stricter administrative controls; and ensuring all pesticide users have personal protective equipment. In a global industry, company training is essential, provided it is reflected in the product price rather than claimed from government levies or development aid funding.

Many innovative programs have been initiated in developing countries to train farmers in Integrated Pest Management strategies. These help farmers reduce their dependence on chemical pesticides, make better decisions, and increase the use of local inputs.

Agrochemical corporations have played a major role in shaping modern agricultural production in both industrialized and developing countries. The products of their research and development dominate the agricultural input market. There are particular problems with this global influence in relation to developing countries, where health and environmental side-effects of the products are often significant. Alternative pest management strategies are recommended, and integrated pest management approaches have demonstrated their benefits. These approaches require support from governments or donors, which makes it difficult for them to compete with the influence of the global market for pesticides.

See Also
World Health Organization; DOC-46

Bibliography

PHARMACEUTICAL INDUSTRY
In 2005 the global pharmaceutical industry was a nearly US$500 billion industry characterized by innovation-driven competition, heterogeneous national regulatory regimes, and product development cycles that were exceptionally uncertain, time-consuming, and resource-intensive. This brief entry will review key characteristics of the worldwide pharmaceutical market, focusing on the ethical pharmaceutical firms that both conduct research to introduce new medicinal remedies for disease and market existing products. (The term ethical pharmaceutical industry refers to those companies whose products are tested and
reviewed by government agencies, such as the Food and Drug Administration [FDA] in the United States.) The first section of the entry provides an overview of the industry; the second describes the importance of proximity and location in each of the stages of the value chain; the third section reviews international collaborations and outsourcing; the fourth section discusses merger activity; and the fifth section describes key issues confronting the global pharmaceutical industry.

The value chain for the world’s ethical pharmaceuticals can be usefully broken down into four principal stages: (1) drug discovery, or the identification of medically active compounds that alleviate the symptoms or causes of disease; (2) development and approval, which is the process of refining molecules and delivery mechanisms, testing them for safety and efficacy, selecting promising molecules for regulatory approval, and applying for approval to enter various national markets; (3) manufacturing; and (4) marketing and sales. Each of these stages involves substantial fixed costs. Strong intellectual property protections in industrialized countries create well-functioning intermediate markets for drugs. This “market for ideas” facilitates collaborations among innovation-focused firms that discover new drugs and those that possess complementary assets in development, manufacturing, marketing, and sales.

Recent estimates suggest that for new ethical pharmaceuticals in the 1990s, drug-discovery research projects lasted an average of between two to three years, during which 5,000 to 10,000 molecules will be screened. Of these, five are selected for development and enter clinical testing, and only one will ultimately be approved for consumer marketing by the FDA.

Although manufacturing expenditure is quite significant, this activity has received relatively little attention from researchers who have attempted to understand the differences in long-term pharmaceutical firm performance; anecdotal evidence suggests that manufacturing may be less significant in driving profitability than other activities (see Wechsler 2002). Research, by contrast, has demonstrated vast differences across drug-discovery research productivity, and this is seen as a critical factor driving competitive advantage in the industry (see Henderson and Cockburn 1994; Gambardella 1995). Academic research on the drivers of productivity in drug development, marketing, and sales is somewhat limited. However, these areas have received attention in the business press as important drivers of competitive success.

The influence of national regulatory agencies is extremely salient in the industry. In most countries, national regulatory bodies approve product entry, regulate market conduct, and often negotiate prices. National agencies do vary significantly in the responsibility they bear for health outcomes and expenditures, and in the extent to which they promote national industrial policy. The characteristics of these bodies, therefore, have a profound affect on the local structure and nature of competition.

Because of the initially high fixed costs of developing new drugs, intellectual property (IP) protection is an issue of great concern to firms in the industry. Equally important, because of the relationship between the strength of IP protection and the costs that local health-care providers must pay, IP is of primary concern to national and international policymakers as well. In industrialized economies, intellectual property rights effectively protect investments in pharmaceutical innovation. As a consequence, markets for IP rights function well, allowing firms to collaborate with or license technology or molecules from other firms. Questions about the role of intellectual property protections in ensuring the development of new medicines for less-developed countries, as well as the distribution of existing medicines to these countries, played a particularly prominent role in industry debates in the first few years of the 21st century.
Proximity and Location

Issues associated with proximity and location are of first-order concern in the pharmaceutical industry, especially in drug discovery, development, marketing, and sales.

As drug-discovery research has become increasingly science-oriented, the importance of geographic propinquity for taking advantage of local knowledge in drug discovery has become increasingly important. As a consequence, firms have begun to collaborate more tightly with those closest to leading-edge knowledge, and they have also begun to establish research facilities near leading knowledge sources.

