

Industry, Innovation and Social Values*

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ABSTRACT: *Remaining important tasks in finding and developing new drugs and vaccines for HIV/AIDS, malaria, cancer and other diseases require continued industry research and development. Industry's research and development pipeline has produced drugs that have saved AIDS victims previously facing certain death, but still no cure nor vaccine is yet available. Experience with the process of research and development indicates that it requires more than a decade of development to produce a new drug with costs in the hundreds of millions of dollars. Intellectual property protection is critically important in assuring that drug development continues. Partnerships between industry and the public sector have increased access to new therapies in developing countries and promise to enhance access to both patented and generic medicines in the future.*

Overview

Given the disease challenges, both in terms of infectious and chronic conditions facing the world today (e.g. AIDS, SARS and heart disease), pharmaceutical innovation and access to health care are two related issues high on the current global economic and political agenda.^{1,2}

HIV/AIDS, which has infected more than 65 million people and killed 25 million people worldwide over the last 20 years,³ is an illustrative example. There is not yet a cure for HIV/AIDS, and a vaccine against this threat will not be available for some years into the future. However, thanks to more than 20 antiretroviral medicines discovered and developed by pharmaceutical companies, AIDS has been translated from death sentence into a lifetime manageable chronic disease at least where the

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available AIDS therapies are accessible to infected populations (largely in the industrial counties).

Given that most biomedical therapies are discovered and developed by industry,^{4,5} often in partnership with public health research institutions, and more than 80 new drugs and vaccines are in industry's pipeline, it is likely that private pharmaceutical and biotechnology companies will be the source of future advances in AIDS therapies and other drugs and vaccines against the broad range of diseases.

The sustained investment in research and development by pharmaceutical companies is prerequisite to developing a successful AIDS vaccine or cure in the future, as well as meeting other health needs of patients worldwide. Because it bears a significant risk burden, it needs to be supported by adequate policies in such areas as intellectual property rights.

In recent years, the pharmaceutical industry has also emerged as an important partner in various health initiatives targeting developing countries. Diverse voluntary contributions of companies complement efforts of other stakeholders in public health, and often are at the heart of successful programs.

Global Public Health – A Need for Continued Innovation

Everything that can be invented has been invented

John Duell, US Patent Commissioner, 1900

We can close the book on infectious diseases

William Steward, Surgeon General of the United States, 1967

Reviewing the global health trends over the last decades, a striking feature is the overall improvement of major public health measures. Be it average life expectancy, infant mortality rates or level of human development, important progress can be observed in all these categories.⁶ It could seem that the world is on the right track to address major health problems, and that the current levels of medical knowledge and technologies are sufficient to do so.

This picture could not be more misleading. In fact, the world's health situation is far from being homogenous: on the one hand, there is a growing disparity in health outcomes between developed and developing countries, and on the other, developing countries themselves experience an increasing heterogeneity in their health profiles.⁷ This phenomenon has been driven by several major developments.

First, there is the continuous threat of communicable diseases linked to emerging and re-emerging epidemics. The Centers for Disease Control and Prevention (CDC) has compiled a list of 29 newly emerging pathogens since 1973⁸ and in the 1990s alone, more than 30 emerging and re-emerging infectious epidemics affected the entire world.⁹ An obvious example of an emerging disease is HIV/AIDS, first discovered in 1983, and now affecting around 40 million people globally, AIDS causes some three million deaths annually. In some African countries, AIDS prevalence reaches 40 percent of the adult population,¹⁰ and it is associated with an important decrease in life

expectancy, estimated at seven years between 1980 and 2002.¹¹ Other emerging diseases include SARS, hepatitis C, or influenza A virus – all identified in the 1990s for the first time.¹²

Among the re-emerging infectious diseases, tuberculosis is the greatest contributor to human mortality. Almost eradicated from much of the world in the 1940s, and now returning at alarming rates in new, more virulent forms, tuberculosis causes 1.5 million deaths annually and it is estimated that nearly a third of the world's population has been latently infected with the mycobacterium.¹³ Other such re-emerging diseases include cholera, dengue fever, malaria or meningococcal meningitis – all reappearing as important public health problems.

