

vices.<sup>4</sup> Maybe, as Tanase argues more generally,<sup>5</sup> Japan's "social blueprint" and contemporary communitarian norms have reasserted themselves robustly against an influx of new legal rules or knowledge practices over the last two decades.

*The Japanese Pharmaceutical Industry: Its Evolution and Current Challenges.* By Maki Umemura. Routledge, London, 2011. xviii, 186 pages. \$148.00.

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*The Japanese Pharmaceutical Industry* is an ambitious, broad-ranging analysis of the postwar history of an industry whose eight per cent share of Japanese manufacturing understates its significance in terms of health and as a barometer for science-based innovation. Based on the author's doctoral dissertation in economic history at the London School of Economics, this book by Maki Umemura constitutes one of a small number of comprehensive analyses of the Japanese pharmaceutical industry.

Similar English-language books have been published by L. G. Thomas and Takuji Hara.<sup>1</sup> Thomas focuses on the shortage of globally marketed drugs in Japan, attributing this to disincentives created by drug pricing policies of the Ministry of Health and Welfare (MHW), protectionist barriers against overseas drugs, anticompetitive effects of drug wholesalers being controlled by major pharmaceutical companies, prescription practices of Japanese physicians, and passivity among Japanese patients. Hara's analysis is more micro-level and biomedically oriented. It centers on case studies of the discovery and development of seven successful Japanese drugs—studies focusing on the company scientists who led these efforts and the organizational and scientific milieu in which they worked.

4. Luke Nottage and Stephen Green, "Who Defends Japan? Government Lawyers and Judicial System Reform in Japan," *Asian-Pacific Law and Policy Journal*, Vol. 13, No. 1 (2011), pp. 129–73.

5. Takao Tanase, *Community and the Law: A Critical Reassessment of American Liberalism and Japanese Modernity*, ed. and trans. Luke Nottage and Leon Wolff (Cheltenham: Edgar Elgar, 2009).

1. L. G. Thomas III, *The Japanese Pharmaceutical Industry: The New Drug Lag and the Failure of Industrial Policy* (Cheltenham: Edward Elgar, 2001), and Takuji Hara, *Innovation in the Pharmaceutical Industry: The Process of Drug Discovery and Development* (Cheltenham: Edward Elgar, 2003).

Umemura's analysis tacks between these two previous studies, and it is the most accessible. It avoids the profuse economic and trade-focused statistical analysis of Thomas's book and also the arcane scientific histories that constitute much of Hara's study. Like Thomas, Umemura emphasizes the negative impact of the policy of MHW (later the Ministry of Health, Labour and Welfare, MHLW) of setting a retail (prescription) price for each new drug and reducing that price over time in a way that rewarded pharmaceutical companies for developing me-too drugs while providing few incentives to invest in the discovery and development of innovative drugs. She and Thomas also emphasize the negative effects of protectionist policies.

The most original insights are in Umemura's two middle chapters which contrast drug discovery and development in antibiotics and anticancer drugs. Each is grounded in case studies that integrate biomedical, historical, and institutional factors. Some, like Hara's, summarize the discovery and development of innovative drugs and show how company scientists kept abreast of worldwide developments and often initiated collaborations with academic researchers. Other case studies show how weak science, small numbers of medical specialists, and conflicts of interest within MHW advisory committees led to the approval and use of several ineffective cancer therapies.

Umemura clearly shows how the inability to obtain product patents on pharmaceuticals prior to 1975 discouraged the development of innovative drugs—an issue glossed over by many English-language academic researchers. Soon after the launch of Meiji Seika's antibiotic, kanamycin, and Kyowa Hakko's novel cancer drug, mitomycin, these companies found sales being undercut by established Japanese pharmaceutical companies copying and marketing the same drugs. Indeed, Umemura's case studies contain tantalizing suggestions that new entrants from other industries had a better record of innovative drug discovery than established pharmaceutical companies. If she had explored this in more depth, along with the inability of most of these new entrants to sustain their initial successes, she might have added new information to the current debate about whether new entrants can spur innovation, especially in countries where start-ups are few.

Umemura's analysis is rooted in the past. Many of the sins she lays at the door of the Japanese government and medical establishment have been substantially rectified. The protectionist industrial policies that she and Thomas criticize have been largely dismantled. Executives of international pharmaceutical companies now rarely complain about an unlevel playing field *vis-à-vis* Japanese companies or about Japan's patent system. Complaints persist about the long time it takes MHLW to approve drugs, both foreign and domestic, compared with the U.S. and European regulatory agencies, but the delay has decreased. Approval of me-too drugs has become substantially harder. Under drug retail licensing requirements



implemented in 2006, most physicians no longer sell drugs, removing a large monetary incentive to overprescribe sometimes marginally effective drugs. U.S. drug companies have detected a tendency for Japanese physicians to be even more interested than their American counterparts in a new drug's mechanism of action and how this might differentiate it from existing drugs.<sup>2</sup> The fixed drug pricing system still exists (as it does in many developed countries). However, to address criticism that it stifles innovation, MHLW implemented innovation price bonuses in 2010 allowing innovative drugs to be sold (and reimbursed under health insurance) at a higher price premium.

