

What are the Prospects for a New Golden Era in Vaccines?



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“Those who cannot remember the past are condemned to repeat it.”

George Santayana



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What are the Prospects for a New Golden Era in Vaccines?

A New Era of Vaccine Innovation?

The prospects for a new era of vaccine innovation - perhaps for a second golden era - will be shaped not only by science and technology but also by the political and economic environments in developed nations like the United Kingdom and the United States¹. The governments of both countries have of late been re-examining their policies on preventive medicines, and there continues to be substantial media concern about sustaining innovation and providing a safe, adequate supply of vaccines in the future². It is thus an opportune time to look back at the first golden era, from 1945 through the 1970s, when 19 new vaccines against a wide



range of infectious diseases were introduced. That burst of innovation, which changed the face of childhood disease in Europe and the United States, prompts us to consider some of the major institutional changes that accompanied that great creative cycle and to reflect on the subsequent efforts to restructure the political economy of vaccines in particular. From that rich historical record we can, I believe, extract some important guidelines for those implementing and attempting to reshape vaccine policy in the present day.

We will explore the following specific questions about the industry and its context: First, what factors have in the past fostered an innovative, productive industry? Second, what developments have led to problems in the sources of innovation and supply? Third, what efforts have been made to mitigate these problems and how successful have they been? Fourth, what are the current and future threats to the successful development of the industry? Fifth, what

does the historical record suggest we should do to encourage the development of this vital industry?

As the public concerns about vaccine supply and innovation suggest, this industry has in recent decades developed what economists and environmentalists call “the problem of the commons.” This situation arises when there is a common or social need to protect something of value to all of those in the society, none of whom have specific responsibility for it. Thus each citizen will act to protect and improve his or her own property, but they are likely to ignore the commons, the plot of land that belongs to an entire town³. In the case of vaccines during and after the industry's contraction, each public and private participant involved was behaving perfectly rationally, seeking to achieve laudable goals, some of which were prescribed by law. But none of the participants was responsible for the long-run performance of the entire global vaccine industry - that is, the “commons” - insofar as innovation and supply were concerned. With this in mind, we will look carefully at how and why the problem arose and why it was so difficult to solve.

The Golden Era

We will begin our inquiry, however, by looking first at an amazingly productive phase of vaccine innovation. The post-World War Two era of preventive medicine and global public health witnessed a series of major breakthroughs in Europe and the United States that had decisive impacts on life expectancy and morbidity throughout the world. None

has been more decisive than the development and widespread distribution of new vaccines. “The ability to grow human viruses outside a living host, in a relatively easy and safe manner, led to an explosion of creative activity in vaccinology....”⁴ In the years following 1945, these scientific and technological advances in the developed world made it possible for the first



time for scientists working together in academe, pharmaceutical companies and governments to discover, produce and deliver safe, effective vaccines against poliomyelitis, measles, mumps, rubella, *haemophilus influenzae* type b, influenza, meningitis, pertussis, hepatitis A and B, tetanus, anthrax, diphtheria, rabies, varicella, rotavirus, and yellow fever - as well as improved vaccines against pneumonia and typhoid fever.⁵

So beneficial were the vaccines developed in the postwar years that the World Health Organisation mounted two global immunisation campaigns. The first was a co-operative effort between WHO, national governments, NGOs and private firms. The goal was the eradication of smallpox, an objective that could be achieved in part because of the use of freeze-dried vaccines and new technologies for injection. The campaign was so successful that by the end of the 1970s, the disease was completely eradicated.⁶ Encouraged by this astonishing accomplishment, WHO and its partners in the Expanded Programme on Immunization launched a second campaign. They set out in the 1970s to provide all children in the world with six vaccines (against tuberculosis, diphtheria, pertussis, tetanus, polio, and measles). With support from a wide range of public institutions, private organisations and NGOs, the Children's Vaccine Initiative succeeded in dramatically improving the vaccination rate among children in the developing nations.⁷

The Golden Era thus represented a decisive and positive turning point in global public health. In countries with advanced economies and formidable medical institutions, the incidence of a number of diseases has been reduced to minor proportions of the population. In Europe, cases of measles have been cut by 95 per cent and diphtheria by 99 per cent in recent years. For the entire world, it is estimated that as many as three million lives are saved every year by immunisation.⁸ That figure is likely to grow higher with the continued success of international efforts to improve immunisation rates. As three distinguished authors with substantial experience in the field noted in the *British Medical Bulletin*, "Vaccination has been demonstrated repeatedly to be cost-effective, indeed even cost saving, a standard rarely expected of other healthcare interventions."⁹ All of the available studies of U.S. paediatric vaccines conclude that every dollar spent results in significant direct medical and indirect savings - with total social saving of billions each year.¹⁰

