

“Technology Transfer”, Capacity Building and the Developing World

The Issue

In recent years, increasing emphasis has been put on the role that multinational companies and developed world Governments should play in supporting technology transfer into developing countries. The context for much of this debate has been Paragraph 66.2 of the TRIPs Agreement which states:

“Developed country Members shall provide incentives to enterprises and institutions in their territories for the purpose of promoting and encouraging technology transfer to least-developed country Members in order to enable them to create a sound and viable technological base”.

Despite this reference to technology transfer in TRIPs, there is no universally recognised definition of what “technology transfer” means. Definitions tend to differ from country to country and organisation to organisation, with some putting a disproportionate emphasis on manufacturing capacity as the most valuable form of technology transfer for developing countries. For GSK, technology transfer represents a mix of “resources” and “know-how” transfer which are made in a commercial and sustainable context. Furthermore, recipient countries are not necessarily least developed countries but are those emerging markets where investment decisions are appropriate and viable can realistically be forecast to succeed.

This paper sets out GSK's approach to investing in, and supporting, developing countries; outlines some of the external conditions which are conducive to this investment; and provides an illustrative overview (at **Annex A**) of some of the capacity building projects we undertake in developing countries.

GSK's Position

- GSK is a global research-based company whose business is to provide innovative medicines to those in need. We are committed to the communities where we operate and our business provides an important contribution to those communities.
- GSK is involved in a number of “know-how” transfer and/or capacity building programmes into the developing world, including voluntary licence arrangements, work with local medical and regulatory professionals, community partnership projects, and clinical trials programmes.
- Taken together these projects contribute markedly to local scientific, regulatory, medical and manufacturing capacity and thereby help to build the necessary sustainable infrastructure to attract and absorb new technologies from other companies and industries.
- GSK considers technology transfer opportunities when they can realistically be forecast to succeed, are practical and appropriate given local conditions, reflect best use of resources and are sustainable.

GLOBAL PUBLIC POLICY ISSUES

GlaxoSmithKline's Position

- Many factors contribute toward a conducive environment in which the pharmaceutical industry will invest in a country or partner with community members. Key amongst these factors are appropriate economic, scientific and market conditions. A robust legal framework is also important. Businesses will migrate naturally to where these conditions exist and are sustainable.
- GSK is involved in a number of manufacturing projects in the developing world. However, it is important that the debate around “technology transfer” or capacity building does not focus disproportionately on local manufacturing. Within the context of the access to medicines debate, locally produced products are not always more affordable.
- A strong intellectual property (IP) system alone will not provide sufficient an incentive to transfer IP protected technology to a country; however, its absence will undoubtedly constitute a major disincentive. Steps that weaken IP protection, such as widespread compulsory licensing, ineffective anti-counterfeiting measures and inadequate data protection, could therefore act as a serious disincentive to investment in developing countries.

BACKGROUND

Conditions Conducive to Inward Investment and Capacity Building

GSK is acutely aware of the economic and related healthcare challenges facing millions of people in developing countries and the link between health and wealth. We are committed to playing a part in helping to address these challenges and the existing unmet medical need in many developing countries. Our response, however, must be sustainable. Our willingness to invest in and partner with developing countries is therefore heavily dependent upon suitably supportive “in-country” business and scientific environments comprising;

- Economic and political stability: There are a number of reasons why a local economic climate can be an attractive place for business in general. These include steady economic growth, stable inflation rates, and low and stable interest rates, open and outward looking markets, with deep and enduring economic linkages with the rest of the world. These factors all support the predictability of the commercial environment.
- Market size and potential; While it is not easy to define the market size or type that will make for viable economic production, it is generally the case that the larger the country or geographic bloc, the greater the market potential and investment appeal.
- Skilled workers: To carry out R&D and high tech manufacturing, it is necessary to have access to highly specialized staff. The availability of scientific research skills and infrastructure will generally outweigh financial incentives or a bw tax climate, although financial factors may be decisive in a choice between two locations with the necessary science base.
- Supportive regulatory environment - A good registration process for pharmaceutical products that enables medicines to meet stringent criteria on quality, safety and efficacy. This will encourage pharmaceutical companies to conduct clinical trials and launch innovative products early.

