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 Trade Related Aspects of Intellectual Property Rights (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*[1] *(LDC) 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 is made in a commercial and sustainable context. Furthermore, recipient countries are not necessarily LDCs but are those emerging markets where investment decisions are appropriate, viable and 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 (Rx), including vaccines (Vx) and healthcare products (Cx), 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 countries where we operate, 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 sustainable infrastructure necessary 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.

– GSK is involved in a number of manufacturing projects (also referred to as production technology transfer) in the developing world. However, it is important that the debate around technology transfer does not focus disproportionately on local manufacturing. Within the context of the access to medicines debate, locally produced products are not always more affordable.

– Production technology transfer is one of many options often considered for increasing the availability of **vaccines** in the developing world, both as a routine public health tool and to ensure health security in the event of a natural or man-made biological event like a pandemic.

[1] As defined by the UN there are currently 47 Least Developed Countries (LDCs). Structural weaknesses, poverty, susceptibility to natural & man-made disasters and to communicable diseases hamper these countries' efforts to improve the quality of life of their people.

- Production technology transfer, however, is not a panacea. In the context of vaccine supplies, for production to be economically viable in terms of facilities and quality assurance, high capital investments can only be justified for sites producing significant doses of bulk antigen ie in the 10s of millions of doses.
- Ultimately, achieving success in vaccination policy requires more than local production capacity. Policies are also needed to make it easy for people to be vaccinated with vaccines once licensed. A robust cold chain, expertise in vaccination and an adequate public health infrastructure are all critical to achieve vaccination coverage.

– Many factors contribute toward a conducive environment in which the pharmaceutical industry will invest in a country or partner with community members. These include appropriate economic, scientific and market conditions; an efficient regulatory authority and a robust legal framework.

– 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, can all act as serious disincentives 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. These include steady economic growth, stable inflation rates, 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 specialised staff. The availability of scientific research skills and infrastructure will generally outweigh financial incentives or a low tax climate, although financial factors may be decisive in a choice between two locations with the necessary science-base.
– A supportive regulatory environment: A good registration process for pharmaceuticals and vaccines 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.
– 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 IP 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 into 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 that only by transferring and building manufacturing capacity in developing countries will 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 medicines.

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 2005[2] 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. The lowest costs will be achieved with high volumes and high capacity utilisation, via concentration in large plants in a limited number of locations. Global 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.

Vaccine Production Challenges

GSK Vaccines is one of the world's leading vaccine innovators and producers. We have developed a network of global industrial vaccine operations spanning 13 sites in 10 countries worldwide. These are made up of a combination of primary and secondary production and comprise a blend of our own operations, joint ventures and collaborations.

The favourable environment described above is particularly difficult to achieve for vaccines, due to the economics inherent in their manufacture. Indeed, several specific scientific, regulatory and economic factors contribute to the cost of, and time required for, vaccine manufacture:

- Vaccines are given to healthy populations, so safety and quality are paramount. Stringent quality processes need to be in place to ensure the safety of these sophisticated products. For example, the production of GSK's 10-valent vaccine against pneumococcal diseases requires 500 quality test steps. Most of these steps involve the execution of complex biological processes.
- Variable costs are low – approximately 15% of total cost base[3]. This has a two-fold effect. First, it makes the favourable difference in low labour costs in developing countries less significant compared to potential savings made in other industries where manufacturing is relocated from developed countries. Second, it generates strong competitive pressures in a high cost of goods industry.
- Historically, the lack of commitment from countries in forecasting their requirement puts manufacturers in a difficult supply position. Uncertainty in forecasting can lead to oversupply or supply shortages due to the lead times required for vaccine manufacture.

March 2019

[2] Kaplan WA, Laing RO, Waning B, Levision L, Foster S. Is local production of pharmaceuticals a way to improve pharmaceutical access in developing and transitional countries? Setting a research agenda.
[3] Salinsky E, Werble C. "The Vaccine Industry: Does it Need a Shot in the Arm?" National Health Policy Forum Background Paper. 25 January 2006.