Optimism and the Golden Era

Whether they were working in the public, the private, or the nonprofit/NGO sectors, almost everyone in Europe and the United States associated with the vaccines of that era had every reason to be proud of what had been accomplished and optimistic about the global future of the vaccine sector.¹¹ The scientists had certainly done their part, providing the means of studying, propagating and attenuating in cultures the viruses and bacteria responsible for many of the diseases



of greatest concern to society. Whether they worked in universities or private firms, researchers had been able to exploit the new technical capabilities and develop effective vaccines for clinical testing.¹² Private firms - some new entrants and others long associated with vaccine innovation - played a central role in large-scale production of the vaccines for distribution by physicians and government agencies.

The optimism of the Golden Era encouraged entry and substantial investments in vaccine research, development, manufacturing, sales and marketing. Demand was large and was growing. There were risks with vaccines, but they seemed to be fairly well defined and significantly lower than those associated with other medicines. In the basic and applied sciences, in the government sector, in the development of private firms and in the interactions between scientific and business establishments, there were strong elements of what social scientists call “path dependency” in this array of institutions.¹³ As the path dependency concept suggests, institutions such as those in the vaccine complex frequently acquire well-rooted patterns of action and interaction, capabilities, and cultures that give them a powerful social momentum. Success of the sort experienced during the golden era helped keep them on a well-established path.

In Europe and America, there were good reasons to believe that the Golden Era would continue through to the end of the twentieth century. As began to

be evident as early as the 1970s, however, the vaccine path was already being altered by problems that none of the participants had anticipated.

The First Vaccine Crisis - a US Problem?



Some of the problems in the United States could be traced to the supply side of the vaccine industry and were an unanticipated consequence of the formidable accomplishments in vaccine use. The wave of new vaccines brought welcome increases in total revenue to the producers, but they were accompanied by increased risks. In most cases, it was possible to calculate the risk of serious side effects from vaccines. But it was difficult for manufacturers to calculate with similar accuracy the risks

associated with the resulting litigation. The problem was particularly acute with paediatric vaccines, which were administered to healthy children. The US courts in the 1970s were inclined to make the manufacturers responsible for damages, even in cases when it could not clearly be established that the vaccine had been the source of damage to the plaintiff. The Swine Flu litigation of the 1970s also had an impact on the industry, threatening further liability for side effects - in this case for Guillain-Barré syndrome. The uncertainties were especially evident with new vaccines because the clinical trials could not establish the likelihood of a side effect that might occur only a few times in a million cases.¹⁴

Meanwhile, costs as well as risks were increasing. New opportunities called for new facilities and personnel for research and development, for clinical studies and for manufacturing, sales and marketing. The high rate of inflation in the 1970s sharply increased the costs of capital. Both personnel and facilities in the vaccine operations were becoming more expensive.

These increased costs would not have been a serious impediment to the private sector firms had there been some relief on the prices they could

charge. Since the state and federal governments purchased many of the vaccines, however, public agencies exerted pressure to keep prices down and, indeed, they were increasing slower than costs. The resulting cost-price squeeze added to the problems being created by liability cases. Capital could be put to more profitable use on pharmaceuticals which were at that time just entering what would be a long period of successful and profitable innovation.

The management at Merck & Co Inc, which was one of the major research firms developing new vaccines, was so concerned about this situation that it commissioned a full-scale internal study of the economic situation in vaccines. The conclusions were startling for the company. In the late 1950s, the company had been able to take advantage of the recent advances in virology to develop new vaccines for measles, mumps and rubella.¹⁵ In the late 1960s, vaccines were making substantial contributions to the firm's revenue growth. But the government's emergency effort to counter an anticipated swine flu epidemic brought to the surface concerns about liability in Merck, about the costs of quickly launching a crash programme to provide large amounts of a new vaccine, and the ratio between costs and profits in the entire vaccine enterprise. The 1979 internal study concluded that vaccines had become low-margin commodities: prices were stable; costs were increasing, so profit margins were being significantly eroded. This was especially true of government purchases.

