



# THE NEW GLOBAL ECONOMICS OF VACCINES: WILL THE SCIENTIFIC POTENTIAL BE REALISED?

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with an introduction by  
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13th Annual Lecture 2006



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## **Office of Health Economics    [www.ohe.org](http://www.ohe.org)**

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# **Introduction:**

## **Professor Patricia Danzon**

### **Background**

For the purposes of defining the economic and policy issues facing the vaccine industry, the comments made here are based largely on the experience in the US, but with some discussion of the global vaccines environment.

Almost every paper in the literature on vaccines starts off with the observation that vaccines are among the most cost-effective of medical interventions, and yet the unfortunate situation (although perhaps not surprising to an economist) is that supply is precarious.

Some facts from the US will help to illustrate this situation. In 1967, there were 26 licensed vaccine manufacturers in the US; by 2004 there were only 12. In addition, and of greatest concern, there are now only one to three producers for each of the main paediatric vaccines. This has resulted in temporary but significant supply shortages for most of these vaccines, involving interruptions to paediatric vaccination schedules, when these suppliers have experienced production disruptions.

Against this pessimistic picture, however, there is now great excitement over the new generation of vaccines. Some of these are emerging from GSK and the other two remaining large multinational producers; however, there are also new entrants into the vaccine market, including a couple of large multinationals that have recently returned to the market, as well as some new small start-ups.

Notwithstanding these recent developments, it is worth revisiting the fundamental economic aspects of the vaccine industry which favour the dominance of a sole supplier. Research indicates that this has been the result of the interaction of supply and demand and, in particular, of the special characteristics of demand and supply in this industry (Danzon et al., 2005).

### **Demand and supply in developed countries**

There is relatively limited demand for childhood vaccines, as annual demand and therefore sales are largely defined by the size of the birth

cohort. In contrast, the general characteristic of chronic diseases is that people take a chronic medication every day for many years, which offers the prospect of much greater annual sales for producers.

Secondly, because of the substantial social benefits from vaccines in the form of externalities, there is a greater role for government procurement. This is the case even in the US, where the government mandates the key childhood vaccines and undertakes procurement for the low-income population. Lessons have been learned over the last couple of decades from the procurement of childhood vaccines in the US. Prior to 1993, the Centers for Disease Control and Prevention (CDC) purchased vaccines using a winner-takes-all approach, with all the business going to the lowest-priced bidder. The result was extreme supply uncertainty for manufacturers because when government purchases represent a significant fraction of the market, failing to obtain that business can leave a manufacturer with a large stock of vaccine but no potential market. Since the 1993 Vaccines for Children programme, the US government's purchasing strategy has changed. Now the CDC solicits bids and posts the prices, but then decentralises purchasing decisions to individual states. Nevertheless, price competition and volume uncertainty remain, albeit reduced by this change in policy, and such uncertainty tends to increase with the number of potential suppliers.

On the supply side, the vaccines sector of the pharma/biotech industry is characterised by high fixed costs and low marginal costs, at least up to a given capacity. 'Fixed costs' here include the regulatory costs associated with the requirements of the US FDA, the UK MHRA or the European EMEA. They also cover plant and capacity costs, determined to a large extent by quality control requirements, and batch-related fixed costs. Marginal cost per unit is minimal up to the fixed annual capacity, after which adding capacity can take years and is extremely costly. One implication of this supply structure is that when one supplier encounters temporary supply problems, due to plant contamination or other factors, it is difficult if not impossible for other suppliers, if they exist, to make up for the shortfall. This situation has occurred with respect to the flu vaccine and a number of paediatric vaccines.

Other supply-related factors tend to exacerbate risks to supply security. First, some of the traditional technologies used in the manufactur-

ing process yield vaccines with a limited shelf life. From the manufacturer's point of view, this means that production that is not sold goes to waste. From the purchaser's standpoint, it means that a steady flow of supply is essential to meeting current demand. Second, liability risks have traditionally been a very significant threat to vaccine suppliers. This threat has been reduced in the US by the creation of the Vaccine Injury Compensation Fund, which provides compensation on a no-fault basis, funded by a tax on vaccines, for covered vaccines. However, liability risks remain an important concern in the event of loopholes in this Act and for non-covered vaccines. A further significant feature of vaccines supply is the absence of cheap generics, due to both the limited size of the vaccine market and the lack of an abbreviated approval process for "biosimilars" through the FDA. Thus, patent life does not determine the end of the economic life of a vaccine. Rather, some vaccines continue to be used for many years and economic life tends to end only when a superior vaccine enters the market.

Putting the two sides of the market together, the US vaccine market consists of several public and private purchasers who take competitive bids from a limited number of high fixed cost firms. If each firm can potentially supply the entire market, then the competitive market equilibrium in this situation results in price falling to the level of marginal cost. However, if price consistently falls to marginal cost, no supplier is able to cover its fixed costs.