Annex A

GSK and Capacity Building in the Developing World

Manufacturing Operations

Across its pharmaceutical and consumer businesses, GSK has 37 manufacturing sites outside Europe and North America. The list includes sites in Algeria, India, Sri Lanka, Kenya, Pakistan, Egypt, South Africa, Malaysia, Singapore, Saudi Arabia, Indonesia, Australia, Japan, China, Argentina and Panama. Collectively they form part of the company'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. By operating these manufacturing sites, GSK promotes the development of skills and technical expertise of the workforce in those countries.

GSK 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.

Joint Ventures

GSK is involved in several joint ventures (JVs), the rationale for which is based on several 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, IP, training requirements, development needs, respect for Good Manufacturing Practices (GMP), independent quality control 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 JVs in China, starting with SK&F discussions in 1983 which resulted in the first Tianjin JV 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.

– Over the last 25 years we have forged a unique partnership - notable in the global health community for its duration, scope and sophistication - with the Brazilian Government's Fundação Oswaldo Cruz (Fiocruz) delivering technology-transfer projects, covering several vaccines (polio, meningitis (Hib), MMR, rotavirus, pneumococcal & MMR-V). We are also working with the Butantan Institute to produce a DTPa vaccine; and, as part of the three-part transaction with Novartis in 2015, we took over a Technology Transfer Agreement with the Ezequiel Dias Foundation (Funed) to produce a Meningococcal C vaccine.

– In January 2013, we entered into an agreement with Biological E Limited (Biological E.), a leading Indian vaccines company, to form a 50/50 JV for the development and commercialisation of a six-in-one combination paediatric vaccine to help protect children in India and other developing countries from polio and other infectious diseases. The partnership reinforces the commitment of both companies to support the WHO's global polio eradication programme.

Scientific Research

R&D Investment

In March 2014, GSK announced plans to establish the world's first R&D Open Lab to increase understanding of non-communicable diseases (NCDs) in Africa. The vision was to create a new global R&D effort with GSK working in partnership with major funders, academic centres and governments to share expertise and resources to conduct high-quality research. At an operational level, GSK scientists collaborate with scientific research centres across Africa and an independent Advisory Board of leading scientists and clinicians informs the strategy and selects the NCD research projects. Five years on, the Open Lab is supporting a total of 20 research projects, enabling researchers across academia and industry to improve understanding of NCDs to help address the specific needs of patients in Africa.

Transfer Programmes

GSK supports the Alliance of Technology Transfer Professionals (ATTP) which is dedicated to increasing technology transfer capabilities across the world and sharing best practice within its member associations. A number of GSK personnel are fully accredited by ATTP and regularly visit universities and SMEs in developing countries to promote higher standards in the technology transfer area.

Scientific Collaboration

'Trust in Science' was established in 2011 as a key element of GSK's efforts to build long-term, meaningful partnerships with key scientific stakeholders in Latin America. It sees GSK provide funding to top local research institutions for the development of patient-focused research programmes that address the treatment of relevant diseases and meet local community needs. The company's support is matched by government research funding agencies. Programmes are selected by an independent scientific panel of eminent local scientists and endorsed by relevant GSK R&D units and independent scientists commissioned by the government funding agencies. The overall aim is to help build understanding of globally and locally relevant diseases, which will help their treatment and prevention. It also aims to create a strong collaborative framework, promoting GSK as a partner of choice.

Trust in Science is an innovative model of public-private partnerships unique to GSK. It was launched first in Brazil and Argentina, and between 2013-15 was extended to a few countries in Africa (Uganda, Kenya and Tanzania).

Clinical Trials

In line with our commitment to develop medicines and vaccines for diseases disproportionately impacting on the developing world such as, TB, malaria, 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 Phase III clinical trials are ongoing in Kenya and Ghana. In coordination with WHO we will also be conducting Phase IV 'observational' studies in Ghana, Kenya and Malawi.