Yet another recent development influencing global public health is the emergence of antimicrobial resistance, i.e. the emergence of drug-resistant strains of bacteria, viruses, parasites or fungus. This presents a particular threat to the world's population, making it extremely vulnerable to the threat of communicable diseases. This important problem is now reaching an alarming scale, with rapidly accelerating antibiotic resistance¹⁴ and its particular linkage to diseases such as *streptococcus pneumoniae*¹⁵ or multi-drug resistant TB.¹⁶ Similar threats of drug resistance have developed for other major infectious diseases, such as malaria¹⁷ and also recently HIV/AIDS.¹⁸

Lastly, the entire world is facing the growing burden of non-communicable and chronic diseases, which are rapidly becoming the leading cause of mortality and morbidity globally, and are particularly gaining importance in developing countries.¹⁹ Many of these diseases, together with the implications of ageing societies, represent significant challenges for public health globally, and can be only partly treated with existing medicines.

All these new developments in global public health are a testimony to the fact that global health needs are subject to constant change. This in turn translates into the continuous need for broad health research and medicines innovation in particular. Various dynamics of health problems exemplified above speak for themselves: we need medicines to fight emerging infectious diseases, as well as new improved treatments, preventive and curative tools to address the re-emerging epidemics. Certainly, the escalating problem of drug resistance magnifies this need. Undoubtedly, intensified R&D efforts in the area of non-communicable chronic diseases are prerequisite for future successful public health strategies.

Sustaining the Flow of Innovative Medicines

Despite many potential defenses – vaccines, antibiotics, diagnostic tools – we are intrinsically more vulnerable than before... We could imaginably adapt in a Darwinian fashion, but the odds are stacked against us... In the race against microbial genes, our best weapon is our wits, not natural selection of our genes.

Dr. Joshua Lederberg, 1958 Nobel Laureate, 1997

There is not yet a cure for HIV/AIDS; furthermore, a vaccine against this threat will not be available for some years into the future.²⁰ But progress has been made in

translating AIDS from a death sentence into a lifetime manageable chronic disease – at least where the available AIDS therapies are accessible to infected populations, largely in the industrial countries. Thanks to more than 20 antiretroviral medicines discovered and developed entirely by research and development within pharmaceutical companies,²¹ death rates from AIDS have plunged by 80 per cent in the US and Europe.²²

The case of HIV/AIDS is illustrative of the process of pharmaceutical innovation. Despite significant progress already achieved in terms of treating AIDS patients, further intensive R&D efforts are needed to develop effective preventive (vaccines) and curative tools, which are considered as the only viable solution to stop the HIV/AIDS pandemic. The pharmaceutical industry continues its effort, and there are currently more than 80 drugs and vaccines in development for HIV/AIDS and its various opportunistic infections.²³

The pharmaceutical industry, often working in partnership with public health research institutions, academia and small biotech companies, has been the principal source of new medicines currently in use. Only 4 of the 47 ‘global’ medicines with annual sales in excess of \$500 million have been developed with any funding support from public research institutions, and such support has been provided at a very early stage.²⁴ The pharmaceutical companies invested almost \$50 billion in R&D in 2002, outscoring the US National Health Institutes—the world’s biggest public health research institution—by 50 percent.^{25,26}