In such a situation, if there is initially competition between multiple suppliers, then the natural equilibrium will tend to result in the exit of all but one firm, leaving a sole supplier as the norm for each type of vaccine. What is interesting about this model is that the few suppliers or sole supplier outcome is not due to regulation of prices, as is commonly alleged, but rather is due to competition in the face of high fixed costs, which drives down prices to unsustainable levels as long as multiple suppliers compete for the market.

While multiple suppliers may co-exist for some vaccines, sole supplier equilibrium in each national market is more likely if there are high country-specific regulatory costs or if the markets are segmented nationally by product type, with reduced potential for global diffusion. Such geographic segmentation by product type could reflect national vaccine policies and preferences. However, it may also reflect the failure of differential pricing, such that manufacturers of the newest

vaccines are unable to sell these new vaccines at lower prices in developing countries without undermining the higher prices they need to charge in developed countries in order to cover fixed costs. In such circumstances, developing countries will be supplied by older vaccine types at lower prices.

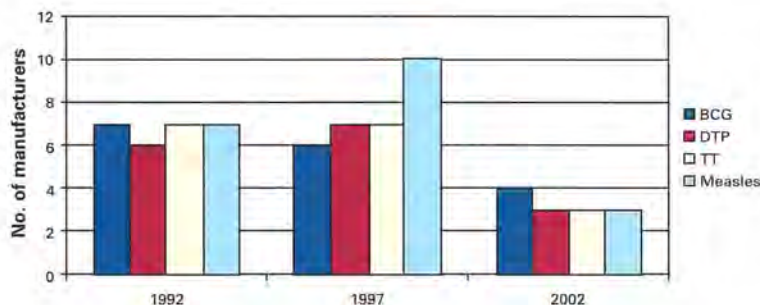
### **Developing country markets – the UNICEF experience**

Developing countries make up a significant proportion of total demand for vaccines. The following draws on a presentation given by Steve Jarrett, then Deputy Director of the Supply Division at UNICEF, at a conference at the Wharton School in 2003. At that time, purchasing by UNICEF on behalf of low-income countries accounted for 40% of global volume, although this represented only 5% of global market value. UNICEF has learned that, in order to maintain multiple sources of supply, it is necessary to contract with several suppliers, rather than award all the business in any year to the lowest bidder.

In developing countries, instead of using the same vaccines as in the higher-income countries at lower prices, the market has essentially segmented such that the products supplied are different from those supplied to the developed economies. Uptake of newer vaccines has remained slow because of higher prices, making them less affordable and less cost-effective than lower priced, older vaccines. One of the challenges for the new generation of vaccines is whether differential pricing will be possible, such that these vaccines can be affordable for developing countries in a timely fashion, rather than with the long delays that have occurred in the past.

The slides from Steve Jarrett's presentation illustrated UNICEF's experience of manufacturers exiting the market so that, by 2002, only three or four suppliers remained for this large segment of the market (Figure 1). Since then, a policy of intentionally allocating total demand between several suppliers has been introduced in order to maintain multiple suppliers.

**Figure 1: Number of manufacturers offering basic vaccines to UNICEF dropped to 3-4 by 2002: developing country manufacturers are now the principal producers**



Source: Steve Jarrett (UNICEF), 2003

Notes: BCG = bacillus Calmette Guerin vaccine, which provides immunisation against Tuberculosis (TB)  
DTP = diphtheria, tetanus, pertussis  
TT = tetanus toxoid

In recent years UNICEF has been buying vaccines from Brazil, Cuba, India, Indonesia, Korea and Senegal, which supply different variants of the standard vaccines (Table 1). For measles a mono-variant is being used, whereas the US and other high- and middle-income countries use the MMR combination. In the DTP combinations in low income countries, whole cell pertussis is being used rather than acellular combinations.



Table 1: divergence of products has emerged between low and high-income countries

Primary disease compared to vaccine	Measles	Diphtheria, Tetanus, Pertussis	TB	Hepatitis B	Haemophilus influenzae type B	Polio
Low Income Countries	mono	wholecell	BCG	mono & in combo with DTPw	in combo with DTPw	OPV
Middle Income Countries	MMR	wholecell in combo	BCG	in combo with DTPw	in combo with DTPw	OPV
High Income Countries	MMR	acellular in combo	none	in combo	in combo	IPV in combo

Source: Steve Jarrett (UNICEF), 2003

Notes: BCG = bacillus Calmette Guerin vaccine, which provides immunisation against Tuberculosis (TB)  
 DTPw = diphtheria, tetanus, pertussis, wholecell vaccine  
 IPV = inactivated poliomyelitis vaccine  
 MMR = measles, mumps, rubella three-in-one vaccine  
 OPV = oral polio vaccine

There are huge price differences between the low-income and high-income countries (Table 2). However, these are not pure price differentials, because they also reflect differences in the products being used, because developing countries are still using the older-generation vaccines, produced by suppliers which are typically WHO authorised as opposed to EMEA- or FDA-authorised.

