

Trends in Local Production of Medicines and Related Technology Transfer



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World Health Organization

Trends in Local Production of Medicines and Related Technology Transfer



**World Health
Organization**

Prepared for the WHO Department of Public Health, Innovation and Intellectual Property by Frederick M Abbott (College of Law, Florida State University).

This report forms part of the project entitled: Improving access to medicines in developing countries through technology transfer related to medical products and local production. It is implemented by the Department of Public Health Innovation and Intellectual Property of the World Health Organization (WHO/PHI) in partnership with the United Nations Conference on Trade and Development (UNCTAD) and the International Centre for Trade and Sustainable Development (ICTSD) with funding from the European Union (EU). The overall objective of the project is to increase access – especially for the poor in developing and least developed countries – to medicines, vaccines and diagnostics.

All reports associated with this project are available for free download from the following website: <http://www.who.int/phi/en/>

This publication has been produced with the assistance of the European Union. The contents of this publication are the sole responsibility of the World Health Organization and can in no way be taken to reflect the views of the European Union.

Editing and design by Inís Communication – www.iniscommunication.com

WHO Library Cataloguing-in-Publication Data

Trends in local production of medicines and related technology transfer.

1.Essential drugs. 2.Technology transfer. 3.Developing countries. I.World Health Organization.

ISBN 978 92 4 150234 4 (NLM classification: QV 704)

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Printed in France

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Contents

Abbreviations	v
Executive summary	1
1. Transfer of technology and local production under the WHO Global Strategy and Plan of Action	5
2. Public health and industrial policy	6
3. Methodology, limitations, structure of report and definitions	9
4. Structure of global production sector	14
5. Local production from the regional perspective	21
6. Technology transfer	63
7. Development of the pharmaceutical production sector	86
8. Recommendations	94
9. Concluding observation	101
References	102
Annex I: Review of literature	109
Annex II: Medicines research and development and transfer of technology programmes not specifically linked to production	170



Abbreviations

AIDS	acquired immunodeficiency syndrome
ANMAT	Administración Nacional de Medicamentos, Alimentos y Tecnología Médica (Drugs, Food and Medical Devices National Administration)
ANVISA	Agência Nacional de Vigilância Sanitária (National Health Surveillance Agency)
API	active pharmaceutical ingredient
ARV	antiretroviral
ASAQ	artesunate–amodiaquine
ASMQ	artesunate–mefloquine
BHF	Business Humanitarian Forum
BIPC	Baz International Pharmaceutical Company
BNDES	Brazilian development bank
cGMP	current good manufacturing practice
COMESA	Common Market for Eastern and Southern Africa
DNDi	Drugs for Neglected Diseases Initiative
EAC	East African Community
EMA	European Medicines Agency
EU	European Union
FDA	United States Food and Drug Administration
FDI	foreign direct investment
GDP	gross domestic product
GMP	good manufacturing practice
GSPA-PHI	Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property
HIV	human immunodeficiency virus
ICH	International Conference on Harmonization
ICTSD	International Centre for Trade and Sustainable Development
IFC	International Finance Corporation
IGO	intergovernmental organization
ISO	International Organization for Standardization
IMF	International Monetary Fund
INVIMA	Instituto Nacional de Vigilancia de Medicamentos y Alimentos
IPA	Indian Pharmaceutical Alliance

IPM	International Partnership for Microbicides
LDC	least developed country
MENA	Middle East and North Africa
MNC	multinational corporation
NEPAD	New Partnership for Africa's Development
NGO	nongovernmental organization
NIPER	National Institute of Pharmaceutical Education and Research
OECD	Organisation for Economic Co-operation and Development
PAHO	Pan American Health Organization
PDP	product development partnership
PEPFAR	United States President's Emergency Plan for AIDS Relief
PICS	Pharmaceutical Inspection Cooperation Scheme
PPP	public–private sector partnership
SADC	South African Development Community
SAGMA	Southern African Generic Medicines Association
SFDA	Chinese State Food and Drug Administration
TB	tuberculosis
UNCTAD	United Nations Conference on Trade and Development
UNDP	United Nations Development Programme
UNIDO	United Nations Industrial Development Organization
USAID	United States Agency for International Development
WHA	World Health Assembly
WHO	World Health Organization
WHO/PHI	WHO Department of Public Health, Innovation and Intellectual Property
WIPO	World Intellectual Property Organization
WTO	World Trade Organization

Executive summary

This report identifies and analyses trends in the local production of medicines in developing countries and related technology transfer. The objective is to assist the World Health Organization (WHO) in its support for Member States in implementing the global strategy and plan of action on public health innovation and intellectual property with particular reference to the promotion of capacity-building for local production in developing countries. The methodology of research included interviews with a range of stakeholders, including industry actors, operators of product development partnerships (PDPs), government officials and members of public health advocacy groups; review of literature and Internet resources; and participation in meetings with stakeholder groups in Africa, Asia and Latin America.

Local production of medicines may be defined by geography and by nationality of ownership. A pharmaceutical manufacturing facility located in a developing country may be owned by nationals of that country, or it may be owned by foreign investors (including multinational enterprises). Although there are reasons why governments may prefer local ownership of manufacturing facilities, benefits from local production facilities may also arise from investments by foreign nationals. This report identifies potential grounds for preference as between local and foreign investors, but it does not suggest that one type of investor should be favoured over another.

Technology transfer is a broad concept encompassing education and training, direct investment, licensing, movement of people, supply of materials and equipment, and other elements. This report uses a broad definition of technology transfer.

From the perspective of global public health, it is important to distinguish between general industrial policy objectives that may argue in favour of local production of medicines in developing countries, and public health objectives for encouraging local production. From an industrial policy standpoint, establishing local production facilities may generate local employment opportunities, stimulate demand for education and training, increase tax revenues and reduce balance-of-payments outflows. Such benefits are not unique to pharmaceutical production and may arise for many industrial sectors. The objective of production-related industrial policy is typically to establish globally competitive and profitable industries. This is likely to generate indirect public health benefits by generally improving the local standard of living.

From a WHO standpoint, one objective of encouraging local production would be to address the unmet medicines needs of the world's population. Medicines may be too costly for the local population, or producers may not supply products specifically adapted to local market conditions because of insufficient monetary demand. There may also be unmet needs for local sources of production that are sufficiently secure and sustainable to address

long-term regional medicines demand that will continue to place strain on public health budgets.

Local production may present disadvantages compared with importation when local manufacturing cannot be undertaken reasonably efficiently, and when local procurement costs exceed costs of importation for a significant period of time. With certain possible exceptions, governments are unlikely to support uneconomic production for sustained periods.

There is fairly broad agreement among experts concerning the desirable elements for establishing and maintaining local medicines production facilities. These include:

- availability of skilled personnel;
- access to investment capital;
- adequate infrastructure development;
- adequate regulatory environment;
- access to relevant technologies;
- availability of suitable input materials;
- achieving economies of scale.

There are substantial differences among developing countries and regions with respect to the presence or absence of these elements. African local producers express considerable concern with respect to each of these elements, and significant investment and effort is required to improve the local production environment in Africa. Some of the larger emerging economy countries of Asia maintain strong local production sectors for medicines and are successful exporters to developing and developed country markets. In Latin America, a substantial part of local demand is met by local generic producers. However, these producers are predominantly reliant on supplies of active pharmaceutical ingredients (APIs) from outside the region, and this dependency presents certain problems. Latin American national producers express concern over access to patented technologies required for the production of newer medicines. It should be noted that most production of medicines is undertaken by private enterprises, and government policies with respect to promotion of local production of medicines are likely to be directed at encouraging private-sector activity.

Almost all elements of the medicines production chain are available for purchase or contracting on the world market. Particularly in light of consolidation and reductions in the workforce among the major multinational pharmaceutical enterprises, a wide range of technical consultants is available for hire. Machinery and equipment and input materials are displayed at international trade fairs. In this context, a private investor or government seeking to establish a pharmaceutical production facility can do so. What is more difficult for many developing countries is the precondition of basic infrastructure, such as appropriate supply of electricity, water and transport –


the absence of which may significantly raise the costs of production (or make it infeasible).

Efficient production of medicines often requires achieving economies of scale, and this may be difficult in smaller countries and markets. Production facilities that are able to supply regional markets are more likely to achieve appropriate economies of scale. However, regional trade in medicines is often made difficult by the cost and effort entailed in registering a medicine in multiple jurisdictions, including in complying with different national regulatory requirements.

Pharmaceutical production technology is transferred through a variety of mechanisms, including foreign direct investment (FDI), joint venture arrangements, licensing (voluntary and compulsory, through pooling arrangements and otherwise), movement of personnel, provision of education and training, and others. There is no identifiable single best mechanism for the transfer of pharmaceutical production technology, and governments are likely to take different approaches to encouraging such transfer.

This report makes a number of recommendations. These are focused mainly on the role that WHO, working in partnership with others, can take with respect to transfer of technology and local production of medicines in developing countries:

- A primary objective must be to identify therapeutic areas and regions for which existing production does not meet local needs, including needs for long-term sustainable supply. The further objectives of the work programme should be designed to address those identified areas.
- A successful national or regional pharmaceutical production sector develops over a significant period of time, through acquiring or developing expertise in the various phases of production. Although some experts recommend development efforts that target more commonly used treatments in order to take advantage of well-known technologies, for the purposes of addressing unmet needs it may be more important to focus on specific technologies that address those needs.
- WHO is in a good position to identify technical experts that can assist in training of personnel for operation of pharmaceutical facilities, as well as technical experts that can aid in the design, construction and initiation of local production.
- WHO technical experts might work with private-sector companies to design and make available “modular packages” for local production facilities suited for developing countries, including advanced formulation facilities. WHO might work with the World Bank to design a financing package for such facilities.
- WHO should continue to work with national and regional regulatory authorities to coordinate and further integrate rules and mechanisms for approving and monitoring operation of pharmaceutical production facilities.
- WHO should assist small and medium-sized pharmaceutical enterprises in developing countries to identify opportunities for serving parts of the



population and markets that are less attractive to well-capitalized larger companies, and that might facilitate negotiation of technology licences and technical support.

- This report identifies the African region as most in need of multilateral support for encouraging local production and suggests that WHO should focus its efforts on this region, while also attending to specific unmet needs in other regions.
- Taking into account all of the foregoing considerations, WHO might establish a resource centre combining human resource and virtual elements as a source of information and expertise to encourage local production of medicines in developing countries.

1. Transfer of technology and local production under the WHO Global Strategy and Plan of Action

On 24 May 2008 the World Health Assembly (WHA) of the World Health Organization (WHO) adopted the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA-PHI).¹ The Member States requested the WHO Director General to support implementation of the GSPA-PHI, and the WHO Department of Public Health, Innovation and Intellectual Property (WHO/PHI) is studying and pursuing mechanisms to carry out this request.²

GSPA-PHI aims to promote transfer of technology between developed and developing countries, and among developing countries and expressly envisages transfer of technology and promotion of “the production of health products in developing countries”. GSPA-PHI specifically addresses investment in building developing country capacity for “local production of pharmaceuticals”.³ With funding from the European Union (EU), WHO/PHI initiated a project to study

1 Sixty-First World Health Assembly, WHA61.21, Agenda Item 11.6, 24 May 2008. Resolution WHA 61.21, Para. 4 adopting GSPA-PHI requests the Director General of WHO: (i) to provide support for Member States, upon request, in implementing the global strategy and plan of action on public health, innovation and intellectual property and in monitoring and evaluating its implementation; and (ii) to support effective promotion and implementation of the global strategy and plan of action on public health, innovation and intellectual property.

2 See also Report by the WHO Secretariat, Sixty-Second World Health Assembly, Public health, innovation and intellectual property: global strategy and plan of action, Provisional agenda item 12.11, A62/16, 26 March 2009, and Add. 1 (Proposed time frames and estimated funding needs), Add. 2 (Proposed progress indicators), and Add. 3 (Open paragraphs on stakeholders).

3 GSPA-PHI incorporates as one of its aims to “(d) improve, promote and accelerate transfer of technology between developed and developing countries as well as among developing countries” (GSPA-PHI, Para. 14(d)). Among the principles of GSPA-PHI, “The promotion of technological innovation and the transfer of technology should be pursued by all states and supported by intellectual property rights” (Para. 19). Element 3 addresses building and improving innovative capacity, and includes among its key areas for investment “science and technology, *local production of pharmaceuticals*, clinical trials, regulation, intellectual property and traditional medicine” (Element 3, Para. 31 [emphasis added]). More specific action items in Element 3 include support for human resources development and scientific institutions, development of regulatory capacity and surveillance mechanisms, development of health innovation models, and strengthening of partnerships and networks (Element 3, Sub-para 3(1)–(5)). Element 4 of GSPA-PHI expressly addresses “Transfer of technology”. It provides, inter alia, that transfer of technology and *the production of health products in developing countries* should be promoted, that possible new mechanisms for such activities should be explored, and that better use of existing mechanisms should be considered “to build and improve innovative capacity for health-related research and development, particularly in developing countries”, including “through investment and capacity building” and “identification of best practices” (Element 4, Sub-para. 4(1) [emphasis added]). Element 4 goes on to support improved north–south and south–south collaboration, local and regional networking, transfer of technology in favour of least developed countries pursuant to Article 66.2 of the World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement), and promoting necessary training to increase absorptive capacity (Element 4, Sub-para. 4(2)).

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and make recommendations regarding mechanisms for promoting transfer of technology and local production of medicines in developing countries.

This paper is a broad survey of trends in this area, describing the structure of the global medicines production sector, the factors that motivate local production, the elements necessary for successful local production, and the extent to which transfer of technology is currently taking place, and ultimately providing recommendations regarding steps that might productively be undertaken to support local production of medicines in developing countries.

2. Public health and industrial policy

The mission of WHO is to support the protection and promotion of public health throughout the world. WHO is not chartered to promote economic development, which is a mission ascribed to other multilateral organizations, including the United Nations Conference on Trade and Development (UNCTAD), the World Bank and the World Trade Organization (WTO). The objective of GSPA-PHI is ultimately to help assure delivery of appropriate health care.

The preponderance of medicines on world markets is produced by private-sector enterprises, not by governments. Although the objective of transfer of technology and local production of medicines in developing countries is to promote public health, the successful establishment and operation of local production facilities is inherently linked to industrial policy (subnational, national, regional and international). Facilities that produce medicines are affected by factors and considerations that affect production facilities for other types of products, whether automobiles, computers or flat-panel televisions. There are, of course, aspects of medicines production that differ from other fields because of the public health impact. For example, there is a high premium placed on assuring the consistent quality and safety of medicines. However, many other industrial sectors must also pay strict attention to quality and safety. In looking at issues relating to local production of medicines, it is important to recognize that such production typically involves commercial business interests as well as public health interests, and that governments take into account both sets of interests when formulating policies.⁴

Governments are more likely to provide support for enterprises that are able to function profitably and contribute to the national economy than to subsidize facilities that drain budgetary and other resources, even if for important purposes. There is a place for “uneconomic production” to supply otherwise

4 Governments often provide direct and indirect support to particular industry sectors in order to promote industrial policy goals. Resources are limited, and policymakers typically must choose the sectors for support that they consider likely to yield the greatest benefits for the local population. Although the protection of public health may be one of the most important functions of a government, it does not necessarily follow that the government of a particular country will choose to provide support for local production of medicines. A government may decide that promoting automobile production will yield the greatest local economic benefits and that medicines will be purchased on the world market. Such a government may not be choosing against public health; it may rather be seeking to maximize overall domestic welfare.

unserved or underserved populations, but this is likely to remain the exception. It is therefore important to focus not only on the location of production facilities but also on the preconditions for establishing economically viable local production facilities.

The foregoing is a preface to the question: why do and should governments encourage local production of medicines? There are direct public health grounds for doing so. Local production facilities may assist in assuring a continuous supply of necessary medicines, particularly in cases of national and international emergency. In addition, a country that faces a comparatively localized threat to public health, such as a tropical disease endemic to a particular region, may find that it must step in to support local production because market-based producers do not adequately address local needs. A local production facility may provide an important link for local medicines researchers who wish to collaborate on the development and supply of new products to treat localized problems (including, for example, fixed-dose combinations that may be particularly suited to local needs). In specific cases such as a country facing a long-term requirement to provide a significant volume of human immunodeficiency virus (HIV)-related medicines to its local population, there are likely to be justifications for local production beyond those taken into account in the type of ordinary cost–benefit analysis typically associated with industrial policy.

Indirect public health and economic benefits of establishing and operating local medicines production facilities may also, however, provide justification for supporting such production. Production facilities provide employment opportunities for the local population. The technical qualifications needed for different parts of a production operation vary considerably, and yet even at a basic level, medicines production facilities require educated employees. The more highly skill-dependent operators of a production facility require university or other advanced technical education, such as training in chemical engineering and computer science. Without available jobs for chemical engineers, the demand for university education in that field is lower. There is a synergistic relationship between employment opportunity and education. Over time, education and employment build on each other, providing the foundation of the well-functioning society and public health system.

On a mainly economic note, producing goods within a country tends to improve the balance of payments and balance of trade (although this depends on the efficiency of local businesses). Local production facilities are likely to generate tax revenues for governments (subnational and national). The presence of a local production facility generates commercial activity for its surrounding community, including demand for housing, food, transportation, entertainment and other requirements. A local market is likely to develop for the supply of intermediate products (e.g. packaging materials). Although governments may profess to be “neutral” about the place where goods are made, this neutrality is belied by the myriad government efforts made to stimulate production of many types of goods and services “at home”. All of

these factors help to explain why governments of developing countries seek to promote local production of medicines.

There are, however, arguments that may disfavour local production, particularly when such production cannot be undertaken efficiently and competitively with the available supplies on the global market. If locally produced medicines are more expensive than imported medicines, then purchasing locally will increase direct procurement costs and strain the public health budget. There may be justification for a modest local production price premium based on the factors discussed above, but a significant price premium may not be sustainable or justifiable in the long run. In addition, although the concept of “medicines security” through local production is appealing, few countries are or will be in a position to produce and supply more than a fraction of the range of medicines necessary to treat the local population, particularly since pharmaceutical producers in most countries rely on importation of active pharmaceutical ingredients (APIs) from relatively few countries. Pharmaceutical production facilities are not readily converted from the production of one class of medicines to another, and the presence of some local production does not assure that a particular medicine will be available in a supply emergency.

A key – and unsurprising – finding of this report is that privately owned pharmaceutical companies tend to establish production facilities commensurate with market opportunities, whether those opportunities are in developed or developing countries. This finding is unsurprising because private pharmaceutical manufacturers are commercial enterprises, and commercial enterprises ordinarily seek to take advantage of market opportunities offering the highest potential returns. Well-capitalized private-sector originator and generics companies are focusing on market opportunities in emerging market countries and on penetrating wealthier developed country markets. Smaller and medium-sized generics companies may focus on local markets in developing countries, mainly because they do not have the resources to expand and compete globally. Industrial policy planners in developing countries tend to focus on improving the global competitiveness and profitability of local industry, and the principal concern may not be with addressing local public health needs.

A question raised by this report is whether the focus of well-capitalized companies and industrial policy planners on commercial market opportunities is having an adverse impact on parts of the world’s population that present lesser market opportunities and, if so, how WHO might facilitate some solution.

Financial and economic planners in developing countries may well view local pharmaceutical production as the potential source of economic benefits arising from creation of employment opportunity, increased taxes and reduced balance of payments outflows. Economic development is likely to enhance general well-being in a community, and this is likely to improve general health conditions among the public. Nonetheless, the focus of the WHO/PHI work on transfer of technology and local production is on whether

and how it can be made effective to supply pharmaceutical treatments to patients who would not otherwise receive them. This is important because a set of recommendations directed solely at the potential industrial policy goals of local production may be different from a set of recommendations directed toward public health objectives and specifically meeting unmet needs. For example, from an industrial policy standpoint, local production of medicines targeted towards competing in wealthy developed country markets might be the most attractive option for developing country planners. Yet, such an emphasis may not result in any appreciable improvement in the supply of medicines to the local population.

WHO/PHI is seeking to develop a set of recommendations regarding transfer of technology and local production that will emphasize the public health objectives. To do this, it must identify gaps in the availability of supply of needed medicines in developing countries and ask whether and how the establishment of local production facilities would address those gaps. This calls for a framework that integrates industrial policy and public health objectives.

3. Methodology, limitations, structure of report and definitions

3.1 Subject matter and limitations

This report addresses local production of medicines in the form of pharmaceutical therapies, including those comprised of small-molecule compounds, plant-based compounds, and other biological material-based treatments. The structure of the industry producing these therapies is described in the following section. This report does not address local production of vaccines, diagnostics or related devices. The production methods for these products differ significantly from those for pharmaceutical therapies, and the characteristics of demand and supply are substantially different. WHO is closely involved in assessment of global requirements for the production of vaccines, and it supports various efforts with respect to the development and distribution of diagnostics and devices. This report does not address those related efforts.

This report specifically concerns production and technology relating to production of medicines. There is considerable activity globally with respect to development of new production technologies, and these activities are addressed. However, this report does not address research and development (R&D) of new medicines.

3.2 Methodology

Several research approaches were taken to identify current trends in transfer of technology and local production of medicines in developing countries. These included: (i) interviews with pharmaceutical industry stakeholders in different industry segments and geographical regions; (ii) interviews with participants in

product development partnerships (PDPs) involved in medicines production; (iii) interviews with government officials; (iv) interviews with members of public health advocacy groups; (v) review of literature regarding transfer of technology with specific reference to local production of medicines; (vi) participation in workshops in Africa, Asia and Latin America with stakeholders involved in production and procurement of medicines, including presentation of interim results; and (vii) Internet-based identification of existing projects and programmes directed towards transfer of technology and local production of medicines.

There are also certain limitations with respect to the type of research materials that were reviewed. People involved in the construction and operation of medicines production facilities are trained in technical specialties, such as the development of machinery and equipment, facilities design and engineering, chemical engineering, and so forth. The literature surveyed for this report addresses policies and practices with respect to local production, and the types of background training useful in this area. It does not, however, survey literature that is used by technical specialists for undertaking their specific tasks (e.g. textbooks on chemical engineering).

In addition, a substantial number of governments maintain programmes of various kinds supporting local production for various sectors of the national economy, including production of medicines. Such programmes may include tax incentives, direct and indirect subsidies, tariffs and quotas, local procurement preferences, and so on. This report describes several of these types of programme operated within specific countries, but it does not canvas the individual industrial policies of WHO Members that may be supportive of or relevant to local production of medicines. Although a complete survey of such policies and programmes at the national level might be useful, it is not within the scope of this report.

Much of the initial research was conducted in the period September to December 2009, with follow-on consultations and discussions taking place throughout 2010, including at workshops. The research has been updated with new data as they have become available.

This research and report is part of a larger project that includes several components in its initial phase. The other components are (i) a survey of stakeholder views regarding local production, (ii) a landscaping of initiatives in this area focused on identifying gaps in therapeutic areas, (iii) eight case studies of local production projects that have been undertaken in developing countries, and (iv) a series of workshops convened to discuss the relevant issue with various stakeholders.

3.3 Structure of report

This report begins by describing the characteristics of local production and the factors currently affecting the global supply of medicines. It then presents the results of research, with respect to Africa, Asia and Latin America, that

seeks to identify the factors or elements necessary for the establishment and operation of local production facilities, particularly in developing countries. This includes research regarding the current situation with respect to transfer of technology and how that may influence capacity for local production. The results of discussions with industry stakeholders regarding their practices and perspectives, and a summary of studies addressing the problem of local production in developing countries broadly, are presented. This is followed by recommendations for a future work programme and the role that WHO might play in such a programme. These recommendations focus specifically on mechanisms that might facilitate access to medicines among those with unmet needs.

To promote “readability”, part of the background research for the report is presented in Annex I: Review of literature and Annex II: Medicines research and development and transfer of technology programmes not specifically linked to production. The body of the report incorporates summaries of literature that are related most directly to local production of medicines and associated transfer of technology. There is considerable additional literature regarding transfer of technology for R&D on new medicines, transfer of technology generally and, recently, transfer of technology to address climate change (which has common features with transfer of technology regarding medicines). This additional literature is identified and briefly summarized in Annex I. Section 6.2 of this report identifies existing projects or programmes specifically supporting local production of medicines in developing countries and associated technology transfer. Annex II identifies projects and programmes that are not specifically related to local production but that undertake or support R&D on new medicines and vaccines, provide financial support, or act as advocate for access to medicines. As noted in Section 6.2, there is not always a bright line between projects or programmes supporting local production and those encompassing other medicines-related activities.

3.4 Definitions

3.4.1 Transfer of technology

Negotiations regarding transfer of technology have taken place in multilateral forums at least since the early 1970s,⁵ and obligations regarding transfer of technology are incorporated in multilateral and bilateral agreements (e.g. see Article 66.2 of the TRIPS Agreement). Still there is no standard definition

5 For example, negotiations on a Code of Conduct for the Transfer of Technology were conducted at UNCTAD in the early 1970s (Patel et al., 2000; Roffe & Tesfachew, 2002).

of the term. For the purposes of this study, a broad definition of transfer of technology was employed:⁶

For working purposes, “transfer of technology” may be considered the conveyance from one party to another of information, know-how and performance skills, technical materials and equipment. Transfer of technology may take place in a variety of settings and ways. Educators and educational resources (books, Internet access, and so on) transfer technology to students. Scientific journals, patents (and patent databases) and other technical information resources transfer technology among the scientific community. Enterprise investors transfer technology in the form of materials, equipment and training among institutions and employees. Public and private patent and know-how licensors transfer technical information, implementing skills and, in some circumstances, materials and equipment. Temporary movement of people, including intra-corporate transferees and exchange of trainers, researchers and students can also provide exposure as well as transfer of know-how and skills. All of these activities may take place in a variety of configurations, whether public or private, institutional or individual, formal or informal, through partnerships or joint ventures, and within or across national borders. Finally, aid and cooperation for development has been pointed to by the literature as a means to design and build an enabling policy environment for technology transfer.⁷

6 This definition was developed in collaboration with experts at the International Centre for Trade and Sustainable Development (ICTSD) and UNCTAD. See also Maskus & Reichman (2004): “International technology transfer (ITT) is a comprehensive term covering mechanisms for shifting information across borders and its effective diffusion into recipient economies. It refers to numerous complex processes, which range from innovation and international marketing of technology to its absorption and imitation. There are also many different channels through which technology may be transferred. One major conduit consists of trade in goods, especially capital goods and technological inputs. A second is foreign direct investment (FDI), which generally transfers technological information that is newer or more productive than that available from local firms. A third is technology licensing, which may occur either within firms or between unrelated firms. Licenses typically involve the purchase of production or distribution rights and the technical information and know-how required to exploit them. ... There are also important non-market channels of ITT. Perhaps most significant is the process of imitation through product inspection, reverse engineering, and trial and error. A related mechanism is triggered when technical and managerial personnel leave a firm and start a rival firm based on information learned in the original location. Still another means is to study information available from patent applications. Thus, patents provide both a direct source of technology transfer, through FDI and licensing, and an indirect source through legally regulated disclosures. Indeed, ‘trade in ideas’ is a significant factor in world economic growth, and developing economies could gain considerably more access to foreign technologies as international firms take out patents in their locations. Nevertheless, this benefit remains dependent on local abilities to learn from incoming technological information, and on the diffusion practices or strategies of technology-exporting firms. ... Much knowledge appears to be transferred through the temporary migration of students, scientists, and managerial and technical personnel to universities, laboratories, and conferences located mainly in the developed economies. Finally, technical information may be available from the public domain, making it free for taking, or from a research commons accessible with certain restrictions.”

7 In specific fields relating to production of or R&D on new medicines, it may be possible to define transfer of technology more narrowly. However, the use of narrower formulations might result in the capture of less information concerning ongoing activities. One participant from an originator pharmaceutical company in a group meeting concerning this overall project proposed further work to establish a narrower definition of technology transfer that would exclude, by way of illustration, corporate collaboration with academic research institutions. However, in light of the focus of GSPA-PHI on R&D collaboration, the author of this report considered that such a restriction might result in an overly narrow examination of the types of collaborative activities that are ongoing.

3.4.2 Local production

Local and foreign ownership

GSPA-PHI expressly refers to promoting capacity for “local production of pharmaceuticals” in developing countries and promoting the “production of health products in developing countries”. The term “local production” can have different meanings when used in the context of manufacture of pharmaceuticals (Kaplan & Laing, 2005). One of the objectives of this overall project is to assess whether there is or should be a preference for the way the objective of local production is implemented, and that may depend upon how the concept of “local production” is defined. From a geographical standpoint, the term “local” is presumed to encompass at least the territory of a single nation-state. “Local production” might also be understood or interpreted to cover manufacturing taking place within a “region”. The term “local” may also be used to imply nationality of ownership, such that “local production” would refer to control over production facilities by nationals of the host country. This would distinguish “local production” from production by subsidiaries or affiliates of multinational pharmaceutical companies.