GLOBAL PUBLIC POLICY ISSUES

GlaxoSmithKline's Position

- A well developed national infrastructure of natural resources, public utilities and transport, along with a robust legal framework will all be considered as part of any investment decision.
- IP protection: The existence and enforcement of an IPR system in a recipient country is generally a prerequisite for any out-licensing / joint venturing decisions. While a strong IPR system alone will not provide sufficient an incentive to transfer IP protected technology, its absence will undoubtedly constitute a major disincentive.

GSK's role in generating many of these conditions is limited. Equally, in the context of Paragraph 62.2 of TRIPs, the ability of developed world governments to encourage investment in a commercially unattractive country through incentives will be limited. Appropriate in-country macroeconomic conditions are not easily created or problems overcome by third party incentives.

“Technology Transfer” and Manufacturing

For many in the developing world, “technology transfer” is seen simply in terms of developing local manufacturing capacity. They argue, post-Doha, that only by transferring and building manufacturing capacity in developing countries will their access to affordable medicines be assured. GSK would question this view. The access debate should not be confused with local industrial policy. The value of “technology transfer” should not be limited to providing manufacturing capacity for products, still less for patented pharmaceutical products.

Manufacturing medicines is a complex, time-consuming, capital intensive, highly regulated process requiring an efficient supply chain and supporting infrastructure of highly qualified staff, and reliable and continuous supplies of water, gas and electricity. A World Bank commissioned study of 2005¹ acknowledged these challenges when it concluded that a critical level of industrial and socioeconomic development and human and technical resources must be reached before any indigenous industry can survive. As a result, manufacturing tends to be concentrated in a limited number of sites in the world.

Manufacturing offers substantial benefits of scale in operation. That is, the lowest costs will be achieved with high volumes and high capacity utilisation – concentration in large plants in a limited number of locations. Manufacturing capacity for pharmaceuticals (if not for vaccines) currently far exceeds demand. Even if current excess capacity were absorbed by increased supply to patients, further demand would, for the most part, best be met by scaling up current efficient operations, not by creating new manufacturing sites.

Approved: September 2007

¹ Kaplan WA, Laing RO, Waning B, Levison L, Foster S. Is local production of pharmaceuticals a way to improve pharmaceutical access in developing and transitional countries? Setting a research agenda.

GSK and Capacity Building in the Developing World

1. Manufacturing Operations

GSK has 46 manufacturing sites outside Europe and North America including one in an LDC (Chittagong, Bangladesh). Here we have contracts with 3 companies for the supply of inhaled aerosol products, penicillins, local solid dose products and Horlicks (see below). The sites form part of the corporation's business strategy and were established in response to a business need or, in some circumstances, because of local government insistence on "local working" as part of the product registration process.

GSK production sites in Algeria, Hungary, Morocco, Nigeria, Sri Lanka and Turkey produce for the domestic market. However, many GSK facilities in developing countries also export to other parts of the world such as is the case in Argentina, Brazil, Costa Rica, Egypt, India, Indonesia, Kenya, Malaysia, Mexico, Pakistan, Panama, Philippines and South Africa. By operating these manufacturing sites, GSK promotes the development of skills and technical expertise of the workforce in those countries.

GSK also has a programme of "know-how" transfer to local manufacturers whereby we outsource production of products as part of a carefully managed production cycle aimed at freeing up GSK production capacity for the development of new drugs and vaccines. Transfer of production usually occurs post-patent expiry for products which local operating units consider of strategic and/or commercial importance in local or regional markets. They remain GSK branded products, sold and marketed by the company; however production is done by a third party contractor, with the necessary regulatory and technical support from GSK to ensure compliance with local and international standards.

Horlicks Production

- *India:* GSK has three Horlicks factories in India dating from 1959, 1973 and 2002 (one in Punjab in the North, one in Andhra Pradesh in the South, and the third in Haryana, which commenced production in 2002). Two of the factories - in Punjab (Nabha) and Andhra Pradesh (Rajahmundry) - buy cow/buffalo milk from around 40,000 local farmers.

When we first started operations in India, local farming families agreed to keep additional animals so that they had surplus milk over and above their family requirements to sell to GSK. We in turn provide aid in terms of veterinary assistance, subsidised cattle feed, artificial insemination, free deworming as well as holding training programmes on animal husbandry to enable the farmers to maximise the output of each animal and enhance the population.