The clustering of pharmaceutical research is not new, however. Pharmaceutical research activities have been concentrated for more than a century in clusters in Basel, Switzerland, the area around London, England, and the Philadelphia-New Jersey-New York region of the United States. At the same time, smaller clusters have persisted in a number of locations (including Chicago), and a few firms, such as Lilly (in Indianapolis, Indiana) and Upjohn (in Kalamazoo, Michigan), succeeded for decades in discovering drugs, while operating in geographic regions that were relatively isolated from other researchers.

Figure 2. Biotechnology clusters around the world, where research activities for the pharmaceutical industry are concentrated.
Drug-discovery laboratory locations were fairly stable in the 1970s, 1980s, and early 1990s, although a number of firms opened laboratories in international locations, while some laboratories were moved or consolidated as a result of mergers. As the pharmaceutical biotechnology industry grew, it concentrated around leading biomedical research facilities. Within the United States, primary clusters emerged in San Francisco and San Diego in California, and in Boston, Massachusetts, while secondary clusters developed around Durham, North Carolina (the so-called Research Triangle); Philadelphia, Pennsylvania; Bethesda, Maryland; and Seattle, Washington. Similar patterns are evident in Europe; for example, biotech clusters in England emerged in the areas around Oxford and Cambridge. Beginning in the late 1990s, as pharmaceutical firms began to seek even closer linkages to universities and biotech firms, they began to establish discovery laboratories in these areas as well. Novartis, for example, announced one of the most dramatic relocation plans, aiming to relocate the bulk of its research and development facilities from Basel, Switzerland, to Cambridge, Massachusetts.

Issues of “nearness” and spillovers play less of a role in drug development, although location is important. Local access to patients for clinical trials and national regulatory issues are extremely significant in development activities. For example, the FDA requires that medications demonstrate safety and efficacy in excess of prevailing treatments to gain approval. Because each new drug must improve on the standard for efficacy of those that preceded it, this policy results in a continuously increasing data burden. In order to accelerate the accumulation of drug data, and to identify cost-effective patient pools for clinical trials, pharmaceutical firms have begun to conduct clinical trials in an increasingly broad set of international locations. For example, a number of firms have begun testing medications in Africa, where patient access costs are lower. The impact of national regulations on location in drug development is also evident. For example, the Japanese requirement that products be tested specifically on Japanese individuals has a clear impact on the “internationalization” of development activities.

Proximity issues seem to play a limited role in pharmaceutical manufacturing. Some manufacturing clusters exist in areas other than those in which research and development is performed (including such diverse areas as Cork, Ireland, and Puerto Rico). Geographic clustering is a more prominent phenomenon in research than manufacturing.

Marketing and sales forces build relationships with physicians, health-care bodies, and (to a growing extent in some countries) with patients. To the extent that these require some specific investments in building relationships with health-care providers, proximity and location issues do play a role.

International Collaborations and Outsourcing

Inter-organizational relationships in the pharmaceutical industry became increasingly prevalent and complex in the final decades of the 20th century. The principal areas in which such collaborations play a role are: (1) technology partnering, in which large firms often obtain access to critical drug-discovery technology platforms developed by smaller firms; (2) in-licensing of drugs by large pharmaceutical firms from smaller, research-focused companies (often biotechnology firms); and (3) cross-licensing or co-marketing agreements, either with large multinational firms or smaller firms whose marketing and distribution capabilities may be limited in particular countries. In recent years, international collaborations have often involved non-U.S. multinationals seeking access to the expertise of American biotech firms. Numerous arrangements exist, however, in which U.S. companies partner with foreign technology and marketing partners.

Technology-platform partnering agreements, such as Roche’s US$280 million deal with deCODE Genetics, are often longer-term arrangements that involve knowledge-sharing, payments for achieving specific milestones, research and development funding, and equity. In recent years, international agreements of this type have often involved non-U.S. multinationals seeking access to the expertise of American biotech firms. For the biotech companies involved in these arrangements, these collaborations provide funding and are often undertaken in project areas that are either emerging or are not the most central areas to these firms’ business. Biotech firms may also collaborate with multiple partners on different projects. For example, Vertex Pharmaceuticals of Cambridge, Massachusetts, has
acknowledged research and development partnerships with a diverse and international set of firms, including Serono, Novartis, Aventis, Taisho, Schering AG, Lilly, Kissei, and GlaxoSmithKline.

An important feature of the pharmaceutical industry is that competition occurs within country-specific therapeutic class combinations. Thus, firms may be collaborators in particular country-therapeutic classes but rivals in others. Unlike technology partnering arrangements (which are often longer-term deals that require extensive, company-specific investments), drug licensing, co-marketing, and co-promotion agreements are often deal-specific, and they are often arranged for the specific purpose of marketing blockbuster drugs and for sales in particular countries. For example, Astra and Merck formed a joint venture specifically for the purpose of marketing Prilosec, a gastrointestinal (anti-ulcer) medication, particularly targeted for the U.S. market.

