as having an increased cardiovascular risk until more is known” (TGA Media statement 20 December 2004). The authors argue that Australia’s regulatory system, the TGA and the PBS, and associated programs for “quality use of medicines”, failed in recognising and acting on early evidence pointing to serious safety concerns.

The second specific theme of the book is the success of the Republic of Ireland in attracting drug company investments. Ireland has figured only peripherally in Australian medicines policy debates. Yet the Irish experience is significant from an Australian perspective — with respect to drug company activity, this small country has achieved what Australian governments have talked about for the twenty years, with disappointing results. As a market, the Republic of Ireland, with a population of about 4 million, is not significant. Australia carries greater weight in this respect — not only because of its absolute size, but because Australia, notwithstanding perennial industry complaints about PBS pricing, has come to be viewed as a prestige market. Commercial success in Australia is seen as potentially valuable in marketing efforts elsewhere. But this has not translated into very significant investments, as distinct from supply through imports.

Astonishingly, Ireland, the “Celtic Tiger”, has emerged as “the biggest net exporter of pharmaceuticals in the world, ahead of Switzerland” (p. 92). Pharmaceutical plants, mostly producing active pharmaceutical ingredients (APIs) rather than final drugs, are concentrated to the Cork region, the second largest city with a population of about 200 000. By 2004 there were 72 pharmaceutical plants in Ireland and thirteen of the global top fifteen companies had established

“substantial operations” (pp. 87–8). Strategic government policy is central to this development, including a very low corporate tax rate of 12.5%. This compares with Australia’s rate of 30% and European Union corporate tax rates typically around 30–35%. A host of other industry support measures and incentives are provided through the Irish Government’s Industrial Development Authority (IDA), as detailed in a chapter by Kathy Glavanis-Grantham. Another significant factor is Ireland’s geographic location as bridgehead to Europe for US companies, particularly in the early stages of European economic integration. While a “partnership” approach, as noted, does not seem significant in Irish medicines policy, Ireland’s overall economic and social development has been framed by a model of “social partnership”.

By contrast, according to a 2005 report by the Economist Intelligence Unit, in Australia “most of the global pharmaceuticals firms restrict their activities ... to distribution”. Only “a small number” were engaged in “secondary manufacturing, and an even smaller number ... in actives manufacturing”. There were only five instances of API production, mostly of a niche character (the alkaloid extraction from poppies in Tasmania is an exception)<sup>1</sup> (pp. 18–19). Governments have introduced one program after another to promote the pharmaceutical industry and make Australia a competitive alternative to Singapore and Shanghai as a location for regional head offices. Yet the results are unimpressive — Australia has made no gains, in relative or even absolute terms, as a global drug industry hub. Indeed, in recent years Johnson & Johnson, Schering-Plough, Bayer, Merck, Sharp & Dohme, GlaxoSmithKline and Wyeth have announced plant closures or redundancies.

What has Ireland then done right — and what are the costs and benefits of major drug-manufacturing operations? This book presents, in several chapters, a critical perspective on these issues. For example, the benefits in terms of employment are less significant than might be expected; relatively few jobs have been created. In 2004 there were about 17 000 employees in this sector with a

similar number of people working in related engineering, maintenance, catering and transport sectors. The explanation is of course that drug manufacturing is highly capital intensive. Each plant typically employs only around 350 people and operations are not closely integrated with the local economy. Companies are thus not necessarily locked in for the long term — manufacturing of this type is relatively footloose and can be relocated if more favourable conditions are offered elsewhere, for example in Eastern Europe where costs may be lower and the infrastructure of similar quality. It would have been interesting to find out more about the environmental aspects of the concentration of API production to a small area around Cork; this issue is referred to only in passing. The environmental impact of such production is increasingly recognised as a problem in developing countries such as India, from where a large proportion of global API supplies is now derived.

It is detailed in several chapters how the sheer economic weight of the industry constrains and influences health and medicines policy. For example, there does not seem to be a mechanism in Ireland for cost-effectiveness assessments before the listing of new drugs under the Community Drugs scheme. Generics have a weak presence; in 2003, only about 19% “of prescription items were dispensed generically” and generic substitution is not allowed (p. 113).

Yet Ireland provides consumers with more comprehensive protection against drug costs than

does Australia. Low income earners entitled to a “medical card” have access to free (no copayments) medical and surgical services and free prescription drugs (no copayments). Between 2001 and 2008 all residents over the age of seventy were entitled to a medical card regardless of means, but in 2009 income and assets tests were introduced. In 2005 around 30% of the population were eligible for free drugs under different schemes while copayments applied for about two-thirds of the population.

This valuable volume is mostly accessible to non-experts including undergraduate students. It is of interest to an international readership concerned with a wide range of medicines policy issues. Through its particular, though not exclusive, focus on Ireland, and its remarkable experience of big pharma activities, it should serve as a useful resource to Australian readers interested in the implications of the NMP objective of sustaining a “responsible and viable medicines industry”. There is unfortunately no comparable book about Australian medicines and pharmaceutical industry policy.

**Hans Löfgren**

**School of International and Political Studies, Deakin University, Melbourne, Vic**

1 Economist Intelligence Unit. Benchmarking study of the characteristics of the Australian and international pharmaceuticals industries. A study undertaken for the Australian Government Department of Industry, Tourism and Resources, Invest Australia and the Victorian Government Department of Innovation, Industry and Regional Development. Canberra: 2005.