Perceived advantages of ownership by local nationals

Interviewees in and from developing countries identified several potential advantages of ownership of production facilities by local nationals. A principal perceived advantage is that nationals of host countries are more likely to maintain local operations in the face of changing economic circumstances than are multinational actors. Because local national owners have stronger ties to the community, and because they may face substantial practical obstacles to moving production outside their home countries, there is a perception that these local owners add an element of stability and continuity to the production and supply environment (including related employment opportunities). This stability and continuity may contribute to security of the pharmaceutical supply chain, including avoidance of supply disruptions. Another perceived advantage of ownership by local nationals is that local owners are more likely to take an interest in the development of domestic technology capacity, including through providing support for training of local personnel. This may involve establishing long-term relationships with local education and training institutions, and may include providing financial and technical support. An additional perceived advantage is that locally-owned enterprises help to establish or maintain a competitive market environment that may constrain the pricing power of multinational suppliers. Another perceived advantage of local ownership of production facilities is that revenues earned from such facilities are more likely to be reinvested in the national economy than are revenues earned by foreign owners (which are more likely to be transferred abroad). Each of these grounds for encouraging local national ownership (compared with foreign ownership) is plausible, recognizing that foreign owners of local production facilities may also provide similar forms of support. Empirically proving or disproving the validity of the perceived advantages of

local ownership from the standpoint of the net result on national public health and welfare would be quite difficult.

Based on interviews and the literature, it is reasonable to conclude that multinational investors and local nationals may have somewhat different motivations for and interests in establishing local pharmaceutical production facilities. Those motivations and interests may result in differentiated behaviours. Whatever might be the consequences of those differentiated behaviours, governments of developing countries are encouraging foreign investment in their pharmaceutical production sectors for a variety of reasons, including generation of employment, technical training of labour and improving security of supply.

In conducting research for this report, the definition of “local production” was not limited to manufacturing facilities owned by nationals of a host country. This report draws a distinction, where appropriate, between different forms of ownership of local production facilities, but it does not presume that GSPA-PHI references to “local production” are limited to facilities owned by nationals of host countries.

4. Structure of global production sector

4.1 Organic chemistry-based production

Production of pharmaceutical products may generally be broken down into stages of the production process (Kaplan & Laing, 2005). These stages involve (i) production or collection of raw materials or basic inputs; (ii) synthesizing the APIs that perform the therapeutic functions of the end products;⁸ (iii) formulation of the APIs with inactive materials that facilitate delivery in the human body, such as combination of APIs with binders and other excipients, and creating tablets, capsules, liquids or other forms of drug delivery; and (iv) packaging and labelling of the finished pharmaceutical products.⁹ Each of these four stages involves a series of processes or steps, the complexity of which varies depending upon the characteristics of the particular pharmaceutical product being manufactured. Furthermore, the production of “biological” pharmaceutical products that are composed of or derived

8 Kaplan & Laing (2005) provide the following definitions: An “intermediate” is a material produced during steps of the processing of an API that must undergo further molecular change or purification before it becomes an API. An “API” is a biologically active compound(s) in a drug formulation that imparts the desired therapeutic effect. APIs are usually first obtained in the crude state (if there is no biological activity, they might be considered “intermediates”), and subsequent production operations convert the crude material to the final API that meets the pharmacopoeial or similar requirements. A sterile API is an API that has been subjected to additional processing steps to remove microorganisms.

9 A product must be developed in a way that will permit it to be manufactured on a significant scale, and suitable production processes must be identified. Assuming the manufacturer intends to rely on external sources of supply for raw materials, APIs or excipients, appropriate suppliers must be identified. A pharmaceutical manufacturing facility must be designed and constructed, or reconfigured, to follow the production processes that have been laid out. The production facility must be put into operation and tested, and it must be approved by local regulators as meeting relevant standards of good manufacturing practice (GMP).

from biological materials involves substantially different types of processing than the production of “synthetic organic chemistry-based” pharmaceutical products.

The raw materials or basic inputs to synthetic chemistry pharmaceutical production are chemicals that usually are readily available on international markets. There are, however, exceptions. Some synthetic compounds use plant materials that may be grown in limited geographical areas, and where large-scale production may involve sophisticated growing techniques. Some synthetic compounds use animal-based raw materials that are subject to supply limitations.

The production of chemistry-based APIs involves a series of steps in the synthesis of chemical compounds, which typically requires close monitoring of chemical reactions, changes in temperature, pressure and other factors. The production of some relatively simple APIs involves limited steps and straightforward technical processes. The production of some relatively sophisticated synthetic chemical compounds may involve more than 100 discrete processing steps and the maintenance of extremely close tolerances (Henry J. Kaiser Family Foundation, 2004).

It is necessary to maintain strict environmental and quality assurance standards in the formulation and packaging and labelling stages of the pharmaceutical production process.¹⁰ However, as a general proposition, these stages are less technologically demanding than the production of APIs. Formulation of pharmaceutical products involves combining active and inactive materials in a controlled environment. This may require close attention to the sensitivity of materials to environmental factors, and close attention to the tolerances of end-products to variability. Packaging and labelling of pharmaceutical products may be more technologically demanding than packaging and labelling of most other consumer products because, for example, of requirements that individual packages be identifiable by code (e.g. for purposes of recall), and sophisticated high-volume manufacturing facilities may employ packaging and labelling equipment that is technologically advanced.

4.2 Biologicals production

It is only in the past decade or so that the production of “biological” pharmaceutical products (or “biologicals”) has become a significant factor in

¹⁰ Formulators produce under national regulatory regimes that apply different standards of GMP, and the level of national regulatory oversight of GMP compliance varies. In order to sell into the United States of America and the European Union markets, a pharmaceutical manufacturer must meet the current Good Manufacturing Practice (cGMP) standards of the United States Food and Drug Administration (FDA) and the European Medicines Agency (EMA), respectively. To sell to the Global Fund and other multilateral procurement agencies, a manufacturer must be approved pursuant to the WHO Prequalification Programme or be determined to already be subject to stringent regulatory standards (e.g. approved by the United States FDA or EMA).

the production sector.¹¹ Biological pharmaceutical products are manufactured using substantially different types of starting materials and production processes than traditional pharmaceuticals produced by synthetic organic chemistry.¹² The production of biological pharmaceutical products is highly dependent upon the creation of the biological source material, which is subject to replication using substantially different techniques and equipment than is involved in synthetic chemistry, and requires close attention to avoidance of contamination.¹³

4.3 Originators and generics

In addition to the division of the pharmaceutical production sector into stages, there is a generally recognized division between originators and generic producers.¹⁴ The originators are the pharmaceutical enterprises that invest in R&D of new therapeutic products, and typically protect their investments with patents and regulatory exclusivity that precludes competitive production by generic manufacturers.¹⁵ The aggregate dollar value of annual global originator pharmaceutical sales far exceeds generic pharmaceutical sales (approximately

11 "Biological products include a wide range of products such as vaccines, blood and blood components, allergenics, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins. Biologics can be composed of sugars, proteins, or nucleic acids or complex combinations of these substances, or may be living entities such as cells and tissues. Biologics are isolated from a variety of natural sources – human, animal, or microorganism – and may be produced by biotechnology methods and other cutting-edge technologies. Gene-based and cellular biologics, for example, often are at the forefront of biomedical research, and may be used to treat a variety of medical conditions for which no other treatments are available" (FDA, 2010).

12 Regarding the development of regulatory standards, see Knezevic (2009). Regarding various uses and definition of the term "biotechnology", see Seuba & Correa (2010, pp. 8–9).

13 As noted in regulatory guidance from the European Union: "Unlike conventional medicinal products, which are reproduced using chemical and physical techniques capable of a high degree of consistency, the production of biological medicinal products involves biological processes and materials, such as cultivation of cells or extraction of material from living organisms. These biological processes may display inherent variability, so that the range and nature of by-products are variable. Moreover, the materials used in these cultivation processes provide good substrates for growth of microbial contaminants.

"Control of biological medicinal products usually involves biological analytical techniques which have a greater variability than physico-chemical determinations. In-process controls therefore take on a great importance in the manufacture of biological medicinal products" (Vol. 4, Annex to Annex 2 of "The rules governing medicinal products in the European Union" containing guidance for the interpretation of the principles and guidelines of good manufacturing practices for medicinal products for human and veterinary use laid down in Commission Directives 91/356/EEC, as amended by Directive 2003/94/EC, and 91/412/EEC respectively (http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol4_en.htm)). See also WHO (2009).

14 On the distinction between the originator and generic pharmaceutical sectors, see Abbott & Dukes (2009).

15 Multinational originator pharmaceutical companies are vertically integrated, at least in significant part. They manufacture or control (through contract) the APIs used in their patent-protected products. A relatively small portion of generic pharmaceutical companies produce the APIs used in their formulations, although the largest and most successful global generics companies are among those that do produce their own APIs.

US\$ 680 billion compared with US\$ 120 billion, respectively), although generic sales substantially exceed originator sales in unit volume.¹⁶

Generic producers often make substantial investments in developing new production processes and techniques and new drug-delivery systems. In addition, although the principal distinction between originator and generic producers is that the former invest in R&D in new therapies while the latter do not, the line between the two types of producers is increasingly blurred. In recent years, originator companies have increasingly moved into generic markets as patent expirations are negatively affecting profits, while several of the more technologically sophisticated generics producers are investing in R&D in new products.¹⁷

In principle, sophisticated generic producers in developing countries are capable of manufacturing the pharmaceutical products of the originator companies. It is not unusual for an originator company based in Europe or the United States of America to contract with a manufacturer in India for the production of APIs or formulated products. Nonetheless, based on interviews with originator enterprises, it appears that these originator companies may limit the stages of production allocated to developing country producers and perform certain “proprietary” stages of production in their own facilities in Europe or the United States in order to maintain control over their patent-protected products. In other words, at least some originator companies are reluctant to outsource the most technologically sensitive aspects of their production processes to contractors in developing countries in order to avoid losing control over their high-margin products.

4.4 Traditional medicines

The term “traditional medicine” describes a group of health-care practices and products with a long history of use. WHO (2008) defines traditional medicine as “the sum total of knowledge, skills and practices based on the theories, beliefs and experiences indigenous to different cultures that are used to maintain health, as well as to prevent, diagnose, improve or treat physical and mental illnesses”.

Traditional medicines may include plant-, animal- and mineral-based substances found in nature but that may be subject to further processing (such as by extraction of active ingredients, purification or the combination of substances). Traditional medicines may be harvested or gathered from their natural or “wild” environment, or they may be cultivated, including through advanced farming techniques. Traditional medicines may contain complex mixtures of organic chemicals, which may vary depending on the variety

16 For 2010 data, see Lewis (2010). For 2009 data, see IMS Health (2009): “IMS Health ... reported today that the value of the global pharmaceutical market is expected to grow 2.5–3.5 percent on a constant-dollar basis in 2009, two percentage points lower than indicated last October, as deterioration in the global economic environment continues to affect market demand. The updated forecast predicts global pharmaceutical sales exceeding \$750 billion for the year, down from the \$820+ billion forecast in October 2008, reflecting both the lower growth rate and currency exchange fluctuations.”

17 E.g. see Boston Consulting Group (2010, slide 14).

of the substance used and other factors related to growth, production and processing (Bent, 2008).¹⁸

4.5 Geographical dispersal of local production

In the following sections of this report, studies with respect to regions are summarized, along with the results of meetings and interviews with industry stakeholders. As a brief summary of the present situation, most pharmaceutical producers located in developing countries are engaged in the later stages of production, including formulation, packaging and labelling. In Africa, there is limited API production in South Africa, but otherwise the region is entirely dependent on imported APIs. In Latin America, Argentina and Brazil maintain some API production capacity, but regional API production on the whole is limited, with principal reliance on imports. The situation for developing countries in Asia is different. India maintains a highly sophisticated API production capacity, and China's API production capacity appears to be evolving rapidly. (The Republic of Korea, Singapore and Taiwan, China are also significant APIs producers, although these countries are not generally considered "developing" (Abbott, 2006).) Sourcing of raw materials for the production of APIs is generally from chemical manufacturers that are distributed widely among developed and developing countries.

Multinational originator pharmaceutical companies are vertically integrated, at least in significant part. They manufacture or control (through contract) the APIs used in their patent-protected products. A relatively small number of generic pharmaceutical companies produce the APIs used in their formulations. The major concentration of vertically integrated generic producers appears to be based in Canada, China, the European Union (EU), India, Israel and the United States. The major concentration of API suppliers to third parties appears to be based in China, India and the Republic of Korea (Abbott, 2006).

Until recently, production of biological pharmaceutical products was essentially limited to originator biotechnology-based originator companies located in a few developed countries. However, enterprises from developing countries have commenced producing biological pharmaceutical products, and some are exporting these products to markets in developed countries (Lewis, 2010).¹⁹ There is a substantial level of commercial interest among developing country pharmaceutical enterprises in entering the biological product market

18 Many traditional medicines have a long history of therapeutic use and claimed health benefits in traditional medical systems such as Ayurveda (traditional Indian medicine). Specific Directive (2004/24/EC) amending, as regards traditional herbal medicinal products, Directive 2001/83/EC, available at <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2004:136:0085:0090:EN:PDF>. Over the past several decades, considerable attention has been paid to identifying and isolating the active ingredients of traditional medicines.

19 Global sales of biologics in 2010 will exceed US\$ 120 billion (IMS Health, 2010). Biosimilar producers include Indian manufacturers and generic producers from Israel (Marth, 2009; Sharma, 2009).

because global capacity in this area is significantly more limited than in the chemistry-based pharmaceutical market.²⁰

Whether or not producers of biological pharmaceutical products in developing countries are authorized to import into the developed country markets, such producers appear likely to supply a share of the developing country market for these products.

There are many developing country “local producers” of pharmaceuticals that meet the regulatory standards (GMP) of their national authorities but are not able to export to developed country markets or supply procurement programmes operated by multilateral agencies. This limits the potential scale of production, the development of production efficiencies, and operating more profitably based on export sales. Limitation of profitability reduces the capital available for reinvestment and, over the longer term, the possibility for investment in R&D on new drugs.

There are private enterprises occupying different levels and niches in the supply chain, and the international market is highly competitive (e.g. Shepherd, 2009). There is a great deal of information available regarding global pharmaceutical market characteristics (e.g. Shepherd, 2009), although data concerning the location and function of production facilities are less transparent (Kaplan & Laing, 2005).

Production of traditional medicines is widely geographically dispersed, although commercial and export-scale production appears to be concentrated in a limited number of countries.²¹ Markets for traditional medicines are large and have been growing significantly,²² including in developed countries. Substantial parts of the populations in Europe and the United States, for

20 A great deal of controversy surrounds technical aspects of producing so-called “biosimilars” or “biological equivalent products”. The developed country enterprises that have originated the biological pharmaceutical products argue that it is very difficult or problematic to produce biological equivalent products without access to the identical starting materials used by the originators. Developing country enterprises seeking to enter the biosimilars market argue that all biological products have a range of tolerance for differences and that originators produce in a range of differences. They argue that they are capable of producing high-quality biological equivalent products.

21 In China, for example, in 2007 the domestic industrial output value of traditional Chinese medicines was more than 177 billion yuan (about US\$ 26 billion), accounting for 26.53% of China’s total pharmaceutical industrial output value (Information Office of the State Council of the People’s Republic of China, 2008).

22 The Indian Government estimates that there is a US\$ 120 billion per year global herbal market (National Medicinal Plants Board et al., 2008).

example, make use of traditional medicines imported from developing countries.²³

For the worldwide generics industry based on synthetic organic chemistry, from a strictly economic standpoint this is a difficult period. There is significant capacity and intensive price competition affecting the market. Inefficient operators are being forced out (Cacciatore, 2009). Generic producers in developed countries with higher fixed and variable costs find it increasingly difficult to compete with efficient large-scale producers from developing countries. At the same time, as major multinational originator companies are facing the imminent expiration of a large number of key patents, these originator companies are focusing on the marketing of “branded generics”, significantly increasing well-financed competition in the generics sector (Boston Consulting Group, 2010; Wilson, 2011). From a strictly economic standpoint, investing in manufacturing facilities for production of chemistry-based generic pharmaceutical products, wherever in the world, means investing in a supply market facing a general situation of overcapacity and aggressive price competition.

4.6 Strategic grounds for investment

Some highly capitalized originator pharmaceutical companies are investing in production facilities in certain developing countries based on corporate strategic interests. As gross domestic product (GDP) in larger developing country markets increases, originator pharmaceutical enterprises are seeking to expand their sales in those markets. From a cost, technical and logistical standpoint, the multinational originators might prefer to supply these emerging markets from large-scale production facilities located in developed or developing countries, but there may be business strategic reasons for investing in local production facilities. National governments in emerging market countries may view foreign investment in local production facilities favourably for a number of reasons. These reasons include industrial policy grounds such as providing employment opportunities for local individuals, increasing the domestic tax base and providing training of local personnel. Reasons also include public health grounds such as improving security of supply of pharmaceutical products. From the standpoint of the originator-investor, it is important to be perceived favourably by the national government. The establishment of a local production facility may facilitate interaction with

23 Regarding reliance on traditional medicine more broadly, see R. Abbott (2009) (“Because traditional medicine (TM) may be more affordable and accessible than western medicine, it has played an important role in meeting the demands of primary health care in many developing countries. For example, data indicates that 70 to 80 percent of the population in India and Ethiopia depend on TM for primary health care. Developed nations have also witnessed renewed interest in the use of traditional medicine. Seventy percent of the population in Canada and 80 percent in Germany are reported to have used it as complementary and/or alternative medical treatment. And yet, TM remains largely marginalised from national health services”) and R. Abbott et al. (2010) (“A recent study of CAM use in the [US] general population reported that in 2007 almost 4 out of 10 adults had used some form of CAM within the past year. In 1998, it was estimated the US public spent between \$36 and \$47 billion on CAM therapies, with \$12–\$20 billion of that total spent out-of-pocket for professional CAM services. (This was more than the out-of-pocket fees for all hospitalizations in that year, and about half the amount paid for all out-of-pocket physician services)”).

regulatory officials in terms of product approvals, and it may facilitate bidding on supply contracts into the local public health system. Although there may be some cost disadvantages to constructing additional production facilities when products could be supplied from abroad, the cost differential may not be so significant as to outweigh the advantages from improving presence in the local market. In this context, national governments in emerging economy countries and originator investors perceive a win–win outcome from local production of pharmaceutical products. This is not to suggest that developing country governments as a matter of principle would prefer foreign direct investment (FDI) to investment by local national entrepreneurs. However, because investment capital is a limited resource for all countries, national governments must balance their approach to distinguishing among sources of investment capital.²⁴

There are only a limited number of developing countries that offer the scale of opportunity for multinational investors such as to justify strategic investment for the purpose of improving presence in the national market.

5. Local production from the regional perspective

5.1 Africa and the Middle East

5.1.1 Africa stakeholder meeting perspective

In December 2009 a meeting of stakeholders from Africa was convened to discuss technology transfer for local production. The meeting was organized by the International Centre for Trade and Sustainable Development (ICTSD) in conjunction with UNCTAD and WHO/PHI (UNCTAD & ICTSD, 2009).

African local producers from throughout the region stressed obstacles they confront in comparison to producers from other regions. First, capital costs, including the cost of borrowing, are very high in the region. This inhibits investment in plant and equipment and adds to the selling price of medicines. Second, supplying to multilateral institutions and foundation programmes requires that the medicine/producer is approved by the WHO Prequalification Programme (alternatively, the national regulatory authority must be considered “stringent”, which is a standard designed to accommodate the United States FDA and EMA).²⁵ Thus, even though an African producer may otherwise be qualified to supply the national HIV/acquired immunodeficiency syndrome (AIDS) treatment programme, if that programme is funded by

24 The foregoing discussion is based on interviews with multinational originator enterprise personnel. The sample of interviewees is not sufficient to suggest a consensus view among the multinational originator companies.

25 These standards generally reflect the guidelines of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). However, the United States FDA and EMA operate on the basis of their own regulatory frameworks, and the requirements of those frameworks are most relevant for producers.

foreign donors the African producer will not be able to participate. This creates a negative feedback loop as exclusion from this market reduces funds available for reinvestment. Some producers (e.g. from Zimbabwe) indicated that the consequence of the WHO Prequalification Programme was to force them out of a market in which they had previously participated. Third, there is a common belief among African producers that pharmaceutical exports from India and China are subsidized by their home governments, exacerbating the difficulties in meeting price competition.

As a general matter, it is difficult for local African producers to compete with foreign suppliers operating large-scale efficient production facilities. Moreover, government tariff and tax policies sometimes operate in favour of imports; for example, governments may limit tariffs on imported formulations but impose significant tariffs on API imports, thus making it extremely difficult for local formulators to compete on price with imported formulations. Local producers, on the other hand, may be given limited pricing preferences for government tenders.

Underinvestment in regulatory capacity leads to a situation in which obtaining approval for construction or completion of a new pharmaceutical production facility is extremely time-consuming. In addition, there is limited local capacity to undertake safety, efficacy and bioequivalence studies and clinical trials that may be required for product registration.

African stakeholders suggested that locally producing medicines already in abundance (e.g. paracetamol) is not the way forward. Development of human resource capacity is very important. Higher education should focus more on production skills and know-how for the pharmaceutical sector. There should be greater interlinkage between universities and industries in the development of products. There should also be practical training in working under GMP-compliant manufacturing standards. In order to improve human resources, job opportunities are necessarily required.

Representatives of least developed countries (LDCs) suggested that the 2016 WTO TRIPS Agreement extended transition deadline for enforcing patents should be extended further. Foreign joint venture partners in local production efforts are concerned about what will happen in 2016.

Integration of the regional market should be encouraged to facilitate trade among countries on the continent. Solutions must be found for reducing intraregional transport costs. There was general support for the integration of the sub-Saharan African pharmaceuticals market to enable producers to improve economies of scale.

Governments should provide incentives to promote joint ventures between domestic and international firms, such as procurement preferences for local production and tax benefits.

There was a suggestion to create integrated web portals providing guidance for regulatory pathways and requirements, and direction to resources for

industrial matters. There should be investment in capacity for drug regulatory authorities, including improved capabilities for assessing bioequivalence and for assessing GMP compliance of local facilities. Steps should be taken to address the adverse consequence of multilateral funding agency guidelines requiring compliance with WHO prequalification or stringent standards.

5.1.2 South Africa and South African Development Community industry group perspective

The head of the South African Generic Manufacturers Association and a new South African Development Community (SADC) regional generic producers association observed that establishing local manufacturing in sub-Saharan Africa is made difficult by tax and tariff policies. For example, in Zambia there are low tariffs on imports of finished products, but there is a 25% tariff on imported APIs, making it economically infeasible to competitively formulate finished products in the local market.

Production facilities established in sub-Saharan Africa tend to have higher production costs than similar facilities in countries such as India. This is because of poor infrastructure, high utility costs (water and electricity), high capital costs and limited availability of experienced personnel. Sub-Saharan African producers have difficulty achieving economies of scale, particularly using older technologies. Sub-Saharan African producers are entirely reliant on imported APIs. African governments are limited in the extent they can purchase from local producers because of higher prices. The weak state of sub-Saharan air transport means that it is typically cheaper to import products from India than to ship between sub-Saharan countries.

A representative of the local industry indicated that security of supply is a major issue for South Africa. During the Beijing Olympics, the Government of China closed chemical factories, and South Africa was faced with shortages of API imports.

African generics producers are confronted with negative advertising campaigns by foreign multinational producers that criticize local African products. It was suggested that WHO might apply pressure on the multinationals to stop this type of advertising.

Support from WHO and others would be particularly useful for training local personnel in achieving compliance with stringent GMP standards.

Representatives of South African industry referred to a proposal for the construction of an API facility in South Africa for antiretroviral (ARV) drugs and suggested that because of the large number of individuals using ARVs in South Africa, this appears to be a reasonable proposal.

5.1.3 Additional expert perspective on local production in Africa

Dr Giorgio Roscigno, Chief Executive Officer of the Foundation for Innovative New Diagnostics, and formerly a senior executive of a major originator company, is a long-time advocate of enhancing local production capacity in Africa. He has been involved in a number of projects intended to facilitate that objective. In an interview, he noted the following: (i) lack of vertical integration and infrastructure in the manufacturing process required to produce good-quality drugs; (ii) lack of training of skilled technicians; (iii) limited industrial know-how in manufacturing; (iv) gaps in quality of analytical technologies; (v) lack of capabilities for local chemistry synthesis procedures; (vi) weaknesses in national regulatory authorities capable of regulating and monitoring manufacturing quality; (vii) lack of government incentives; and (viii) lack of access to the donor market.

Dr Roscigno suggested that these barriers can be overcome through targeted technology transfer and focused training. With appropriate capacity building, a sustainable technological platform can be created. He suggested that the advantages of transfer of technology in the pharmaceutical sector are fostering national scientific and technological capacity. Local pharmaceutical manufacturing can be a focal point for a knowledge- and skills-oriented society, and for a transition into value-added manufacturing. Local manufacturing has a high impact on educational level and local education systems and increases employment. It enhances economic self-sufficiency, improves substantially national pharmaceutical policies, diminishes the risk of counterfeit drugs, and provides long-term sustainable conditions for R&D capacity for drugs for neglected diseases.

Dr Roscigno suggested that a business model for encouraging the development of local production capacity in Africa be based on voluntary licensing from the originator sector to enterprises in Africa. This would include transfer of manufacturing technology (including know-how) and training in achieving stringent GMP compliance. Licences should permit competitive marketing and sales in the private sector but should also require low-cost supply to the public sector. Public-sector sales would be given priority over private-market sales as part of the voluntary licensing agreement. Governments would play a role by providing financing support for the marketing launch of the African private sector licensee.

Dr Roscigno observed that to take full advantage of building capacity, a country must address all elements of the value chain. Unless a country has the capacity to synthesize active pharmaceutical ingredients, its R&D must be out-licensed to foreign manufacturers that will capture the value added. Both Japan and the Republic of Korea followed industrial policies that forced foreign companies to conduct clinical trials in those countries in order to have medicines approved, resulting in local industry developing expertise in conducting clinical trials. Industrial policy measures are necessary for developing local industry.

5.1.4 Literature on African local production

Overview

IFC (2007)

The International Finance Corporation (IFC) of the World Bank Group, with funding from the Bill & Melinda Gates Foundation, and with information gathering and analysis by McKinsey & Company, completed a study in late 2007 that examined in some detail the state of local manufacturing of pharmaceutical products in sub-Saharan Africa. Some of the key findings of that study are:

- More than 70% of sub-Saharan Africa's US\$ 1 billion in annual pharmaceutical production is concentrated in South Africa. Nigeria, Ghana and Kenya together account for about 20% of the region's production. Kenyan manufacturers export 35–45% of production value to the East African Community (EAC) and Common Market for Eastern and Southern Africa (COMESA) countries.
- Thirty-seven sub-Saharan African countries have some pharmaceutical production capacity, with 34 of these having capacity for formulation. Only South Africa has limited API production capacity.
- Local producers have low participation in the donor purchasing market because they lack WHO prequalification or have not met stringent regulatory standards. Only two sub-Saharan manufacturers offer WHO-prequalified products.
- Sub-Saharan African producers typically operate at a cost disadvantage to large Asian generic manufacturers. A substantial part of that cost disadvantage is based on absence of economies of scale.
- Both fixed and variable (including labour) costs are higher for sub-Saharan African producers than for Asian producers, with higher financing costs, less than optimal or outdated facility design, and tariff policies that may increase local production costs.
- Freight costs for intra-sub-Saharan African trade may exceed freight costs for importation from Asia, and intraregional trade is often subject to the same tariffs as extraregional import trade.
- Sub-Saharan manufacturers benefit from (i) preference policies for public tenders, (ii) tax benefits on raw materials, intermediates and final products, and (iii) import bans on selected medicines.
- Evidence is unclear as to whether local production would improve the level of quality or reduce the introduction of counterfeits in the region.
- Stakeholders expressed concern over security of supply and suggest that local production will increase such security. Availability of APIs represents a key potential vulnerability, although it may be difficult to establish local API production (given scale and expertise disadvantages). An alternative is for local manufacturers to acquire offshore API sources.

Suggestions in the study for improving local manufacturing competitiveness include:

- increasing the scale of manufacturing to reduce unit costs and improve the prospects for obtaining WHO prequalification;
- aggregating national markets into regional markets;
- entering into partnerships (including licensing) or contract manufacturing arrangements with multinational companies;
- focusing on the commercialization of drugs to address infectious and neglected diseases endemic to the region, including forming associations with PDPs.

*Gulmier et al. (2004)*²⁶

The issue of domestic production of drugs in developing countries has provoked lively discussion since the end of the 1970s. During this time period, several international organizations, including the United Nations Industrial Development Organization (UNIDO), supported efforts to establish pharmaceutical industries in these countries in order to reduce dependence on imported drugs, create employment, and earn foreign exchange as well as improve access to drugs. However, few of these efforts were successful, and international interest in supporting drug production in these countries waned.

The concept of access to drugs has continued to evolve, and is often defined in terms of four dimensions relative to access to quality drugs, i.e. those that are manufactured in plants that meet Good Manufacturing Practice (GMP) standards, are properly registered, and that reach the end-user through distribution systems that include quality assurance systems. These four dimensions include: geographical accessibility, physical availability, acceptability, and affordability. Of these, the first two are largely dependent on functioning distribution systems rather than the location of drug manufacturing and the third is often dependent on marketing, as end-users in developing countries may need to be persuaded to choose domestically produced drugs over imports. This leaves affordability as the primary opportunity for domestic production to have an impact on access to drugs.

The recent focus on ensuring access to the drugs used to treat HIV/AIDS, tuberculosis (TB), and malaria, diseases which disproportionately affect the populations of Sub-Saharan Africa (SSA), and to ensure their quality, has raised the question of whether the production of these drugs in the region can improve affordability while meeting quality standards. As of June 2004, no enterprise within SSA had been prequalified by the World Health Organization (WHO) for drugs related to these diseases. However, within the past year, several initiatives to start up production, especially of anti-retrovirals (ARVs), have been launched in SSA in order to increase their affordability.