Other large US companies were also concerned as vaccines drifted toward commodity status. The firms that re-examined their investments in vaccines were all major companies with significant research and development as well as manufacturing and sales capabilities. Eli Lilly was deeply concerned about the risks associated with vaccine production. All it took in this setting was a production problem - and vaccines had always been more difficult to standardise than pharmaceuticals - or a problem with unanticipated side effects to persuade company executives to shift their investments to other products. Both difficulties hit Lilly's research with pneumococcal polysaccharide vaccines, and the company decided to leave the vaccine business to other American firms.¹⁶ It was not alone in reaching this decision. Pfizer had also dropped out of vaccine



research and production, as had Dow and Richardson-Merrell. Five major firms were left in the large American market: Lederle, Parke-Davis, Merck, Wyeth, and Connaught.¹⁷ The United States was, with very little notice or discussion, steadily drifting into a “problem of the commons” in vaccines.

The European vaccine industry appeared to be self-contained and protected from the changes taking place in America. The major innovators were all continuing to develop and produce vaccines for their respective national markets. The purchasing was done almost exclusively by their governments, all of which favoured their national champions.¹⁸ Burroughs-Wellcome and Glaxo served the United Kingdom's market; Pasteur and Mérieux supplied France; Behringwerke (a division of the giant Hoechst firm) Germany; and Sclavo supplied Italy. The big three in Europe were Behringwerke, Mérieux, and Pasteur (which was owned by the French government). Insofar as these nationalistic preferences prevented people from receiving the best vaccines available on the global market, the non-tariff national barriers to trade probably had a negative impact on the populations served by the European champions. The barriers did, however, prevent further contraction in the number of competitors in the global industry, a development that actually favoured innovation over the long-term. Soon, however, that situation would also change, and the US problem of the commons would become a global problem.

The decline in the number of US vaccine operations was ominous for the global industry. If it foretold further decline, there were likely to be fewer innovators and the remaining firms were likely to concentrate on fewer products. In the mid-1970s, there were eight US firms producing influenza vaccines, but only four companies took part in the emergency swine flu program. A few years later another producer dropped out of the flu vaccine business. As these changes in the industry took place, there was good reason to be concerned about the future of vaccine innovation and supply.

Public and Professional Responses to the Problem of the Vaccine Commons

While this restructuring of an industry vital to public health was gaining momentum in the United States, both government and nonprofit organisations began to take note of what was happening. In 1977, the National Immunization Work Groups, convened by the Office of the Assistant Secretary of Health, made a series of recommendations for public responses to the problems of vaccine innovation and supply. Two years later, the Congressional Office of Technology Assessment re-examined the issues and also proposed options for a federal response. Neither study, however, was able to move the government to take any action. The groups disbanded, and media and public interest evaporated. This cycle would be repeated again and again in the next two decades.



In the 1980s there was finally a partially successful response to the problem, and it came from a nonprofit organisation and not the government.¹⁹ The Institute of Medicine, an organisation chartered by the National Academy of Sciences, established a Committee on Public-Private Sector Relations in Vaccine Innovation and launched a study of vaccine innovation.²⁰ The National Academy was and is a high-status, professional organisation whose leaders and activities command respect in the nation's capital.

The Committee approached the problem by first sponsoring a conference on the barriers to vaccine innovation in 1983. "All of the committee's discussions were based," the ensuing report noted, "on the premise that a domestic vaccine industry is essential to ensure vaccine innovation and availability in the United States. This assumption derived from an understanding of the unique features of vaccine production: the difficulty of quality control for biological products, the length of the production cycle, and specific problems that would

be created by sole reliance on foreign manufacturers.”²¹ The European healthcare systems were thus not alone in favouring national champions.

The Committee's 1985 publication, *Vaccine Supply and Innovation*, focused attention on the problems that appeared to block the development of new vaccines: “Technical problems, high research and development costs, the expense and logistics of clinical testing and surveillance of reactions; the risk of litigation over untoward events associated with vaccine use (whether causally related or not), and limited sales.”²² As the Committee recognised, the government could employ a state-owned enterprise (SOE) in vaccines, but the Committee's report opted for a less radical solution using the existing private organisations in the vaccine industry: “A government production bureaucracy in the role of a sole supplier might not be subject to the market pressures that often lead to innovation and the application of new technologies.”²³

The primary barrier in the private sector, the Committee concluded, was the common-law tort system of handling liability for vaccine-related injuries. This approach “had left manufacturers apprehensive and uncertain about the extent of their responsibilities beyond proper manufacturing and labelling.” Recent decisions had left manufacturers liable for injuries even when the vaccines were properly produced and labelled. The Committee called on the government to develop a new compensation system for those injured by vaccines.²⁴

The Committee and the National Academy were successful in solving one part of the problem of the commons in vaccines.²⁵ Given the lack of any government response to the previous studies of the vaccine problem, one might have expected that the report would be followed by polite acknowledgements and political inaction. But that was not the case.