Outsourcing is particularly important in the development phase of the pharmaceutical value chain, although contracting for manufacturing and sales services is becoming more common as well. Such arrangements play a limited role in drug discovery, in part because of the importance of this activity for competitive advantage.

Drug development is characterized by the need to conduct large numbers of clinical trials to ascertain and document a drug's safety and efficacy. Pharmaceutical firms will conduct at least some clinical trials using their own in-house personnel for each product they develop. They are, however, subcontracting an increasing portion of these activities to outside organizations. Contract research organizations (CROs) have emerged as important partners in the development and approval process, especially in the United States. Among their activities, CROs design protocols for clinical trials, enroll patients, administer medications, record and analyze data, and assist in compiling regulatory submission packages. Parexel, one of the largest CROs in the United States, estimated that approximately US$6.5 billion would be spent on CRO services in 2000 (Parexel 1999).

Contract research organizations can be valuable for all firms attempting to minimize the amount of time that drugs spend in clinical trials, and they can be particularly helpful partners for firms with limited experience outside their home markets. Parexel has amassed clinical trials expertise in numerous countries and prepared development data for multiple regulatory authorities. As of 2001, the firm operated in 36 countries, including each of the world's major health-care markets, and it generated nearly 40 percent of its revenue outside the United States. In addition to reducing the time that a drug spends in development, pharmaceutical firms are conducting international clinical trials in lower-wage countries in order to reduce development costs. It is somewhat surprising, however, given the number and the frequency of clinical trial outsourcing, that most relationships with CROs are arm's-length rather than relational (see Azoulay 2001).

Although slightly more than one-third of pharmaceutical manufacturing expenditures are outsourced—34.7 percent of US$29.4 billion in 1998 (Birch 2002)—these are not viewed as important for achieving competitive advantage, and manufacturing costs account for a limited fraction of the total pharmaceutical costs.

As the biotech industry grew in the 1980s and 1990s, contract sales organizations (CSOs) emerged offering complete marketing and sales services, from prelaunch marketing to product positioning. In 1997, these accounted for about US$1.4 billion, approximately 3.4 percent of global sales and marketing costs (Birch 2002). Thus, while they may be important vehicles for international entry, their significance for value creation and capture is not yet extensive.

Mergers, Acquisitions, and Spin-offs
During the final decades of the 20th century, a wave of mergers and acquisitions substantially reshaped the global pharmaceutical industry, resulting in a smaller number of large, integrated firms that compete and collaborate with numerous smaller research-focused firms. Indicative of the trend were the US$90 billion acquisition by Pfizer of Warner-Lambert and the US$180 billion merger of Glaxo Wellcome and SmithKline Beecham (each of which had been the product of 1990s mega-mergers) in 2000.

Managers suggest that such mega-mergers result in economies of scale and scope (as well as spillovers) in therapeutic-class research and development. These mergers and acquisitions also appear motivated by the search for increased market access and increased power in negotiating with regulatory agencies. (Danzon, Epstein, and
Nicholson [2004] review evidence on pharmaceutical mergers more completely.)

In addition to mergers and acquisitions among domestic and international competitors, multinational pharmaceutical firms have been consistently active in taking equity stakes in biotechnology firms. For example, in one of the earlier and more prominent deals, Switzerland’s Roche participated in a US$2.1 billion merger with San Francisco-based Genentech in 1990. Such deals have been driven principally by the goal of accessing leading-edge science and technology.

In the final years of the 1990s and the early part of the new millennium, a number of larger biotech firms acquired other biotech firms. In 2001, Vertex Pharmaceuticals purchased Aurora Biosciences for nearly US$600 million. In the largest acquisition in the pharmaceutical sector of that year, Amgen purchased Immunex for US$16 billion. These transactions serve multiple goals, including enhancing R&D capabilities and assembling complementary assets that further enable these firms to capture the value associated with their innovations.

Global Issues

One of the most serious challenges facing international institutions and the global pharmaceutical industry is the need to supply current medications to and develop new medications for lower-income countries. Some of the difficulties associated with supplying medicines to such countries are related to the nature of fixed costs in the industry, the potential for free-rider problems, and the possibility that local governments will expropriate efficacious new medications. At the same time, however, some of the difficulties associated with effectively distributing medicines to lower-income countries are not related to intellectual property issues. At the same time, however, some of the difficulties associated with effectively distributing medicines to lower-income countries are not related to intellectual property issues. (Michael Kremer examines such issues in greater depth and works to propose frameworks that may enable national and international institutions to address such problems. This section draws, in particular, on Kremer’s research.)