This study seeks to contribute to the discussion of domestic production by analyzing, from a business context, whether or not such production of drugs

²⁶ Author's executive summary.

in SSA is sufficiently profitable to enable an enterprise that produces drugs to be a going concern while at the same time enabling increased access to drugs by providing them at prices lower than those available from international sources.

When the factors that affect the operations of a going concern in SSA are examined, including those related to the country environment, government strategy and policy, and potential market size, a few countries appear to offer a moderately favorable climate for pharmaceutical production in terms of political risk and human resource availability, but throughout the region drug manufacturers face obstacles in terms of access to financial capital, technical know-how, purchasing and maintaining equipment, and obtaining spare parts. Furthermore, domestic producers face several challenges in the market place. First, institutions and governments will be major buyers of the currently recommended drugs to treat HIV/AIDS, TB, and malaria and will be obliged to respect the procurement guidelines of major donors. For domestic producers, this means that the drugs they manufacture for these buyers have to meet international quality standards, such as those of WHO prequalification, as well as be competitive in price with drugs that are produced on a large scale by international competitors. Second, most national markets in SSA are too small alone to absorb the production of drugs to treat these three diseases. This requires domestic manufacturers to develop an export strategy, which will require registering their products in each of the countries they export to as well as negotiating and obtaining licenses, where necessary, for the right to export drugs still under patent to countries that are signatories to the Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement.

To examine the potential for a going concern that manufactures drugs to operate under these conditions, this study uses a model to simulate the cost structure of an imaginary enterprise manufacturing quality drugs, based in West Africa and serving a market covering 236 million people (i.e. 35% of the entire population of SSA) in 12 countries. This region was chosen because the proximity of countries belonging to different economic trading blocs and different language zones presents opportunities as well as constraints. ...

In conclusion, it appears that under certain conditions (i.e. at prices that are competitive with those of imported drugs, with significant market share, a stable political context, and the production of drugs to treat both priority diseases and conditions of lesser public health importance etc.) domestic production in SSA has the potential to be financially viable as well as to offer the possibility of a modest reduction in the ex works prices of quality drugs. However, there is no guarantee that all of the drugs produced will necessarily meet widely accepted international quality standards, because the WHO prequalification only covers a limited set of drugs. The financial viability of the enterprise appears fragile because it depends on two significant factors which it cannot totally control: the price of API and market share. The inability to obtain favourable prices for API from suppliers, or failure to obtain needed market share would threaten the ability of the enterprise to continue as a going concern. In addition, the enterprise will: (i) have to ensure that the products

which it will sell through international and national tendering procedures are prequalified by the WHO (or registered in a country that is a member of either the International Conference on Harmonization, ICH, or the Pharmaceutical Inspection Cooperation Scheme, PICS); (ii) successfully register all of its products in each country it exports to; and (iii) obtain compulsory licences and voluntary licences as needed to produce patented drugs for both domestic consumption and export requirements. Lastly, the logistics for supplying API, equipment, spare parts, and ensuring maintenance will have to be assured in order to avoid costly delays and interruption of production.

Further research is needed in several areas, particularly those related to manufacturing and quality, distribution, and intellectual property.

- To reinforce manufacturing quality, operational research could help better define the human resource needs and additional costs that current manufacturers would incur in order to consistently meet GMP standards and to prepare comprehensive dossiers for their products.
- Exploring the possibility of subsidizing API. Just as the prices of products which are considered vital are subsidized in many countries, this intervention could help make essential drugs more affordable, whether or not they are made domestically.
- Drug regulatory authorities and quality assurance systems need to be reinforced to ensure that only quality drugs reach the end-user through distribution systems.
- Distribution needs to be made efficient, so that the large mark-ups that are commonly added in both public and private distribution systems do not outweigh or even negate the impact of lower ex works prices for manufactured drugs.
- Lastly, research is needed to further explore how the compulsory licensing provisions provided for in TRIPS might affect the potential for domestic manufacturing to provide increased access to existing drugs patented before 2005 as well as the new drugs which will be patented after 2005.

WHO (2005)²⁷

World medicine production is on the increase but is concentrated in a few industrialized countries. Despite the growth observed in global medicine production over the years, studies indicate that Africa's share of world medicine production continues to decline. With a view to strengthening regional local production capacity and improving access to essential medicines, the Regional Committee for Africa formerly adopted resolutions AFR/RC38/R19, AFR/RC49/R5 and AFR/RC54/R5. These pertain to local production of essential drugs in the Region; a situation and trend analysis of essential drugs in the Region; and improving access to care and treatment for HIV/AIDS, The 3 by 5 Initiative. Most production of medicines in the Region is limited to compounding and packaging, repackaging, and processing bulk medicines into dosage forms using imported raw materials. The majority of the production facilities are privately-owned. Mainly generic medicines are produced, and they satisfy only a small

27 Author's summary.

proportion of national requirements. The viability of local production is influenced primarily by the size of the market; existence of other production capacity in the Region; size and procurement preferences, especially of public sector market, physical infrastructure and human resources. This document examines issues, challenges and perspectives and advises governments on the way forward with local production of essential medicines, including antiretrovirals, in the African Region. The Regional Committee is requested to review and adopt the orientations contained in this document.

Ghana

Harper & Gyansa-Lutterodt (2007)

Although Ghana's pharmaceutical market is composed of 30% locally produced products and 70% imported products, Ghana has a well-established pharmaceutical manufacturing base. The authors describe Ghana's manufacturing base as proactive but constrained by barriers that result in a more than 50% underutilization of manufacturing capacity. The barriers that impede Ghana's manufacturing base include an unregulated pharmaceutical distribution chain, focus on production of over-the-counter drugs, inability to produce essential medicines that meet WHO prequalification standards, limited attention to R&D, and the escalating threat of counterfeit and diverted medicines. Due to the increasing political and economic stability in Ghana and countries in the subregion, the time is ripe to address local pharmaceutical development issues to help eliminate Ghana's dependency on imported pharmaceuticals and the poverty–sickness cycle. The authors propose a number of recommendations, including legislation for and stronger enforced regulation of pharmaceutical development at both the national and subregional level, avoiding the introduction of parallel pharmaceutical trade until regulation is harmonized at the subregional level, revision of Ghana's patent law, creating a subregional legal framework that effectively implements the TRIPS Agreement, and conducting training workshops and follow-up technical assistance to implement effective technology transfer for the local pharmaceutical industry.

Rwanda

Chiwandamira & Kamanzi (2006)

This report explains how incorporating the TRIPS Agreement flexibilities into Rwanda's otherwise obsolete patent law will facilitate production of essential drugs at the local level. Rwanda is an LDC with a weak manufacturing base, and its public health sector is heavily dependent on imported generic pharmaceuticals from India. Rwanda's dependency on imported pharmaceuticals is due to a lack of awareness of intellectual property rights, of the TRIPS Agreement and the ramifications it has on the local economy, and of the overall legal framework regarding access to medicines. This report proposes ways in which the TRIPS Agreement flexibilities might be incorporated into

Rwanda's intellectual property law, thereby allowing for local production of necessary drugs. The report asserts that incorporating the TRIPS Agreement flexibilities, coupled with the inception of a national drug authority, will foster local production of pharmaceuticals in Rwanda and therefore provide for a more attractive investment environment.

South Africa

*Walwyn (2008)*²⁸

Over the last three decades, there have been numerous attempts to stimulate investment in the pharmaceuticals sector, and in particular the local production of active pharmaceutical ingredients (APIs). Almost without exception, these initiatives, whether led by government, parastatal organisations or the private sector, have failed. The local API industry remains tiny in comparison to the national demand and South Africa imports the bulk of its API requirements. This experience is in stark contrast to the substantial growth in API production within other developing countries including India, South Korea and China. Over the same period, these countries have successfully built strong pharmaceutical value chains extending from fine chemicals to finished product.

Two of the major constraints for local industry have been the low volumes of the domestic market and the lack of real competitive advantages vs the main players in the global market. The huge scale of the HIV epidemic, which is now upon us in all its ramifications, has changed this situation. South Africa is a major portion of the global antiretroviral (ARV) market. We are already treating 460 000 patients with ARVs and this number is growing. Moreover only 29% of patients requiring ARVs are actually on the treatment programme; if universal coverage were to be achieved, we would represent nearly 40% of the global market. By 2014 it is estimated that the procurement cost of ARV APIs alone will be about R3.5 billion p.a. (2008 R).

As for most of the other APIs, all of our API requirements for the ARV treatment programme are imported, mainly from India and China but also from the developed countries. This situation is not sustainable for several reasons. Firstly HIV is our problem and the production of ARVs is not particularly attractive for any country. It has become a technically challenging, low margin business which requires high standards of quality management and process technology. We cannot continue to rely on other countries to supply products for which we require a high level of quality and security of supply for the ARV treatment programme.

28 Author's summary.

Secondly the pharmaceuticals sector has for good reason been identified one of four lead sectors which could be used to diversify South Africa's industry (away from its predominantly resource-based nature) and to address a worsening trade balance problem (present trade imbalance for the sector is R11.8 billion alone). Recently the government has called for the fast track implementation of sectoral strategies and for a "leveraging of the state's pharmaceutical procurement programme" in order to stimulate the local production of APIs.

In response to these imperatives, two proposed incentive schemes/initiatives have been developed as follows:

- *ARV APIs*: given the urgency of the supply situation and several other characteristics of the ARV market, it is proposed that government should form a public private sector partnership (PPP) which will result in the establishment of a local ARV API production facility. Such a facility should be focused on at least two of the key high volume APIs which are used in the present first line treatment regimen (such as efavirenz, tenofovir, lamivudine, zidovudine or nevirapine) and be scaled to manufacture at least 500 Tpa of API.

A detailed analysis of the techno-economics for ARV APIs has shown that the production margins are tight and for the first generation APIs such as zidovudine and lamivudine, these margins are negative (such products tend to be sold on the basis of the direct costs only). For the proposed PPP to generate a positive return on investment, government will be required to finance the plant construction and commissioning costs (about R564 million; such a PPP is referred to as a "concession agreement with fully funded infrastructure") and to offer some initial security of off-take (such as a supply agreement for the public sector procurement programme). In return the private sector partner must provide state of the art process technology, manufacturing expertise and a clear link to a local formulation facility.

The economic benefits of this PPP will include local value added (R1.05 billion contribution to gross domestic product), foreign exchange savings (R1.7 billion p.a.), increased security of supply, development and diversification of the chemicals sector, job creation, more control over medicine quality and human capital development.

- *Other APIs*: ARVs are not the only pharmaceuticals whose local manufacture would be advantageous from a strategic perspective. Other APIs include those used to treat TB, diabetes and heart disease. It is proposed that government develops a sectoral-specific rebate incentive scheme (similar to that developed for the film industry), which will provide up to 30% of the initial construction and commissioning costs in the form of a performance-related refund. The scale of the recommended investment by government is about R500 million p.a. for five years. Such a scheme will be important in allaying at least the capital portion of the risk associated with an investment in local API production, and help to diversify the number of companies which will participate in this section in addition to the proposed PPP, resulting in a R5 billion p.a. local API industry (turnover).

These two proposals have arisen from a detailed assessment of the advantages to the South African public of local pharmaceutical production. We agree fully with the Minister of Finance, who in his 2008 budget speech stated that:

“Business development is not a core responsibility of government, but where it contributes to broadening opportunities, to drawing the marginalised and excluded into the mainstream of economic activity, then it has a rightful claim on public support ... this House and every taxpayer shares with us a responsibility to question continuously whether our incentives are based on sound policies and criteria, not on favours or special interests masquerading as the public good.”

The incentives proposed in this document are indeed based on sound policies and criteria; the pharmaceuticals sector can contribute to broadening opportunities and to the stable management of South Africa’s economy. Furthermore it is a sector which has an important role to play in this country’s battle against HIV/AIDS; for this reason alone we are compelled to carefully consider our investment options and to build API capacity in support of the ARV treatment programme.

United Republic of Tanzania

Losse et al. (2007)

Due to the significantly large donor market in the United Republic of Tanzania that is capable of accommodating Tanzanian producers, the authors contend that there is a case for promoting the local production of pharmaceuticals in the United Republic of Tanzania. In the United Republic of Tanzania’s case, the TRIPS Agreement flexibilities are not as imperative as originally anticipated: Tanzanian producers formulate APIs into ARVs, meaning they import the APIs and then formulate the combination and package for the ARVs. There are three primary challenges of local production competitiveness in the pharmaceutical sector: the achievement of international quality standards, regional cooperation, and human resource development. The authors claim that the facilitation of knowledge transfer or advisory services to the Tanzanian Food and Drug Regulatory Authority will contribute to the improvement of quality standards. The challenge regarding regional cooperation entails the extent to which Tanzanian producers will be able to meet foreign standards and consumer expectations while competing with well-established producers such as India and China. Finally, because of a lack of generalized education and specialized workforce, pharmaceutical companies in the United Republic of Tanzania must recruit staff from India and China to be competitive.

5.1.5 Regional initiatives

African Union/New Partnership for Africa's Development

National governments in Africa operating through the African Union are developing a programme to promote local production of pharmaceuticals. The African Union Assembly in 2005 mandated the African Union Commission to develop a Pharmaceutical Manufacturing Plan for Africa within the framework of the New Partnership for Africa's Development (NEPAD). The African Union Commission (2007) conducted a local pharmaceutical production capacity mapping exercise, and an initial document was prepared for the Third Session of the African Union Conference of the Ministers. The report proposed the creation of a Technical Committee to facilitate implementation and monitoring of the Pharmaceutical Manufacturing Plan for Africa, and the Conference of the Ministers of Health endorsed that proposal.²⁹ Technical experts met in South Africa in February 2010 and in their meeting summary and recommendations stated (NEPAD & COHRED, 2010):

A special meeting of the African Union's Extended Technical Committee on the Pharmaceutical Manufacturing Plan for Africa convened in Pretoria, South Africa, on February 18–20, 2010. This meeting was held to consider the results of the study on Strengthening Pharmaceutical Innovation in Africa done jointly by COHRED and NEPAD, with contributions from the George Institute for International Health. The study provided the first practical tool to operationalise global and African strategies to improve access to essential medicines. ...

The meeting focused on the review and evaluation of a new tool (the "Pharmaceutical Innovation Framework and Grid") that supports countries to assess their current situation and future intentions for pharmaceutical innovation, and to design national and regional action plans for innovation, access and local production of medicines, diagnostics and vaccines. Participants found the tool useful and provided suggestions for its improvement, including reference documents and examples illustrating the range of policy instruments and resources available in countries. They emphasised that access and innovation must go hand-in-hand and that the tool should encompass all stakeholders including civil society and private sector. ...

Participants recommended a number of practical steps forward, including:

- Using the tool to make a valuable contribution to achieving the goals of the Pharmaceutical Manufacturing Plan for Africa and the

29 Johannesburg Declaration of the Third Ordinary Session of the African Union Conference of Ministers of Health, Johannesburg, South Africa, 13 April 2007. CAMH/MIN/Draft/Decl.(III) (http://www.afro.who.int/malaria/publications/johannesburg_declaration_au.pdf). See also WIPO (2007–2008). In February 2010, the Technical Committee convened in Pretoria, South Africa, to prepare a technical report on pharmaceutical innovation in Africa and a summary policy document.

Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property.

- Providing strong support for the development and implementation of a business plan for the Pharmaceutical Manufacturing Plan for Africa; the meeting invited partners to assist in its development and implementation – by providing resources and ensuring synergies with the private pharmaceutical sector.

Southern African Development Community

There are other regional efforts under way to improve cooperation and consider approximation of regulatory approval requirements to enable the operation of larger-scale and more efficient production facilities by opening opportunities for African intraregional trade.

SADC, a 14-country trade community in the southern African region, adopted a policy in 1999 to promote regional harmonization of pharmaceutical regulation. Working groups have been established to facilitate this process (Matsoso, 2003).

On 3 December 2009, the Southern African Generic Medicines Association (SAGMA) was inaugurated, to be officially launched in March 2010. Its press release stated:

The inauguration of the Southern African Generic Medicines Association (SAGMA) today is an important development for the future of generic medicines in SADC and its fourteen member countries. The Mission of SAGMA is to achieve self-sufficiency and reliability in the local production and/or promotion of affordable, efficacious, quality generic medicines in the Southern Africa Development Community (SADC). This initiative has been sponsored by the United Nations Industrial Development Organization (UNIDO) and spearheaded by the National Association of Pharmaceutical Manufacturers of South Africa (NAPM) together with active participation from other SADC member countries.

5.1.6 Middle East and North Africa³⁰

The regional situation

The total pharmaceutical market of the Middle East and North Africa region (MENA) is in excess of US\$ 12 billion per annum, serving a total population of approximately 340 000 000 people.³¹ There are 280 pharmaceutical manufacturers in the MENA region, producing mainly generics in limited therapeutic territories. Saudi Arabia and Egypt are the largest markets in dollar terms. Demand is met largely by imported products, although there is

30 The MENA region includes countries in Asia and Africa. The discussion is included here but is also relevant to Asia. Representatives from Jordan participated in the regional workshop for Asia discussed in the following section.

31 This section of the report relies on data compiled and presented by Hanan Sboul, Secretary General, Jordanian Association of Pharmaceutical (Sboul, 2009). See also Kurdi (2010).

significant local production, with well over 50% of demand by volume being met by local production in Egypt, Morocco and the Syrian Arab Republic. MENA may be characterized as a fast-growing pharmaceutical market.

MENA pharmaceutical exports are valued at approximately US\$ 1 billion per annum, with Jordan anticipating exports of US\$ 450 million in 2009. Jordanian manufacturers view advantages in a relatively large pool of skilled labour with relatively lower wages and lower manufacturing costs compared with the United States and the EU, high-standard manufacturing sites and accumulated regulatory and marketing expertise. The industry faces a number of challenges, including rising manufacturing costs, regulatory compliance costs, strong competition from foreign imports, emerging local industries and price controls in major export markets. Challenges facing the region include fragmented regulatory regimes, and distribution structures that favour vertically integrated supply chains. Branded generics producers are advertising heavily.

Jordanian industry perspective

The Jordanian local producers express particular concern with the introduction of product patent protection and regulatory data protection, as a consequence of both the TRIPS Agreement and bilateral and regional trading arrangements in MENA. Local patent offices have limited capacity to review patent applications, resulting in grants of weak patents. Databases are not well developed with search capabilities. Originator companies encourage broader interpretation of regulatory data protection requirements than is required by international agreement. A study conducted under the auspices of the Medicines Transparency Alliance indicates that the introduction of generic medicines in Jordan has been delayed as a consequence of amended patent and regulatory data rules, with a significant monetary cost to consumers (R. Abbott et al., 2010).

Taking the above into account, Jordanian domestic producers are encouraged for the future because of the strong rates of economic growth in many countries of the region, and the consequent beneficial effects of stronger consumer demand for good-quality pharmaceutical products.

5.2 Asia

5.2.1 Regional workshop Malaysia

A dialogue was held in Kuala Lumpur, Malaysia, bringing together experts from industry, government, public health advocates and academia from a wide range of countries in Asia, as well as facilitators from ICTSD, UNCTAD and WHO.³²

32 Asian Dialogue on Technology Transfer for Local Manufacturing Capacity of Drugs and Vaccines, 29–30 April 2010, Kuala Lumpur, Malaysia, organized with the support of WHO and the EU. A formal report was prepared by the organizers (ICTSD et al. 2010).

There was recognition that a number of countries in Asia are among the leading “local” producers of pharmaceuticals in the world, but also that the situation differs substantially among countries of Asia. There is no one-size-fits-all approach suitable for promoting local production throughout the region. For example, some Asian countries are major recipients of inward FDI in their pharmaceutical production sectors, while others receive little in the way of FDI. Also, in some countries the government provides significant direct and indirect support for the pharmaceutical production sector, while in others the government role is more limited.

With that said, there were several themes common throughout much of the discussion:

- Education and training play a key role in the development of local pharmaceutical production, and policies to support basic education and technical training should be emphasized.
- Different regulatory standards for each country create obstacles to intraregional trade in pharmaceutical products, limiting possibilities for exports and achieving appropriate economies of scale. Consideration should be given to improving regulatory cooperation and approximation of rules.
- Patents and other forms of intellectual property protection, including regulatory data-based exclusivity, present an obstacle to meeting local health needs through local production, and mechanisms for overcoming restrictions based on intellectual property are needed. Voluntary licensing and joint ventures may be the first best solution, but alternative approaches for overcoming intellectual property-based obstacles may also be necessary. It was commonly emphasized among industry participants that governments in Asia should not give up existing TRIPS Agreement-based flexibilities in bilateral and regional trade negotiations.
- For a number of countries in the region, support is needed to improve GMP compliance, both to improve quality for local distribution and for potentially entering export markets. Training assistance is required generally for quality control and quality assurance, in addition to GMP. WHO could establish a pool of experts to provide appropriate technical assistance.
- Cooperation and coordination among government agencies regulating the pharmaceutical sector needs to be improved. Transparency in government regulation must also be improved.
- Local production in some countries of the region is significantly hampered by lack of adequate infrastructure development.
- Pharmaceutical producers in Asia are significantly interested in expanding production of biological products.
- The pharmaceutical subject matter scope of the Medicines Patent Pool might be expanded beyond medicines for the treatment of HIV/AIDS.

There were a number of observations made with respect to specific settings:

- The success of the Jordanian generic pharmaceutical sector has been supported by a strong industry association. It is notable that the Jordanian local industry is reliant on imported APIs, but with emphasis on high-quality

production standards it has gained an excellent reputation and a strong export presence throughout the MENA region. Nonetheless, local Jordanian manufacturers are pressured by new rules negotiated under bilateral free-trade agreements, and are hampered by a lack of transparency regarding patents filed in Jordan and elsewhere in the MENA region.

- The local generic industry in Bangladesh has made considerable progress and supplies a substantial part of local pharmaceutical requirements. However, that industry is reliant on imports of APIs and is hampered by a weak domestic regulatory framework. It is important to Bangladesh as an LDC that the TRIPS Agreement exemption for providing patent and regulatory data protection is extended beyond the current 2016 deadline.
- Indonesia presents substantial opportunity for growth of local production because there is presently limited FDI in that sector, with the exception of FDI from Japan. However, legislation requiring vendors of drugs in Indonesia to produce locally may increase investment by multinational firms. This represents a potential threat to existing local industry.

5.2.2 India

Indian Pharmaceutical Alliance

Dilip Shah is the Secretary-General of the Indian Pharmaceutical Alliance (IPA).³³ The following section is based on an interview with Mr Shah and a published study by him (Shah, 2007). Mr Shah stressed the importance of recognizing that the development of a robust local manufacturing sector and R&D capacity in the pharmaceutical sector is a medium- to long-term exercise. The stages of development of the Indian pharmaceutical sector are illustrative of this development cycle.

The development of the globally successful Indian generics industry was the product of deliberate Indian Government policies carried out since the early 1970s. In 1971 the Indian Government abolished pharmaceutical product patent protection, while retaining protection for process patents. Around the same time, the Indian Government instituted a formal system of price controls for medicines that effectively forced local companies to become efficient producers.³⁴ Indian Government policies also included the establishment of

33 IPA is an organization representing the interests of a number of the largest pharmaceutical producers based in India (Cadila Healthcare, Cadila Pharmaceuticals, Dr Reddys, Glenmark, Intas, Lupin, Sun, Micro Labs, Torrent, Unichem, USV and Wockhardt).

34 Regarding price controls, see Department of Pharmaceuticals (2009a), including "Price control of scheduled drugs through the National Pharmaceutical Pricing Authority (NPPA)" and "Price regulation of non-scheduled drugs" (stating "the NPPA monitors the prices of other medicines not listed in the DPCO Schedule, such that they do not have a price variation of more than 10% per annum"). One of the stated objectives of the campaign is to "Develop a model which can be replicated not only in India but also in other less developed countries in their common goal of improving quality affordable healthcare by improving access to quality medicines at affordable prices for all".

public-sector units and support for small-scale industrial units,³⁵ forcing both domestic and foreign companies to invest in and undertake production of APIs and to use specified shares of indigenous materials as against imported materials, and mandating dilution of equity holdings by foreign companies. Indian industry in the 1980s and 1990s concentrated on reverse engineering and refinement of production technologies. Concentration on production technologies enabled Indian producers to produce at substantially lower cost than originators from the Organisation for Economic Co-operation and Development (OECD), leading to contract in-sourcing from the originators.

By the time the TRIPS Agreement was adopted in 1995, the local industry had become highly proficient in reverse engineering pharmaceutical products and in developing production processes that were substantially improved over those used by foreign industry.

In 1995 total spending by Indian pharmaceutical manufacturers on R&D was US\$ 30 million per year. When the TRIPS Agreement was signed, the industry recognized that it would need to transition to R&D, and by 2005 the annual R&D spending of Indian manufacturers was US\$ 600 million. There was a 20-fold increase over a 10-year period, and the Indian Government provides only about 10% of the R&D funding. In recent years the local industry has generated enough capital to invest in R&D on new medicines, which represents a new phase in the development of the Indian pharmaceutical sector.

Recognizing that how developing countries are classified is a difficult issue, he suggested in terms of pharmaceutical capacity looking at three levels of development:

- *India–China–Republic of Korea*: with complete production capacity (from bulk materials to APIs to finished products), and R&D capacity for new medicines.
- *Brazil–Mexico–South Africa*: with some capacity for API production, good formulation capacity, and less robust R&D capacity.
- *Nigeria–Libyan Arab Jamahiriya–Ghana–Kenya*: sufficiently large consumer markets to support development of production capacity.

A country should start by developing good formulation capacity under GMP standards, focusing on the 15 most widely used drugs in the country. This will help develop financial, technical and human capacity. The key is to train people, including by sending them on programmes in India, Brazil and South Africa. This initial phase may take 5–7 years.

35 E.g. see Department of Pharmaceuticals (2009b). This brochure, distributed at the India Pharma Summit 2009, notes: "A sizable number of [small-scale industrial] Pharma Units have been closed down due to inability to meet expenditure requirement for up-gradation to revise Schedule 'M' Standards ... subsequent to the notification in 2005. Therefore it is necessary to enable them to upgrade not only in terms of Plant & Machinery (P&M) but also manufacturing processes." The Department of Pharmaceuticals has identified 179 required plant and machinery equipments and related technology that would enable the small-scale industrial units to meet the mandatory schedule "M" compliance standards. Of 179 new technologies/equipment/accessories, 135 are for manufacturing of formulations and 44 are for manufacturing of bulk drugs.

The next step is a relatively simple, small-scale API production facility, such as for paracetamol. Local market needs can be calculated fairly easily, and presumably a plant with capacity of 15–20 tons could be used. It will likely take 3–5 years of producing API in bulk for skills training to have developed sufficiently to proceed to more complex molecules. At that point, a stage of more complex API production can be initiated.

Only when local producers are generating sufficient revenues is it feasible to turn to R&D on new medicines, which may involve shifting 6–12% of revenues to R&D, with long-term development costs and high expenses connected with obtaining approval, particularly in developed country markets. Even for Indian companies, one of the reasons for partnering with foreign originator companies is the high cost and long lead time involved in the development of a new medicine, and the cost of litigation.

In sum, there may be a 30-year timescale from initiating GMP-compliant formulation to a move into R&D on new products, and this assumes healthy development of the industry.

Indian R&D is not directed primarily to local diseases but is directed to diseases prevalent in the more lucrative markets of the developed countries.

It is necessary to meet the safety and efficacy standards of WHO, and Indian facilities of IPA members meet the highest worldwide standards.

It is unrealistic to think that a country or region can move from a relatively undeveloped pharmaceutical sector to complex API production and R&D on new medicines in a short period of time. There is a learning curve involved in manufacturing that requires a substantial number of years of experience.

The fact that India, China, the Republic of Korea, Brazil, Mexico and South Africa may be further along the development curve in the pharmaceutical sector than other developing countries does not mean that inward technology transfer is unnecessary or unimportant for these countries.

5.2.3 China

Stakeholders in the Chinese pharmaceutical sector working in academic institutions, Chinese government regulatory agencies and private-sector industry groups were interviewed. According to the results of these interviews, the pharmaceutical industry in China has developed quickly, with the Chinese government encouraging foreign multinational pharmaceutical enterprises to do business in China. The Chinese government has provided industrial policy incentives such as tax benefits to encourage development and investment. Subsidizing foreign investment in local production of medicines is both an industrial policy and a public health policy.

The pharmaceutical industry is still transitioning from planned economy to free market economy, with the Chinese government increasingly leaving medicines production to the private sector. Many domestic Chinese pharmaceutical

companies are family-owned small or medium-sized enterprises, but consolidation is occurring as the market becomes more competitive. The Chinese state still owns a substantial number of pharmaceutical manufacturing facilities, but the industry is now open to everyone, foreign and local, and the industry has become very market-oriented. The Chinese government is increasingly seeking to exit from the industry.

Most multinational pharmaceutical corporations are now doing business in China. Foreign companies are building their own production facilities in China and hiring locally, partnering with domestic companies, or outsourcing aspects of the production process. Foreign companies have the benefits of producing lower-cost products and expanding their presence in China and other parts of Asia.

Most of the generics produced in China are for domestic use, although a number of Chinese companies are now producing generic medicines or branded medicines under licence for export to developed country markets such as the United States. Foreign regulatory agencies inspect local production facilities under agreement with the Chinese State Food and Drug Administration (SFDA).³⁶ Medicines produced for domestic use are subject to a lower regulatory standard based on WHO GMPs. However, stakeholders in China consistently expressed the view that gaps between Chinese GMP standards and United States FDA/EMA GMP standards would be diminishing in the not distant future.