Responding to the call for a statutory solution to the liability issue, Congress passed the National Childhood Vaccine Injury Act in 1986. The new law created a system involving government-funded compensation for children injured by vaccines along the lines of the existing programs in other countries, including the United Kingdom.



The UK's Vaccine Damage Payment programme clearly was more efficient and effective than the common-law tort system in protecting both citizens and companies supplying vaccines.²⁶ Concerned about the sudden and sharp decline in the number of manufacturers producing paediatric vaccines, Congress also funded the National Childhood Vaccine Injury Program in 1987 to administer the new system.²⁷



The Committee and the National Academy were less successful, however, in dealing with the problem produced by the industry's low profit margins. The Committee recognised that the costs of developing new vaccines were out of line with the sales that could be anticipated by the manufacturers. The perfectly rational response was to spend less on research and development in vaccines, and indeed, new product introductions had gradually declined in the 1970s. Looking for the source of this problem, the report acknowledged that patents played only a minor role in vaccines and that the manufacturers thus had less protection than firms producing pharmaceuticals. Regulation also imposed more of a constraint on vaccines than it did on pharmaceutical producers because of the relatively small revenues in preventive medicine.

That brought the study to the heart of the matter - the market for vaccines - but the Committee found it difficult to confront this issue. The report observed that a significant percentage of the industry's revenues (40 per cent or more) came from government purchases and that this gave the buyers substantial market power against suppliers. In effect, large government purchases constituted an "oligopsony," a situation that exists when a small number ("oli") of buyers dominate a market. Economist John Kenneth Galbraith analysed oligopsony in his lucid 1952 study of the dynamics of institutional change, *American Capitalism: The Concept of Countervailing Power*.²⁸ Galbraith pointed out that strong buyers tend to produce strong sellers on the other side of the market: thus, "Economic power is held in check by the countervailing power of those who are subject to it."²⁹ Indeed, the Commission noted that the decline in the number of firms providing vaccines had gradually created a "loose oligopoly" on the seller's side of that market. But the Committee did not follow that line of reasoning to its logical conclusion: oligopsony was

producing oligopoly, a structural response to market power and low-margin sales. On this point, the Committee concluded, rather tepidly, that it did not have the information it needed to deal with this issue in detail. Instead, the report employed the customary academic and bureaucratic gambit of tossing the issue into the hands of some future group of analysts: “Further actions should be considered if the available protection of property rights appears insufficient to stimulate the desired level of innovation.”³⁰

The 1985 study left little doubt, however, that there were serious problems - a common or social problem involving both innovation and supply - in the vaccine markets. It was unlikely that the decline in suppliers would be reversed by the new legislation reducing risk for part, but not all, of the vaccine products. It was unlikely that government or private purchasers of the industry's products would look for and then find ways to pay more for vaccines and reduce the burden of the cost-price squeeze on manufacturers. Public agencies faced their own fiscal problems and were unlikely to engage in economic engineering that contradicted the public health quest to provide the most assistance, including immunisation, to the most people. Public health has a powerful ideology and its practitioners were likely to see and condemn any such effort as a nefarious form of corporate welfare.

This left the United States and very soon the global industry with a classic case of “the problem of the commons.” All of the participants in the vaccine market were seeking to achieve their individual goals. But none of the participants was responsible for the long-term performance of the entire vaccine industry - that is, the commons - or any distinct branch of it insofar as innovation and supply were concerned.

So despite the expressed interest in restoring the vaccine industry to the condition that had existed in the golden era, the issue fell off the public agenda - but only for a few years.

Globalisation and the Second Vaccine Crisis

In the following years, dramatic changes in the global economy and in the pharmaceutical industry produced a second wave of changes in vaccines. The age of national champions gave way to a determined drive by the developed nations to lower barriers to trade. Globalisation in the last two decades of the twentieth century opened overseas markets to the small number of firms left in the vaccine industry.³¹ No longer were European



healthcare systems insulated from the effects of the contraction in the industry. In effect, the commons was now global.