Table 2: Large price differences between high and low income countries reflect different products and producers: decline in differential pricing

Primary disease compared to vaccine	Measles	Diphtheria, Pertussis, Tetanus	TB	Hepatitis B	Haemophilus influenzae type B	Polio
Low Income Countries	14c	7c	7c	32-90c	\$3.10	10c
High Income Countries	\$15.50	\$10.65		\$9.00	\$21.38	\$8.25

Source: Steve Jarrett (UNICEF), 2003

With respect to the new vaccine technologies which are emerging, the big challenge being addressed in the policy debate is the optimal way to stimulate the production and commercialisation of the resulting vaccines, with much of the debate centring around 'push' versus 'pull' subsidies. 'Push' subsidies, in the form of contributions from public and philanthropic donors such as the Bill and Melinda Gates Foundation and other international donors, have had some success in generating new vaccine candidates, mainly by channelling funds to the R&D efforts of public-private partnerships. 'Pull' subsidies, which are now the focus of great interest, would involve the establishment of an Advanced Market Commitment whereby purchasers commit to purchasing a vaccine that meets prespecified requirements at a specified price. It is hoped that this type of arrangement would give sufficient market certainty such that private sector suppliers would be willing to make investments in the fixed costs of expanding plant capacity to serve developing countries and, ultimately, to invest in R&D for new vaccine development.

Thus, supplying new vaccines to developing countries entails a chicken-and-egg problem: suppliers are not willing to make investment commitments until they are confident of adequate demand and ability to pay, while purchasers - developing country governments and philanthropic donors - are reluctant to commit to purchase without assurance of product efficacy, safety, quality and price. These features of the market provide the context for the environment which Dr Stéphenne faces with some of the new vaccines that GSK has developed.

## Reference

Danzon P M, Pereira N S, Tejwani S S (2005). Vaccine supply: a cross-national perspective; how do the economics of vaccines differ in the United States from other countries, both industrialized and developing? *Health Affairs* 24(3):706-717.

# **THE NEW GLOBAL ECONOMICS OF VACCINES: WILL THE SCIENTIFIC POTENTIAL BE REALISED?**

**Jean Stéphenne**

## **Background**

In attempting to provide some answers to the questions identified by Patricia Danzon, it is worth highlighting a feature of the market not previously discussed, namely that the development of a new vaccine today (with testing in 10,000 or 20,000 children or adults) is almost as expensive as the development of a drug. Given an environment in which the development process and requirements for quality in manufacturing of modern vaccines imply costs approaching those of other medicines, the question is whether the return on investment in the vaccines industry can compete with that in pharmaceuticals. The answer put forward here is that it can, and for two reasons.

The first is the high failure rates in drug development and the consequent (minor) crisis in the pharmaceutical industry where innovation is generating insufficient numbers of new drugs and consequently insufficient return on investment. The second reason is the advantage vaccines have due to their biological basis. Reinforcing Patricia Danzon's point about the lack of cheap generics for regulatory reasons, the complexity of manufacturing biologicals also means that price cuts at patent expiry are likely to be less than for non-biological medicines, given that payers and regulators are concerned to ensure high quality.

When a medicine is produced, it is known that at the expiry of the patent its price falls by a substantial percentage. While Pfizer's Lipitor has \$10 or \$12 billion of annual sales now, on the day of patent expiry, these will fall dramatically in value terms. An important factor from an economic viewpoint is that, with the new and more complex technology in vaccines, they will probably have a longer time to recover their investment than many new medicines. Indeed, this is likely to be the

only means of achieving an adequate return.

In the UK it is important to re-state the achievements that vaccines have already made, because the British press has a tendency to be critical of vaccines and their value has often gone unrecognised. However, a new era is dawning and the next five years may well prove to be a golden age for the vaccine industry. As a result of the efforts which have been made during the last 20 years, many new vaccine products will reach the market.

There are two major challenges for the industry. The first is to make new vaccines available. The second is to enhance the value of vaccines, whose prices should be commensurate with their value. It should be noted that a price of 7¢ or 8¢ at which some existing vaccines are sold will not support the manufacturing costs of modern vaccines.

### **The achievements of vaccines in the UK**

Vaccines represent major achievements in the fight against smallpox, polio, measles, diphtheria, tetanus, rubella, meningitis and hepatitis B. If there is a measles epidemic today, it is because the vaccine is not used<sup>1</sup>. Disease outbreaks mean that people do not yet recognise the value of the vaccine and reflect the difficulty of convincing people of the benefits that vaccination provides, not only from an individual perspective but also from a societal point of view. There is still a need to educate those who do not vaccinate that they are putting others at risk as well as themselves.