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.

Good Clinical Practice (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.

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. One recent example includes GSK sponsorship in March 2017 of a three-day International Conference on Harmonisation (ICH) Workshop on Chemistry, Manufacturing & Controls (CMC). Organised by Duke-NUS Medical School its primary objective was keeping regulatory professionals up to date with innovative approaches and ensuring alignment in the understanding, interpretation and implementation of ICH quality guidelines. Sixty-one participants from regulatory agencies, industry, academia, and research institutions attended the Workshop, including 13 participants from 7 ASEAN regulatory agencies (Brunei, Cambodia, Indonesia, Lao PDR, Malaysia, Thailand, Vietnam).

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. Standardisation 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.

The areas of greatest opportunity for global sourcing and standardisation have been R&D (*see above*), manufacturing and IT, due to the size of their expenditure 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. GSK projects include:

– A Pack Artwork Shared Service Delivery Centre in India where GSK employs up to 140 FTE's in low-cost creation of packaging artwork, proof reading and completion, for GSK Rx,Vx and Cx.
– 80 offshore analysts based in Hyderabad, India supporting our Rx, Cx and Vx businesses with supply chain Incident Management, Request Fulfilment and Problem Management processes.

Community Partnership Programmes

GSK's community partnership activities 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 couple of examples of the developing world projects we run:

– Our work with malaria and health systems strengthening has expanded through our five-year, £22 million partnership with Comic Relief. Launched in December 2015, the partnership works with organisations fighting malaria and improving health in Tanzania, Mozambique, Ghana, Sierra Leone and the Greater Mekong sub-region.
– As part of GSK's global partnership with Save the Children, we are currently working together on programmes in 45 countries worldwide. Together, we are combining our efforts to deliver interventions such as upgrading health centres, training and equipping community health workers and giving families and communities access to healthcare provision and services. We jointly advocate for universal health coverage, with a particular emphasis on increased and improved healthcare for children.

- In September 2018 GSK announced a collaboration with the USAID and the scientific organisation, USP, to help increase the availability of Umbipro (a gel form of the life-saving WHO-recommended antiseptic, chlorhexidine, to prevent umbilical cord infections in newborns). Umbipro was developed by GSK in 2016 in response to a call from the UN for manufacturers to develop chlorhexidine products for newborn umbilical cord care, with the aim of saving up to 422,000 lives over five years. Through the collaboration, GSK is sharing manufacturing expertise and specifications for Umbipro in order to stimulate local production and sustainable access to this critically needed medicine in developing countries.

GSK and Sub-Saharan Africa

GSK has a long track record of working in Africa and in the context of GSK's ambition to be one of the world's most innovative, best performing and trusted healthcare companies, in 2017 we reviewed the sustainability of our business in Sub-Saharan Africa to ensure we have the right commercial model in each market. We believe it is only through a sustainable business over the long term that we can continue our efforts in supporting access and addressing Africa's healthcare challenges. We have therefore restructured our operations such that we:

- Run fully serviced local GSK businesses in two key markets: Kenya and Nigeria.
- Have retained our South Africa business (run in an alliance with Aspen Pharmacare)
- Have restructured 31 markets and now manage them from a UK-based Export Markets hub. We have ceased marketing and promotional activities to healthcare professionals in these markets and have adopted a distributor-led model.
- Work directly with governments or supranational organisations in 11 markets.

Patient access to medicines and vaccines remains our priority as we leverage the strength of our distributor partners, governments and WHO/GAVI/UNICEF arrangements to make our medicines and vaccines widely available to patients across Sub-Saharan Africa. We are continuing our efforts aimed at strengthening healthcare infrastructure, combating child mortality, tackling tropical diseases and driving innovation in R&D through the Africa Non-Communicable Diseases Open Lab.