Meanwhile, consolidations transformed pharmaceuticals and spilled over into the vaccine business. New approaches to competition policy facilitated mergers and acquisitions, as did the drive to get up to scale for innovation, production, and distribution on a global basis.³² Burroughs Wellcome and Glaxo merged in 1995 to form Glaxo Wellcome. The following year Ciba-Geigy and Sandoz Laboratories merged to form Novartis. Pasteur had meanwhile been acquired by Mérieux and the combination had later been absorbed into Aventis, which in turn merged with Sanofi; the vaccine organisation thus became Sanofi Pasteur. As a result, the number of major vaccine producers in the world actually declined in the years following the Institute of Medicine study and the creation in the United States of a new government programme to reduce the risk of supplying paediatric vaccines. During these years, competitors in the industry also had greater freedom to develop alliances, such as the joint venture for the EU between Pasteur Mérieux and Merck Sharp & Dohme.³³

It was in this setting that the second vaccine crisis began with a political attack on the industry from an entirely new angle. No longer were the central concerns innovation and supply. In 1993, the Clinton Administration charged vaccine producers with preventing the immunisation of American children by

charging high prices for paediatric products. There was no reliable evidence that this was true, and there was substantial evidence to the contrary. But legislators could not appear to be opposed to preventive medicine for children, and Congress duly passed legislation to promote immunisation of certain selected groups of children.³⁴

After the smoke had cleared from this political imbroglio, the public concern about vaccines in America and Europe shifted back to the two issues of greatest concern in the 1980s: innovation and supply. There were also periodic concerns about the safety of vaccines. These normally declined after the media stopped raising the issue, but underplayed the effects that such crises can have on both the supply of vaccines and confidence in them.³⁵ Nevertheless, the concerns were strong enough to persuade the World Health Organisation to create a Global Advisory Committee on Vaccine Safety in 1999.³⁶ The safety issue was important primarily because it impaired the industry's public image and thus its ability to work with governments to solve the problems related to innovation and supply. The latter problems, much deeper problems, would not go away.

The safety issue was magnified because it developed at a time when the public image of pharmaceuticals had reached a low point. Concern about the HIV/AIDS crisis in the developing world, about increases in pharmaceutical prices, and about the problems arising in healthcare in all of the developed nations combined to focus media attention on the negative aspects of the entire industry. This swirl of journalistic criticism came at a time when the pharmaceutical industry was most vulnerable because it had hit a flat phase in new drug development and could not point to its record of blockbuster innovations to counter the critique.³⁷

The safety and supply issues in vaccines were compounded in 2004 when the United Kingdom's regulatory authority (MHRA) suspended the manufacturer's licence of the Chiron flu vaccine plant in Liverpool, England. An investigation prompted the company to delay shipments before the suspension of the licence. Because the plant was scheduled to supply 46 to 48 million doses to the United States, the US Congress became involved, as did the US Securities and Exchange Commission. This intensified a crisis that was already forcing

public officials to be concerned about the small number of producers for vital vaccines. It was a year before the Chiron plant began shipping vaccines again.³⁸

The Chiron problem had one prominent silver lining, because it was followed by a decision on the part of Novartis to buy the share of Chiron that it did not yet own. The Swiss firm already owned 42 per cent of Chiron, and after completing the purchase of the remaining shares, it set out to increase its role in the global vaccine business. This was the type of research-oriented firm with significant production and distribution capabilities that the vaccine business had lost in the years since the mid-1970s. Novartis was the world's fourth largest pharmaceutical company (based on sales in 2006) and by purchasing Chiron, it immediately became the world's fifth largest vaccine firm. Novartis is now providing vaccines against: meningococcus C, rabies, tick-borne encephalitis, *Haemophilus influenzae* type b, polio, mumps, measles, rubella, diphtheria, tetanus and whooping cough (pertussis). To promote its growing vaccine business, Novartis is investing £100 million in a new, state-of-the-art manufacturing facility in Speke, Liverpool.



Thanks to scientific progress in molecular genetics and biotechnology, a number of small research firms also entered what had become a truly global industry and began to focus their attention on vaccine research and development. These firms did not have the clinical and production capacity to bring new products to market, but they could, if their research was successful, join forces with larger firms for the clinical testing, regulatory procedures, production and distribution phases of the vaccine business. By themselves, however, the biotechs were no more able than governments or professional organisations had been to solve the problem of the commons in the vaccine business. For insight into what might be the solution to that problem and appears to be the first phase of recovery from the decline of the 1970s, we need to look into recent developments in the UK vaccine industry.