If proof were needed of the achievements of vaccines, they are amply illustrated by the observed re-emergence of disease as soon as people stop vaccinating. Greater awareness of the benefits of vaccination is needed, but sadly the best awareness campaign, and the best marketing tool for vaccines, is the re-emergence of infectious diseases. Today, everyone knows about the flu pandemic and link it with the need to vaccinate.

Table 3 gives some statistics on the impact of vaccines in the UK, where a remarkably successful vaccination programme has yielded, for many diseases, major advances in disease control. An even more impressive picture for the UK would emerge from the addition to the table of meningitis C, for which the US is a good example. The difficult task is remaining vigilant to ensure that these achievements continue.

<sup>1</sup>In recent years, outbreaks of measles and mumps have occurred in Germany and the UK, respectively.

Table 3: Vaccine achievements – UK examples

Disease	Before immunisation			After immunisation		
	Year	No. of deaths	No. of cases	Year	No. of deaths	No. of cases
Diphtheria	1939	2,133	47,061	1996	0	12
Tetanus	1960	32	n.a.	1996	0	8
Pertussis	1956	92	92,410	1996	2	2,387
Haemophilus influenzae type b	1991	22	417	1996	0	38

*Note:* n.a. = data not available

It should be borne in mind that, despite the achievements of vaccines, utilisation globally is still limited. For example, while the Haemophilus influenzae type B (Hib) vaccine is widely used in the developed world (the US and Europe were the first two areas to adopt), the proportion of developing countries using the vaccine is probably less than 30%. Similarly, the benefits provided by the measles (rubella) vaccine have been concentrated on the developed world. The number of countries vaccinating against measles/mumps/rubella outside the wealthier countries is still limited.

### The future outlook

The outlook for vaccines is promising. Good research has been carried out in the last 20 years, with the right investment decisions being taken 10 or 15 years ago. Investing in R&D firstly requires a vision; secondly, work needs to be conducted on diseases where there is a medical need; and thirdly research must be focused on the right technology. Finally, it has to be done at the right time since development times for vaccines are as extended (i.e. 10 to 15 years) as those for other pharmaceutical products.

With this background in mind, there are two main reasons why a better period for developing vaccines beckons. Firstly, new vaccines are being developed as a result of new technology and, secondly, new markets are emerging. Today, it is possible to sell a flu vaccine at a higher

price to the private market in China than the average price at which it can be sold in the UK. India is another country where some people can buy the vaccine at a relatively high price. At the same time, the vaccine industry has a moral obligation to supply to all strata of society and the pressure is on the industry to do so. On the one hand, there is a need to defend higher pricing for those who can afford the vaccine but, on the other hand, there is a need to make sure that vaccines are available to the poorest. In the US, a balance has been found between the private market and the public market.

One aspect of vaccine development in which GSK has been an industry leader is in improving the adjuvant used in vaccine manufacture. A major hurdle is that, whenever a component of a vaccine is changed, its safety has to be demonstrated. The ability of aluminium to stimulate the immune system was recognised in 1925 and is still used today by the older vaccines. In the meantime, the progress made in immunology has resulted in substances with which certain cells of the immune system can be targeted to generate a better immune response than that achieved with aluminium. Demonstrating this to the regulatory authorities, however, has taken many years of research.

GSK was at the forefront of the developments of new adjuvants. MPL was licensed in 1991 and another adjuvant, QS21, was licensed in 1992, with the emulsion developed at around the same time. The history of these developments stretches back 15 years, when GSK decided to invest in basic research to develop a new substance which would stimulate the immune system.

The new adjuvants induce a stronger and longer lasting immune response. In addition, the immune system is taught to respond correctly to an antigen. The importance of teaching the immune system to respond correctly can be illustrated by the parallel of allergies. These affect so many people (as we are beginning to understand today) because they give the wrong response to the antigen. With a vaccine, the antigen which is presented to the immune system must elicit the correct response. Major progress has taken place in that regard, with the ability to target the immune system effectively being an important advance.

Much has been learnt with malaria, in which GSK has worked for 25 years with the US Army, about the stronger immune response provided by better adjuvants. The advantage of the malaria model is that it has been possible to have 'human challenge'. This involves giving

adults the candidate vaccine, exposing them to mosquito bites and subsequently monitoring the level of protection obtained. In attempting to understand what the vaccine does to the immune response, a range of adjuvants has been tested and developed.

A further advantage of improved adjuvants is that the active dose of vaccine can be reduced, thereby generating savings in terms of capital outlay. This is a significant issue given the complexity and expense of manufacturing vaccines, involving huge capital investments.

### **Current and future vaccine developments**

Since the mid-1980s, the explosive growth in vaccines has resulted in many new products appearing on the scene, such as HPV, meningitis, rotavirus, pneumococcal and dengue vaccines (Figure 2).