- *Bangladesh:* Bangladesh receives Horlicks DMI (Dry Mix Ingredient) from Slough in bulk Vitamin premix. Fine crystalline sugar and ferric pyrophosphate are added in the DMI at a third party, Mutual Foods Bangladesh, and packed into the consumer pack. Other variants of Horlicks (Junior, Mothers & Chocolate), Viva and Maltova are supplied in bulk from India and packed at Mutual Foods Bangladesh, who also add vitamins to some of the products.

GLOBAL PUBLIC POLICY ISSUES

GlaxoSmithKline's Position

2. Joint Ventures

GSK is involved in a number of joint ventures, the rationale for which is based on a number of contributory but essential factors. Careful consideration is given to all aspects of the agreement between GSK and the JV partner, including the rights and liabilities of the contracting parties, confidentiality matters, intellectual property, training requirements, development needs, respect of GMP, independent QC or National Control Authorities. External factors also play a large part such as market size, a favourable climate for foreign direct investment and opportunities for export. Examples of existing projects include:

- GSK (via its legacy companies) has a long history of joint-ventures in China, starting with SK&F discussions in 1983 which resulted in the first Tianjin joint-venture TSK&F in 1987. This ownership was 55:45 and it was one of the three most successful foreign pharmaceutical businesses in China throughout the 1990s. In 1996 it reached a production level of more than 1.2 billion capsules per year, mostly of OTC-type products Contac (for colds) and Fenbid (the non-steroidal ibuprofen for a variety of aches and pains). Both achieved market leadership. These volumes have remained at a steady level since.
- In 1997, GSKT, the second manufacturing Joint-Venture in Tianjin (at 90:10) was approved. This became operational in January 2001 with the launch of Avandia. GSKT is now registered to supply Zantac to 10 markets and has been supplying finished packs to the UK since 2006.
- In 1998 GSK signed a technology transfer, supply and licence agreement with the Brazilian Government's Fundação Oswaldo Cruz (Fiocruz) for the formulation and filling of our Haemophilus influenzae type B meningitis vaccine. At the end of 2003, a second contract of the same type was signed with Fiocruz for our measles, mumps and rubella vaccine.

3. Scientific Research

R&D Investment

In May 2007, GSK R&D announced the set up a new R&D center in Shanghai, China. GSK R&D China will focus on research into neurodegeneration with the objective of creating new medicines for such severe disorders as multiple sclerosis, Parkinson's disease, and Alzheimer's disease. The center will eventually direct the global discovery and development activities within its therapeutic area, from drug-target identification to late-stage clinical studies, while collaborating with research institutions elsewhere in China and other countries. It is hoped that up to 1,000 high skilled jobs will be created at the site by Year10, making it GSK's third largest R&D base.

Transfer Programmes

- In 2000, GSK signed an agreement with the Shanghai Institute Materia Medica whereby initially two chemists from Shanghai spent three months in GSK high-throughput chemistry laboratories being trained in state-of-the-art chemistry techniques. These Chinese chemists then went back to their Institute to spread the technology within their own group. We now support eleven scientists in Shanghai who synthesise quality chemical arrays in collaboration with GSK and to the benefit of the local academic science base in Shanghai.

GLOBAL PUBLIC POLICY ISSUES

GlaxoSmithKline's Position

- The UK India Education and Research initiative is a joint initiative between R&D and GMS (our manufacturing division). Through collaboration with The British Council, up to 20 Indian graduates from premier Indian universities spend one year in GSK, either in R&D or GMS. Ten students (from all parts of India) started in November 2006 (5 in each area) and 15 students will be recruited to start in the autumn of 2007.
- In July 2005, GSK and Oxford University's Department of Clinical Pharmacology established a collaboration creating the first Indian cancer-trials network comprising a number of India's leading comprehensive cancer centres.

Each Indian site has a clinical co-ordinator who has received on-line training from the University of Oxford prior to visiting Oxford to acquiring additional hands-on experience working for a brief period in the Oxford clinics. The primary purpose of this training is to increase the Indian clinicians knowledge of Good Clinical Practice in order that they can take this back to India and put it into practice.