Monopsony and Oligopoly in the United Kingdom



The vaccine sector in the United Kingdom is similar to that of the United States, but the demand side of the UK market is very close to being a monopsony (with a single buyer). The Department of Health, General Practitioners, and the NHS Trusts all purchase vaccines, following EU procurement directives.³⁹ For a substantial number of their products, the Department and the NHS Purchasing and Supply Agency

(the Agency) use restricted bidding: only those invited to participate are allowed to present tenders - that is, make bids. Other vaccines are tendered under open procedures. Both the Department and the Agency receive technical guidance on the need for vaccines, on immunisation practices, the quality of vaccines, and other specific matters from a Joint Committee on Vaccination and Immunisation and sub-groups of experts within the Committee.

Predictably, the Department and the Agency attempt to encourage competition and the development of more than one source of supply. Increased competition on the supply side increases the market power of the monopsonist. This creates a paradox because “The main reasons for the narrow market relate to the high and increasing cost of vaccine development and production, mergers of manufacturers and the relatively low profit margins compared with other pharmaceutical products.”⁴⁰ In that regard, the UK and the US demand-side situations were producing similar results: in the short term, narrow profit margins; in the long term, concentration on both sides of the market. The major differences between the two markets were the large size and lower level of concentration on the demand side of the American market.

Despite the problems of confronting monopsony in the UK, the major firms have remained innovative - in part because globalisation leaves them less

dependent upon any single national market. GlaxoSmithKline (GSK) became a prime global competitor and innovator in vaccines following the 2001 merger of Glaxo Wellcome with SmithKline Beecham.⁴¹ The company, headquartered in London, now produces a number of the important vaccines used in the UK, and its global vaccine business had sales in 2007 of £2 billion - an increase of 20 per cent over the previous year.⁴² The firm's leading products include its hepatitis A and B vaccines, its combination A/B vaccine, its new vaccine against human papillomavirus (HPV), and its flu vaccine. In 2007 GSK had sales of £146 million for its pre-pandemic vaccine. The company, which has been investing heavily in new vaccine research and production facilities, has in recent years developed a vaccine that could prevent relapse in cancer patients. GSK Bio currently has 24 vaccines in clinical trials - many of them the combined vaccines that facilitate immunisation.⁴³

Both GSK and Novartis have also tackled the thorny problems of discovering and producing vaccines for the developing world. Since neither individuals nor national health systems in the developing countries can afford to pay for the preventive medicines they badly need, research for vaccines against tropical diseases has lagged badly. Now, however, GSK Bio is working on vaccines that could be effective against malaria and Dengue fever. The Novartis Vaccines Institute for Global Health is also focusing its research efforts on diseases that have been devastating to the populations of developing nations.⁴⁴

Sanofi Pasteur MSD combines in a joint venture the vaccine capacity and research facilities of two leading vaccine companies. Sanofi Pasteur has roots that reach back into the beginnings of modern medicine and the era of the world's first successful vaccines and serums. Sanofi Pasteur, which is the vaccines division of sanofi-aventis group, provided global markets in 2006 with over a billion doses of vaccine directed against 20 diseases. The firm has a strong position in flu vaccines and the joint venture with MSD supplied several of the top vaccines (by global sales) in 2007. In addition to the flu vaccine, the joint venture's leading products included paediatric combination vaccines, travel vaccines and a vaccine against pneumococcal infection.⁴⁵ MSD's contributions to the joint venture also include vaccines against human papillomavirus, rotavirus, and shingles.⁴⁶

Wyeth Vaccines is responsible for introducing the world's first billion dollar vaccine: *Prevenar* prevents serious diseases caused by *Streptococcus pneumoniae*. Wyeth also produces a meningococcal C vaccine and distributes a flu vaccine for the UK market. Given the recently reported incidence of pneumococcal and meningococcal diseases across Europe, the demand for these two vaccines is likely to grow substantially - as is the demand for flu vaccine.⁴⁷

The threat of new influenza pandemics and the political concerns about adequate supplies of vaccine have encouraged the existing suppliers to increase their capacities and have brought two other major competitors back into the industry. In October 2006, Pfizer acquired PowderMed, a UK-based firm with capabilities in DNA vaccines. Pfizer's pipeline now includes vaccines against influenza, HPV, and hepatitis B. Meanwhile, AstraZeneca has acquired MedImmune, a US firm, and with it the FluMist vaccine.⁴⁸ Baxter International Inc supplies pandemic influenza vaccine, and Solvay Pharmaceuticals is producing seasonal flu vaccine. UK biotech firms have been less aggressive about vaccine research than the US biotechs, but Oxford-based British Biotech has engaged in vaccine research, as has Acambis, which became a primary supplier to the United States of smallpox vaccine. Oxford BioMedica, Cobra, and Xenova have also been involved in research on a number of experimental vaccines.⁴⁹