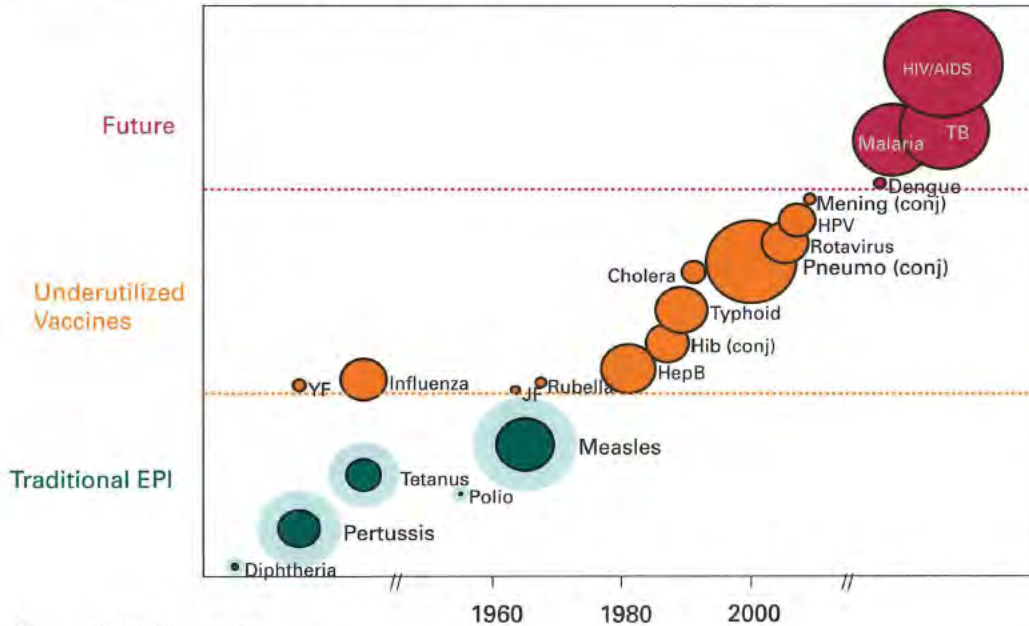
Work is currently underway to harness the benefits of new adjuvants to improve existing vaccines. For example, the flu vaccine, which has existed for many years, is known to be not particularly effective in the elderly since an elderly person's immune response is not as strong as that of a 20 year old. However, it is possible, with the adjuvants available today, to rejuvenate the immune system.

A new adjuvant has been applied to the human papillomavirus (HPV) vaccine, which GSK expects to launch in 2007, offering broader and longer-term protection. In the case of hepatitis B, it is known that some people do not respond to the vaccine but, with the new adjuvant, a response can be seen in people who might not otherwise respond, such as haemodialysis patients. Consequently there is now a candidate vaccine for such patients.

Another development in the pipeline is a pandemic flu vaccine or, to be more accurate, a 'flu pre-pandemic' vaccine. GSK's reasoning is that it is better to have a modern vaccine which could be used before a pandemic is declared rather than attempting to vaccinate during the chaotic conditions of the pandemic itself. GSK has carried out clinical trials of such a vaccine and is about to file for registration firstly in Europe and subsequently in the US.

The vaccines in GSK's portfolio include not only those being developed against infectious diseases, but also vaccines against cancer, a disease for which a number of products are likely to emerge in future

Figure 2: Vaccine development through time



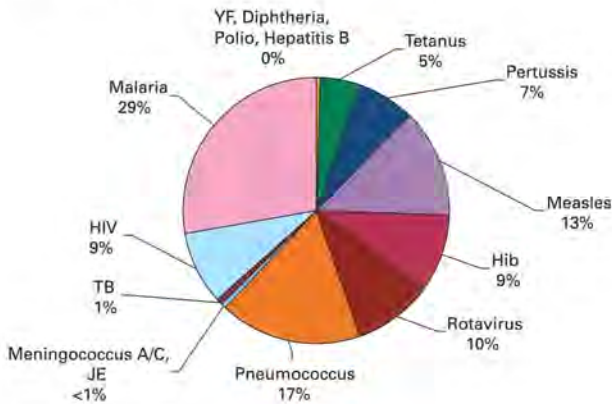
Notes: conj = conjugate vaccine  
 EPI = Extended Programme of Immunisation  
 JE = Japanese encephalitis  
 YF = yellow fever



years. For instance, GSK is currently testing a vaccine called MAGE-3 in melanoma and lung cancer. Although it will not avoid the need for surgery, chemotherapy or radiotherapy, it should help to prevent redevelopment of the cancer. In June 2006, GSK published results showing that the vaccine improves survival in lung cancer, an extremely severe form of cancer, by 30%, which is a huge improvement. Following this initial trial, the potential of a new version of the vaccine to improve on that figure will be tested. Combining new vaccines, which are described as 'immuno therapeutic', with 'gene profiling', it is possible to predict the response to a cancer vaccine. In future, cancer vaccines are likely to become a reality, as will allergy vaccines, for which the science base will also develop in the years to come.