Pharmaceutical companies are reluctant to develop medicines for (or distribute existing medicines in) countries that do not offer sufficient intellectual property protection. For example, medicines for tropical diseases constituted only approximately 1 percent of all medicines licensed worldwide between 1975 and 1997 (Pecoul et al. 1999; Kremer 2002). The economic rationale for such reluctance is that weak intellectual property rights lead to circumstances in which the firms may not be able to recoup the costs invested in developing new drugs, either because governments may appropriate the IP rights or because other firms may be able to take advantage of new discoveries to produce medications at substantially lower average costs (because they do not have to bear the costs of researching and developing new drugs).

For most of the 20th century, intellectual property rights varied substantially across countries and such rights were weaker in developing and less-developed countries. The agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPs), a product of the Uruguay Round of the General Agreement on Tariffs and Trade that became effective in January 1995, was designed in large part to address these issues. The TRIPS agreement curtailed differences in international property rights protections. According to the agreement, nations that are members of the World Trade Organization (WTO) must establish minimum standards of intellectual property protection for foreign and domestic products and processes, including those for the pharmaceutical industry (Bass 2002). With respect to the pharmaceutical industry, developing countries were granted a 10-year grace period (until January 2006, with the possibility of additional extension). In a prominent example of a country’s effort to adjust its national policies to fit the requirements of the WTO, India amended its 1970 Patent Act in Spring 2005 to extend local patent protection to products as well as processes. Although theory suggests that these developments may lead to increased development of new drugs for such countries, more time is needed to determine whether these initiatives have been successful. (For a deeper discussion of these issues, see Lanjouw and Cockburn 2001.)

While issues associated with intellectual property rights are of considerable importance for developing medicines and for introducing medicines into lower-income countries, many of the difficulties that such countries face are unrelated to intellectual property issues. For example, Kremer notes that, at the beginning of the 21st century, health-care spending in the relatively small U.S. state of Connecticut exceeds that of the 38 low-income countries of sub-Saharan Africa.
Africa combined (Kremer 2002). Indeed, many combinations of off-patent vaccines and low-cost medications are not delivered to children and other at-risk groups in such countries because of limited health infrastructures and other local institutional difficulties.

See Also
AIDS; Health; Intellectual Property; Trade-Related Intellectual Property Rights; DOC-52; DOC-53; DOC-126

Bibliography
Philanthropic foundations have played a major role in the internationalization of the world, and they are making an increasingly significant contribution to current globalization processes. In the course of their modern history, philanthropic foundations have created dense national, regional, and international networks. Because of the absence or inadequacy of state and intergovernmental initiatives, these networks often involve significant flows of money, ideas, research, experts, and intellectuals. Historically, states frequently expanded into areas after foundations did so, either easing out the foundations, incorporating them, or forming important state-private networks that shared responsibilities. Since the early 1980s and the Reagan-Thatcher era of “rolling back the frontiers of the state,” foundations have become more significant at the global level, especially in attempts to construct a “global civil society,” which purportedly increases levels of citizen participation in global affairs, creates more accountable global institutions, and humanizes globalization itself. Major global foundations include the Ford, Gates, and Turner foundations in America; Europe’s Bosch, Bertelsmann, Fondation de France, and Olivetti philanthropies; Japan’s Sasakawa Peace Foundation; and George Soros’s Open Society network. These and other philanthropies have also developed extensive and multilayered strategic organizational networks that span and unify the globe, encouraging the spread of philanthropy and linking together the world’s regions. Due to the historical power of American foundations, U.S. philanthropy is at the forefront of this development.

Historical Origins
Philanthropic foundations may (cynically) be defined as pots of money surrounded by people who want some, as Dwight MacDonald famously remarked. More commonly, they are regarded as sources of charitable giving (or in the United States, “scientific giving”) located beyond the realms of the market and politics, beyond business interests and the state. Thus, philanthropy is often viewed as part of a “third [or nonprofit] sector.” More specifically, philanthropy refers to the voluntary use of private finances for public purposes.

The historical strength of U.S. foundations in global philanthropy is such that they are widely viewed as an American invention. But while the American model has been adopted across the Western world, the Global South lacks the resources to engage in global philanthropy. In the South, philanthropic models have developed that reflect the lack of legal, tax, and other incentives for potential philanthropists. Broadly, however, global philanthropy shares in common a religious inspiration, especially among Protestant Christians (e.g., Rockefeller and Carnegie in the United States, Rowntree in the UK, and the Bertelsmann Foundation in Germany), and across Islam (where the paying of Zakat is a pillar of the religion),