According to a Chinese regulatory official, as the pharmaceutical industry in China has experienced technical improvements, so must SFDA update its regulatory work, generally following the trends of international development. SFDA would benefit from new technologies to help improve regulation; in particular, SFDA would benefit from legal assistance and technical guidance. WHO has helped to provide information in this field, but more assistance is necessary.

Many APIs are manufactured in China and exported to the United States and the EU. However, China remains a net importer of medicines. The amount of imported medicines is increasing, with China importing both raw materials and finished dosage forms.

China is still developing its human resource capacity for local medicines production. As more foreign companies invest in China, this may help provide Chinese scientists with additional training and business skills. China already has a robust educational system that emphasizes science-based teaching.

Intellectual property is always an issue for developing countries and can be a barrier to accessing medicines. The example of second-line ARVs for the treatment of HIV/AIDS that remain under patent is an illustration. However, SFDA does not consider patent status in its applications: SFDA is a drug regulatory authority and not an intellectual property authority. Under Chinese

³⁶ Information concerning SFDA is available in English at <http://eng.sfda.gov.cn/eng/>.

provisions, a submission for medicines approval should include information on intellectual property. It does not appear that compulsory licensing of patented medicines has occurred in China.

China's public universities are engaged with assisting private-sector enterprises in commercial activities. Pharmaceutical manufacturers in China come to the medical and pharmaceutical schools for assistance relating to medical technology, and to law schools for advice on business and legal matters, such as protection for their proprietary information, assistance with initial public offerings, and consultations with respect to the TRIPS Agreement.

5.2.4 Literature review on Asian local production

Overview

Abbott (2006)

This paper analyses the emergence of successful local pharmaceutical manufacturers in Asia, including in China, India, the Republic of Korea and Singapore, and the strategies being pursued by the existing dominant pharmaceutical market actors based in the United States, Europe and Japan to protect their global market position. These strategies include promotion of strong intellectual property standards and enforcement mechanisms, integration of patent and health regulatory mechanisms to forestall entry of generic competition, and use of mergers and acquisitions to limit emergence of global competitors. This paper recommends that Asian governments consider placing limits on foreign acquisitions, including through the use of competition law, during the transition of their local industries from generic to originator enterprises, to allow the emergence of globally competitive locally based industry.

*Grace (2004a)*³⁷

To meet obligations under the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS), China enacted regulation in 2002 extending pharmaceutical patents to twenty years, and data-exclusivity for six years and India plans to amend its patent laws by 2005 to allow for pharmaceutical product patents on any product with a patent issued after January 1, 1995.

Why is the introduction of product patents in India and China important? Firms in these countries are important suppliers of low-priced active pharmaceutical ingredients and finished products domestically and to developing countries, and many fear that the introduction of product patents will destroy these industries and lead to increased drug prices. DFID has consequently commissioned this study to answer some emerging policy questions:

37 Excerpts from study.

- What will happen to the pharmaceutical industries in these countries? Will Indian and Chinese pharmaceutical firms be displaced as MNCs [multinational corporations] enter their domestic markets, or become multinationals themselves, governed by the same incentive structure?
- What will happen to the supply of low-priced medicines within these countries as well as internationally (where India and China export ingredients or finished products)? Will January 1, 2005 be the start of the doomsday many have feared?

The line of reasoning that connects IP, the pharmaceutical industries in India and China and access to medicines is not a direct one, so deserves clarification. Enhanced IP protection can close off certain revenue options and cause a reorientation of firms' strategies. This reorientation can affect industry structure and types of competition, and this can lead to changes in prices, quality levels and physical availability. Similarly, access to new medicines can also be affected by enhanced IP protection, but indirectly, through IP's influence on a firm's market orientation, and thus, the incentive structure to invest in R&D. The incentive to invest in R&D has implications for the number and type of new drugs that are developed through this investment.

This study reveals that enhanced IP protection in China and the approaching introduction of product patent law in India are already having an effect on the product and market strategies of Indian firms. The introduction of product patents means that Indian firms will have reduced revenue options for the sale of drugs domestically, since generic copies of newer drugs will become illegal. To compensate for this revenue loss, Indian firms have increased their emphasis on exporting to the more profitable regulated markets, as evidenced by the large concentration of FDA approved manufacturing plants (more than any other country besides the US, numbering 60). There is also an increased focus on product innovation, with the most successful firms investing an increasing amount in R&D, including in partnership with MNCs, and with increasingly positive results; one-third of all FDA applications came from India in 2003, and this number is expected to be one-half in 2004. MNCs have been interested in working with Indian firms for some time, attracted by the lower cost structure – estimated to be one-eighth (in R&D) to one-fifth (in manufacturing) compared to Western firms; advanced chemistry and process engineering skills; and large market size. In conclusion, the prospects are extremely positive for the future of the Indian industry, in contrast to what many would predict.

The Chinese industry has different strengths and weaknesses versus the Indian industry. At this time, China is primarily still thought of as the lowest-cost source of pharmaceutical ingredients and plain vanilla generics, rather than the source of more innovative products. However, some of the major current domestic generic producers are migrating towards innovative R&D, at least as a longer-term goal. Within the innovative products category, Chinese firms appear to be focused on opportunities with biotech and traditional medicine primarily, with a lesser emphasis on small molecules, the traditional area of expertise of MNCs and Indian firms. Although China's expertise in selected sectors (e.g.

biotech) already stands out at the international level, the industrialisation of this expertise is under-developed. Co-operative relationships between MNCs and Chinese firms are also not exactly comparable to the Indian situation either, as many MNCs are put off by the language barriers, relatively lower level of chemistry skills in China, relatively inferior quality, insecure institutional environment for intellectual property protection, long registration approval processes, and regulatory favouritism towards local firms.

Although some have feared that the advancing product and market strategies of Indian and Chinese firms would cause them to lose interest in serving their traditional low-priced/high-volume markets, there is ample reason to believe that these firms will not reject the markets that have been their bread and butter for several decades. Low-priced/ high-volume markets have been and are likely to remain relatively more attractive to Indian and Chinese firms, given the lower cost structure of these firms, their existing expertise in serving these markets, and their need to balance their more risky forays into the regulated markets with more advanced products.

There exist theoretical arguments to predict as well as some evidence to reveal what effect changing IP is having on the pricing and availability of medicines within China and India. The good news is that the availability and pricing of approximately 90% of medicines in India and China, including most the WHO Model List of Essential Medicines, should not be affected by the introduction of product patents.

With the introduction of product patents in India, the category of products that will be immediately affected will be those patented after 2005, and, depending upon how TRIPS is translated into domestic law, perhaps those medicines patented between 1995 and 2005 as well. The latter includes some of the newer ARVs and some important anticancer drugs. Access may be impeded for these categories of products in terms of price or even lack of physical availability at any price. China is already experiencing access problems within the category of newer drugs. Some important ARVs are simply not physically present on the Chinese market, while others are present, but at prices aimed at skimming the wealthy market segment.

As for access to new medicines, as mentioned above, changing IP is influencing the business strategies of firms in India and China, and the incentive to invest in R&D in order to move up the product/market hierarchy. Thus, indications are that enhanced IP is encouraging increased development of new medicines, which is a good thing for access. However, there is mixed theory and evidence to support the idea that Indian and Chinese firms may be more likely than MNCs to devote R&D expenditure towards the development of products for neglected diseases.

Worldwide access to medicines, where India and China provide products or sources of price competition, is affected not only by the parameters discussed above which determine domestic access in India and China, but also by the IP situation in the importing country. Many African countries already

implemented domestic patent legislation in line with the more regulated markets. Thus, although generic copies of, for example, older ARVs will be able to remain on the market in India, domestic legislation would not authorise generic copies in these African countries unless the patent holder has waived its rights or licensed the patents to generic firms. Where the patent holder is not willing to do this, the options include trying to access differential prices of the originator's product through "access" programmes, pooling demand for bulk purchasing, tapping in to less expensive sources of the originator's product through parallel importing, issuing a TRIPS-compliant compulsory license, or in eligible countries, amending domestic legislation to take advantage of the TRIPS extension for least developed countries until 2016. All of these options have their practical difficulties.

The final section of the study offers ideas for initiatives that public funding bodies may wish to support with the goal of improving access to medicines.

Bangladesh

Da Cunha (2007)

Bangladesh, as the only LDC with sufficient capacity to produce and export generic versions of patent-protected medicines, manufactures high-quality drugs and is able to meet the requirements for WHO prequalification. However, a number of barriers obstruct Bangladesh's ability to become "a second India". The authors propose a number of measures that would enhance Bangladesh's role as a supplier of generic drugs, such as: technical assistance, including technology transfer for production of APIs and selected finished drugs; providing information on the TRIPS Agreement opportunities and limitations to eradicate confusion surrounding the Agreement and the implications of the waiver for LDCs; counselling for nongovernmental organizations (NGOs) on development of business opportunities in essential drugs exportation; assistance in complying with international quality standards and certification; and providing market information to facilitate access to developing country markets. The authors argue that if Bangladesh is able to overcome certain barriers, then it has the potential to substitute Indian and Chinese providers to developing country markets of both finished drugs and APIs, notably in antibiotics, antiulcer drugs, antihypertensives and antidepressants.

India

Chaudhuri (2005)

This comprehensive study focuses on the role of patents in the development of the pharmaceutical industry in India. It stresses that India's generic pharmaceutical sector was able to challenge the dominance of multinational producers otherwise prevailing in much of the world because the India's patent law did not provide pharmaceutical product patent protection before 1 January 2005 (in conformity with international rules). The author challenges the assumption that introduction by India of pharmaceutical product patent

protection will increase FDI in the pharmaceutical sector. The author further suggests that secondary patents taken out in India by multinationals may inhibit introduction of generic products by local producers, blocking market entry. The author posits that in the absence of price controls, the introduction of pharmaceutical product patent protection in India will increase prices to consumers in India, and in developing countries more generally. This study includes extensive compilation of data with respect to production, trade and pricing of pharmaceutical products, and the structure of the Indian and global pharmaceutical industry over time.

*Chaudhuri (2010)*³⁸

The Indian pharmaceutical industry occupies a special position among developing countries having demonstrated strong innovation capabilities, strength in developing cost-efficient processes and significant capacity in setting up manufacturing plants for drugs satisfying international quality norms, earning worldwide recognition as the “pharmacy of the developing world”. This study examines how Indian generic companies are responding to the new policy environment of the TRIPS regime, the impact on their growth and the fruition of the promises of the TRIPS regime to deliver increased, more relevant R&D. The analysis of the performance of the Indian pharmaceutical industry is largely based on a sample of 166 large and medium sized Indian companies. The study explores changes in the domestic and export markets as well as in the research and development area.

In terms of the domestic market, the study finds that Indian companies continue to maintain their dominance though there is renewed interest from MNCs. Changes in the domestic patented market are yet to take effect fully and will be heavily influenced by the manner in which India’s amended patent law is applied. The Indian companies are taking various responses including filing oppositions to ensure the robust application of India’s patent law, exploring voluntary licensing, engaging in patent disputes and resisting the enforcement of greater patent rights in order to restrict the scope of the patented market.

The domestic generic market, which comprises the bulk drugs market and the retail formulations market on the other hand, has seen significant changes. For bulk drug manufacturers, TRIPS hardly makes a difference as they already operate in a very competitive environment and will continue to do so even after patents expire. In the post-TRIPS situation large firms that cannot initiate the manufacturing of new drugs as they did earlier will be the most adversely affected. Anticipating the shrinkage in domestic operations due to TRIPS, Indian companies have been introducing new products and promoting these aggressively resulting in the expansion of the retail formulations market. Market concentration is also rising with negative implications for pricing. The market share of the top 20 companies has increased while more than half of

38 Excerpt from author’s summary.

the small-scale pharmaceutical units operational in India have closed down in the last two years.

In terms of exports, the study finds that the export market is larger than the domestic market not only for large companies but also for smaller companies. However, only a small number of companies have been able to undergo the full transition to exports to regulated markets. For the larger companies, there is an increasing interest in developed markets like the US (which is now the largest export partner in both bulk drugs and formulations) and their role in these markets ranges from supplying generics where patents have expired to an increase in their own patenting practices and patent challenges. Exports to developing countries including LDCs is an area that will be most affected after the TRIPS regime when patents are granted in India and to utilize India's capability and capacity for enhancing the access to essential medicines in developing countries, compulsory licensing or other measures will be of vital importance. To facilitate their international operations, Indian companies have also set up subsidiaries and acquired companies abroad. Some of these acquisitions however have caused severe financial strains for some companies. They are also facing MNCs as competitors in the generics market. Certain policy initiatives and actions at the behest of MNCs and developed countries are also jeopardizing exports such as the seizure of several consignments of Indian exports meant for Africa and Latin America at European ports on allegations of the violation of intellectual property rights at the transit point.

Relationships between the generic industry and foreign companies are also changing including tieups for marketing and distribution, increasing mergers and acquisitions as well as contract research and manufacturing. For instance, recent acquisitions include Ranbaxy by Daiichi Sankyo and strategic alliances have been reported between Pfizer and Aurobindo and between GSK and Dr. Reddy's. The Study finds that in the pre-TRIPS situation, because of competition in patented drugs in India, both consumers and Indian producers were able to benefit from the policy environment. After TRIPS, the new policy environment has led to collaborations between Indian companies and MNCs that are restricting competition and both of them are gaining at the cost of consumers.

The study also specifically explores the claim that strong patent protection will be beneficial for India.³⁹ The TRIPS negotiations were driven by specific claims that TRIPS-compliant patent protection would prompt developing-country companies to conduct greater R&D for the development of new drugs more suited to local needs. The study finds that among a sample ... of 166 companies only 37 were major R&D spenders (increasing steadily from 3.89 percent in 2001 to 8.35 percent in 2005/06) while the rest maintained their R&D expenditure around 1 percent. As seen above, the Indian pharmaceutical industry is highly export oriented. Significant R&D efforts are directed towards developing processes and products to get regulatory approvals for entry and

39 Although the present study does not generally address R&D on new drugs, this paragraph and the next are included here to maintain the subject matter integrity of the UNDP author's work.

growth in patent-expired generic markets in developed countries. Thus much of R&D by Indian pharmaceutical companies is not related to TRIPS. It is the result of increasing export orientation of Indian pharmaceutical companies and diversification to the regulated markets, particularly to the US.

While for the R&D spenders there has been a significant amount of investment, no NCE [new chemical entity] developed by an Indian company has yet been approved for marketing in India. For companies that invested heavily in NCE development there have been significant setbacks to the extent that eventually these companies have had to reduce their R&D expenditure and some have de-merged their NCE R&D business. The study also finds that the anticipated benefit of TRIPS that the product patent incentive will prompt local companies to put resources in developing drugs more suited to developing countries has not materialized with NCEs being developed by Indian companies aimed at global diseases that have lucrative markets.

While the Indian pharmaceutical industry has performed well since the beginning of the TRIPS regime it is also very heterogeneous. The larger and export oriented companies have done much better than the smaller and domestic market oriented companies. However there has been a sharp decline for the medium and smaller sized companies. Even for the larger companies, the figures hide some important differences.

Highlighting these differences, the study presents case studies of the strategies of key Indian generic companies including Ranbaxy, Dr. Reddy's and Cipla. Ranbaxy and Dr. Reddy's have pursued a "high-risk high-gain" strategy investing in NCE R&D, while Cipla, the other company in the group of "Big three", opted for a "safer" strategy. Interestingly enough, in the post-TRIPS situation, Cipla, which is more critical about the advantages of TRIPS, has done much better than Ranbaxy or Dr. Reddy's, with Ranbaxy having reached a point where it was sold to Daiichi Sankyo, a Japanese multinational company. The general picture that comes out from the case studies is that companies which have been able to expand in the domestic market and which have avoided high risks in foreign markets and in R&D have done well.

Analyzing the findings the study concludes that little has changed to dispute the conventional wisdom that developing countries should not grant product patent protection in pharmaceuticals. They are already paying the cost of high prices of patent protected products without having seen the supposed concomitant technological benefits. While R&D activities have diversified, efforts in the full development of NCEs are yet to succeed and are focused on lucrative developed country markets; there have been several setbacks and the partnership model has not always worked properly. What Indian companies have really demonstrated is the ability to develop generics – an ability acquired and improved during the pre-TRIPS period. Industry gains are evident in the new relationships with MNCs. But from a public health perspective these can hardly be a justification for a country such as India to grant such patent protection. The author accordingly recommends as follows:

- *Policy implications:* The Government must continue to play an important role in the development of the pharmaceutical industry in India as it has in the past and adopt policy initiatives that ensure a larger space of operations to generic companies which will in turn drive down prices.
- *Preserving generic competition:* In the immediate context, the Government should utilize fully the flexibilities provided under TRIPS, and reject TRIPS-plus measures including those being pushed through Free Trade Agreements (FTAs). In particular the Government could introduce an easy to use compulsory licensing system. In this regard the procedure in the Indian law is overly complicated as it allows patent holders to delay the process. A significant step to improve access to essential medicines without violating TRIPS is to revive and utilize the capacities of public sector units to manufacture patented drugs and supply these through public health care facilities on a no-profit basis.
- *Addressing pricing:* Controlling the prices of patented drugs as well as the improvement of public healthcare and insurance facilities are also required.
- *TRIPS review:* Finally, the Indian experience as evidenced in the study, along with that of several other developing countries and LDCs, provides sufficient evidence for a proper review and renegotiation of TRIPS. Indeed, with fifteen years of experience with the TRIPS regime, such a review is overdue.

*Chaudhuri et al. (2006)*⁴⁰

Under the TRIPS Agreement on Trade-Related Intellectual Property Rights, the World Trade Organization members are required to enforce product patents for pharmaceuticals. In this paper the authors empirically investigate the welfare effects of this requirement on developing countries using data for the fluoroquinolones subsegment of the systemic anti-bacterials segment of the Indian pharmaceuticals market. The results suggest that concerns about the potential adverse welfare effects of TRIPS may have some basis. The authors estimate that the withdrawal of all domestic products in this subsegment is associated with substantial welfare losses to the Indian economy, even in the presence of price regulation. The overwhelming portion of this welfare loss derives from the loss of consumer welfare.

*Dhar & Rao (2002)*⁴¹

This project consists of three case studies of sectors where the selected developing countries have demonstrated their ability to create new productive capacities and successfully participate in the world market. The case studies are intended to identify factors that could enable firms in developing countries to upgrade technologies or develop new technologies with a view to enhancing their productivity.

40 Author's abstract.

41 Portion of author's abstract.

This specific paper examines the Indian pharmaceutical industry and the factors that helped the nation build domestic capacity and integrate into the global economy. India claimed a niche for itself providing low-cost and good quality generic bulk drugs, by keeping the prices low and the patent rules applicable at the birth of the industry, namely the 1970 Patent Act. The Act adopted a process patent regime and shorter patent terms, which in turn made the country unattractive for foreign companies to register for patents in the pharmaceutical sector. This gave the Indian firms the opportunity to copy technology and first cater to the domestic market, and later, when the patent expired, to export. The Indian firms could gain experience through a reverse engineering process, acquiring production capabilities based on indigenously generated technologies. Additional factors that aided India's success in the pharmaceutical industry include government incentives for firms to invest in research and development and institutional support from publicly funded laboratories, such as the Council for Scientific and Industrial Research (CSIR).

Presently, India is self-sufficient in up to 70 per cent of bulk drugs and almost all formulations. The proactive government policies and the global developments in the pharmaceutical sector helped change the mindset of Indian drug manufacturers. Moreover, the contribution of industry visionaries also greatly helped the development of the pharmaceutical sector.

*Fink (2001)*⁴²

This study examines the role of patent protection on the behavior of transnational corporations and market structure in the Indian pharmaceutical industry. The method of analysis is the calibration of a theoretical model to firm-level data from two therapeutic groups of the Indian pharmacy market, and a simulation analysis asking the hypothetical question of what the market structure would be if India granted patent protection to pharmaceutical products. The model developed for the simulation analysis explicitly accounts for the complex demand structure for pharmaceutical goods that result from the presence of therapeutic substitute drugs, and product differentiation among chemically equivalent drugs.

*McKinsey & Company (2009)*⁴³

This paper has been prepared for the "India Pharma Summit – 2009" organised by the Department of Pharmaceuticals, Government of India, in collaboration with the Federation of Indian Chambers of Commerce & Industry. It synthesises views on India's strategic importance in the global pharmaceuticals industry. The objective of this paper is to facilitate the discussions and deliberations at the summit. Thus, it is not a comprehensive articulation of McKinsey & Company's perspectives on the topic.

42 Author's abstract.

43 Excerpts from original text.

The current trends in the globalization of the pharmaceutical industry include the rise of emerging markets, innovative approaches in R&D, outsourcing and off-shoring to control markets and the rise of biologics. These are defined to give context to India's unique position in the global pharmaceutical industry. Their position is underpinned by several factors. To begin with, even within emerging markets, the market opportunity stands out due to a strong and sustainable growth momentum, and the diversity of business opportunities. Next, contrary to other emerging or developed markets, strong process chemistry skills lead to truly competitive manufacturing cost structures. Finally, a successful local industry and entrepreneurship culture spur partnership opportunities and business development.

For India to realise its full potential in pharmaceuticals, several challenges need to be overcome. These include low healthcare spends and insufficient infrastructure, limited access to insurance, shortage of specialised talent, funding gaps, and aspects related to production quality. To overcome these challenges, the industry and the government will need to make concerted efforts.

The "India Advantage" has gathered momentum, and domestic and global pharmaceuticals companies are increasingly recognising this. However, they are yet to comprehend and leverage India's true potential. Despite the country's impressive track record, sheer momentum alone may not be enough to capture this opportunity. Industry and government will need to make concerted, scaled-up and sustained efforts. And most importantly, the global industry will need to fully acknowledge and wholeheartedly embrace the "India Advantage".

Leveraging India's manufacturing competitiveness: The global pharmaceuticals manufacturing outsourcing industry is expected to grow to US\$ 100 billion by 2015, driven in large measure by margin pressures and patent expirations. India has the potential to capture 8 to 10 per cent of this industry by 2015. This potential is distributed across opportunity segments along four dimensions: stage of production, stage in product lifecycle, technology type and customer segment.

APIs and intermediates will account for up to 70 per cent of the US\$ 8 to 10 billion potential, with finished dosage formulations (FDFs) accounting for the remainder. Mature and generics drugs account for more than half of the potential and on-patent drugs another 25 to 30 per cent. While biologics manufacturing will grow, small molecules will account for more than 95 per cent of the opportunity by 2015. Within customer segments, large and mid-sized pharmaceuticals companies will account for up to 70 per cent of the opportunity with generics companies capturing the remainder.

Several large-scale collaboration opportunities exist beyond plain contract manufacturing of specific products. One obvious opportunity lies in the sourcing of branded generics with a focus on emerging markets. Others include the sourcing of biosimilars for emerging markets and Europe, and the lifecycle management of mature products supported by capabilities in formulations development and drug delivery technologies.

The Department of Pharmaceuticals, Ministry of Chemicals and Fertilizers, Government of India has supported the establishment of the National Institute of Pharmaceutical Education and Research (NIPER). Initially there was a single NIPER campus at Nagar, but there are now an additional six institutes at Ahmedabad, Guwahati, Hajipur, Hyderabad, Kolkata and Rae Bareilly. NIPER operates graduate-level (MSc, PhD, MBA) programmes with specific emphasis on education and research for the pharmaceutical sector. NIPER collaborates with academic institutions in developed and developing countries, and with domestic and foreign pharmaceutical enterprises. In addition to graduate-level training, NIPER conducts research across a broad spectrum of pharmaceutical-related subject matter. Activities of NIPER have been funded by the World Bank, the International Foundation for Science and the Third World Academy of Sciences. Masters programmes at NIPER include medicinal chemistry, natural products, pharmaceutical analysis, pharmacology and toxicology, pharmaceuticals, biotechnology, pharmaceutical technology (formulations), pharmaceutical technology (bulk drugs), pharmaceutical technology (biotechnology), pharmacy practice, pharmacoinformatics, regulatory toxicology and traditional medicine. MBA programmes include pharmaceutical management.

NIPER incorporates training programmes for other countries of South-East Asia and Africa. Over 25 countries have been represented in such programmes. Some scholarships are provided for foreign participants.

Mergers and acquisitions

India's domestically owned producers have been subject to merger and acquisition attention from foreign multinationals. Table 1 lists recent acquisitions.⁴⁴

Table 1 Recent acquisitions of Indian pharmaceutical producers

Date	Acquirer		Target company
	Company	Country	
June 2008	Daiichi Sankyo Co., Ltd.	Japan	Ranbaxy Laboratories
August 2008	Fresenius Kabi AG	Germany	Dabur Pharma
June 2009	Pfizer (animal health business)	United States	Vetnax Animal Health Ltd (earlier ICICI Venture acquired from Ranbaxy)
June 2009	Vetoquinol SA	France	Wockhardt (animal care subsidiary)
July 2009	Abbott Laboratories	United States	Wockhardt (nutrition business)
July 2009	Sanofi Aventis	France through Mèrieux Alliance	Shantha Biotech (increased stake from 60% to 80%)

44 Table provided by DG Shah, Indian Pharmaceutical Alliance.

IPA has suggested that the companies targeted for acquisition tended to be involved in costly R&D activities that required external sources of funding.

Financial news media reports have suggested additional acquisition activity (e.g. Reuters, 2009; Shukla & Swati Bharadwaj-Chand, 2008). Although companies involved have denied interest in being acquired, the reports are illustrative of a perception in the financial media that successful Indian manufacturers represent attractive opportunities for developed country multinationals, because among other reasons this would provide entry into the growing Indian domestic market.

5.3 Latin America

5.3.1 Latin America stakeholder meeting perspective

A meeting of stakeholders was convened under the auspices of ICTSD in Buenos Aires, Argentina, in March 2010. Stakeholders included national drug regulatory authorities, representatives of national and regional pharmaceutical industry associations and individual private-sector firms, intellectual property and R&D promotion office representatives, academics and NGOs. The discussion at this meeting focused on the effects of patents and regulatory marketing exclusivity rules on locally owned pharmaceutical manufacturers; the reliance of Latin American pharmaceutical manufacturers on imported APIs; the effects of a lack of harmonization or mutual recognition among national drug regulatory authorities; and the generally low level of private-sector R&D.

Representatives of regionally based manufacturers indicated that they are unable to obtain voluntary licences for producing newer on-patent medicines from originator enterprises based in developed countries. Recent years have witnessed a substantial rise in the number of pharmaceutical patents granted in the region. Many of these patents, in the view of the local producers, are granted without sufficient attention to the criteria of patentability. Most national patent offices do not have the technical capacity to properly assess patentability. There is a general lack of appreciation of patenting standards among the judiciary. These factors combine to permit foreign multinational companies to exercise substantial market power. In countries that have negotiated bilateral or regional free trade agreements with developed countries, new marketing exclusivity rules based on regulatory submissions are compounding the problems with maintaining access to the market.

Producers in the region are hampered in achieving significant economies of scale because of a number of factors. Intraregional trade in pharmaceuticals has traditionally been at a low level. One reason for this is a lack of regional regulatory cooperation or absence of mutual recognition of regulatory approvals. In addition, because producers in the region are generally reliant upon imported APIs, they are not able to achieve levels of profitability comparable to those of vertically integrated producers based in Europe, the United States, India, China and Israel. Critically, few local manufacturers meet the GMP standards of the United States FDA, EMA or WHO prequalification

programme. As a consequence, exports to developed country markets and to large-scale purchases by multilateral institution buyers are quite limited.

A significant number of the stakeholders at this meeting emphasized the importance of making use of the flexibilities in the TRIPS Agreement to overcome market access barriers presented by patents and regulatory marketing exclusivity rules. They encouraged multilateral organizations, including WHO and the Pan American Health Organization (PAHO), to support the use of these flexibilities.

A significant number of stakeholders expressed the view that national governmental and regional authorities should promote regulatory cooperation and mutual recognition and should make efforts to ensure that national and regional public health requirements are the central focus of integration efforts.

There was substantial support for greater government involvement in promoting transfer of technology, including through the participation of the national drug regulatory authorities in the licensing process. There was also substantial support for improving the capacity of national patent offices and the judiciary to better assess the patentability of pharmaceutical inventions so as to reduce the level of market restrictions.

There was support for additional programmes to encourage the manufacture of APIs in the region, including through government support of local manufacturers. There was support for government assistance through financial support for achieving compliance with GMP standards that would encourage participation in export markets.

5.3.2 Literature review on Latin America local production

Brazil

*Abbott (2007)*⁴⁵

About 65% of the dollar value of sales in the pharmaceutical market in Brazil⁴⁶ is captured by foreign multinational enterprises, while 35% is captured by domestic generic producers.⁴⁷ Brazil runs a heavy trade deficit in the pharmaceutical sector because of its reliance on foreign originator products.⁴⁸

45 Excerpted and adapted by study author.

46 Brazil has a population of about 190 million, GDP of US\$ 1.65 trillion (PPP) or US\$ 967 billion (official exchange rate), and a per-capita GDP of US\$ 8800 (PPP).

47 E.g. see Chamas (2005, pp. 83–84).

48 See De Lemos Capanema (2006, p. 203), using 2005 data showing a deficit of about US\$ 2 billion, and Oliveira et al. (2004, p. 171), showing a seven-fold increase in the pharmaceutical deficit between 1993 and 2002, rapidly accelerating in 1996.