The need for vaccines is illustrated by Figure 3 which shows the WHO estimate of the number of deaths of children under five years old in 2004.

**Figure 3: Causes of 4.1 million deaths in under-fives (out of 10.5 million total deaths) in 2002**



Source: World Health Report 2004

Notes: JE = Japanese encephalitis

YF = yellow fever

It is hoped that after 2010 vaccines against three worldwide threats – malaria, HIV and TB – will become a reality. While HIV/AIDS probably represents the most complex of the three, the other two diseases represent more immediate targets. GSK is currently working on a malaria vaccine which will be entering Phase III trials in 2007 with the

intention of providing a vaccine for Africa while, in tuberculosis, the development programme has reached Phase II. Vaccines have the potential to prevent many of the vast numbers of deaths attributable to these three diseases.

As Figure 4 shows, vaccine development is an extremely active area of research. Excluding HIV and TB but taking all other diseases into account, GSK will have a vaccine against 90% of the infectious diseases which kill children under the age of five. However, only 1.5% of the drug spend is currently devoted to vaccines. Considering the current pipeline, the aging population and the diseases that vaccines could help to tackle, the proportion of spending accounted for by vaccines needs to increase. Vaccines can play a major role in years to come, in treatment as well as prevention, but there must be an appropriate budget to reflect the contribution of vaccines to the world and the investment in their development. Once vaccines have been developed, the question is whether they will be utilised, given the need to reach nearly six billion people, comprising 900 million in the industrialized countries and five billion in developing countries. This is no longer a challenge for the scientific community but, especially in relation to developing country diseases, is one for the world.

### **Vaccine funding requirements**

In high income countries the vaccines budget needs to be increased by a multiple of its current size. In the case of the UK, the vaccines budget needs to be quadrupled in order to provide access to new vaccines over this period. Germany is in a better position because *Streptococcus pneumoniae* vaccine has already been introduced.

In low income countries billions of dollars are needed to put vaccination programmes in place. To reach the target reduction in child mortality proposed by Chancellor of the Exchequer Gordon Brown by 2015, GAVI (formerly the Global Alliance for Vaccines and Immunisation, which relates to countries where average annual income is below \$1,000 per head) needs to spend \$18 billion on new vaccines in the years to come. These figures assume that the HPV vaccine against cervical cancer, which is a vaccine for all women, will be restricted to a cohort of 10 to 12-year-olds, otherwise the numbers would be much larger. The issue facing every country of the world is whether the money can be found to fund vaccination programmes.

**Figure 4: GSK Biologicals' vaccine pipeline**

March 2006-GSK Biologicals

Pre-clinical	Phase I	Phase II	Phase III / Filed
Staph.aureus *	HIV	<i>Mosquirix</i> *	<i>Cervarix</i> *
Allergy *	TB *	Flu improved	<i>Simplirix</i>
SARS *	Varicella Zoster	Epstein-Barr virus *	DTPw-HepB-Hib-MenAC
Chlamydia *	S. Pneumo elderly *	MAGE-A3 NSCLC & Melanoma (1) *	PHiD-CV *
	HER2 (breast cancer) (1)	Hib-MenCY-TT	<i>FluLaval</i>
Other Cancer *	P 501 (prostate cancer) (1)	MenACWY-TT	Flu Pandemic
Respiratory Syncytial Virus	S. Pneumo paediatric	Hepatitis E	<i>Priorix Tetra</i>
Flu cell culture		Flu intranasal	
Men B		Dengue *	



Vaccine candidate containing a GSK's proprietary adjuvant system

\*In-license and other alliance relationship with third party  
(1) Antigen Specific Cancer Immunotherapies

The commitments of GSK are two-fold. Firstly, they are to R&D to address all the major diseases of the world. Secondly, they are to globalisation. Just as the car industry manufactures its cars in China or India, the vaccine industry will also manufacture vaccines in middle-income countries. GSK has already made progress on this front and will continue to do so. Given that quality must be maintained at a consistent level, vaccines need to be manufactured in cheaper locations if they are to be offered at differentiated prices.

### **Vaccines R&D in and for developing countries**

Patricia Danzon covered issues of supply to the developed and the developing world. Today GSK manufactures annually 1.2 billion doses of vaccines, 90% of which go to developing countries. GSK is the primary supplier to UNICEF, GAVI and the PanAmerican Health Organisation (PAHO).