Clinical Trials

The number of global R&D trials conducted outside traditional US and European countries has increased considerably over the past few years (from 9% of new patients in 2003 to 29% in 2007 YTD). This has been supported by an appropriate increase in investment both in operational headcount and in infrastructure development. The expansion in our oncology portfolio, for example, has led to increased investment in infrastructure to support these trials - ranging from building additional storage facilities for clinical files at the National Cancer Institute (INEN) in Peru, to the provision of high speed internet access, air conditioning units for drug storage areas, and secure filing at an oncology centre in Lahore, Pakistan. These measures permit the centres to more efficiently run Clinical Trials to GCP. In addition, the placement of study-funded co-ordinators at selected high-recruiting sites enables investigators to focus on the patient-facing component of the research, and to maintain their studies to the highest standards despite the increased flow of work.

GCP-training of staff is a high priority in all countries, but none more so than non-traditional markets where experience of conducting global trials is still growing. Investigator GCP-training workshops are sponsored by GSK in many countries. In Korea, for example, there is a well-established GSK-sponsored accreditation programme which receives excellent feedback.

In line with our commitment to develop medicines and vaccines for diseases disproportionately impacting on the developing world such as, TB, malaria, dengue, HIV and HPV, GSK is currently undertaking clinical trials in countries across the globe where such diseases are prevalent. For example, GSK has invested more than two decades in the effort to develop a successful malaria vaccine and in collaboration with leading research institutions based in Africa, a series of clinical trials are ongoing in Mozambique, Tanzania, Kenya, Gabon, and Ghana.

In malaria treatment studies, GSK has worked with sites to improve internet connectivity, electricity supplies and requisite storage facilities for drug supplies and study documentation. There has also been upgrading of clinical rooms, wards, and laboratories with training and improved capacity for specialist laboratory testing.

GLOBAL PUBLIC POLICY ISSUES

GlaxoSmithKline's Position

The International Region is now involved in more studies, utilising more countries and enrolling substantially more patients into R&D studies than in previous years

Regulatory Conferences and Workshops

Competent regulatory authorities are important to the pharmaceutical industry. They speed up product registration in support of public health and they relay a valuable message to the broader business community regarding the importance a country attaches to effective governance and high standards, as well as establishing regulations – allied to workable systems and processes – for ensuring protection of public health. As a global pharmaceutical company GSK works closely with other companies to help build capacity in the regulatory area across the developing world. This commitment is ongoing, takes a number of forms and brings tangible benefits to both sides.

- **Regional Regulatory Conferences:** In collaboration with other members of EFPIA, the European Trade Association, GSK supports a series of annual regulatory conferences. The series began in 1996 with the Middle East Regulatory Conference and has been mirrored since in Asia and Latina (in collaboration with the International Trade Association, IFPMA). Representatives from the local and regional Regulatory bodies are invited to hear Regulators from ICH countries, as well as the R&D-based Industry discuss best practice. Horizon scanning issues are also discussed, such as the likely impact of genomics on pharmaceutical regulatory processes. The World Health Organisation is closely involved in the development and delivery of these Conferences.
- **Workshops:** The Conferences outlined above are also supplemented by one-off workshops for Regulators on specific issues such as GMP and support for global clinical development. Again, representatives from ICH Regulatory Authorities, such as the FDA or EMEA are invited by industry to speak/train their counterparts in developing countries and thereby facilitate know-how transfer. Such Workshops are generally supported by Industry, include organisation and some degree of funding.
- **Contact facilitation and Training:** In recent years, industry has supported and delivered trainings to the Chinese Regulatory Authority to support the review of investigational new drug (IND) applications and IND variation applications, specifically in order to facilitate a common understanding of the product development process for new chemical entities, and to improve understanding of the types of technical changes that may occur so that regulatory approval procedures and approval times can be adhered to. At a company-specific level, via GSK's dedicated International Regulatory Affairs Department, GSK regularly facilitates meetings between developing world Regulators and their European or American counterparts. We also stand ready to work with Regulatory Authorities on training programmes.

4. Global Sourcing

Global Sourcing is about accessing world-class talent pools, patient pools and infrastructure in low to medium cost locations and sourcing direct materials from low-cost, high capability locations. Standardization is about applying proven local best practices and processes more broadly across the company without adding bureaucracy, resulting in reduced complexity, increased productivity and improvements in the quality of outputs.