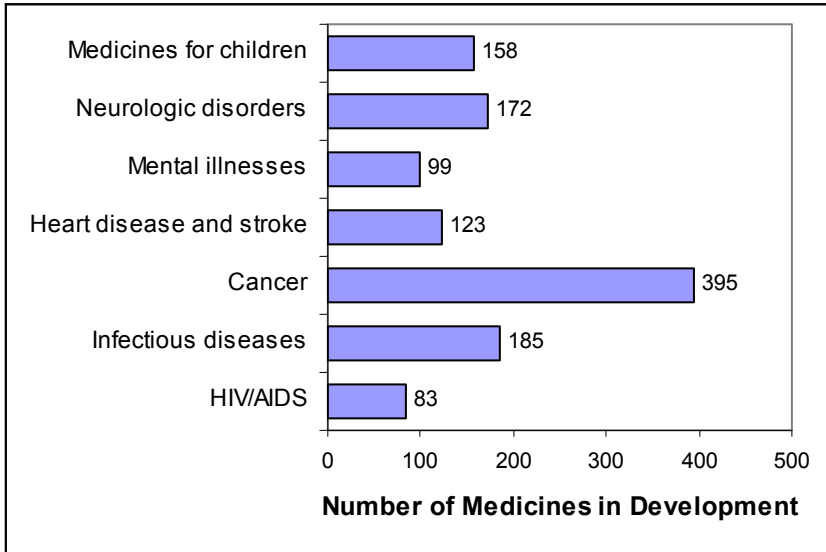
R&D efforts of the pharmaceutical industry spread over a broad range of diseases and thus attempt to address all major public health needs. Figure 1 illustrates these endeavours, showing the number of drug and vaccine candidates currently in the industry’s development pipeline. Altogether, there are more than 1,200 new drug and vaccine candidates in clinical development, and the total number of medicines in research and development, i.e. including drug/vaccine candidates in early discovery and preclinical development, was the highest ever, reaching more than 7,300 drug and vaccine candidates.²⁷

The social and economic value of medicines innovation generated by the pharmaceutical industry is difficult to overstate. Health-related technology improvements led by the introduction of new medicines are estimated to have reduced human mortality by upwards of 50 percent between 1960 and 1990.²⁸ Various studies provide evidence of a clear link between innovative medicines and disease prevalence,²⁹ mortality rates,³⁰ and overall economic growth.³¹ Also, innovative medicines may be a source of important budgetary savings for health systems, reducing hospital stays, surgical interventions and other non-drug costs.^{32,33}

A very good illustration of the value of medicines innovation is provided by vaccines, which have long been considered as one of the most cost-effective interventions in health. For example, the increased global immunisation coverage, reaching 80-90 percent of infants in the late 1990s,³⁴ had a significant impact on the infant mortality rate, which dropped by 50 percent in least developed countries over last 25 years.³⁵ The pharmaceutical industry has developed the bulk of existing vaccines³⁶ and among more than 70 vaccines currently in development pipeline, there

may be future vaccines for HIV/AIDS, infant diarrhoea, malaria, tuberculosis, pneumonia, dengue fever, influenza and many other communicable diseases of high risk.

**FIGURE 1. DRUG AND VACCINES IN DEVELOPMENT
BY MAJOR DISEASE CATEGORIES**



Source: PhRMA, Medicines in Development Surveys 2003-2004.

Understanding the Process of Medicines Innovation

The patent system... added the fuel of interest to the fire of genius in the discovery and production of new and useful things.

Abraham Lincoln, Congressman and US President, 1859

(...) we strongly believe that strong intellectual property protection will enable us to protect our investments in research.