The economics of vaccine manufacture mean that economies of scale can be exploited by designing the manufacturing process and manufacturing plant to produce global volumes. An important part of the strategy, therefore, is to produce for the world, and not just for the US or Europe.

Vaccines cannot be provided to developing countries at the same price as elsewhere in the world. Europe and the US must accept that they have to pay a higher price to subsidise research for the benefit of developing countries. This is the model which GSK promotes, politically and publicly, and is the way in which GSK has provided all its vaccines to developing countries.

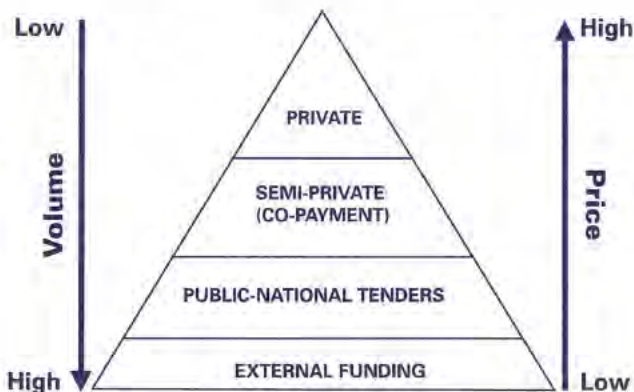
To exploit the full value of vaccines, they need to be rapidly introduced in developing countries. The characteristic delay of 20 years for vaccines, such as hepatitis B or Hib, to be introduced in a developing country after being introduced in Europe or the US, has to change. Vaccines must be introduced simultaneously in developing and in developed countries, a model which was initially put into practice by basing the development of rotavirus vaccines in Latin America. GSK received a mixed reaction to this initiative but it was felt to be necessary because of one major difference between developed and developing countries. Whereas rotavirus is killing children in Latin America, it does not kill children in the UK.

Introducing a vaccine in a developing country first means developing it to the same standard that applies in the developed world. From a public health point of view, Latin America is a good test bed for introducing a vaccine because of the high rate of vaccination among children. In Brazil, the percentage of children who are vaccinated is probably higher than in the UK. Hence GSK is locating its development in Latin America and will continue to pursue the model of launching vaccines first in developing countries.

### The new availability model

Reasonable pricing for vaccines needs to be accompanied by sustainable financing. In order to introduce a vaccine in a developing country, it is necessary to make sure that the government there has sufficient funds to spend. GAVI is playing a major part in this effort, and the UK's Chancellor of the Exchequer Gordon Brown has also played a critical role. Satisfying the 'new availability model' (Figure 5) for the introduction of vaccines means creating new market segments and implementing tiered pricing within a country. The implication of this for the industry is that it is critical to have a private and a public market in each country.

**Figure 5: New availability model**



The private component of the model applies to the wealthier sections of society who can pay for the vaccine themselves. A 'semi private' market would be for those who can pay for part of the vaccine, with the government making an additional contribution in accordance with the person's income. Public-national tenders comprise a third element while external funding is the only means for people in Africa, for example, to purchase vaccines. In other countries, such as India and China, there is no reason why a private market cannot exist for higher income individuals there. Given that China may be the largest economy in the world in a few years' time, it is logical that some people there should be able to pay for a vaccine.

The 'semi-private' market refers to the idea that people pay for some goods such as television sets on a monthly basis. GSK has successfully introduced a scheme along these lines for vaccination in one or two countries, whereby people take out a loan to pay for the vaccine. This can help families to vaccinate their children in circumstances where the government cannot provide the necessary funding. This is a feasible approach because families want to take care of their health and, especially, that of their children.

While responsibility for implementing vaccination recommendations and policies rests with PAHO, the WHO and national ministries of health, support is needed (what Patricia Danzon called the 'push' mechanism) for R&D for the poorest countries. In that regard, the Bill and Melinda Gates Foundation, with a budget amounting to billions of dollars is the main provider of funds, because Europe and the US are not organised to fulfil this role. The efforts of individuals are privately making a bigger contribution than governments to drive forward research and implementation for vaccines in developing countries.

Public funding by the richer countries is, however, likely to become more important. The two mechanisms that the British government has supported are the International Financing Facility (IFF) and Advanced Market Commitments (AMCs). AMCs have been developed as a way of stimulating research into medicines and vaccines for diseases of developing countries and may become a reality in 2007, with support from the British and Italian governments.

Multilateral organisations such as GAVI and UNICEF are needed for the implementation and introduction of new vaccines. In particular,

UNICEF is playing a critical role in countries where there is little infrastructure. It is worth noting that the viability of the model presented here, and UNICEF's role in it, is underpinned by the general absence of counterfeiting in vaccines. While 10% (and rising) of the world's drugs are counterfeit, it is to be hoped that this will not affect the vaccine market.