The benefits of these reforms may not be fully evident for several more years. Nevertheless, rather than focusing on the past and plowing ground already covered by Thomas, Hara, and others, Umemura might have considered the degree to which Japan is emerging as a more "normal" environment for pharmaceutical innovation and whether this will solve its "underachievement" in pharmaceutical innovation. In the process, she might have provided unique insights into the prerequisites for a supportive environment for innovation, for not only pharmaceuticals but also other industries.

The initial assumption in Umemura's book is that Japan is an underachiever in pharmaceutical innovation. In terms of global sales, launches of globally marketable new drugs, and innovativeness of domestically discovered drugs, Japan clearly lags behind only the United States. Compared to any other country (except Switzerland, taking into account its small population and gross domestic product), Japan's lag is not profound. Despite all the disincentives to innovation, Japanese corporate researchers, sometimes in collaboration with university scientists, have invented a respectable number of medically important drugs. In terms of new drugs recently approved by the U.S. Food and Drug Administration, Japan ranks second in the world as the source of new globally marketed drugs, behind only the United States (although both the United Kingdom and Germany follow close behind Japan). Japan is also second behind the United States in terms of sales of globally marketed new drugs, and in this regard only Germany is close behind.<sup>3</sup>

When Japan's new drugs are classified according to innovativeness (new versus old mechanism of actions, or drugs that offer substantial benefit over currently marketed drugs versus those that do not), subpar performance

2. Jonathan D. Rockoff, "All Drug Marketing Is Local," *Wall Street Journal*, September 30, 2011.

3. This analysis excludes drugs developed just for the Japanese market. These findings are based on an analysis of the discovery origins of all the 252 new drugs approved by the U.S. FDA from 1998 through 2007. See Robert Kneller, "Importance of New Companies for Drug Discovery: Origins of a Decade of New Drugs," *Nature Reviews Drug Discovery*, Vol. 9 (2010), pp. 867-82.

becomes more evident. Despite the above-noted innovative drugs, most Japanese drugs are based on previously proven mechanisms of action and do not offer substantial benefits over currently available drugs. But in this regard, Germany is exactly the same. Furthermore, in Japan and continental Europe, almost all drugs are discovered in the laboratories of established pharmaceutical companies (hereinafter, pharmas). The vast majority of these in-house discovered drugs are not innovative, excepting those from Switzerland. The United States, Canada, and Australia are the only major pharmaceutical countries that discover more innovative than noninnovative drugs. In these three countries, the majority of innovative drugs are discovered either in new companies (hereinafter, biotechs) or in universities that initially partner with biotechs to develop the drugs. North American pharmas are more innovative than Japanese and continental European pharmas but not as innovative as North American biotechs. When the same analysis is repeated for sales, rather than number of drugs, the distributions are very similar. The picture that emerges is of two innovation ecosystems. The much more innovative one is based largely upon biotechs that are innovative in their own right and that tend to pick up the vast majority of innovative university discoveries, while the less innovative one is based almost exclusively on pharmas which discover noninnovative drugs.

Umemura faults Japan for a low output of cancer drugs. However, its output is no worse than that of any continental European country. Over half of cancer drugs are discovered in the United States, and over half of all cancer drugs are discovered either in biotechs or in universities that partner with biotechs for initial development.<sup>4</sup> Umemura is correct to note that cancer drug discovery tends to be more science based than antibiotic discovery. As new companies are much more likely than old ones to develop scientifically novel drugs, it is not surprising that the discovery and development of oncology drugs is concentrated in countries where biotechs are active in drug discovery.

The in-house drug discovery teams in established Japanese companies are probably no less able than the drug discovery teams in somewhat larger overseas multinationals. An examination of the pipeline drugs (those in phase 1, 2, and 3 clinical trials) of Schering Plough, Abbott, and Bayer compared with those of the eight largest Japanese pharmaceutical companies in 2003 showed that the number of internally discovered new mechanisms of action drugs was about equal in both groups of companies.<sup>5</sup> So the main

4. For institutional and geographic origin of the discovery of active therapeutic compounds in new cancer drugs, 1998–2007, see *ibid.*

5. Kneller, "Autarkic Drug Discovery in Japanese Pharmaceutical Companies: Insights into National Differences in Industrial Innovation," *Research Policy*, Vol. 32, No. 1 (2003), pp. 1805–27.



reason for Japan's underachievement in pharmaceuticals is neither inferior scientists in its established companies nor inferior management through the clinical trial stage of development. Rather, it probably is related to Japan's lack of vibrant new companies engaged in drug discovery.