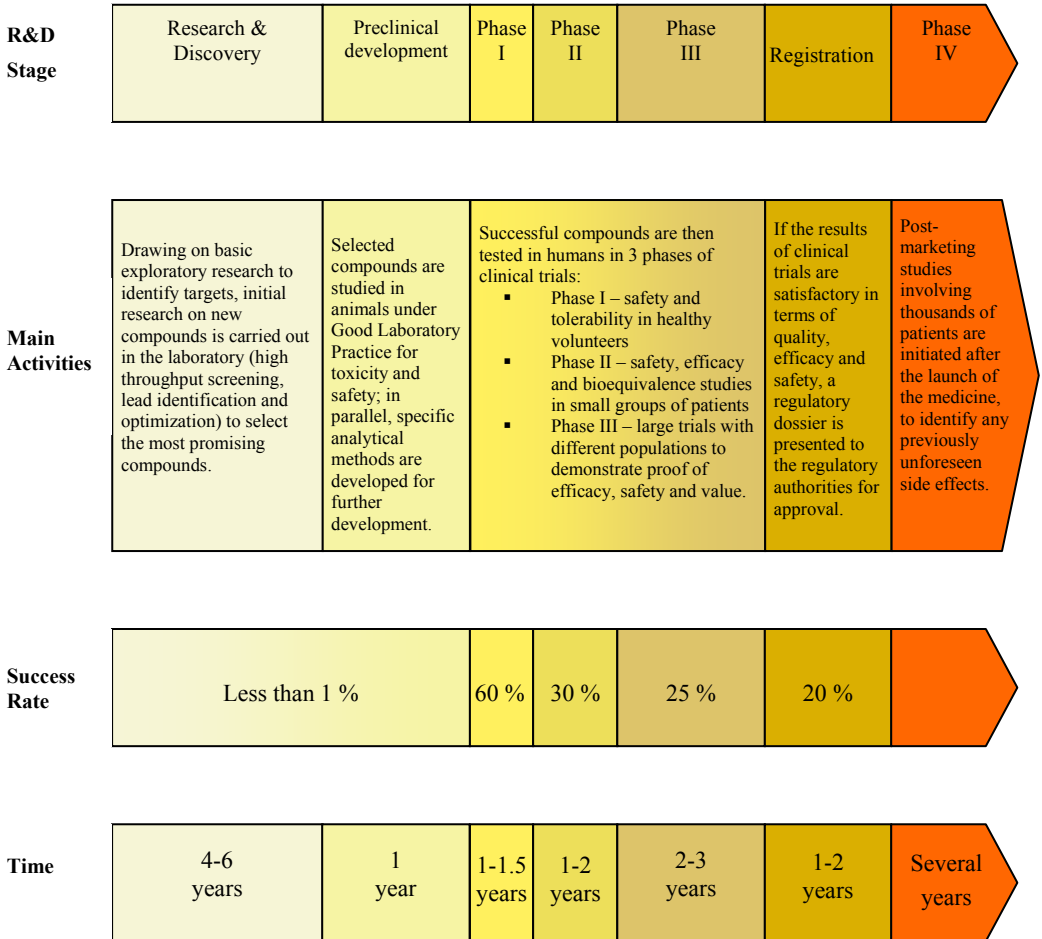
An environment which fosters and protects research discoveries and processes will lead to the innovations and medicines of the future.

Nicholas Piramal India Ltd. Annual Report 2001-2002

The process of pharmaceutical innovation has several distinct characteristics, as illustrated by Figure 2. It is a very complex, multistage process requiring sophisticated skills, knowledge and capacities. An integral element of pharmaceutical innovation is risk—developing a successful medicine necessitates deployment of substantial financial resources over long time periods, with very little chance of succeeding at the end.

Consequently, the average cost of bringing a new product to market in the US, where most new medicines are invented today,³⁷ was around \$800 million in year 2000 dollars, a 2.5 fold increase over the average cost in 1990.³⁸ This amount further increases if the post-market approval expense for assessing long-term safety and efficacy is included in these calculations.³⁹ On average, it takes in excess of 12 years to discover and develop a new medicine that can be delivered to patients.

FIGURE 2. PROCESS OF PHARMACEUTICAL R&D



A long list of factors is needed to create an environment enabling medicines innovation, spreading over human, technical, financial, organisational and institutional requirements.⁴⁰ Describing them all is however, beyond the scope of this paper. One particular element—intellectual property rights—is worth more attention though, given its centrality to the process of pharmaceutical innovation.