### **Promoting the value of vaccines**

Turning to the value of vaccines, for many years there have been stories in the British press about the measles/mumps/rubella vaccine. These stories have damaged confidence in vaccination and, by laying criticisms which have no scientific merit against a product, undermine the credibility of all vaccines.

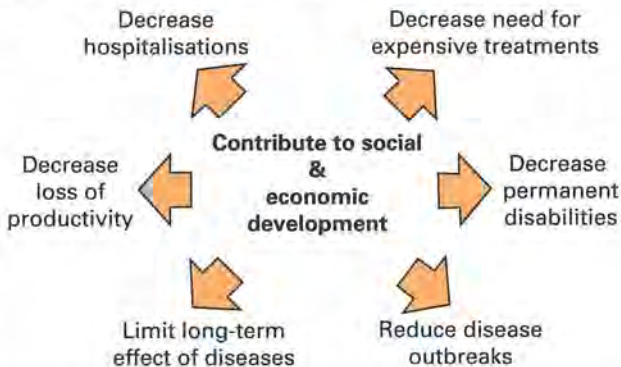
A similar crisis in relation to hepatitis B and multiple sclerosis arose in France, again with no scientific foundation. People need to be persuaded that vaccines are critical to society and could become more important with global warming if, as the models predict, there is as a result a greater likelihood of viruses, bacteria and other diseases returning. There is a need for education about infectious disease and the propensity of viruses and bacteria to exploit any opportunity to spread. Behaviour is important, with recent press reports suggesting that European statistics reveal a rising trend in HIV infections. The reason for the spread of this disease is that people are taking fewer precautions.

Although it is a matter of individual choice whether or not people are convinced of the need to protect themselves and their families by vaccination (the best advertisement for which may be the re-emergence of disease), there is a societal and economic aspect to disease and its prevention.

For society, the contribution of public health is well established and can be likened to that of drinking water or education. Without clean drinking water, infectious diseases will proliferate while, like education, vaccination is something people want for their children. Moreover, there is evidence that vaccination in a developing country such as Mozambique helps children to learn and grow, thus enhancing their contribution to the country's economy. This message needs to be better explained.

Another difficult point to explain in our individualistic societies is that what is called 'herd immunity' leads to global protection. The refusal of some people to be vaccinated means that they are putting others at risk. Vaccination cannot be imposed on society but the risks for society need to be explained. People need to be educated that vaccination is performed not only to prevent infectious disease, but also so that people remain healthy and contribute to the wealth of the economy (Figure 6).

**Figure 6: The value of vaccines – the economy**



*Source: International Federation of Pharmaceutical Manufacturing Associations, May 2003*

One aspect of Figure 6 to which it is worth drawing attention is the impact of vaccination on productivity losses. If vaccination is discussed in these terms rather than purely in terms of infectious diseases, people may be better able to understand that, in not vaccinating, they are putting at risk not only their life and the wealth of their family, but also the economy of their country. More can be done in terms of education to enhance the value of vaccines by challenging conventional thinking that vaccination is done solely to prevent disease. Other messages need to be given, with the involvement not only of healthcare workers but also of the entire community.

An illustration of educational messages about vaccines is the reporting by the British press in 2004 of GSK's announcement that HPV vaccine would become available in the following few years. The press pro-



vided a great deal of education on HPV vaccination when the medical community had not taken the time to explain what HPV is. It is important that consumers (the people who will use the vaccine) are better educated.

Governments also need to recognise the value of vaccines as one of the most cost-effective interventions. Vaccines should not be seen as a cost but rather as an investment in health and wealth. Political will and commitment on all sides are needed to change perceptions.

### **Conclusions**

It is generally agreed that vaccines have a major impact on public health. The rapid development of new science and new technologies has resulted in major breakthroughs. However, the level of readiness amongst governments in terms of budgeting for the future is low.

GSK is committed to making vaccines available to everybody, no matter where they live in the world. It is critical that vaccines attain global coverage, if the experience of HIV in South Africa is not to be repeated. This commitment is exemplified by the refusal, at the time of the merger between SmithKline and Beecham in 1989, to switch vaccine production away from polio vaccine into a different vaccine. The company was then (and still is today) manufacturing 800 million doses per year for the developing world. Since that time, the task with polio vaccine has been to realise more of its value (it was sold for 2¢ and is now sold for 20¢) in order for its production to remain viable.

Vaccination should be valued as highly as education and all people throughout the world should enjoy the benefits of vaccines. Commitment and partnership from all sides are needed to achieve this. It is important that there is worldwide support for Gordon Brown's initiative, because the poorest countries suffer the most from infectious disease and are in greatest need of help.

GSK has been able to build a vaccines business generating as great a profit as its other pharmaceuticals and has contributed to the development of many new vaccines which have reached the poorest countries of the world. This is a major achievement which has succeeded in striking the right balance between rewarding the shareholder and doing good for society.

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