Brazil has identified the pharmaceutical sector as one of four key sectors for an industrial policy initiative launched in 2003 (in addition to semiconductors, manufacturing equipment and software).

PROFARMA (through BNDES, the Brazilian development bank) is a support programme for the pharmaceutical supply chain.⁴⁹ PROFARMA provides loans for upgrading pharmaceutical production facilities, including to achieve compliance with United States FDA cGMP and other relevant international standards. One major objective is to strengthen the international competitive position of the Brazilian producers. To date, PROFARMA has financed 32 transactions with respect to production facilities, totalling approximately US\$ 225 million.⁵⁰

A second element of the sectoral programme involves financing and support for mergers and acquisitions among domestic pharmaceutical companies. In 2005, Aché acquired Biosintética with financial support from this programme, creating an enterprise with annual revenues in excess of US\$ 750 million. BNDES extended a loan for approximately US\$ 150 million in connection with this transaction. BNDES is currently attempting to induce further combinations in the Brazilian pharmaceutical sector.⁵¹

The third element of the sectoral programme involves R&D. In this programme, BNDES provides loans and equity participation. Lending for innovation may be up to US\$ 250 million, whether for new laboratory or production facilities. BNDES may invest on the basis of equity participation, up to 35% of the enterprise value.⁵² BNDES expects to offer its equity shares to the public within 3–5 years of its initial investment.⁵³ To date it has engaged in ten transactions regarding R&D totalling approximately US\$ 60 million.⁵⁴

49 See De Lemos Capanema (2006) and http://www.bndes.gov.br/SiteBNDES/bndes/bndes_en/.

50 Financing terms for loans under the production programme are generally at a long-term interest rate defined by BNDES plus a remuneration to BNDES that is 3% per annum for large enterprises and 1% per annum for micro, small and medium-sized enterprises. The method of calculation of the long-term interest rate (TJLP) can be found at <http://www.bndes.gov.br/english/tjlp.asp>. For the period July to September 2007, the rate was 6.25%. The rate appears to be variable and to fluctuate depending on the rate of inflation. LIBBS Farmaceutica, one of the Brazilian companies that participated in meetings with the Colombian pharmaceutical enterprises involved in this project, has been a significant recipient of loans under the PROFARMA programme. The first Profarma loan of approximately US\$ 8.5 million was to LIBBS for the construction of a new production facility (see <http://www.bndes.gov.br/noticias/2004/not893.asp>). Provision is made for payment grace periods (up to 3 years) and amortization (up to 7 years). BNDES may participate with loans up to 90% of appropriate covered costs.

51 Loan terms are the long-term interest rate, plus 3% per annum remuneration to BNDES, for a maximum period of 10 years. BNDES may participate with loans up to 75% of appropriate covered costs (see http://www.bndes.gov.br/english/profarma_in.asp).

52 An interviewee at BDNES indicated the maximum equity percentage as 40%, while the BNDES website indicates 35%. Interview with Pedro Lins Palmeiro Filho, Head of Department, Intermediate Products and Pharmaceuticals, BNDES, Rio de Janeiro, 26 February 2007.

53 Source: interview with Pedro Lins Palmeiro Filho, Head of Department, Intermediate Products and Pharmaceuticals, BNDES, Rio de Janeiro, 26 February 2007.

54 E.g. a BNDES Profarma loan of approximately US\$ 8 million was made to LIBBS for R&D on five new products. Loans terms are at a fixed annual rate of 4%, for a maximum term of 12 years, with BNDES loan participation up to 90% of appropriate covered costs (see http://www.bndes.gov.br/english/profarma_in.asp).

Brazil introduced pharmaceutical subject matter patent protection in 1996. At about the same time the Brazilian Government modified its industrial policy to reduce tariff and taxation preferences for local fine chemical producers. Since the early 1990s, Brazil's API industry has gone from supplying 55% of the country's domestic requirements to supplying less than 5%.⁵⁵ Brazilian API producers have not been able to negotiate patent licences with multinational firms (Chamas, 2005, p. 94; Oliveira et al., 2004).

With the support of the Brazilian Government, the Federal University in Rio de Janeiro and other institutions are conducting research with respect to uses of patent information to identify products and processes in the pharmaceutical sector that may be of use to Brazilian industry without infringing on the rights of patent holders. Researchers at the Federal University have compiled an impressive list of technologies that may be pursued by local industry.

It should be noted that a large number of patent applications in the pharmaceutical sector have been filed by foreign nationals in Brazil during the past 5 years.⁵⁶

There is considerable interest in Brazil, including at BNDES, in reinvigorating the API production sector. At the moment, local API producers suffer from high labour costs and Government bidding rules that mandate the award of contracts to the lowest-cost supplier (which favours Indian and Chinese producers). Although domestic API producers must comply with stringent Agência Nacional de Vigilância Sanitária (National Health Surveillance Agency; ANVISA) GMP requirements (including inspection), ANVISA does not apply the same standards to foreign API exporters. ANVISA is planning to modify this policy and to conduct inspections of foreign plants, which should help equalize the competitive environment (and improve the quality of finished products). Paradoxically, in light of efforts to promote local production of APIs, Brazilian tax policy effectively discriminates in favour of imported APIs, providing about a 19% advantage. Although the Brazilian Government is aware of this, it has been slow to readjust the system.

There are no publicly traded domestic pharmaceutical companies in Brazil. Local experts attribute this to the fact that these companies are family-owned and are resistant to the transparency and loss of control that may result from public share offerings.

A significant part of Brazilian public pharmaceutical demand, including for ARVs, is met by formulation–production from public manufacturing facilities, such as those of FarManguinhos (part of the Oswaldo Cruz Foundation or Fiocruz) (Bermudez et al., 2004). FarManguinhos purchased a large “excess-capacity” manufacturing complex from Glaxo (which had opened a new local

55 BNDES officials indicated in interviews that from a statistical standpoint (i.e. percentage of APIs market supplied) there is currently almost no production of APIs in Brazil. See data in de Lemos Capanema (2006).

56 See data in Oliveira et al. (2006, pp. 165–70). Supplemented by interview information from Jorge Avila, Director of INPI.

facility). In 2007 FarManguinhos was in the process of initiating production in that facility.

In April 2007 the Brazilian Government granted a compulsory licence for public use of Merck's Brazilian patent on the ARV efavirenz.⁵⁷ This ARV is used in the treatment of approximately 75 000 of 200 000 people with HIV/AIDS being treated in Brazil.⁵⁸ Brazil estimates a cost-saving of US\$ 30 million per year to its public health procurement budget from shifting to generic imports. As of late 2007, FarManguinhos was planning to commence local production of efavirenz.

Production of APIs in Brazil declined substantially over a decade commencing from the early 1990s, and the speed with which its domestic API industry will recover is difficult to predict. A substantial amount of public and private capital has already been invested in making Brazil's local pharmaceutical industry more globally competitive, and yet Brazil's net balance of payments outflow in this sector continues to expand. The capacity of the Brazilian national pharmaceutical sector to overcome the challenges of foreign competition has yet to be manifest in a way that could be characterized as an industrial policy success. This does not mean that success will not be achieved as the policies take hold, but rather makes clear that this process is at a relatively early stage.

*Bermudez et al. (2004)*⁵⁹

Brazil has been implementing a broad range of initiatives to expand access to medicines, which can provide examples for other developing countries. Of special interest is the universal access to anti-retroviral drugs program that the Ministry of Health established in recent years, which is discussed in this chapter. These initiatives must be considered not as isolated actions but as a sequence of steps that have enabled Brazil's national health system to make advances. This chapter of an edited compilation briefly describes and analyzes the most important government policy initiatives of the pharmaceutical industry and access to medicines.

*Pinheiro et al. (2006)*⁶⁰

Objectives: To present direct manufacturing costs and price calculations of individual antiretroviral drugs, enabling those responsible for their procurement to have a better understanding of the cost structure of their production, and to indicate the prices at which these antiretroviral drugs could be offered in developing country markets.

57 See Q&A from the Brazilian Ministry of Health on the efavirenz compulsory licence. Official translation from the Ministry of Health available at www.aids.gov.br.

58 Ibid. Merck offered to lower the annual per-patient price of its drug from US\$ 580 to US\$ 400, but there are generic versions available from India at US\$ 165 per patient per year (Cohen, 2007).

59 Author's introduction.

60 Author's abstract.

Methods: Direct manufacturing costs and factory prices for selected first and second line antiretroviral drugs were calculated based on cost structure data from a state-owned company in Brazil.

Prices for the active pharmaceutical ingredients (API) were taken from a recent survey by the World Health Organization (WHO). The calculated prices for antiretroviral drugs are compared with quoted prices offered by privately-owned, for-profit manufacturers.

Results: The API represents the largest component of direct manufacturing costs (55–99%), while other inputs, such as salaries, equipment costs, and scale of production, have a minimal impact. The calculated prices for most of the antiretroviral drugs studied fall within the lower quartile of the range of quoted prices in developing country markets. The exceptions are those drugs, primarily for second-line therapy, for which the API is either under patent, in short supply, or in limited use in developing countries (e.g. abacavir, lopinavir/ritonavir, nelfinavir, saquinavir).

Conclusion: The availability of data on the cost of antiretroviral drug production and calculation of factory prices under a sustainable business model provide benchmarks that bulk purchasers of antiretroviral drugs could use to negotiate lower prices. While truly significant price decreases for antiretroviral drugs will depend largely on the future evolution of API prices, the present study demonstrates that for several antiretroviral drugs price reduction is currently possible. Whether or not these reductions materialize will depend on the magnitude of indirect cost and profit added by each supplier over the direct production costs. The ability to achieve price reductions in line with production costs will have critical implications for sustainable treatment for HIV/AIDS in the developing world.

Colombia

*Abbott (2007)*⁶¹

This study examines Colombia's pharmaceutical production sector and government policies related to this sector, and compares the same sectors and policies in Brazil, Mexico and Singapore. The study considers potential measures for promoting transfer of technology to the Colombian pharmaceutical sector to improve the international competitive position of the local industry and improve public welfare. The study notes that achieving improved economies of scale through exports to the United States or the EU will require investments in upgrading facilities to meet United States FDA or EMA GMP standards, which investments might not be cost-effective for local Colombian producers in the absence of external funding support. Achieving improved economies of scale through intra-Latin America exports requires overcoming inefficiencies created by differential national regulatory requirements, suggesting that Colombia would benefit from improved intraregional regulatory coordination. The study recommends that the Colombian Government consider the type

61 Excerpted and adapted by study author.

of financial incentives provided by the Brazilian Government for upgrading facilities and inter-enterprise consolidation.

Colombia's⁶² locally owned pharmaceutical sector is today comprised wholly (or almost wholly) of producers of off-patent generic products. These companies control a substantial share of the domestic market for pharmaceuticals. In dollar terms, foreign multinational companies completely occupy the 60% of the market composed of originator products, as well as a substantial share of the generics market.⁶³ A report by Proexport suggests that cancer and HIV/AIDS treatments form an important and growing share of the import market for originator products (Proexport Colombia, 2007, p. 11).

Colombia has a large balance of trade deficit in the pharmaceutical sector. According to numbers furnished by Proexport, in 2006 Colombia exported US\$ 300 million and imported US\$ 735 million in this sector, with imports having risen 67% in the period between 2003 in 2006 (Proexport Colombia, 2007, pp. 8–11). Venezuela, Ecuador, Panama and Peru occupy the predominant export markets for Colombian pharmaceutical products.⁶⁴

Colombia imports virtually all APIs used by its manufacturers, whether locally owned or foreign owned. There is one API manufacturing facility in Colombia.⁶⁵ The requirement to import virtually all APIs negatively affects Colombia's balance of trade in the pharmaceutical sector.⁶⁶

Many developing countries, including Colombia, maintain their own cGMP standards (often based on internationally recognized standards, such as those promulgated by WHO or the International Organization for Standardization, ISO) and maintain programmes for the inspection and certification of facilities. However, these standards and inspection processes are different from those used in much of the OECD. There is no "mutual recognition" of cGMP certification between the United States FDA and EMA, although progress is

62 Colombia has a population of approximately 44 million, 30% of whom are aged 0–14 years and 5.4% aged 65 years or older. Colombia has a GDP of approximately US\$ 176 billion using current International Monetary Fund (IMF) data or US\$ 374 billion using PPP. GDP per capita per year is US\$ 8600 using PPP or US\$ 4000 using current IMF GDP data. This is 10–20% of the United States GDP per capita, depending on whether the current exchange rate or PPP figures are used.

63 A study by ANDI (2006), using IMS Health data, showed that of the top ten pharmaceutical sellers in Colombia, only two were locally owned (Genfar and Lafrancol), with a combined 6.3% share of the market, while eight foreign multinationals held 34% of the market. These data differ from a compilation by Proexport, which shows Tecnoquímicas with US\$ 250 million in annual sales, making it the leading pharmaceutical seller in Colombia. However, Tecnoquímicas has a broad product line beyond pharmaceuticals, and this may account for the difference between the ANDI/IMS and Proexport numbers.

64 Political events involving Colombia and Venezuela in 2009 have significantly affected the volume of cross-border trade and almost certainly have had a significant impact on exports of Colombian pharmaceuticals to Venezuela (e.g. El Universal, 2010).

65 Industria Química Andina is reported by industry sources to manufacture paracetamol. ANDI (2006, e.g. pp. 15 and 34) shows some exports of "basic materials". However, the study includes within the scope of those materials components of vitamins, glucose, caffeine and other products that are not generally considered active "pharmaceutical" ingredients.

66 This also leads to significant quality control issues because of the difficulty in exercising control over the quality of exported products at their source (e.g. in China or India). Exporters of APIs differ substantially in terms of quality control in production, which may be significantly influenced by the regulatory control exercised by the country of import.

being made toward this end (e.g. HHS Task Force on Drug Importation, 2004). There is no mutual recognition of cGMP certification between Colombia's Instituto Nacional de Vigilancia de Medicamentos y Alimentos (INVIMA) and the regulatory authorities of OECD countries. If a Colombian pharmaceutical manufacturer wishes to export to the United States or Europe, its production facilities must be inspected and approved or certified by United States FDA or EMA personnel.⁶⁷ At the present time, there appears to be no Colombian pharmaceutical manufacturing facilities certified by the United States FDA or EMA,⁶⁸ and there are no pharmaceutical product exports to the United States or Europe.⁶⁹ Because a significant part of United States FDA and EMA cGMP requirements relate to the manner in which pharmaceutical plants are constructed, upgrading domestic Colombian manufacturing facilities to meet requirements for export to the United States or Europe is likely to involve significant cost for many (but not all) Colombian producers.

Pharmaceutical quality regulatory requirements differ not only between the OECD and developing countries, but also among developing countries. The regulatory authorities of Brazil (ANVISA) and Argentina Administración Nacional de Medicamentos, Alimentos y Tecnología Médica (Drugs, Food and Medical Devices National Administration; ANMAT) maintain GMP and other standards that differ from those of Colombia, creating significant barriers to trade between the three countries. Colombian generic producers have experienced substantial difficulty in exporting to Brazil and Argentina because of regulatory obstacles.⁷⁰

There is an important distinction between Indian and Chinese exports to the United States and Europe (and most other OECD countries), and Indian and Chinese exports to the developing world, particularly in the field of APIs. Indian and Chinese exporters of APIs to the developing world are not subject to United States FDA/EMA plant inspection, and the domestic regulatory capacity of Indian and Chinese authorities is limited.⁷¹ APIs may be shipped

67 For a description of the United States FDA regulatory process applicable to importation of pharmaceuticals, including the inspection and approval of foreign production lines, see HHS Task Force on Drug Importation (2004, e.g. pp. 4–5), including cross-citations to relevant legislation and regulations, e.g. 21 CFR Part 211. For EMA, see Inspections: Good manufacturing practice (<http://emea.europa.eu/Inspections/GMPHome.html>). Technically, the United States FDA may approve a production line for a particular product within a plant that is also operating unapproved production lines. EMA refers to inspection and certification of a manufacturing site for an authorized product. These technical differences may have consequences with respect to the cost of bringing a production line or site into cGMP compliance with the relevant set of regulations and inspection procedures.

68 Some people in the local pharmaceutical industry have suggested there may be one such facility, but this information has not been verified.

69 ANDI (2006) shows some exports of basic materials and semi-finished products to France and Italy. However, the ANDI study encompasses materials that are not generally considered "pharmaceutical" products, such as vitamins and caffeine, and so the statement in the text and the ANDI study are not necessarily inconsistent.

70 This is reported by Colombian producers and is evident from export data (ANDI, 2006, pp. 14–15).

71 As a consequence, there is less assurance that exports of products other than to the United States or Europe (or to other OECD countries with similar regimes) will be of expected quality. If goods are inspected after arrival and transshipment to local facilities, this presents significant problems for manufacturing flow in Colombia to reject goods and secure alternative materials (Tayler & Seiter, 2009).

by maritime transport. Ocean crossing from India or China to Latin America may be a matter of weeks. As a practical matter, Colombian manufacturers are substantially dependent on the quality of APIs shipped to them, and finished products in Colombia are likewise affected by the quality of those APIs. This provides a reason for increasing regulatory vigilance at the point of origination, requiring importation only from United States FDA/EMA approved or certified facilities, or increasing local capacity in Colombia to produce APIs.

Colombia's domestic producer pharmaceutical market is characterized by small to medium-sized enterprises with relatively limited capital base. There are no Colombian pharmaceutical companies traded on the national stock exchange, which means that no company has taken advantage of local or global public equity investment.⁷²

According to data from Proexport, in 2005 pharmaceutical sales in Colombia totalled US\$ 2.6 billion. Foreign-owned enterprises have a 100% share of the originator pharmaceutical market (which constitutes 60% of the dollar value of the entire market). Foreign-owned enterprises also maintain some substantial share of the Colombian generics market (although data available for this study do not yield a percentage figure).⁷³ According to Proexport data, the largest dollar value seller in Colombia in 2005 was a Colombian company, Tecnoquímicas, at US\$ 250 million.⁷⁴ The next largest Colombian seller, in tenth place, was Procaps, at US\$ 80.5 million. The remaining top 15 sellers are affiliates of foreign multinationals. Although it is difficult to break down the data precisely, Colombia's generic producers appear to maintain some substantial part of the domestic market. If, hypothetically, that generics market share is 50% by dollar value, then this would, according to Proexport data, amount to approximately US\$ 520 million in annual sales.⁷⁵

The current situation presents an apparent policy conundrum for the Colombian Government. There are clear policy advantages to improving production infrastructure within the country. The most important benefit would be to improve and assure the quality of products delivered to the consumer. The second benefit would be to open up export possibilities for domestic manufacturers. That said, requiring the domestic industry to absorb

72 Anecdotally, there appear to be three factors underlying this phenomenon. It has been suggested that arranging a public share float in Colombia is expensive and that there is a limited public equity investment culture in the country (limiting potential public interest in equity share offerings). It also appears that pharmaceutical companies in Colombia are largely "family-owned" businesses. Entering the public equity market implies an element of loss of control over business management, which may not be attractive to family owners. Of course, there is a potential upside to entering the public equity market, which might offset concerns over loss of control.

73 According to ANDI (2006, p. 7), the two top-selling Colombian-owned companies are reported to have a 6.3% share of the total national market (including originator products)

74 Tecnoquímicas sells a broad line of consumer products, and this figure appears to reflect sales of Tecnoquímicas's full product line. IMS data used for the ANDI (2006) study do not list Tecnoquímicas in the top ten Colombian sellers in 2005. Different selection of product lines for inclusion in aggregate data may explain the different results.

75 Colombian pharmaceutical industry associations were asked for more precise data, but at the time of writing these data were not available. Recall that foreign originator products account for 60% of the total market, leaving the remaining 40% for generics. Fifty per cent of the generics sector would be 20% of the total market.

the costs of compliance may trigger a loss of market share. This suggests that Colombian Government policy should seek a way to assist domestic manufacturers to upgrade their manufacturing facilities without significantly adding to their cost structure. This is where policy options for government aid in financing must be considered, including the potential for seeking assistance from multilateral institutions with interest in promoting development and improving public health.⁷⁶

Domestic companies may also pursue financial opportunities through joint venturing with foreign enterprises, or by taking advantage of public equity markets. Encouraging the development of a “public share” mentality among the domestic pharmaceutical producers might provide a mechanism for funding upgrade of pharmaceutical plants or consolidation. Some mechanisms of government encouragement, such as tax incentives, might be made available to stimulate interest in this type of proposal.

In a number of areas, access to foreign technological expertise would be required to successfully undertake upgrading of local production capacity. Meeting United States FDA/EMA cGMP requirements would require engaging foreign technical experts with experience in plant design and quality control processes. The identification of such experts should not be considered a substantial obstacle.⁷⁷

In a similar vein, moving towards production of APIs would require foreign technical expertise since Colombian manufacturers have not participated in this aspect of the business. Such expertise is available either through joint venturing or through the retention of independent technical experts.

Proexport is actively encouraging FDI in Colombia by offering tax and other incentives to investors that meet certain targets regarding investment level or employment of Colombian nationals. The Proexport programme might be used to encourage investments in API plants by foreign investors. It is important in the development of such investments to include participation by Colombian national enterprises and Colombian technical experts so as to improve the possibilities for diffusion of technology into the Colombian pharmaceutical sector.

76 Note that, as reported in Annex I, a proposed investment by the International Finance Corporation in Tecnoquímicas “will allow for them to expand and upgrade its manufacturing facilities, possibly acquire pharmaceutical companies or facilities in the Andean region, provide general corporate expenditure and long-term working capital”.

77 Experts with industry experience have offered to be of assistance or to help identify other relevant experts. There are, in addition, a number of firms that provide such expertise on a contract basis.

Cuba

*Kaplan & Laing (2005)*⁷⁸

As early as 1972, the Cuban government established Medicuba, a state enterprise, for the purpose of importing and exporting pharmaceutical products and medical equipment. In the pharmaceutical area, the importation of finished medicine was gradually reduced to the current level of 18%, while Medicuba concentrated on arranging the importation of base chemicals for manufacture of products in Cuba. Early Cuban exports were “traditional” medicines on the World Health Organization’s essential medicines list. Cuba’s pharmaceutical trade was not insignificant, and by 1987 Cuba imported \$34.6 million worth of chemicals, largely from market economies, and exported approximately \$70 million of pharmaceutical products, principally to the West and particularly to Latin America.

Cuba’s pharmaceutical production capacity is backed by strong government support. In 1993, it was estimated that 1150 biologic and diagnostic products, as well as 30 nonprescription drugs and 132 generic products, were manufactured in Cuba. The growth of the local pharmaceutical industry, which by the mid-1990s was bringing Cuba some 100 million dollars a year in export earnings, has not only covered domestic demand for medicines, but has also led to the development of products that compete on the international market. Cuba is the only country in the world, for example, that has come up with an effective vaccine against meningitis B. The vaccine is administered free of charge to all children in Cuba, and sold to countries like Argentina, Brazil, Colombia and Mexico. With low, stable prices, China provides around 40 percent of the raw materials used by Cuba’s pharmaceutical industry, although the distances involved mean transportation of the products often takes a month and a half or even longer. At present, nearly 80 percent of finished pharmaceutical products used in Cuba are locally made.

78 Excerpted from Kaplan & Laing (2005, p. 16) (footnotes omitted).

6. Technology transfer

6.1 Direct investment

6.1.1 Multinational ownership and intra-enterprise technology transfer for local production

There is a great deal of exchange of technology across borders within individual multinational originator companies and through a wide variety of transnational arrangements entered into by those companies. When a multinational originator company establishes a production or related R&D facility in a developing country, the originator provides the facility with technology generated over a period of years. It provides equipment directly to the facility or furnishes access to equipment in laboratories elsewhere within the company. These intra-company activities involve transfer of technology from developed to developing countries (as well as reverse transfer from developing to developed countries). There is an exchange across borders of scientific information and know-how.

The results from this type of intra-company technology transfer over the short to medium term are likely to be closely held, whether in terms of being kept confidential or being used as the basis for patents that restrict third-party use of the technology. In this regard, it is necessary to distinguish between transfer of technology in the sense of providing public access to usable information and know-how, and transfer of technology restricted for commercial gain. In other words, the fact that technology is being transferred from developed to developing countries does not necessarily mean that the public stock of usable knowledge is being increased in developing countries over the short to medium term (although the public may benefit from products developed on the basis of that knowledge).

Ownership of the technology developed through intra-company activity will be held in the private sector and, with some exception, used for commercial gain. That commercial gain eventually flows to shareholders of the company that invested in the technology. For today's multinational originator companies, shareholding may be presumed to be widely dispersed, though concentrated in OECD countries. In that respect, the benefits flowing to developing countries are circumscribed by the fact of foreign ownership of the products of R&D.

Over the longer term, as scientific employees of multinational originator companies establish their own enterprises, move to locally based companies, to academic institutions or elsewhere, basic scientific know-how will go with them. Technology protected by patents will enter the public domain. Because innovation in the production sector entails less risk and cost than innovation with respect to new medicines, there is reasonable prospect that locally based entrepreneurs and enterprises will have the financial resources to effectively employ learned technology to develop new production processes, new drug-delivery systems and new formulations.

Multinational originator companies rely substantially on outsourcing of production, including to developing countries. This also involves the transfer of technology and enhances the technical capacity of the scientific and technical staff of developing country enterprises performing outsourcing work. The multinational transferor may deliberately limit the steps in the production process performed by any particular contract outsourcing company, retaining critical production steps in-house. Nonetheless, transfers of technology from multinational to outsourcing contractor will add to the technological capacity of the contractor and its employees (as well as reverse technology transfer to the multinational). The benefits to the developing country may be limited by proprietary controls over intellectual property (including through patent and trade secret), but such controls should not preclude knowledge from diffusing over the medium to longer term.

6.1.2 Local production from the perspective of the enterprise

Most of the world's pharmaceutical production capacity is owned and controlled by private-sector companies. The author of this report has interviewed a significant number of owners and senior staff of these companies.

The multinational originator perspective: Company A (Switzerland)⁷⁹

Company A is based in Switzerland. It manufactures originator pharmaceutical products (protected by patent), generic products, vaccines and diagnostics, and a broad range of consumer health products. Company A operates approximately 90 manufacturing sites, from smaller-scale to large facilities, and employs a total of 30 000 people in all manufacturing and supply operations. Company A manufactures APIs and biological products, and performs formulation and final packaging.

From a product quality and an efficient manufacturing perspective, it is generally preferable to operate larger facilities because of economies of scale. It is, however, possible to operate profitably at a smaller scale, depending on the type of product, production volumes and the requirements of the regional market. For example, local packaging is more feasible than manufacturing APIs or sterile products, which require special and expensive technology.

Governments seek local production facilities for a number of reasons. These include increasing local employment and moving up the technology development ladder. Some emerging market country governments seek multinational pharmaceutical producers to produce locally.

There is growing demand for pharmaceutical products in larger economy markets in Africa, Asia and Latin America. The establishment of local production facilities as part of an overall corporate presence may improve access to these markets. The process of obtaining regulatory approval for products may

⁷⁹ This section is based on interviews conducted at the headquarters in Switzerland of a major originator pharmaceutical company. The company approved the use of its name in this report, but the author has redacted it to avoid any appearance of favouring a particular company.

involve continuing interaction with local regulators, and that interaction may be facilitated by an established local presence. Products may require adaptation for the local market in areas such as packaging and labelling, and that adaptation may be facilitated by a local presence. Proximity to the local market may also be helpful in responding to government and other purchasing tenders. In summary, although it may be most cost-efficient to construct and operate large-scale production facilities, there are other factors that are also considered in determining whether and where to locate facilities.

Company A contracts with manufacturers in different countries for the supply of parts of its production. This requires Company A to perform close due diligence, provide technical assistance and oversee contract suppliers. Company A has a global quality team that reviews local operations, production policies, and so forth. It is a major challenge to identify necessary high-quality contract producers. For branded pharmaceutical products, patent protection is an important issue that can influence where manufacturing takes place.

Company A produces a large volume of an artemisinin-based combination for malaria, which it sells at not-for-profit prices to public-sector buyers in developing countries where malaria is endemic. The product is manufactured at two sites, one in the United States and one in China, with a combined capacity of 100 million treatments per year. Company A has provided technical support in China for GMP-conforming production of artemether, and it has transferred process technology to China for the synthesis of lumefantrine. Company A assisted in transitioning from the harvesting of wild artemisinin to commercial plantation cultivation in China. Until recently, artemisinin was sourced solely from China, but Company A has attempted to diversify supply by supporting and transferring technology to farmers in east Africa for growing the plant. This transfer-of-technology project has encountered some difficulty. The yield of active ingredient from African plants has initially not been as good as that from comparable Chinese plants, which is due to the different stage of Africa's cultivation and extraction industry on the learning curve. For China this learning started in the 1970s, but for Africa it began only 5 years ago. Company A continues to support the project in Africa in an effort to geographically diversify the supply of artemisinin.

Company A is engaged in collaborative production-related ventures with enterprises in China.

The vertically integrated generics perspective

*Company B (India)*⁸⁰

Company B exemplifies the development of the Indian pharmaceutical sector. The company is one of the largest in the Indian formulations market, with operations around the world and international sales contributing over 33%

⁸⁰ This section is based on interviews conducted by the author at the headquarters of Company B in India. Company B approved the use of its name in this report, but the author has redacted it to avoid any appearance of favouring a particular company.

of revenues. Today it is investing 6% of revenues per annum in R&D on new molecular entities, biologicals and new drug-delivery systems. It employs more than 10 000 people in 18 countries. The company is a fully integrated producer, operating three API production facilities in India that manufacture over 60 APIs, and supplying to its own formulation facilities and by contract to third-party producers in regulated markets. Two of its multipurpose API facilities are approved by the United States FDA and EMA. Company B continually invests in the improvement of production processes, including with the assistance of international expert consultants.