This brief survey of the UK industry suggests that the global vaccine enterprise is on the threshold of a new era of expansion and innovation, an era that could witness the global vaccine commons restored. The causes for this revival cannot be traced to the public sector either in the UK or the US. Nor is it a product of the excellent professional studies that have been focusing attention on the problem of the vaccine commons for the past quarter of a century. The two influencing factors are instead the lower levels of innovation in pharmaceuticals and the new science and technologies flowing from the molecular genetic revolution and biotech. This push and pull has edged some of the world's large pharmaceutical firms back into a business they formerly eschewed.⁵⁰

These transitions swung the balance in supply and to a lesser extent in innovation of vaccines back toward Europe and away from the United States.

While North America is still the largest single market for vaccines, almost 90 per cent of the world's production now takes place in Europe. Only about a third of the sales are in Europe; most go to North America and the developing countries. But two-thirds of the vaccine R&D is now being conducted by European firms. Almost all of the European investment in R&D (22.5 per cent of sales) comes from the private sector, and almost all of it is focused on new vaccines.⁵¹ If these developments continue, we may indeed have a second golden era of vaccines.

What are the Current Threats to Innovation and Supply of Vaccines in the UK and US?

While the vaccine industries in both nations have thus experienced encouraging entries and increased capacity, it should be apparent that nothing has, or is likely to be done, to remove the threat to the commons - that is, to the ability of the industry to develop the innovations needed and ensure adequate supplies of vaccines.

Margins will remain tight and may become tighter.⁵² Pressure to reduce healthcare costs in both nations are likely to continue for many years, as reflected in the UK's concern with the Pharmaceutical Price Regulation Scheme and in the steady

decline of health insurance protection in America. There is no mechanism in either country for ensuring that each individual purchasing organisation will not drive the best bargain possible for its clients. Indeed, all are under significant pressure to continue doing just that. Where they have market power, they are likely to exercise it and once again threaten the commons.



Any general economic decline that reduces public health budgets for preventive medicine such as vaccination will negatively impact investment in R&D and in increased capacity in areas such as influenza.⁵³ As the American situation of the 1970s and 1980s clearly indicates, governments are slow to

respond to the sort of structural change that took place in vaccines. As the political attacks of the Clinton Administration clearly indicate, there is substantial political capital to be acquired by attacking big pharma on almost any issue, including vaccines. If such attacks and narrower margins start another wave of decline, the public sectors in both nations will probably be as poorly equipped as they were in the past to introduce measures that will restore the health of this vital industry.

Does that mean we can do nothing to improve the prospects for a new golden era in vaccines? No, I think there are three measures that will help ensure a golden future in this wing of preventive medicine. First, we should continue to support the basic science that was the necessary foundation for the successes of the past and which promises to play the same role again. Second, we should do everything possible to prevent or counteract poorly conceived political and media attacks on the industry, like those that were launched in the United States in the early 1990s. Third, we should attempt to promote in all of our public health agencies attitudes toward negotiating that recognise the long-term needs of society as well as the short-term needs of the agencies' budgets.

What are the chances that we can be successful on all three counts? The first proposal seems achievable in both the United States and the United Kingdom without radical changes in either the public or private sectors. The second calls for statesmanship and greater political collaboration, both of which are likely to be in greater supply in the UK than in America. The third will be the most difficult to achieve in the foreseeable future. The problem has been well-defined for over two decades now. But the solution may require more transparency, industry-government collaboration, and compromise than either nation is capable of mustering. That being the case, we may be facing more tragedies of the vaccine commons.

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- ³ Garrett Hardin, a professor of human ecology, has written extensively on the problem of the commons; see, for instance, his article in *Science*, 162 (1968), 1243-48. As he notes in *The Library of Economics and Liberty*, William Forster Lloyd of Oxford University pointed out the problem in 1832 "looking at the recurring devastation of common (i.e., not privately owned) pastures in England...." www.econlib.org/library/Enc/TragedyoftheCommons.html.
- ⁴ Susan L. and Stanley A. Plotkin, "A Short History of Vaccination," in Stanley A. Plotkin and Edward A. Mortimer, Jr., *Vaccines* (Philadelphia, 1994), 5-6, including Table 1-1.
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⁹ D.M.Salisbury, P.C.L. Beverley, and E. Miller, “Vaccine programmes and policies,” *British Medical Bulletin* 2002, 62, 201. See also UVIG, “Vaccination: a good investment for society,” July 2007.