GLOBAL PUBLIC POLICY ISSUES

GlaxoSmithKline's Position

The areas of greatest opportunity for global sourcing and standardization have been R&D (see *above*), manufacturing and IT, due to the size of their spend base and the global potential of existing talent. We believe we are at the forefront of industry global sourcing in many areas and in IT in particular.

Specific GSK projects include:

- Significant amounts of IT work to India with over a thousand full-time equivalent (FTE) employees working on GSK projects at vendor offshore locations
- A Global Pack Management Centre in India where by the end of 2007 GSK is on course for employing up to 140 FTE in low-cost creation of packaging artwork, proof reading and completion serving International markets and catering for work overflow from Europe.
- The creation of close to 500 FTE's across several functions in Finance, HR, R&D, and Commercial in several countries in the developing world, Outsourced services include processes such as accounts payable, general accounting, helpdesk, and travel & expense, R&D processes such as data management, biostatistics & programming, and medical writing.

5. Community Partnership Programmes

While none of GSK's community partnership activities is designed to increase the sale of GSK products, they deliberately go beyond traditional philanthropy and are aimed at building strategic, sustainable partnerships that generate mutual benefit for GSK, its partners and beneficiaries of the programmes.

Given GSK's principle commercial activities and the skills of our people, the focus of our programme is on improving health and education – critical areas where we can really make a difference. The following are a few examples of the developing world projects we run;

- GSK's Thai Rural Nursing Excellence programme sponsors female high school graduates from rural areas to complete nursing degrees with the aim of training 200 nurses over five years. Once qualified, the nurses return to work in their communities for at least three to four years.
- In Vietnam, a similar GSK programme provides scholarships for 500 women to be trained in community healthcare. This is a unique training programme, based in Tu Du Hospital, Ho Chi Minh City, that aims to reduce childbirth complications and decrease newborn fatality from 6% to zero% in some of the more remote and poorest communities in Vietnam. The project is training midwives who will return to their villages to provide healthcare services for vulnerable mothers and newborn babies
- GSK's PHASE (Personal Hygiene And Sanitation Education) programme is a simple handwashing programme for schoolchildren that saves lives. By teaching hygiene and sanitation skills, PHASE aims to reduce diarrhoeal-related disease. Children are encouraged to act as agents of change by applying what they have learnt to their home environments and teaching their families. PHASE is implemented in partnership with NGOs Plan International and AMREF.

GLOBAL PUBLIC POLICY ISSUES

GlaxoSmithKline's Position

As part of a post-tsunami reconstruction programme in Nias (off western Sumatra, Indonesia), GSK is working with Save the Children to incorporate PHASE as the health and sanitation component of a comprehensive school health programme.

- GSK is also working with JHPIEGO and local partners in Indonesia to improve the skills and knowledge of the faculty of Takengon Midwife Academy and to help supply this school for midwives with necessary teaching equipment and supplies.
- In Pakistan, GSK has supported a Primary Health Care Extension programme to reduce maternal & infant mortality
- GSK's Positive Action programme to fight the HIV/AIDS pandemic has been running for 15 years and supports innovative community-focused projects providing education, prevention, care and support; treatment literacy; advocacy; information sharing and dissemination.
- GSK's African Malaria Partnership supports three behavioural change initiatives to improve individual and community responses to malaria, encouraging the use of insecticide-treated bed nets (ITNs), intermittent presumptive treatment of pregnant women (IPT) and prompt, effective treatment of malaria fevers in young children. The partnership is reaching almost two million people at risk from malaria.

6. Voluntary licences

As noted in the WHO Commission on Macroeconomics and Health Report of 2001, "voluntary licenses" (VLs) are seen by some as a valuable technology transfer tool from North to South.

They enable local manufacturers to produce and sell generic versions of patented products. GSK's association with them dates back to 2001 when we granted our first VL for the manufacture of anti-retrovirals in Africa. We have now negotiated eight licensing agreements covering a mix of individual countries, trade blocks or all of sub-Saharan Africa.

Any decision by GSK to grant a VL depends on a number of factors including the severity of the HIV/AIDS epidemic in that country, local healthcare provision and the economic and manufacturing environment. Selecting the most appropriate licensee is key. We need to be sure that the manufacturer will be able to provide a long-term supply of good-quality medicines and will implement safeguards to prevent the diversion of medicines to wealthier markets.