Company B produces and exports biological equivalent pharmaceutical products, and engages in R&D in development of process technologies in this area.

Company B seeks to secure licensing rights for the manufacture and distribution of proprietary products from foreign companies. Unlike a number of other Indian exporting companies, Company B does not seek market entry by challenging originator company patents in developed country markets.

Company B takes advantage of a strong Indian university system for skilled employees, including research scientists, some of whom have also trained in the United States and Europe. Company B has two manufacturing facilities outside India, in Japan and Brazil.

Indian Government support for the pharmaceutical industry makes India an attractive place to establish and operate manufacturing facilities. Company B has an active interest in exploring opportunities to manufacture products such as vaccines and biologicals at locations outside India.

Company C (Israel)⁸¹

Company C is a large independent generics producer based in Israel. Company C is vertically integrated, manufacturing a substantial part of its API requirements. Company C's manufacturing facilities are concentrated in Israel and Europe. Company C assesses its production facility requirements from the standpoint of efficiency, economies of scale and quality control. As a general rule, these requirements are best met with large-scale, closely supervised facilities based in countries with good infrastructure and a highly skilled workforce. Company C constructs and operates all of its production facilities using stringent global GMP standards, regardless of the location of the production facility or the destination of exports. Company C operates its facilities under the quality control supervision of PhD-level scientists.⁸²

81 This section is based on interviews of Company C executives conducted by the author at a generics industry conference in late 2009. The author has redacted the name of the company to avoid the appearance of favouring a particular company.

82 Company C representatives observed that several decades ago the company operated some production facilities using different GMP compliance standards, depending on the location of the facility and purchasers.

According to Company C, the international generics market is highly price-competitive, and there is not a good economic case for building and operating smaller-scale plants. When considering locations for production facilities, among Company C's principal concerns are availability of skilled labour and tax structure. The international generics sector is highly competitive, and a seemingly small difference in tax rates may have a significant impact on the ability to offer competitive prices on products.

Developing countries seeking to attract local production might concentrate on development of scientific skills in the pharmaceutical sector. Governments seeking to attract investment should focus on providing an environment that will permit the investor to operate price-competitively. Taxation policies are particularly important.

Company C is conducting substantial R&D on biological products.

Although Company C is principally a generics producer, the company supports strong intellectual property protection and is concerned with protecting against unauthorized technology leakage.

The least developed country enterprise perspective

As part of this overall project, UNCTAD has undertaken a case study of the experience of Quality Chemical Industries, based in Uganda.⁸³ Quality Chemical Industries is a producer operating under licence from Cipla (India). Quality Chemical Industries produces ARVs and antimalarials. Approximately US\$ 40 million was invested in the company's state-of-the-art formulation facility, but the facility has not been prequalified by the WHO. Because Uganda is an LDC, it is permitted pursuant to Paragraph 7 of the Doha Declaration on the TRIPS Agreement and Public Health not to enforce patents until 1 January 2016. At the regional stakeholder meeting in Cape Town, South Africa, a representative from Quality Chemical Industries indicated that the management of its Indian partner is concerned about what will happen at the expiration of the extended TRIPS transition period. UNCTAD has been consulting with the Ugandan Government regarding the legal situation at the end of the transition.

6.1.3 Local production and the product development partnership: an alternative model

The Drugs for Neglected Diseases Initiative (DNDi) has worked with different partners in establishing production for antimalarial combinations in developing countries.⁸⁴

DNDi developed the new fixed-dose combination of artesunate–amodiaquine (ASAQ) and licensed it to Sanofi-Aventis for industrial production. ASAQ is

83 Information available at <http://www.qcil.co.ug/>. Because Quality Chemicals is the subject of a separate case study by UNCTAD and is identified in that case study, the author has included its name here.

84 This section is based on the author's interview of Dr Bernard Pecoul, Executive Director of DNDi.

manufactured at a Sanofi-Aventis facility in Morocco, where 95% or more of the staff are local. More than 20 million tablets of ASAQ were distributed in 2009. The product is registered in 24 countries in Africa and in India. DNDi developed artesunate–mefloquine (ASMQ) in collaboration with Farmanguinhos/Fiocruz in Brazil. The product is registered in Brazil, and registration procedures are under way in other Latin American countries. DNDi is also working with Cipla in India on production processes to make the drug available in Asia.

A difficult problem arose in connection with production of ASMQ as Company D ceased manufacture of mefloquine in 2007, and DNDi had to find a new source for this complex API. It finally contracted with an Italian firm, but at a high cost. Company D was unwilling to transfer technology for this production. Moving into production of the formulation in Brazil has involved a long lead time, as developing formulation processes took longer than expected and there were delays in licensing the manufacturing facilities. Moving into production through Sanofi in Morocco has also been a lengthy process, including the need to obtain approval from the WHO prequalification programme. Dr Pecoul thinks it is very important for Africa to produce its own antimalarial drugs. Because Africa is the highest malaria-endemic region, it will otherwise be faced with continuing outflows of financial resources. The model for this needs to be sustainable.

6.2 Existing programmes promoting transfer of technology and local production

6.2.1 Multilateral initiatives

Multilateral organizations have developed a limited number of programmes that promote transfer of technology and local production of pharmaceutical products in developing countries. UNIDO indicates that it is supporting local production of pharmaceuticals, and it has provided specific financial support to a programme in industrial pharmacy in the United Republic of Tanzania (along with GIZ; see below). The IFC division of the World Bank offers loans to support local production of pharmaceuticals in developing countries, and several recent loans can be identified. UNCTAD conducts research and offers support for technology transfer initiatives for local production, but is not directly involved in specific production efforts. WHO, through its prequalification programme, provides support for achieving GMP compliance at production facilities in developing countries. Notwithstanding the aforementioned multilateral organizations and programmes, it is difficult to identify a multilateral organization project or programme involving a major financial or technical commitment to establishing local pharmaceutical production facilities in developing countries (noting that the situation for vaccine production, which is not encompassed by this report, may be different). This relative lack of multilateral support for local production appears to be the result of a studied determination, at least in the case of the World Bank, that the private sector is adequately addressing global pharmaceutical supply needs and that significant-scale multilateral support for such endeavours is not warranted.

6.2.2 Bilateral and regional development aid initiatives

The EU is providing support for this WHO PHI research initiative regarding local production in developing countries. The Government of Germany, through GIZ, provides support for transfer of technology and development of local production facilities in least developed African countries. GIZ provides financial support for a programme in industrial pharmacy in the United Republic of Tanzania, which contemplates the eventual strict GMP qualification of a pilot-scale production facility.⁸⁵ The Government of the United States, through its United States Agency for International Development (USAID) arm, has provided technical and financial support for improving GMP compliance by local production facilities in developing countries. The Government of Brazil is supporting a local production initiative for HIV/AIDS treatments in Mozambique. The Government of Cuba offers technical support for production facilities in developing countries. As with respect to the multilateral organizations, however, it is difficult to identify a significant-scale systematic programme among developed country governments for promoting local production of pharmaceuticals in developing countries.

Some multinational pharmaceutical originator companies provide technical support to third-party producers in developing countries with respect to a limited number of products directed to treating neglected diseases.

6.2.3 Assistance with legal issues

Pharmaceutical producers in developed and developing countries typically rely upon private legal counsel to represent their interests in licensing negotiations, patent validity challenges and seeking government action to facilitate access to technology. In most developing countries, there is an association of local producers that may generally represent interests of the industry in discussions with government. Some multilateral organizations provide training and guidance with respect to the legal rules applicable in these areas, including WHO, the World Intellectual Property Organization (WIPO), WTO, UNCTAD and the United Nations Development Programme (UNDP). Such training and guidance is generally at the “macro” level in the sense of providing guidebooks and general information, and does not involve

⁸⁵ In Africa, several experts teach a certificate programme in industrial pharmacy at the St Luke Foundation/Kilimanjaro School of Pharmacy. Financial support has come from GIZ and UNIDO, and a pilot-scale drug development facility has been established with this funding. Attendees are professionals from national drug regulatory authorities, African pharmaceutical companies and African universities. The programme provides training in quality-assured drug production, drug development, and detecting counterfeit and substandard drugs. At the request of attendees and in collaboration with the Tanzanian University in Dar es Salaam (MUHASA), the curriculum is being expanded to offer a Master’s programme, beginning in March 2011. Two of the companies with attendees in this programme have used this training to assist their submission of dossiers for HIV/AIDS drugs to WHO for prequalification. With additional funding, the programme plans to upgrade the development facility to cGMP so that it can sell initial quantities (a few metric tons) of United States FDA-approved drugs to the Government through programmes such as the United States President’s Emergency Plan for AIDS Relief (PEPFAR). When the technology is transferred to local producers and they become WHO prequalified, the programme will switch to a new drug to keep the cycle turning. (Based on email correspondence with Professor Joseph Fortune, 24 September 2010.)

providing legal support for particular enterprises. Governments may typically request specific assistance.

In addition to support for multilateral organizations, a number of NGOs and intergovernmental organizations (IGOs) provide general and specific legal support for facilitating access to technology for production. There are NGOs and IGOs operating at the “macro” level, such as ICTSD and the South Centre. There are also a number of “legal clinics” associated with universities that may offer assistance to specific enterprises, although this is not a systematic practice.

6.2.4 Internet-based identification of existing programmes

Internet-based research was conducted to identify projects and programmes intended to facilitate local production of medicines in developing countries, including related transfer of technology. The objective was not to identify more general national industrial policy programmes, such as tax incentives and subsidies, that are intended to facilitate the promotion of local industrial development, but rather to identify transfer-of-technology programmes specifically intended to improve capacity for local production of medicines in developing countries.

This Internet-based research suggests that there are a limited number of projects and programmes specifically directed towards encouraging the production of medicines in developing countries. Projects and programmes intended to facilitate production of vaccines appear as common as such projects and programmes for conventional medicines.

On the other hand, there are a significant number of projects and programmes that are designed to facilitate R&D on new medicines (including vaccines and diagnostics). A substantial number of such projects and programmes involve improving capacity for the conduct of clinical trials in developing countries. Most of such R&D projects and programmes address type II and III diseases.

The information identified and presented in this section is dependent on “self-reporting”, meaning the activities identified are those that companies, organizations or initiatives have reported themselves.

The projects and programmes specifically referring to facilitation of “local production” are listed below. There is not always a bright line that divides projects and programmes facilitating local production and projects and programmes directed to R&D. A project that successfully develops a new medicine in a developing country may well lead to local production, whether or not that was specifically contemplated by the researchers. Annex II gives a more complete compilation of projects and programmes directed towards R&D, technology transfer, financing and advocacy with respect to medicines for developing countries. The results in Annex II of Internet-based research do not purport to identify all of the programmes and projects currently in and for developing countries. There are a large number of such programmes and projects around the world. The report has endeavoured to identify at

least representative programmes and projects addressing different areas. It is hoped that publication of this listing and the development of a public access portal to information will encourage other programmes and projects to identify themselves and provide information.

African Union

The African Union, pursuant to a decision taken by the African Union Assembly in 2005, mandated the African Union Commission to develop a pharmaceutical manufacturing plan for Africa within the framework of NEPAD. The African Union Commission conducted a local pharmaceutical production capacity mapping exercise, and an initial document was prepared for the Third Session of the African Union Conference of the Ministers (African Union Commission, 2007). The report proposed the creation of a technical committee to facilitate implementation and monitoring of the Pharmaceutical Manufacturing Plan for Africa, and the Conference of the Ministers of Health endorsed that proposal.⁸⁶ In February 2010, that Technical Committee convened in Pretoria, South Africa, to prepare a technical report on pharmaceutical innovation in Africa and a summary policy document (NEPAD & COHRED, 2010). The summary report from that meeting is excerpted earlier in this report.

Aspen Pharmaceuticals

Aspen Pharmaceuticals, South African's largest generic pharmaceutical company, entered into an agreement in 2006 with Bristol Myers Squibb, a global pharmaceutical company. The agreement grants Aspen Pharmaceuticals "a non-exclusive license and technology transfer collaboration agreement ... for the manufacture and distribution of Atazanavir, a new generation antiretroviral" (Aspen, 2006).

Business Humanitarian Forum

Business Humanitarian Forum (BHF) is a non-profit-making association based in Geneva, composed of senior representatives from humanitarian organizations and private companies. BHF's mandate is "to encourage and develop new and innovative ways to bring the resources, energy and creativity of the private sector to bear where it is needed most for job creation and humanitarian assistance" (BHF, 2008). In collaboration with entrepreneur Dr Karim Baz, BHF built a generic medicines plant in Kabul, Afghanistan. The factory, operating as the Baz International Pharmaceutical Company (BIPC) was created to manufacture generic medicines for distribution within Afghanistan. Construction of the factory was completed in December 2007, but due to political turmoil within Afghanistan, the generics plant has been unable to operate as planned. In 2008 the European Generics Association secured donations of generic medicines to be distributed by BIPC, and Dr Baz

86 Johannesburg Declaration of the Third Ordinary Session of the African Union Conference of Ministers of Health, Johannesburg, South Africa, 13 April 2007. CAMH/MIN/Draft/Decl.(III) (http://www.afro.who.int/malaria/publications/johannesburg_declaration_au.pdf). See also WIPO (2007–2008).

indicated that until the situation was more stable to begin production, he would continue to import and distribute generic medicines.

Drugs for Neglected Diseases Initiative

DNDi was founded in 2003 as a non-profit-making PDP for facilitating R&D on treatments for the world's neglected diseases, including human African trypanosomiasis (sleeping sickness), visceral leishmaniasis (kala-azar), Chagas disease and malaria. DNDi's founding partners are the Oswaldo Cruz Foundation of Brazil, the Indian Council for Medical Research, the Kenya Medical Research Institute, the Ministry of Health of Malaysia, the Pasteur Institute of France and Médecins sans Frontières (MSF), with the Special Programme for Research and Training in Tropical Diseases (WHO/TDR) as a permanent observer. DNDi as a non-profit-making entity operates as a form of research coordinator and hub, identifying promising targets for research, contracting for and coordinating R&D activities, overseeing processes for conducting clinical trials, coordinating drug registration and arranging for manufacturing and distribution of products.

As discussed earlier, DNDi developed new fixed-dose combinations of artesunate–amodiaquine (ASAQ) and artesunate–mefloquine (ASMQ) and participates in production-related activities regarding these medicines.

Gilead

Gilead is a research-based biopharmaceutical company. "Gilead has signed non-exclusive licenses with multiple generic manufacturers in India. Under these agreements, [Gilead's] partners will produce high-quality generic versions of Viread [for] 95 resource-limited countries, which are home to 95 percent of the world's HIV-infected people. We expect that multiple manufacturers will ensure competitive pricing, thus promoting broad access to our products for patients in developing countries with HIV/AIDS."⁸⁷

GlaxoSmithKline

GlaxoSmithKline (GSK), a global pharmaceutical company, issued a public policy position paper in September of 2007 entitled "Technology transfer, capacity building and the developing world" (GlaxoSmithKline, 2007). This policy highlights GSK's work and its role in technology transfer. GSK reported that it has manufacturing sites in over 46 countries, including many developing countries. Having manufacturing sites in these countries increases the transfer of know-how and training for a skilled local workforce. Furthermore, often GSK outsources products after the patent has expired to other manufacturing

87 Gilead offers two programmes to facilitate access in the developing world. One programme focuses on access to medicines for people with HIV/AIDS. Gilead offers tiered pricing for HIV/AIDS medicines to developing countries, and provides medicines free of charge for use in clinical trials in "limited resource settings". Gilead also owns the patented product AmBisome, an effective treatment for visceral leishmaniasis and works with WHO and other NGOs to provide AmBisome at preferential prices for countries greatly affected but without the resources to purchase the treatment.

companies, resulting in transfer of technology, including intellectual property and manufacturing capabilities. GSK has a few joint ventures, which also promote technology transfer. Two are located in China and produce over-the-counter medicines and pharmaceuticals. GSK also entered into a joint venture with Fiocruz, a pharmaceutical company in Brazil, where GSK entered into technology transfer, supply and licence agreements for the production of the meningitis vaccine and the mumps, measles and rubella vaccine. In the area of R&D, GSK participates in several programmes that support training and higher education. The programmes include training Chinese chemists in new techniques, and training Indian clinical researchers in good clinical practices for use in cancer clinical trials in India. In an effort to expand GSK's own clinical trial network, GSK has contributed to improvements of facilities in Pakistan, Peru, Mozambique, Ghana, Gabon, the United Republic of Tanzania and Kenya. GSK has entered into eight voluntary licensing agreements for the production of ARVs in Africa in an effort to provide access to more affordable medicines.

GIZ

GIZ is a German-owned enterprise that supports Germany in achieving its development policy objectives but also provides support and analysis to other governments and international institutions. Four studies have been conducted by GIZ on the feasibility of local capacity in developing countries for pharmaceutical production. GIZ is supporting directly the pharmaceutical sector of Ethiopia and of the EAC region, through improvement of the quality infrastructure and the quality management systems in the companies, building up of training and educational facilities (vocational training and academic) including R&D facilities, strengthening regional coordination in the fields of building a regional association, harmonizing intellectual property rights legislation and pharmaceutical action plans, and supporting a regional bioequivalence centre.

Hisun Pharmaceuticals

Hisun Pharmaceuticals is a Chinese API manufacturer and R&D company. Hisun partners with the Lilly MDR-TB Partnership and is a Lilly transfer of technology partner, receiving technology, know-how and training in GMP for the production of capreomycin, an antibiotic used to treat multidrug-resistant TB.⁸⁸

Hoffmann-La Roche Ltd

Hoffmann-La Roche Ltd is a research-focused health-care company based in Switzerland. Roche published a paper entitled "Roche position on R&D for neglected tropical diseases" to highlight its activities and contributions to R&D for treatment of neglected tropical diseases (Roche, 2008a). In an effort to combat malaria, Roche provided expertise in industrial malarial drug development to Medicines for Malaria Venture. In 2003, Roche donated

⁸⁸ See http://www.lillymdr-tb.com/media_center.html.

the manufacturing and technologies to produce its patented medicine for treatment of Chagas disease to the Brazilian Government.⁸⁹

Roche committed to an AIDS Technology Transfer Initiative in 2006 (Roche, 2008b). This initiative is aimed at transferring technology and enhancing the manufacturing capabilities of manufacturers in developing countries to produce second-line HIV medicines. As of November 2008, Roche had signed agreements with manufacturers in Kenya, South Africa, Bangladesh, Ethiopia, Zimbabwe and the United Republic of Tanzania and was reviewing a number of proposed agreements.

International Finance Cooperation

IFC is part of the World Bank Group and provides financial capital and advisory services to the private sector in developing countries. Several loans from IFC over the past 5 years have been given to pharmaceutical companies in developing countries that are seeking to increase their capacity for local production of medicines or APIs, or increase their capacity for R&D. Some recent relevant projects are described here:

- *Bharat Biotech* is a biotech company located in Hyderabad, India involved in the development and production of vaccines, contract development and manufacturing for developed country pharmaceutical/biotechnical companies, and development of its own line of molecules. The company received a loan in 2006 from IFC to upgrade and expand its current facilities, increase contract manufacturing, increase marketing and sales to expand revenue in India and for exports, and increase R&D efforts (IFC, 2005a).
- *Dabur Pharma* is an India-based company that markets oncology formulations and APIs. An IFC loan was given to the company in 2005 to “leverage its manufacturing expertise and its research and development efforts over the last few years and to grow significantly by expanding its international market reach and commercializing new products” (IFC, 2005a).
- *Dishman Pharmaceuticals and Chemicals Limited*, a contract research and manufacturing company based in India, began an investment programme with IFC in 2009, which includes “the construction of new facilities at its existing manufacturing site in India, the establishment of a greenfield manufacturing facility in China and investments in overseas subsidiaries and joint ventures” (IFC, 2009). The anticipated development impact of the project includes “south–south investment of Indian company into China and transfer of knowhow for USFDA-approved standards; lower the overall costs of medicines R&D and manufacturing for customers thus facilitating a more affordable end price of medicines for consumers; technology transfer to Dishman from its global pharmaceutical market clients and from Dishman of its knowhow in API manufacturing to its joint-venture partners; and a demonstration effect for others in the sector through Dishman’s

⁸⁹ In partnership with WHO, Roche has provided assistance in stockpiling Tamiflu for the management of bird flu in developing countries, and has continued assisting in research and clinical testing for child-sized portions of the treatment. In an effort to identify treatment for diarrhoeal diseases, the Institute of OneWorld Health has been granted access to the Roche library to identify potential effective compounds.

commitment to intellectual property rights and adherence to Indian environmental performance and labor standards” (IFC, 2009).

- *Ocimum Biosolutions* is an R&D company based in India that provides contract resource outsourcing services (IFC, 2006b). IFC has invested in the company and its plans to expand through acquisitions and investing in the R&D infrastructure in India. The IFC investment is expected to have a “high development impact” in India, building up the life sciences sector, encouraging research scientists to remain in India, supporting an internationally competitive Indian-based contract research outsourcing company and fostering technology transfer from north to south.
- *Shanghai Fosun Pharmaceuticals Company Limited* is one of the largest pharmaceutical companies in China. The company has R&D capacities, and manufacturing and distribution throughout China (IFC, 2006a). The project with the IFC is to support Fosun Pharma’s operating activities and to support China’s medical sector reform and the development of antimalarial drugs.
- *Tecnoquímicas* is a Colombian generic pharmaceutical manufacturer distributing the majority of its products within Colombia and a small amount to other Latin American countries. IFC’s investment in the company will allow Tecnoquímicas to expand and upgrade its manufacturing facilities, and possibly acquire pharmaceutical companies or facilities in the Andean region, providing general corporate expenditure and long-term working capital (IFC, 2008).

LIFElabs

LIFElabs, a biotechnology regional innovation centre, was created and funded by the South African Government to encourage investment and expand the biotechnology industry in South Africa. One of the unique programmes that LIFElabs offers, in partnership with the Research Office of University of Kwalzu Natal, is the National Genomics Platform. This is equipped with high-technology equipment for research in genomics and the facility is made available to selected research projects. Two projects currently using the National Genomics Platform are studying HIV and extremely drug-resistant TB.⁹⁰ Arvir is a biotechnology company owned by LIFElabs.⁹¹ Arvir seeks to build South Africa’s capacity for manufacturing APIs for ARVs. Arvir also conducts research on medicinal uses for traditional South African medicinal plants that have antiviral activity and has developed a unique low-cost process technology for an API used in ARV manufacturing.⁹²

Lilly MDR-TB Partnership

This is an international public–private partnership formed to combat multidrug-resistant TB led by Eli Lilly and Company, a global pharmaceutical

90 Three new projects for the National Genomics Platforms. *LIFElabs*, 2008, 4:3 (<http://www.lifelab.co.za/>, accessed 16 December 2009).

91 Arvir. *Overview*. Johannesburg, Arvir. (<http://www.arvir.co.za/index.php?q=con,5,Overview>) (accessed 15 December 2009).

92 Arvir. *Technology*. Johannesburg, Arvir. (<http://www.arvir.co.za/index.php?q=con,6,Technology>) (accessed 15 December 2009).

company. "Since 2003 the Partnership has worked to provide access to medicines, transfer manufacturing technology to the developing world, train healthcare workers, raise awareness and promote prevention and research, while providing support for communities and advocating on behalf of patients" (Lilly MDR-TB Partnership, 2010a). The Partnership is interested in providing developing countries with sustainable access to multidrug-resistant TB treatments. In an effort to support this interest, the Partnership has provided all information and technology to the manufacturing plant partners located in developing countries, as well as funds to purchase necessary equipment for manufacturing capabilities (Lilly MDR-TB Partnership, 2010b).

Partners associated with the Lilly MDR-TB Partnership include Aspen Pharmacare, South Africa; Eli Lilly and Company; Harvard Medical School and Partners in Health; Hisun Pharmaceuticals, China; International Council of Nurses; International Federation of Red Cross and Red Crescent Societies; International Hospital Federation; Purdue University, United States; RESULTS Educational Fund; Shasun Chemicals and Drugs; SIA International/Biocom; Stop TB Partnership; TB Alert; The Advocacy Partnership; United States Centers for Disease Control and Prevention; World Economic Forum; WHO; and World Medical Association (Lilly MDR-TB Partnership, 2010b).

Merck

Merck, a global pharmaceutical company, has formed partnerships with several public–private partnerships to address the need for new medicines for diseases that most commonly afflict developing countries. Many of these partnerships include the licensing of Merck's intellectual property. Merck has granted royalty-free licences for production of an ARV to five South African generic manufacturers (Merck, 2008). Merck entered into an agreement with DNDi, granting DNDi a nonexclusive royalty-free licence to some of Merck's intellectual property for the purposes of early development programmes in an effort to find effective treatments for neglected tropical diseases. Merck has granted Medicines for Malaria Venture an exclusive royalty-free licence for an investigational drug candidate to treat malaria. If the drug candidate proves to be successful, it will be offered to people infected in the developing world. International Partnership for Microbicides (IPM) also received from Merck a non-royalty-bearing, nonexclusive licence for a novel ARV, allowing IPM to develop, manufacture and distribute the treatment for protection of women from HIV in developing countries. In an effort to create affordable vaccines, Merck has also partnered with the Wellcome Trust to create Hilleman Laboratories in India, a non-profit-making laboratory focused on discovery and development of vaccines for diseases common in developing countries. The purpose of Hilleman Laboratories is to create a sustainable entity to develop innovative vaccines for diseases that most commonly affect low-income countries and are affordable and practical. Hilleman Laboratories will be based in India and staffed with 60 researchers and developers. The laboratory will work with manufacturers to ensure the cost-efficient production of vaccines to meet the needs of developing countries (Merck, 2009).

Medicines Patent Pool

The Medicines Patent Pool is an initiative aimed at promoting production of pharmaceuticals in and for developing countries that has been established through the work of UNITAID. The independent Medicines Patent Pool obtains voluntary licences from originator pharmaceutical companies, research institutes, governments, universities and other sources, and out-licenses that technology to manufacturers for the production of essential medicines needed in developing countries, such as ARVs. The Medicines Patent Pool acts as a conduit for the transfer of technology in the form of patents to local producers. The Medicines Patent Pool does not serve as a producer but relies on private and government sector producers.

Novartis

Novartis produces a large volume of Coartem, an artemisinin-based combination for malaria, which it sells at non-profit-making prices to public-sector buyers in developing countries where malaria is endemic.⁹³ The product is manufactured at two sites, one in the United States and one in China, with a combined capacity of 100 million treatments per year. Novartis has provided technical support in China for GMP-conforming production of artemether, and it has transferred process technology to China for the synthesis of lumefantrine. Novartis assisted in transitioning from the harvesting of wild artemisinin to commercial plantation cultivation in China. Until recently, artemisinin was sourced solely from China, but Novartis has attempted to diversify supply by supporting and transferring technology to farmers in east Africa for growing the plant.

Shasun Chemicals and Drugs

Shasun Chemicals and Drugs, an India-based pharmaceutical and API manufacturer, is part of the Lilly MDR-TB Partnership and benefits from the technology transfer practices undertaken by this partnership. Shasun has produced the API for cycloserine, an antibiotic that treats multidrug-resistant TB.

United Nations Industrial Development Organization

UNIDO is undertaking a global project entitled “Strengthening the local production of essential generic drugs in developing countries”. The project aims to expand and upgrade small and medium-sized enterprises in selected developing countries, mainly in Africa, for the local manufacturing of essential generic drugs, with the objective of enhancing access of poor people to these drugs at affordable prices. This objective is pursued through a combination of advisory, promotional, institutional capacity-building and enterprise-level

⁹³ In addition to interviews at Novartis headquarters in Basel, sources of information regarding Coartem production and transfer of technology include a presentation from Frank Petersen, Executive Director, Natural Products, Novartis Institutes for BioMedical Research, Case Study 1: Novartis, European Federation of Pharmaceutical Industries and Associations, Seminar on Biodiversity, 7 November 2006.

activities. At the enterprise level, the project supports companies in developing countries to produce good-quality medicines that meet international standards. Training measures for production staff and technical advice on production technology are important contributions in pursuit of higher-quality standards. Furthermore, UNIDO supports sector associations and institutions to provide services to the industry. Finally, to ensure that companies and governments work together, UNIDO facilitates public-private dialogue on the operating conditions for pharmaceutical manufacturers.

United States Agency for International Development

USAID provides funding and expertise for projects related to development outside the United States. It has provided funding and expertise for upgrading pharmaceutical manufacturing facilities in several developing countries (e.g. USAID, 2009).

6.3 Literature concerning transfer of technology for local production

The literature summarized below is generally concerned with technology transfer relevant to local production of medicines, as compared with the more regionally oriented literature summarized earlier in this report. Except with respect to legal mechanisms for addressing patent barriers, there is not a great deal of general literature concerned with technology transfer for local production. Most studies with respect to technology transfer relating to medicines are concerned with promoting R&D on new medicines (which is not within the scope of this report).

There is a substantial body of literature addressing legal mechanisms by which third parties may be authorized to make use of technology protected by patent without the consent of the patent holder (e.g. compulsory licensing), including literature published by WHO and other multilateral organizations.⁹⁴ Local production of medicines may require addressing legal barriers established by patents, and literature concerning mechanisms for addressing patent barriers is relevant to transfer of technology for local production. To date, compulsory licensing of patents for purposes of directly undertaking local production has not been widely practised (Abbott & Reichman, 2007). This report does not independently summarize or review the literature relating to compulsory licensing of patents. The potential role of such licensing is addressed in Section 7.5.