¹⁰ See CDC, “Achievements in Public Health, 1900-1999: Impact of Vaccines Universally Recommended for Children - United States, 1990-1998,” *MMWR*, April 2, 1999, 48 (12), 243-48. Fangjun Zhou, et al., “Economic Evaluation of the 7-Vaccine Routine Childhood Immunisation Schedule in the United States, 2001,” *Archives of Pediatrics & Adolescent Medicine*, 159, 12 (December 2005), 1136-44. Walter A. Orenstein, “Testimony on the Immunisation Grant Program of the PHS Act”, May 6, 1997, www.hhs.gov/asl/testify/t970506a.html.

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¹² Rino Rappuoli, Henry I. Miller, and Stanley Falkow, “The Intangible Value of Vaccination,” *Science*, 297 (August 9, 2002), 937-39. Maurice R. Hilleman, “Vaccines in historic evolution and perspective: a narrative of vaccine discoveries,” *Vaccine*, 18 (2000), 1436-47.

¹³ See Paul A. David, “Path Dependence, Its Critics and the Quest for ‘Historical Economics,’” in P. Garrouste and S. Ioannides, eds., *Evolution and Path Dependence in Economic Ideas: Past and Present* (Cheltenham, 2001); and “Clio and the Economics of QWERTY,” *American Economic Review* 75 (May 1985): 332-37.

¹⁴ E. W. Kitch and E. A. Mortimer, Jr., “American Law, Preventive Vaccine Programs, and the National Vaccine Injury Compensation Program,” in Plotkin and Mortimer, Jr., *Vaccines*, 933-57. I am distinguishing here between risk, which can be managed insofar as it has certain well-defined aspects, and uncertainty. Uncertainty is characteristic of situations in which the variables cannot be specified or understood well enough to be anticipated or otherwise managed. Frank Knight, *Risk, Uncertainty, and Profit* (Boston, 1921).

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¹⁶ Lilly continued to produce rabies vaccine because it was the only company supplying the U.S. market for this product. The information on Lilly's decision is from a "History of Pneumococcal Research" in the Merck Archives.

¹⁷ The Merck study concluded that "No company currently not in the vaccines business would (logically) choose to get in." H. Lipmanowicz, "Vaccine Study - 1979 (Merck Archives, August 1979).

¹⁸ Merck's international division, Merck Sharp & Dohme International, could not at that time make any vaccine sales in Britain, France, Germany or Italy.

¹⁹ The study did, however, receive financial support from the Food and Drug Administration, the Department of the Army, and the Centers for Disease Control, as well as private firms and foundations.

²⁰ The mission of the Institute, which was chartered in 1970, was "to enlist distinguished members of the appropriate professions in the examination of policy matters pertaining to the health of the public."

²¹ Institute of Medicine, *Vaccine Supply and Innovation* (Washington, D.C., 1985), ii, v-vi. The Committee's Government-Industry Liaison Panel included representatives from the following private organisations: Burroughs Wellcome Company; Wellcome Research Laboratories; Lederle Laboratories; Mériex Institute; Wyeth Laboratories; Merck Sharp & Dohme Research Laboratories; Parke-Davis; Cutter Laboratories; Connaught Laboratories, Limited; Eli Lilly and Company.

²² *Ibid.* 4.

²³ *Ibid.* 5-6. There was, however, an implied threat that "direct government production" might be required at some time in the future. It would not be too many years before that possibility would arise again.

²⁴ *Ibid.* 12-13, 65-122.

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²⁶ The UK introduced its Regulatory Reform (Vaccine Damage Payments Act), Order 2002, in 1979. The plan provides a one-off, tax-free, lump-sum payment to those severely disabled by vaccination. The sum increased over the years and is currently £120,000. www.opsi.gov.uk/si/si2002/20021592.htm. The plan was introduced following the report of the Pearson Commission in 1978 recommending a no-fault scheme of compensation that would replace civil law with an administrative, non-adversarial programme.

²⁷ E. W. Kitch and E. A. Mortimer, Jr., "American Law, Preventive Vaccine Programs, and the National Vaccine Injury Compensation Program," 933-57. The number of producers had dropped from 7 to 2 for DPT (diphtheria-tetanus-pertussis combined vaccine); from 3 to 1 for oral poliovirus vaccine; and from 6 to 1 for measles vaccine.

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³⁰ Institute of Medicine, *Vaccine Supply and Innovation*, 45-64.

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