The dependence of the pharmaceutical industry on intellectual property protection (IPP), and in particular of the temporary exclusivity granted by patent protection, is

arguably the highest when compared to other industries.^{41,42,43} IPP transforms the intangible capital generated by pharmaceutical companies during the process of R&D into financial flows indispensable to continue the cyclical process of innovation and to sustain the successful business model pursued by pharmaceutical industry. *As such, it should be regarded as the heart of the whole system of pharmaceutical innovation.*

Patents for products last nominally for twenty years from the time of grant by national patent offices of all WTO members who have implemented the WTO's Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS). However, meeting the exacting technical regulatory requirements of the product licensing authorities now takes, on average, ten years from the point at which a patent is granted for an invention, which is the effective starting point for the product development process. It should be noted that, in practice, the period of market exclusivity due to patent protection is much shorter, as a result of therapeutic competition, i.e. the introduction of competing products in the same therapeutic class shortly after the launch of the breakthrough product. By way of example, major products launched in the late 1980s enjoyed market exclusivity of 4 to 6 years, while products launched a decade later could only benefit from 0.5 to 2 years of exclusivity.⁴⁴

Data exclusivity is another form of intellectual property protection independent of patent protection. Developing a patented discovery into an approved saleable product requires amassing large amounts of data over many years on pharmacology, toxicology, clinical trials, manufacturing processes and product quality etc. These data are submitted in confidence as a single dossier to the relevant technical regulatory approval body in national (or EU) jurisdictions to gain a license to sell the product by the innovator. Article 39(3) of the TRIPS Agreement obliges WTO Member States to ensure that this data package shall be maintained confidential or exclusive to the originator for a fixed period from the date at which it was submitted to the government authorities.^{45,46}

Perhaps the most telling example of the importance of intellectual property protection for pharmaceuticals is the fact that between 2002 and 2007 the value of US patents that will expire on 35 drugs (based on current global sales) is more than \$73 billion.⁴⁷

The Pharmaceutical Industry and Developing Countries

The analysis of global public health could not be complete without particular emphasis on developing countries. Specificity of these countries, in terms of their health status and underlying socio-economic conditions, has largely influenced the global agenda⁴⁸ and has had an important impact on the pharmaceutical industry itself.^{49,50}

Arguably, the most important aspect of this problem concerns the issue of access to needed medicines in developing countries, and the alleged barriers that might be created by pharmaceutical patents. In order to see things in the right perspective, it should be noted that patents are in force on only about 30-40 percent of the global prescription volume.⁵¹ Also, it is important to retain the fact that the great majority of

diseases affecting developing countries can be effectively treated with the off-patent medicines from the WHO's Essential Drug List.⁵² Actually, out of more than 300 medicines on this list, only a handful of products are still protected by any patents.⁵³ At the same time, in most poor countries, only 30-50 percent of the population has access to these essential medicines.

Clearly, factors other than patents are responsible for this *status quo*, including unavailability of health services and infrastructure, inappropriate government prioritisation and failure to use prevention and treatment strategies.⁵⁴ Responding to this crisis, the pharmaceutical companies have mobilised substantial resources and emerged as an important stakeholder in the global effort to improve the health situation of developing countries. A new form of collaborative action—public private partnerships—has now become a distinctive feature of the global health landscape,⁵⁵ and the pharmaceutical industry has been a critical stakeholder in these endeavours.⁵⁶

The involvement of the pharmaceutical companies in health partnerships spreads over diverse activities, from providing free-of-charge or highly discounted medicines, through training and capacity building, to conducting R&D to diseases exclusively affecting developing countries. Many of these programs have yielded important results improving health of the world's poorest populations, including the following:⁵⁶

- More than 150,000 AIDS patients received triple antiretroviral combination through the Accelerating Access Initiative
- Over 3 million doses of Diflucan have been distributed free-of-charge to AIDS patients in 16 African countries through the Diflucan Donation Program
- By the end of 2003 almost 80 million people in 37 countries received free treatment for lymphatic filariasis through the Global Alliance to Eliminate Lymphatic Filariasis
- Around 30 million people receive annual free treatment to protect them from river blindness through the Mectizan Donation Program.

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