Attridge & Preker (2005)

By examining the manufacture and distribution of medicine by focusing on the potential utility of ideas from agency theory, transaction cost analysis and contemporary ideas from strategy theory, the authors provide theoretical frameworks for policy-makers. For LDCs, there is a lack of realistic scope for cost-efficient local manufacture. Therefore, the primary objectives for LDCs must encompass seeking donations and educational training packages from

⁹⁴ See recently UNAIDS et al. (2011).

R&D-based multinational companies (MNCs) on a selective basis to high-priority needs, participating in international bulk purchase initiatives, and investing funds in improving public-sector demand-side health infrastructures for diagnosis and development, among others. For large middle-income countries such as India and China, the authors suggest that the countries must seek to build R&D capabilities on to the existing generic manufacturing and export industry platforms. For Latin American and Asian middle-income countries, joint ventures of local companies with R&D-based MNCs where there is constant access to innovative new products and technologies is an attractive possibility.

*Fink (2000)*⁹⁵

This dissertation analyzes the economic implications of a move toward stronger IPRs [intellectual property rights] in developing countries, with a focus on the implications of stronger IPRs on the behavior of transnational corporations (TNCs) in developing countries. The relationship between IPRs and TNC activity is of interest for several reasons. First, TNCs are significant producers of intellectual property and one would expect this type of firm to be highly sensitive to the protection of IPRs. Second, the developing world has experienced a sharp increase in FDI from industrial countries over the past decade and it is important to know about the behavior of TNCs in light of a changing environment for IPRs. Third, FDI is considered to be an important vehicle for the transfer of technology and IPRs protection is likely to affect the extent and quality of technology transferred to developing countries.

The dissertation consists of three self-contained, but connected studies, where the common objective of these studies is to gain insight in how IPRs reforms in developing countries affect the behavior of TNCs as well as market structure and welfare in reforming countries. Fink concludes with recommendations for future research, which may enhance understanding of the economic implications of IPRs protection in developing countries.

*Grace C (2004b)*⁹⁶

Technology transfer (TT) is defined here as the dissemination of knowledge and expertise in the pharmaceutical sector from developed country organisations to organisations in developing countries. Recognising that technology transfer is potentially a very important activity for the international community to encourage, particularly when such transfers further public health objectives, this briefing paper documents a variety of TT experiences and analyses the motivations behind the enabling agreements. These experiences range from those that occur spontaneously, sometimes between relatively equal partners engaging in more of a technology exchange, to those taking place in countries with industries in more nascent stages of development, as well as those where

95 Author's introduction and conclusion summarized.

96 Author's summary.

public bodies sometimes impose obligations or offer incentives, including through public–private partnerships (PPPs), to bring parties together.

On the obligation side, the TRIPS agreement is weak on imposing technology transfer obligations in developed countries as a legal requirement, although the statements referring to TT as an objective may be used as an interpretative device, either to inform the application of other parts of the TRIPS Agreement, or as the basis for political objection to the manner in which the Agreement is being interpreted and applied by developed members. On the incentive side, developed country examples where governments have offered incentives to industry to engage in TT are limited. However, non-governmental and international organisations have been active in this field, and their engagement well noted in the examples.

Regardless of where the TT experience fits within the “spontaneous/purely commercial” versus PPP continuum, sustainable arrangements have required a solid business rationale for engaging in any such technology transfers. Many of the technology transfer experiences have involved an element of public funding or technical support that serve to “sweeten” the deal, making it a sound business investment for the technology donor and/or recipient.

It is difficult to generalise about the kind of incentives that can be offered to bring together such TT deals, since the appropriate incentive and the business case it supports, will differ according to such (usually difficult to uncover) factors as the particular company’s history and past investments, perceived competitive advantages and future strategic goals. In some instances, the business case for the participating firms may be immediately obvious, short-term, and easily attributable to the TT experience. Alternatively, the business case may be more subtle and long term – for example, a response to public pressure or a desire to fulfil overall company strategic objectives.

As for how changing intellectual property (IP) can be expected to impact TT, as long as the institutional and governance structures are aligned with increasing protection of IP, then we might expect to see more willingness of firms to license and contract out increasingly important/proprietary technologies to developing country firms. However, the opposite argument has also been made – that strong intellectual property protection is liable to stifle technology transfer as technology owners exploit their market power. The technology/patent-holder will no doubt need to consider all types of costs and benefits when choosing the most appropriate contractual/ownership mode and the degree of technology that can be successfully transferred.

*Janodia et al. (2008)*⁹⁷

Intellectual property is an important aspect for country’s technological, economic and social development. It is observed that normally technologies are created in developed countries and benefits of these technologies are not spilled over to people in the developing countries. It is essential to make

97 Author’s abstract.

these technologies easily and economically available to developing countries. By transferring technologies, firms can recoup a substantial portion of investment. Government, industry and academia can join hands in developing and distributing technologies to all the stakeholders. Licensing (in-licensing and out-licensing) is one such phenomenon of technology transfer that has gained momentum in pharmaceutical industry whereby pharmacy companies can contribute to research and development. This article identifies some aspects of technology transfer that is shaping pharmaceutical industry and its research and development activities to meet the newer challenges and some relevant examples of technology transfer in pharmaceutical industry.

Kaplan & Laing (2005)⁹⁸

Local production of pharmaceuticals in developing countries may be seen as helping to stimulate industrial policy and/or as stimulating pharmaceutical “access” to needed medicines. However, if a developing country with manufacturing facilities is able to finish off bulk active ingredients sourced from developed or other countries at high costs, such manufacture may have no impact whatever on patient access to needed medicines. There has been some critical thinking in the past regarding whether or not small developing countries should make their own pharmaceuticals, but no recent comprehensive summary of the issues and policy options. This paper summarizes the issues surrounding “local production” from a policy and public health viewpoint. It provides four brief country-level case studies, and reviews the evidence supporting the industrial policy assumptions underlying the goal of local production. In brief, in many parts of the world, producing medicines domestically makes little economic sense. If many countries begin local production, the result may be less access to medicines, since economies of scale may be lost if there are production facilities in many countries. The document concludes by providing a research agenda specifically designed to test assumptions about local production of pharmaceuticals.

Management Sciences for Health (1997)⁹⁹

Chapter 9 – Pharmaceutical Production Policy

Policy-makers must be concerned about pharmaceutical production for the same reasons that underlie other policy and legal decisions: drugs can be dangerous as well as lifesaving. Health professionals and patients have no ready way of making judgments about drugs without public surveillance as a guide.

Problems of lack of access, high prices, and poor drug quality in many markets have prompted public and political interest in finding reasonable alternatives to dependence on outside suppliers. These alternatives to dependence on outside suppliers. These alternatives have often been formulated in terms of local production to promote self-sufficiency achieve independence from powerful international suppliers, develop local industrial capacity, and create

98 Authors' abstract.

99 Authors' summaries.

jobs. Basically, the reasoning has been: if we develop our own production capacity, we'll be free from dependence on unreliable outsiders. To ensure that major public needs are met, the public sector has often become involved in local production.

Experience over the last two decades has demonstrated that this perspective is sometimes flawed. Ample evidence indicates that production by public agencies is often not the wisest courts. Many failed attempts at such production, together with rapidly expanding markets and communication systems, have reduced earlier pressures for direct public sector involvement in manufacturing. The principle policy question is often not make or buy but rather what to buy and where to buy it.

Three important findings of the last twenty years guide this chapter:

1. Drugs are potentially life-saving and life-threatening. Drug production requires precise standards, quality control, a skilled labor base, capital, and management. Modern drug production often uses raw materials that are most economical in the international market. This means that high-quality, low-cost drugs are not likely to be produced from the raw-materials stage in countries that do not have the required market size and resources in terms of skilled people technology and quality control.
2. Where private manufacturing initiatives have proved successful, pharmaceutical manufacture has remained a high profitable industry. [I]n a market that is large enough, local manufacturers can carve out a role even when they are starting way behind the international producers. Section 9.1 describes the range of production options, from primary manufacture of raw materials to the packaging of finished products that policy-makers must consider.
3. Since consumers are unable to judge medicines safely on their own, policy-makers must be concerned about regulating production quality, whether drugs come from international or domestic sources. Whether policy-makers take an active or passive role, they must recognize that the regulations and incentives existing in a country always affect drug production. The most constructive stance may be to shape policies and working regulations that promote the goal of a reliable access to effective, safe and inexpensive medicines rather than focusing on where the production takes place.

Chapter 19 – Small-Scale Local Production

Local pharmaceutical production can be conducted on a large scale (usually on a national level by the private-sector pharmaceutical industry or by the public ministry of health). It can also be done on a small scale, perhaps at a regional or local level by private non-governmental organizations (NGOs) or not-for-profit mission organizations. This chapter focuses on small-scale local manufacturing and repackaging operations capable of producing non-sterile and sterile pharmaceuticals. It provides information to help program managers decide whether it is logical to begin small-scale local production, and if so, how to plan and carry it out.

In order to decide whether it small-scale local production is a valid option, production capability and resources must be assessed. After a decision to produce pharmaceuticals locally is made, product selection and preparation, quality control, and pricing must be thoroughly studied and a plan of development established. When properly carried out, local pharmaceutical production and repackaging may significantly improve primary health care services.

Because of the multitude of difficulties encountered and the level of sophistication requires, large-scale production is often not realistic in developing countries, at least when attempted by the public sector. Nevertheless, the need for some locally produced pharmaceutical and laboratory reagents may exist, and if this need cannot be adequately met by an existing large-scale facility, hospitals (or associations of facilities) may have to produce what is needed on a much smaller scale. The rationale for local pharmaceutical production is to save lives that may be endangered by shortages of commercial products.

It was only in the last thirty years that the United States, under pressure from the pharmaceutical industry and strict government regulation, removed much of the preparation of simple pharmaceuticals (including IV fluids) from hospitals. The increased threat and expense of lawsuit splayed a major role in this decision to leave manufacturing in the hands of the pharmaceutical industry. In many developing countries legislation still promotes the local production of pharmaceuticals. The long experience of high-quality, small scale production by hospital pharmacies, which continues in many European countries should not be forgotten in developing countries. However, quality must be assured.

Drug prices have skyrocketed in recent years to the extent that some products can be safely manufactured locally are simply not affordable if purchased and imported into developing countries, especially for the public health sector, with its meager resources. This means that some small-scale local production is likely to be cost effective in many countries, but it requires that management personnel ensure its safety and effectiveness. The experience of many countries confirms that this is possible, but the potential problems and risks should not be underestimated.

*Tybout (1998)*¹⁰⁰

Manufacturing firms in developing countries have traditionally been relatively protected. They have also been subject to heavy regulation, much of it biased in favor of large enterprises. Accordingly, it is often argued that manufacturers in these countries perform poorly in several respects; markets tolerate inefficient firms, so cross-firm productivity dispersion is high; small groups of entrenched oligopolists exploit monopoly power in product markets; many small firms are unable or unwilling to grow, so important economies of scale go unexploited. [The author] assesses each of these conjectures, drawing on plant- and firm-level studies of manufacturers in developing countries. [The author] finds systematic support for none of them. Turnover is substantial, exploited scale economies are modest, and convincing demonstrations of monopoly rents are generally lacking.

Overprotection and overregulation are probably less a problem in developing countries than are uncertainty about policies and demand, poor rule of law, and corruption.

[The author] does find evidence that protection increases firms' price-cost margins and reduces average efficiency levels at the margin.

And although the econometric evidence on technology diffusion in developing countries is limited, it does suggest that protecting "learning industries" is unlikely to foster productivity growth.

All of which suggests that the general trend toward trade liberalization has yielded greater benefits than the traditional gains from trade.

*UNIDO (1980)*¹⁰¹

World sales of drugs in developed market economies are concentrated in the hands of transnational corporations. [There has been an] increasing share in the production of drugs by developing countries from 1960 to 1980.

This increase in production will involve much higher capital investment than normally envisaged, because, of 110 developing countries, only about 10 have formulation and bulk production plants, while some 50 have only formulation plants and the rest only import the finished products. Therefore, most of them now only carry out the final stages of manufacture, that is, formulating imported bulk drugs into finished preparations or repackaging imported finished drugs. Backward integration of industries in these countries to go into more basic stages of manufacture will involve considerable capital investment without reflecting significantly on the value of output. Ancillary industries such as the production of packaging materials and associated engineering industries for making simply equipment must also be established. These measures will result in a considerable increase in the value added and reduce

100 Author's summary.

101 Author's introduction.

dependence on imports. With a simultaneous development of the chemical and chemical-based industries, where feasible, the developing countries will have more self-sustaining industries.

The trends from 1980 onwards are difficult to forecast because of political, social, economic and technological factors that are likely to play increasing roles in the development of the pharmaceutical industry throughout the world. The growth of the industry will probably be more regulated to meet the urgent health needs of each country instead of the laissez-faire policy followed at present in many countries, especially as the right to health care will become widely established as a major socio-political goal. This development will also mean higher levels of government economic controls on prices, profits, and foreign capital investment. To correct the present concentration of drug distribution in urban centers and make drugs available in the rural and more remote parts of developing countries, the trend will be toward public acquisition of the drug distribution systems. Traditional medicine will also play a more important role in the health services, and greater attention will have to be paid by governments to the standardization and upgrading of products from this source.

World Bank (2005)¹⁰²

Pharmaceuticals are essential in every health care system. The objective of pharmaceutical policy is to make sure that there is a reliable supply of good quality medicines at affordable prices. Local manufacturing is sometimes offered as a potential solution to the “access” problem. Supporters of this concept suggest that local production in a developing country should result in a cheaper final product. Skeptics argue that small manufacturing units don’t achieve economies of scale, and that higher unit costs outweigh potential advantages such as lower transportation costs.

Another factor in this discussion is the TRIPS agreement. TRIPS requires all countries (except the least developed) to introduce patents for pharmaceuticals in 2005. There are mechanisms in place, for example compulsory licensing, to balance the interests of patent owners with public interests in countries affected by a health crisis such as HIV/AIDS. So, for example, a country may declare that a health crisis makes it imperative for them to have access to a particular drug, and there is an established process through which the country can issue a license (whether or not the patent holder agrees) to a company to manufacture or import the drug. But it is not yet clear whether these mechanisms work well for countries that rely on imported pharmaceuticals only. Thus, the question of local manufacturing comes up, as a way to bypass the complexities of licensing agreements that cover more than one country.

This paper reflects on aspects of health policy and industrial policy relevant to local manufacturing, which need to be balanced according to development priorities. It advocates for a sound assessment of costs and benefits as the basis for rational decision making on pharmaceutical manufacturing.

102 Author’s introduction.

7. Development of the pharmaceutical production sector

The preceding review of trends regarding local production of medicines in developing countries and related technology transfer, based on interviews and the literature, yields a fairly consistent set of elements or factors that are important to the development of a successful local production sector within a country or region:

- *Availability of skilled personnel:* basic education, specialized technical education, experience.
- *Access to investment capital:* equity and loans – public and private, national and international.
- *Availability of suitable input materials:* basic chemicals, biological starting materials (including plant-based), APIs, excipients.
- *Adequate infrastructure development:* water, electricity, transport, environmental controls.
- *Access to relevant technologies:* machinery and equipment, supply-chain controls (e.g. computer software to monitor movement through chain), production processes, chemical and biological formulae for medicines (including authorization for use).
- *Adequate regulatory environment:* regulatory oversight, approval of facilities, manufacturing to GMP standards, export and import controls.
- *Achieving economies of scale:* sufficient market size to allow efficient manufacturing, adequate marketing and distribution channels.

7.1 Availability of skilled personnel

A significant number of technically trained individuals are required in the operation of a pharmaceutical manufacturing facility. The level of technical training required will vary depending on the type of facility in question. An advanced API production facility or a facility for the manufacture of biological products may require personnel with a highly specialized scientific/technical background. A formulation facility requires individuals with skills in the analysis and testing of chemical compounds, and environmental control and computer software engineers. Maintenance of sophisticated manufacturing equipment, including packaging and labelling equipment, requires specialized knowledge.

Much of the scientific training for pharmaceutical industry personnel takes place in the university setting (e.g. coursework in chemical engineering). As is the case for most industries, however, on-the-job work experience is necessary to complete the training process. Most of such practical training takes place in the ordinary course of business in an established pharmaceutical facility where experienced employees are involved in the training of junior employees. It is not uncommon in the pharmaceutical sector to find that senior executives of generics companies in developing countries began their careers as employees of multinational originator companies. For developing countries without established pharmaceutical manufacturing facilities, the possibility for on-the-job training of personnel is limited.

Notwithstanding existing possibilities for on-the-job training, some developing countries with advanced pharmaceutical industries are strongly supporting education programmes specifically intended to support the local industry. An example is found in India, where a set of education institutions known as National Institutes of Pharmaceutical Education and Research has been established to provide targeted training and support for all aspects of the pharmaceutical sector, from scientific research to marketing and sales. India is not alone in providing such support. Other developing countries with comparatively strong pharmaceutical industries, such as Argentina, Brazil and China, are providing support for industry-specific training.

For developing countries with comparatively small pharmaceutical sectors, and for countries with less availability of scientific training at the university level, there is a gap that is not easy to close. If there are limited employment opportunities in a particular sector, students are unlikely to train for employment in that sector. Universities and other training institutions are less likely to develop curricula relevant to the area because of a lack of student demand. On-the-job training opportunities are by definition limited.

One of the key problems for promoting local production of pharmaceutical products in developing countries is to provide mechanisms for the education and training of personnel for the specific sector. This is addressed further in Section 8.

7.2 Access to investment capital

Particularly among stakeholders in the pharmaceutical manufacturing sector in Africa, the high cost of investment capital is identified as a major obstacle to local production. There is little history of venture capital investor participation in the local pharmaceutical sector, and local pharmaceutical producers do not participate in public securities markets. Capital for investment in local manufacturing facilities principally comes from borrowing and reinvestment. Borrowing costs in Africa are generally higher than in other regions. Pharmaceutical manufacturing carries a significant degree of commercial risk, and borrowing costs in this sector are affected by the level of risk.

Local producers in Africa consistently identify the regulatory certification requirements of international purchasers of HIV/AIDS drugs as having a particularly adverse impact on their sales opportunities on the continent. All, or virtually all, procurement authorities operating with the support of multilateral funding mechanisms require that products be prequalified by WHO or are otherwise approved by stringent regulatory authorities. There are few local African producers that meet these regulatory requirements, and they are thus shut out of selling to the largest buyers of pharmaceutical products. Although this is a regulatory problem, and not strictly speaking an access-to-capital problem, it becomes an access-to-capital problem as African producers find it more difficult to generate profits that can be reinvested in local production facilities.

In other regions, local pharmaceutical manufacturers face access-to-capital problems typical of those of other industries. Some developing countries' governments, through their industrial development bank facilities, provide lending support for the pharmaceutical sector. The IFC division of the World Bank provides loans to pharmaceutical manufacturers in developing countries, although the level of lending activity is relatively modest.

As noted earlier, the generic sector of the global pharmaceutical industry is highly competitive and operates on relatively low margins. With few exceptions, the much more highly capitalized multinational originator companies are in a better position to finance or expand operations. This (i.e. access to capital) is one of the reasons why successful generics producers in India and elsewhere are being acquired by, or entering into joint venture arrangements with, originator companies.

7.3 Adequate infrastructure development

Pharmaceutical manufacturing is particularly reliant on the quality of material inputs, including ultra-pure water. Because of the close tolerances involved in manufacturing processes, a continuous supply of electricity is important. Environmental conditions must be closely controlled (e.g. clean air). As in other industries, transport is important to supplying both local and foreign markets.

Many developing countries face challenges in providing appropriate infrastructure for pharmaceutical manufacturing. African local producers in particular identify the high price and potentially intermittent availability of electricity as problematic. African producers also highlight air transport problems. Air transport between countries in Africa is routinely more costly than air transport arriving from outside the continent, compounding the difficulties that African local producers face in competing with imported products. It is not uncommon for an intra-Africa air shipment to be routed through Europe.

The requirement of adequate infrastructure development is certainly not unique to pharmaceutical manufacturing. Infrastructure development is a challenge for many developing countries, and its absence affects social welfare in a variety of ways. There are mechanisms for supporting infrastructure development for specific industries, including the pharmaceutical industry, but this presents a choice between alternative allocations of scarce resources.

7.4 Adequate regulatory environment

One of the most difficult challenges facing local producers in developing countries is complying with local and international pharmaceutical regulatory standards, in terms of both production and registration. In virtually every country, a pharmaceutical manufacturer must demonstrate compliance with domestic regulatory standards to operate its facility. Each country has its own production-related regulatory requirements and regulatory authority.

The stringency of the regulatory requirements and the technical capacity of the regulatory review authorities vary substantially between countries. In addition, for sales to certain export markets, and particularly to the United States and Europe, manufacturers must comply with the production-related regulatory requirements of the importing country, also entailing site visits by the foreign regulator. Finally, as noted in the preceding section, certain types of sale funded by international procurement authorities require production facility approval by the WHO prequalification programme or by a stringent regulatory authority, typically the United States FDA or EMA.¹⁰³

African local producers in particular expressed concern over national regulatory authorities in their home countries that are underfunded and understaffed and may lack certain technical expertise. These characteristics, it is argued, inhibit bringing production facilities online in a timely way.

Producers in developing countries in general face difficulty in complying with cGMP requirements and review of production facilities by regulators from the major potential developed country export markets, the United States and the EU. Compliance with cGMP standards of the United States FDA and EMA is often substantially more costly than compliance with local regulatory standards, and in any event entails a time- and staff-consuming process. Producers from only a few developing countries have received the necessary production-related approvals to import into the United States or the EU.

As noted earlier, African producers in particular have expressed concern regarding requirements to be prequalified by WHO for undertaking sales to internationally funded HIV/AIDS-related procurement authorities. Some of these producers indicate that, as a consequence of these requirements, they were shut out of national procurement programmes in which they previously participated.

In addition to production-related regulatory review requirements, pharmaceutical products must be registered with national regulatory authorities before they may be placed on the local market. Each country maintains its own drug registration authority. The level of scrutiny an application for registration undergoes may vary significantly between countries, depending among other things on the capacity of the national regulatory authority. Pharmaceutical manufacturers in different regions express concern that technical drug registration requirements may in some cases be adopted for the purpose of protecting the local industry against foreign competition. For example, in the view of some manufacturers, countries may adopt stability testing requirements that vary among neighbouring countries, mainly for the purpose of protecting local producers.

There are legitimate public health-related reasons why individual national drug regulatory authorities may adopt standards for the registration of

¹⁰³ As noted earlier, the United States FDA and EMA regulatory frameworks may be largely consistent with ICH guidelines, but the United States FDA and EMA operate pursuant to their own statutory and regulatory mandates.

drugs that differ from those adopted by other countries. Differences may be based on geography/climate conditions unique to a country or region (such, for example, that there will be different concerns regarding temperature or humidity sensitivity), the prevalence of certain types of disease in the local population and the susceptibility of that population to a particular condition, or a particular way that drugs are distributed in a country. National regulators do not always agree on the degree of risk that patients might be exposed to in a particular situation. Nevertheless, economies of scale in local production of medicines are an important factor in achieving competitive pricing, and regulatory cooperation and harmonization efforts, at least among relatively homogeneous geographical regions, would appear to be a logical step towards encouraging development of local production capacity.

7.5 Access to relevant technologies

The technologies necessary for local production of pharmaceutical products range across a wide spectrum of knowledge. At each stage of the production process, different technologies will be used. These range from the technologies applicable to producing the raw materials; the technologies used in constructing facilities, and acquiring, installing and testing equipment; the technologies involved in synthesizing APIs and formulating final pharmaceutical products; the computer software technologies used in controlling production processes and tracking products; and logistics and transportation technologies. Virtually all such technologies are available for purchase on international markets, whether through purchasing of materials and equipment or by hiring of experts to perform the various tasks. Some of the technologies may be protected by patents or other forms of intellectual property rights, but at least in terms of production-related equipment there are substitute sources of supply sufficient to maintain competitive markets.

The technology necessary to produce pharmaceutical products by and large is not “secret”. There are many qualified individuals inside and outside pharmaceutical companies with the relevant expertise to build and operate pharmaceutical manufacturing facilities. Virtually all types of necessary equipment can be identified and purchased at trade shows open to the public. It is a different question as to whether nationals or residents of particular developing countries have the relevant expertise to install and operate the equipment. In that regard, many developing countries do not presently have locally available technology – but that obstacle can be remedied through the establishment of local training programmes relying on imported technical experts at least during transition to more autonomous local production. Training local personnel is dependent on a certain baseline of education in relevant scientific and technical fields. The potential lack of individuals with sufficient baseline skills is a more difficult problem to overcome than lack of specialized expertise. Nonetheless, basic training can be provided through temporary residence and training abroad, or by temporary reliance on imported teaching staff.

A separate side of the question regarding access to technologies involves potential restrictions on access based on patent, trade secret and data-exclusivity protection. A local producer in a developing country may have the technical capacity to produce a particular pharmaceutical product but is precluded from doing so because an originator company has exclusive rights within its market (including export markets). The grant of market exclusivity in one form or another is based on the idea that investments in R&D should be protected for at least a limited period of time in order to promote a continuing stream of new investment in R&D.

Lack of access to patented technologies relevant to particular pharmaceutical products cannot typically be overcome through purchasing or licensing on the international market. Originator pharmaceutical companies that have invested substantially in the development of new drugs generally do not out-license distribution rights to third parties. In principle, there are mechanisms that can be used by governments to compel the grant of access to patented technologies (e.g. through the grant of compulsory patent licences), but for a variety of reasons governments have been reluctant to make use of such mechanisms.

The problem of access to technology needed to manufacture pharmaceutical products may be exacerbated as the TRIPS Agreement product patent transition came to an end for developing countries in 2005, and will end for LDCs (unless extended) in 2016.¹⁰⁴ Until 1 January 2005, developing countries that are Members of the WTO and that had not provided pharmaceutical product patent protection when the agreement entered into force were entitled to delay implementation of that protection. This particularly affected India, a developing country that had built up significant pharmaceutical production capacity in terms of medicines covered by patents in developed countries with production capacity, and that exported such products to other developing countries. As of 1 January 2005, India implemented pharmaceutical product patent protection for new inventions and also commenced a review of patent applications that had collected in its "mailbox" during the 10-year TRIPS transition period. The consequence is that global availability of off-patent versions of newer originator medicines available from India is diminishing. In the future, new drugs such as second- and third-line ARVs will be available only from the originator patent-holder companies, and foreseeably at higher prices than those that would have been charged by generic manufacturers in India. The Indian Government could ameliorate the impact of the end of the TRIPS transition period by issuing compulsory licences, including compulsory licences for export (under the WTO 30 August 2003 waiver decision), but so far it has not moved forward in this area.

Although the pharmaceutical product patent transition period ended for developing country Members of the WTO on 1 January 2005, a similar transition period will not end for LDC Members until 1 January 2016, and then might be further extended. That raises the possibility from a legal standpoint

¹⁰⁴ Regarding the legal implications of the end of the TRIPS Agreement transition period, see Abbott (2004).

that production of pharmaceutical products on patent in developed and developing countries could be initiated in LDCs during this extended transition. This has to a certain extent taken place in countries such as Bangladesh and Uganda. However, it should be noted that the off-patent pharmaceuticals manufactured in these countries may be exported only to other countries where the pharmaceuticals are similarly off-patent (including to other LDCs that currently are authorized under the TRIPS Agreement to disapply existing patents), and not to developed or developing country markets where patents have been secured (and have not expired or been subject to voluntary or nonvoluntary licensing). It is doubtful that LDC production of off-patent pharmaceuticals can effectively substitute for the large-volume production of India within a period of a few years.

With the end of the TRIPS pharmaceutical product patent transition period in view, developing countries at WTO initiated and completed negotiation of the 30 August 2003 waiver that authorizes the grant of compulsory licences for export to countries with insufficient manufacturing capacity.¹⁰⁵ It was contemplated that countries such as India might be able to continue their traditional role of manufacturing and supplying lower-priced generic versions of newer medicines on patent in developed and developing countries after 1 January 2005. It remains unclear whether the 30 August 2003 waiver (and the corresponding Article 31bis amendment to the TRIPS Agreement) will be effective in allowing use of the technology necessary to maintain continuity of supply of necessary treatments.

7.6 Availability of suitable input materials

Local production of pharmaceutical products in most developing countries today typically involves the steps of formulation, packaging and labelling. Such production relies on imported APIs and other inactive ingredients. As noted earlier, in order to import pharmaceutical products into the United States or Europe, a manufacturer and its facility must be approved by the United States FDA or EMA, respectively. This applies to both API materials and finished/semi-finished products. This regulatory requirement largely ensures that the finished products formulated in the United States or the EU will be of adequate quality.

Developing country producers may purchase and import APIs from a range of manufacturers, including those qualified for export to the United States and Europe, but also many that are not. The APIs approved for export to the United States and Europe are likely to be more expensive than those exported to other markets; because producers in developing countries are seeking a competitive edge over their rivals, they may purchase APIs from low-price sources. Although developing country producers will ordinarily test API inputs before use in formulations, it may be difficult to determine whether such input materials are of appropriate quality. Moreover, transit costs and times are important elements in the production cycle, and rejecting, replacing and

¹⁰⁵ Regarding the 30 August 2003 decision and its implementation, see Abbott & Reichman (2007) and Abbott & van Puymbroeck (2005).

recovering the price of API inputs that do not strictly meet quality standards can be a significant problem. The net result of the different approach to regulation of API imports is that developing country producers tend to face a heightened risk that finished products will not meet the same quality standards as products produced in the United States or Europe.