The components of a supportive environment for science-based entrepreneurship and the reasons new companies are better innovators than old in such an environment are complex and subject to debate. Two important features of the U.S. environment are generous funding from the National Institutes of Health for basic biomedical research allocated by a competent system of scientific peer review and large numbers of skilled, mobile biomedical researchers. As Umemura, Thomas, and Hara suggest, minimal controls on drug prices in the United States and attendant opportunities for substantial profits may be another. However, these factors should benefit biotechs and pharmas relatively equally. Indeed, there are reasons new companies are likely to be more innovative than old ones in a supportive environment, not only in pharmaceuticals but also in many other industries, as discussed elsewhere.<sup>6</sup>

It is probably no accident that countries where innovative drug discovery is based largely upon new companies are liberal market economies, while those where drug discovery is noninnovative and confined mainly to in-house laboratories of established companies are coordinated market economies. In the "varieties of capitalism" literature,<sup>7</sup> the former (including the United States, Canada, and Australia) are characterized by relatively high labor mobility, low job security, low reliance on in-house training, minimal government and organized labor involvement in business decisions, and a tendency for equity as opposed to loan financing for business expansion. The opposite features characterize coordinated market economies, such as those of Japan and continental Europe. The contrasting patterns of drug discovery in North America and Australia compared with continental Europe and Japan suggest that liberal market economies tend to encourage innovation in new companies while coordinated market economies tend to confine innovation to old companies. The greater propensity for new companies to undertake radical innovation may be a key missing link between the tendency for radical innovations to arise from liberal market economies, while coordinated market economies excel in incremental innovations.

As Japanese electronics makers are now struggling and even auto man-

6. See Robert Kneller, *Bridging Islands: Venture Companies and the Future of Japanese and American Industry* (Oxford: Oxford University Press, 2007), and Kneller, "Importance of New Companies for Drug Discovery."

7. See, for example, Peter A. Hall and David Soskice, "An Introduction to Varieties of Capitalism," in Hall and Soskice, eds., *Varieties of Capitalism: The Institutional Foundations of Comparative Advantage* (Oxford: Oxford University Press, 2001).

ufacturers are under pressure, pharmaceuticals no longer stand out as a laggard among Japanese industries. While an analysis of Japan's pharmaceutical industry from the 1970s to 1990s may have justifiably focused on factors that held it back relative to world-leading Japanese industries during that era, it is not surprising that an analysis of the industry since 2000 points to problems shared by many other Japanese manufacturing industries. One of Japan's fundamental problems is that too many of its great human and financial resources are locked up in old organizations doing old things. This problem must be addressed, but in a careful way that recognizes the complex institutional and social factors that underlie it.

*Changing Power Relations in Northeast Asia: Implications for Relations between Japan and South Korea.* Edited by Marie Söderberg. Routledge, London, 2011. xvi, 188 pages. \$130.00, cloth; \$130.00, E-book.

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Marie Söderberg's edited volume is likely to become the standard reference for the study of contemporary Japan–South Korea relations. Hitherto, the definitive book for this bilateral relationship was Victor D. Cha's *Alignment Despite Antagonism: The United States-Korea-Japan Security Triangle*. According to Cha, the United States is the key driver of relations between Japan and the Republic of Korea (ROK), and this explains the volatility in ties between the two “quasi-allies” in Northeast Asia. He wrote: “The primary determinant of these variations is the fear of U.S. abandonment. When this fear is high, as a result of weak U.S. defense commitments and/or salient external threats, Japan and Korea are more willing to put aside friction arising from conflicting abandonment/entrapment concerns and show greater cooperation.”<sup>1</sup>

Cha's elegant model plausibly explained why Japan-Korea relations blew hot and cold in alternation notwithstanding latent historical enmity during the cold war era. However, Söderberg notes that although the cold war persists in Northeast Asia (primarily due to an incorrigible and nuclearized North Korea), the world has become globalized, China is rising rapidly, and economic and cultural ties are deepening between Japan and South Korea. Paradoxically, the historical issue occasionally became more problematic between the two neighbors than in earlier decades.

1. Victor D. Cha, *Alignment Despite Antagonism: The United States-Korea-Japan Security Triangle* (Stanford: Stanford University Press, 1999), p. 206.