7.7 Achieving economies of scale

A number of the factors or elements referred to above help determine the extent to which developing country producers are able to achieve the economies of scale in production that are necessary to achieve price-competitiveness with imported products. Perhaps the most important is the requirement to register products in each export destination, and the problem that national regulators apply different approval standards. Better-capitalized producers have advantage in complying with different national regulatory requirements because they can absorb the cost. If a developing country pharmaceutical producer intends to export to the United States or Europe, it must meet the cGMP requirements of those countries, including inspection requirements. In Africa, achieving economies of scale is also made difficult by transport infrastructure obstacles, the high cost of capital and the relative weakness of regulatory authorities.

Alternatively, a developing country might be satisfied with a local production sector designed to meet only the national requirements for certain essential drugs, and might be willing to subsidize local producers to meet those requirements. If that is the objective, then issues involving heterogeneous regulatory requirements diminish in importance. For a producer in Africa seeking to supply the national market with HIV/AIDS-related drugs, there may remain problems associated with restrictions on procurement funding from international sources. But that is a specific and limited case.

8. Recommendations

The foregoing analysis leads to the following recommendations regarding a further work programme of WHO/PHI with respect to technology transfer and local production in developing countries.

8.1 Matching local production to public health needs

Developing country governments may have important industrial policy interests in encouraging local production of medicines, such as providing employment and reducing balance-of-payments outflows. As a consequence of WHO's public health mission, WHO/PHI is principally concerned with the question of whether local production can be employed to address unmet public health needs. Such needs may arise from an absence of potentially available treatments at affordable prices. Such needs may arise from decisions by manufacturers not to produce products for which there is insufficient demand from low-income patient populations, including decisions not to produce specific formulations that might be useful to low-income populations. Such needs may be present in a country or region that faces long-term requirements for large volumes of medicines, such as to treat HIV/AIDS¹⁰⁶ or malaria,¹⁰⁷ for which both security of supply and long-term economic sustainability is important. WHO/PHI is concerned with ensuring that medicines supplied by local producers in developing countries are produced to appropriate production and quality standards.

From a public health perspective, a first order of business for a continuing work programme should be to identify those specific areas in developing countries in which there are unmet needs, as described above. Once those needs are adequately identified, local production should be facilitated to meet the needs. This is where the general lessons of this report will assume their role. That is, WHO and Member States, along with industry and other stakeholders, can implement manufacturing solutions that are sustainable, inter alia, by establishing appropriate regulatory frameworks to enable production at suitable economies of scale; identifying and addressing infrastructure requirements; assisting with procurement of suitable machinery and equipment, and design of facilities; assisting with the establishment of technical training programmes; and identifying and assisting with securing the technologies needed to allow production. WHO can work with established local manufacturers to improve production standards for purposes of assuring the supply of good-quality products to patients at all income levels.

106 A large part of the population of Africa in need of ARV treatment is currently unserved, mainly because of a shortage of financing for antiviral procurement, rather than because of unavailability of adequate global supply capacity. Because ARV treatment is required for lengthy periods, and because supply interruption cannot be tolerated by patients, there are sound public health-related reasons for promoting increased production capacity for ARVs in Africa.

107 There was indication that supply of antimalarial medicines for Latin America was in comparatively short supply. DNDi and Fiocruz have teamed up to produce an antimalarial compound that is designed to treat the type of malaria endemic to Latin America and that is effective for the local population.

This report has not found evidence that small-molecule chemical pharmaceutical production capacity, in general, is inadequate from a global standpoint. Producers of generic medicines worldwide refer to a situation of overcapacity and aggressive price competition. Moreover, it appears that in many developing countries, a large part of generic pharmaceutical supplies are locally manufactured (at least in the sense of formulation). Multinational originators tend to dominate developing country markets in terms of dollar revenues, but this is a consequence of market exclusivity enabled by patents and regulatory data protection.

There is a fundamental question of whether developing country local production is optimally or quasi-optimally suited to addressing local public health needs, or whether better use of existing production facilities could be made. It is possible, for example, that local production in developing countries is currently directed more towards satisfying consumer preferences, as in “lifestyle products”, and less towards meeting the basic health requirements of local populations. It is possible that local producers focus on exports to more lucrative markets, including developed country markets, and do not address the requirements of local populations with equal attention. It may be that existing developing country pharmaceutical producers are currently capable of addressing unmet medicines needs. The more specific problem may be one of providing sufficient economic incentive to do so.

Because local pharmaceutical producers in developing countries may rely on sales to government-sponsored public health programmes, there is reason to expect that there is a reasonable match between genuine public health requirements and profit optimization. It is unlikely that government procurement authorities for the local public health sector forgo purchasing products needed for basic treatment and instead allocate resources to lifestyle products. Nonetheless, it may be prudent to further study the relationship between public health demand and the components of supply of local production to determine whether there is a reasonable match between production and public health needs, or whether some recommendations might be required for adjusting that mix. This might be of particular relevance to countries where local producers are focusing on export markets while paying only modest attention to domestic consumption needs.

8.2 From back to front through the production cycle

Operation of pharmaceutical production facilities requires technical knowledge gained through experience. Unless local industry intends to remain dependent on foreign technical experts, it is necessary to gain hands-on experience through operation of the different levels of pharmaceutical production. Experts from countries such as India that have successfully developed high-quality production facilities recommend that local production begin with formulation and proceed to production of relatively simple APIs, before finally embarking on production of complex APIs. It is difficult to bypass a significant transition period in the development of an advanced pharmaceutical production sector, which may require 10–15 years. Where a developing country currently has

limited pharmaceutical production capacity, initial efforts should be directed towards building formulation facilities meeting high GMP compliance standards.

From the perspective of WHO it is critical that the objective of developing local production capacity that addresses unmet patients' needs is kept in view. Industrial policy interests may suggest that support efforts should be directed towards use of commonly available technologies or supply of the most profitable market segments, more or less irrespective of local public health needs. Even at the early stages of planning for development of local industry through the entire production cycle, focus should be directed towards what is necessary for treating patients.

8.3 Education and training as a key factor of success

Construction and operation of a pharmaceutical manufacturing facility is a complex technical exercise that requires advanced education and training. That education and training must begin with early education where the foundations of mathematics and science skills are laid. A country with a weak educational infrastructure is unlikely to develop a strong pharmaceutical manufacturing sector. During a transition period, advanced education used in pharmaceutical manufacturing can be provided by training programmes outside the host country environment or can be provided by visits of technical experts to the host country. WHO is in a good position to recommend technical experts or programmes for such purposes.

It is very difficult to tackle a general problem such as inadequacy of basic education infrastructure as a prerequisite to addressing a specific problem such as advanced scientific training for the pharmaceutical sector. Nonetheless, it is at least worth emphasizing that support for basic education is important to a number of social welfare goals, including promoting local production of pharmaceuticals.

8.4 The virtues of the global marketplace

A developing country is not constrained in developing pharmaceutical manufacturing capacity by a shortage of available high-technology equipment. With limited exception, virtually any component needed for pharmaceutical manufacturing can be purchased on the global market. Although some technologies must be adapted to the specific operation, such as supply-chain management software, there are major computer software providers that specialize in production facility implementation. In addition to equipment, almost any skill set needed for the operation of a pharmaceutical manufacturing plant is available through the hiring of expert technical consultants. There has been a significant consolidation of pharmaceutical production facilities over the past decade, and there is substantial independent expertise available for hire.

An organization such as WHO could facilitate access to relevant technical expertise by maintaining updated lists of experts with current contact information.

8.5 Development of pharmaceutical manufacturing modular packages for developing countries

It should be practicable for WHO to develop, with the assistance of relevant experts, modular packages for the construction of pharmaceutical production facilities in developing countries. Such a programme could begin with the plans for a relatively straightforward formulation plant and could include design blueprints, construction flowcharts, necessary equipment, infrastructure input requirements (water, electricity, environmental protection and hazardous waste disposal), a list of potential suppliers of APIs and inactive materials, and so forth. Alternative modular package proposals could be assembled by private-sector companies, including pricing proposals that would include technical training, and it appears that certain private-sector companies already offer such modular packages.

For many developing countries, a main issue will be capital financing for establishing such production facilities. The World Bank might be solicited for proposals of long-term financing.

8.6 Regulatory capacity and cooperation

For developing countries at all stages in the pharmaceutical production arena, it is useful to be able to take advantage of export markets in order to produce at significant economies of scale, thereby reducing unit costs. It is a significant hindrance to such economies of scale to be required to seek regulatory approval for the marketing of medicines in each potential export market. In addition, multiplication of approval requirements increases the number of regulatory authorities that must be financed and staffed. There are compelling reasons from a public health standpoint for seeking to consolidate regulatory functions, at least at the regional level.

At a first stage, it would be very useful for governments at the regional level to seek to harmonize or approximate regulatory requirements for medicines so that producers could operate to a single standard. Although there may be some circumstances in which different public health requirements would necessitate differential requirements (e.g. significantly different climatic conditions), in most cases this should not have adverse public health consequences.

At a second stage, the establishment of regional-level regulatory authorities would appear to provide substantial benefits, including enabling greater specialization within the regulatory agency and reducing overall regulatory costs for producers and the public. The EU has taken significant steps towards consolidation of medicines regulatory approval at the regional level, although the EU experience teaches that there are substantial obstacles to overcome in achieving this objective. This report does not suggest that the establishment

of regional regulatory authorities is a simple and straightforward matter. But, even if achieved over a period of decades, this would yield long-term benefits.

8.7 Improving production processes and regulatory compliance

Local production throughout much of the developing world would benefit from upgrading of equipment and facilities to meet more stringent GMP standards. Improvements in cGMP compliance would help to ensure the quality of pharmaceutical products on local markets. In the case of Africa, compliance with stringent GMP standards is necessary if local producers are to be able to supply internationally financed procurement tenders. More stringent GMP compliance may be useful in making export opportunities available so that local producers can achieve greater economies of scale, thereby reducing unit costs. The same level of production control is not required with respect to all medicines; some are more tolerant of minor variations than others. The cost of upgrading facilities will vary depending on the type of medicine being produced. But currently many local producers choose not to upgrade facilities because of the expense involved.

This suggests the development of a programme that would assist in upgrading manufacturing facilities to meet stricter GMP regulatory compliance requirements. Such a programme could include technical expertise and, of necessity, a funding mechanism.

8.8 Access to technology

Issues surrounding access by developing country producers to originator-funded technology have been debated for many years, and there is no straightforward solution to the problem of pharmaceutical-related technology imbalance on the horizon. In terms of local production, some of the most advanced production technologies today are developed and maintained in developing countries such as India. But access to production technologies does not correspondingly ensure access to the legal right to produce new drugs. The Medicines Patent Pool is one initiative to address the problem of access to use of new drug technologies. Various PDPs such as DNDi use novel approaches such as the allocation with originators of marketing rights along geographical or market segment criteria to facilitate access to technology. This report does not make a specific recommendation on addressing potential barriers to local production arising from intellectual property protection, but it calls attention to the ongoing need to address the situation as a component of facilitating local production in developing countries.

WHO is principally interested in local production in developing countries from the standpoint of addressing unmet patients' needs. Often, patients in developing countries do not enjoy access to medicines because of inadequate financial resources – their needs are unmet because they cannot pay. Because private-sector pharmaceutical companies do not find adequate market opportunity among such populations, it is reasonable to expect that larger private companies would be more willing to make available their proprietary

technology, including patents, to smaller local producers seeking to supply underserved patient populations. WHO might assist smaller local enterprises in identifying unmet public health needs and facilitate linkages with larger companies that may be willing to transfer technology in circumstances where potential competitive threat is minimized. This should be complementary to the activities of the Medicines Patent Pool.

Dr Giorgio Roscigno pointed out that technology licensing can be undertaken in a way that targets therapeutic areas and populations in need, including by negotiating licences that allocate market opportunities, whether along geographical or public/private sector lines. He suggests there are adequate mechanisms to provide incentive for larger, better-capitalized companies to undertake voluntary licensing while protecting their perceived longer-term interests.

For developing countries with more advanced local production sectors, transferring technology and establishing or improving facilities for production of biological drugs may be useful. In this area, intellectual property rights may constitute a more significant barrier than for chemistry-based pharmaceuticals because the preponderance of biological drugs is new. As with respect to chemistry-based local production, from a public health standpoint it is important to identify therapeutic areas where biological drugs are currently not accessible by the local population.

More generally, it is evident that there are numerous complementary mechanisms by which technology is and may be transferred from developed and developing countries, and among developing countries. Debate may be had over the relative merits of FDI as a means to transfer technology, as compared with joint ventures and independent licensing. There does not, however, appear to be a practical reason for attempting to narrow the scope of available options. A mix of policies and practices will be used, depending on the informed views of governments and private-sector actors. Some governments may attempt to promote the indigenous development and implementation of pharmaceutical production technology. Some may promote FDI in the pharmaceutical production sector. Some may use industrial policy mechanisms to encourage joint ventures. Some may attempt to promote licensing of technology by providing tax or other economic incentives. Some may attempt to compel the transfer of technology. This report does not identify a single “best” mechanism for the transfer of technology for local production of medicines. There appear to be a number of ways to achieve the desired end.

8.9 Narrowing the geographical focus and support for existing initiatives

Different regions of the world are in substantially different situations regarding local production of pharmaceutical products. Africa is identified by studies, academic literature and experts as currently lacking significant capacity for the production of APIs, and more generally facing difficulties in support of local production. A good part of Africa confronts significant limitations on access

to essential medicines by the local populations. This situation seems to argue for directing efforts towards improving local production capacity principally to Africa because this may have the most significant long-term public health benefit.

It is also important to note that political leaders in Africa through the African Union have already taken steps to establish an initiative to support local production, thereby manifesting the political will to move forwards in this area. This argues in favour of providing support to the African Union initiative because government support is essential to facilitating transformation of infrastructure and providing other incentives. Moreover, government support for action to improve cooperation among regulatory authorities is critical.

This does not mean that other regions do not require support for local production initiatives. But for other regions, the public health gaps are narrower and might be addressed by more specifically tailored projects and programmes, such as programmes to facilitate production of APIs specifically required to address public health needs, upgrading production facilities to meet stricter GMP compliance standards, supporting further cooperation and integration of rules among regional regulatory authorities, and supporting production of biologicals.

8.10 A WHO resource centre

A number of the recommendations in the preceding paragraphs refer to actions that WHO may take to facilitate identification of appropriate technical experts, identify potential sources of materials, equipment and technology, and establish links with potential financing mechanisms. Taken as a whole, these recommendations suggest that WHO might encourage local production of medicines in developing countries by establishing a “resource centre” where such information and expertise are made available. Such a resource centre might combine human resources and virtual elements.

9. Concluding observation

Local production of pharmaceutical products may provide a variety of benefits to the economy and social welfare of a developing country. Education and employment opportunities are mutually reinforcing. The development of a pharmaceutical manufacturing sector requires infrastructure that is important for other sectors of the economy. Local pharmaceutical production may result in increased tax revenues and improve the balance of payments. A successful local pharmaceutical production sector may ultimately generate sufficient revenues to enable advanced R&D on new products.

WHO's role in encouraging local production is necessarily focused on how this will benefit public health, in particular by facilitating access to medicines among those currently in need. Although it is important that pharmaceutical production facilities operate cost-effectively in order to be sustainable over the long term, WHO's efforts should not focus on maximizing market opportunities and profitability. This is the natural domain of private-sector companies, and promoting industrial policy is the objective of other multilateral institutions. WHO should instead focus on a framework for identifying unmet needs and how local production might be employed to address those needs.

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Annex I: Review of literature¹⁰⁸

AI.1 Technology transfer and research and development regarding medicines

Agarwal et al. (2007)

Weaknesses in the current technology transfer mechanism and policies were identified through an examination of the status of technology transfer-related issues in pharmaceuticals and biotechnology sectors in India, and R&D and technology transfer models. Fiscal incentives and tax concessions available for the R&D industry are lacking because of the lowering of tariff and tax rates in the context of the WTO and liberalization policies. Additionally, because the issue of R&D support to industry is not covered in the WTO as in the case of subsidies, the government must re-examine existing promotional measures for R&D. To encourage technology transfer and make it more effective for the growth and competitiveness of the industry, the authors suggest a technology transfer management model and tailoring FDI policies to encourage technology transfer.

Brewster et al. (2005)¹⁰⁹

This paper seeks to raise awareness about the importance of managing IP [intellectual property] to facilitate humanitarian use and applications. The goal is to identify intellectual property approaches that can promote access to and use of health and agricultural product innovations by poor and disadvantaged groups, particularly in low-income countries. The paper encourages more public-sector IP managers to understand and employ strategies that will accomplish these goals. Humanitarian use approaches should become the norm, as we seek to help private-sector licensees understand the rationale and potential benefits behind such strategies. This paper focuses on the pharmaceutical and agricultural sectors, but the principles noted could potentially be applied to other areas as well.

There are key moments when technology managers can improve the likelihood that their IP will benefit people in need: when they decide 1) who will receive a license, 2) whether the license will be exclusive, 3) what types of applications will be covered, and 4) how long the duration of the license will be. In addition, if and when technology managers reach the stage of negotiating license terms, particularly in an exclusive license, they may be able to include legally enforceable provisions to protect in advance the possibility of sharing their IP with third parties for the benefit of people in need. These humanitarian license provisions may define beneficiaries by the field in which the IP would be applied, by geographic region, by national income level, or by market (e.g., “subsistence farmers”). License terms may also require the licensee to meet specific milestones related to availability or price in order to ensure that the

108 The author acknowledges valuable research assistance by Rene Casey Larkin and Maegan McCann in the preparation of this annex.

109 Authors' abstract.

IP benefits the target populations. The license agreement can further increase access through specific terms that govern the use of the technology for research, the licensee's freedom to grant sublicenses, and the treatment of follow-on innovations developed by the licensee.

The paper acknowledges that improved IP management cannot by itself solve the access crisis. Even if technology managers adopt humanitarian IP management strategies, they will need to connect with development partners who can utilize the protected technologies. In some cases, these partners may not yet exist. But when partners are found, it will be important to establish simple, efficient ways for them to identify technologies that public sector institutions are willing to share.

Coe & Helpman (1995)¹¹⁰

Investment in research and development (R&D) affects a country's total factor productivity. Recently new theories of economic growth have emphasized this link and have also identified a number of channels through which a country's R&D affects total factor productivity of its trade partners. Following these theoretical developments we estimate the effects of a country's R&D capital stock and the R&D capital stocks of its trade partners on the country's total factor productivity. We find large effects of both domestic and foreign R&D capital stocks on total factor productivity. The foreign R&D capital stocks have particularly large effects on the smaller countries in our sample (that consists of 22 countries). Moreover, we find that about one quarter of the worldwide benefits of investment in R&D in the seven largest economies are appropriated by their trade partners.

Correa (2000)¹¹¹

This document discusses possible elements to be considered in patent laws in order to develop a health-sensitive approach that facilitates access to drugs, especially by the poor. The basic premises of this work are that, within the limits imposed by international obligations, notably the TRIPS Agreement of the World Trade Organization, developing country patent laws should be: a) designed to serve the interests of all groups in the society, and b) responsive to health policy objectives and, in particular, to the needs of the poor. The document acts as an extensive guide for policymakers in developing countries for developing a patent legislation.

Europe Economics (2001)¹¹²

This report seeks to contribute to the debate on how best to improve the availability of essential medicines to people living in low-income countries, and how to encourage more R&D of new medicines to treat the illnesses prevalent in these countries.

110 Authors' abstract.

111 Author's summary.

112 Summarized author's executive summary.

The main policy implications to be drawn from this review are:

- Neither the problem of improving access to health care and to existing treatments, nor that of encouraging research that will lead to new medicines, is amenable to quick solutions. It will take a long time to improve health care infrastructure, and an equally long time to increase R&D expenditure and convert it into effective new products. A high-quality sustained strategy is required.
- It is essential to be clear about policy objectives and to recognize that measures to encourage one objective may conflict with another. Notably, policies that might improve affordable access to patented medicines in the short term through copying or licensing would discourage future investment in R&D for new medicines.
- The essential first step in many countries is to develop an effective health-care-delivery system, comprising trained nurses, doctors and well-equipped clinics and hospitals.
- The intellectual property system is the fundamental arrangement through which private-sector R&D into new and improved medicines is financed and incentives are provided for new research. It depends on (i) the prevention of copying – i.e. the effective protection of the intellectual property that results from successful research; and (ii) the medicines that are successfully patented finding a market.
- Currently, despite the lack in many countries of effective national intellectual property protection, because there is no international patent exhaustion, companies are generally willing to make patented products available at much lower prices in developing countries than in developed markets; this is economically efficient.
- The great majority (over 90%) of molecules on the WHO Essential Drugs List are out of patent. These can be supplied by whichever producers can deliver the right quality at the most competitive price; this is likely to be achieved in future through international trade rather than local production.
- Developing countries differ substantially with regard to health care. Some suffer from extreme poverty, have few resources, and may need institutional support. Others have sizeable numbers of relatively affluent people and better infrastructure, as well as much poverty, and may be the base for companies capable of supplying generics on a worldwide basis.
- In addition to confidence in the long-term commitment of developing country governments to effective intellectual property protection, new approaches to funding R&D and ensuring speedy and successful commercialization of new products are needed. Much work still needs to be done to further explore how packages of incentives or rewards such as up-front research grants, stage payments for development work, flexible product-to-product or country-to-country patent exchanges, and pre-commitment to purchase medicines in the R&D pipeline can be developed within new public-private structures.

*Fink (2004)*¹¹³

This chapter investigates the link between IPRs [intellectual property rights] and TNC [transnational corporation] activity empirically. It econometrically estimates the effect of different IPR regimes on U.S. and German international transactions in various manufacturing industries in a cross section of industrial and developing countries. International transactions in this context are broadly considered to be foreign sales of goods that were produced with knowledge developed by domestic firms. By definition, such international transactions are dominated by TNCs. The empirical investigation focuses on both total international transactions and individual modes of delivery – exporting, foreign production, and licensing arrangements.

The basic findings can be summarized as follows. For the United States, IPRs do not seem to play an important role in influencing total international transactions of U.S. firms. Only in chemicals and allied products and in electric and electronic equipment could a negative relationship be identified, but this link was not robust across the different model specifications. These conclusions were largely confirmed when the effect of IPR protection was evaluated on the individual modes of delivery – arm's-length exports and sales by affiliates. In the case of chemicals and allied products, the negative relationship could be confirmed for sales of affiliates, but again this relationship was not robust across the different model specifications. Arm's-length exports were consistently found to be unaffected by the degree of IPR protection in U.S. partner countries.

In view of the theoretical considerations outlined in the second section of this chapter, the absence of a link between the degree of intellectual property protection and U.S. international transactions may be attributed to two factors. Either positive and negative effects offset each other, or IPRs are simply not important enough to have a measurable effect on the aggregate data analyzed in this study. The latter possibility is supported by the fact that not all international transactions by U.S. and German firms are in knowledge-intensive goods.

The estimation results obtained for total German exports suggested that the strength of IPR protection has a positive influence on total German exports. This result is in accordance with previous empirical evidence on the IPR-trade link from Fink and Primo Braga (see chapter 2) and Maskus and Penubarti (1995). However, IPRs were found to be irrelevant in explaining the direct investment stock of German firms in foreign countries.

Finally, German receipts for patents, inventions, and processes were found to be positively related to the degree of IPR protection, especially in the chemical and oil processing industries, where firms make extensive use of patents to protect new products and technologies. Whether this positive link is attributable to more technology being transferred at arm's length, to higher

113 Author's summary.

royalties and license fees, or to increased use of the IPR system to repatriate profits remained an open question, however.

*Friede (2009)*¹¹⁴

Increase of influenza vaccine production capacity in developing countries has been identified as an important element of global pandemic preparedness. Nevertheless, technology transfer for influenza vaccine production to developing country vaccine manufacturers has proven difficult because of lack of interested technology providers. As an alternative to an individual provider–recipient relationship, a technology and training platform (a “hub”) for a generic non-proprietary process was established at a public sector European manufacturer’s site. The conditions for setting up such a platform and the potential applicability of this model to other biologicals are discussed.

*Ghaffar A et al. (2008)*¹¹⁵

This report is the result of a collaborative project to define practical ways in which health research capacity strengthening can be systematically operationalized to improve the performance of national health research systems, particularly in low- and middle-income countries. As most contributors attest in this report, a significant paradigm shift is urgently needed in order to align research capacity strengthening with other health-related changes, and to move health research itself closer towards centre stage at the national level in low- and middle-income countries. There is an urgent need to move beyond the idea of research capacity strengthening as primarily related to individual researchers, through the evident institutional capacity challenges, to a more comprehensive, holistic and demand-driven model of national research systems. Such a model genuinely engages policymakers, government officials, the media, health-care professionals, private companies and insurers, patient advocacy groups, community-based organizations, and the general public, as well as the full spectrum of other social, cultural, civil society and faith-based institutions.

The report concludes by recommending 12 priorities for action: (1) Expand to a demand-driven model of national research capacity strengthening; (2) Introduce a rights-based framework for research capacity strengthening; (3) Strengthen general health systems; (4) Address the broader determinants of health; (5) Engage different stakeholder groups; (6) Apply Essential National Health Research strategy; (7) Combine shared ownership of research coordination with accountability; (8) Galvanize different parties through national leadership; (9) Enhance research capacity strengthening investments; (10) Devote 2% of national health budgets to research; (11) Establish international research networks; and, (12) Monitor and evaluate institutional research capacity strengthening.

114 Author’s abstract.

115 Sections of authors’ executive summary.

*Hill & Johnson (2004)*¹¹⁶

The study was undertaken to meet the following aims:

- To describe current drug regulation and registration processes in selected countries, in order to understand how they affect the quality and availability of medicines in developing countries
- To develop policy recommendations as to how systems can more efficiently allow appropriate quality drugs to market
- To discuss emerging challenges and requirements posed by compulsory licensing, drugs for neglected diseases, anti-retroviral (ARV) and anti-tuberculosis (TB) drugs.

As a “desk-based” study, the major source for the mapping of current drug regulation was the comprehensive multi-country study undertaken in 1998–1999 by the World Health Organization (WHO). The key issues identified in that study were that effective drug registration depends on appropriate legislation with adequate administrative structures, to ensure that the scientific assessment of new products (generic or innovator) can be undertaken in a rigorous and efficient fashion. Political support and financial and other resources are critical.

Since that study was carried out, the pressures on regulators in developing countries in particular have included having to respond to international political issues such as TRIPS and free trade agreements, as well as having to respond to the need for access to essential medicines for epidemics such as HIV. From the reviews and documents available, in general, many developing country regulatory systems have not been able to respond effectively. The problems include:

- Lack of effective legislation to allow use of so-called “TRIPS flexibilities” such as compulsory licensing;
- Lack of adequate quality manufacturing capacity;
- Lack of adequate regulatory science capacity to assess generic products that potentially meet the need for essential drugs;
- Lack of adequate human resources; and
- Inadequate funding for drug regulatory activities

To address these problems, it is clear that a coordinated approach at country and regional level is the only solution. Regional cooperation is needed to ensure that the scientific capacity is developed. In addition, development of regional manufacturing capacity appears to be the most likely way to simultaneously enable economic feasibility, meet adequate quality standards and comply with international trade requirements. It is the legislative requirements and political requirements, however, that seem to be the most critical; countries need to have support to develop effective national legislation, as well as cooperating regionally to ensure that legislative variation between one country and another does not hamper access to essential medicines.

116 Authors' executive summary.

In terms of scientific capacity development, the WHO is continuing to play a major role, through its prequalification project and other activities. Given that the quality of pharmaceuticals generally is such a major issue, the WHO and other international authorities, such as developed country drug regulatory authorities, should be encouraged and supported to expand their current programmes that are designed to support developing countries. In addition, developing country capacity needs to be strengthened, not only to assess and register new products, but also to carry out the clinical trials of new drugs for neglected diseases that are necessary to establish safety and efficacy. Again, this is an activity that should be carried out at regional level. Mechanisms to retain trained personnel also need to be adequately addressed in any capacity development programme. Although outside the scope of this study, drug regulation should also be seen as encompassing the post-marketing activities and surveillance of products after marketing authorizations are issued, and mechanisms to develop effective post-marketing surveillance need to be incorporated into any drug regulatory authority (DRA).

Finally, there needs to be a reaffirmation that the purpose of drug registration is to protect the public health, not to facilitate profit of pharmaceutical manufacturers. Registration should not be seen as a detrimental hurdle to be avoided; it needs to be seen as a critical step in ensuring access to effective and safe medicines.

IFPMA (2003)¹¹⁷

In today's world there is a strong link between a nation's economic success and its capacity to carry out R&D of an international standard. Innovation specifically in health is additionally important both for the social as well as the economic well being of nations.

Economists have identified three inter-related mechanisms involved in economic growth.

The first of these is the productive capital of a country – the plant and equipment of the business sector, and the human capital that results from investments in education, health, and on-the-job training.

The second mechanism in economic growth is technological advance. Improvements in technology lead both to new goods and better ways of producing goods. Each new technological innovation triggers yet further innovation, in a kind of chain reaction that fuels long-term economic growth. Thus, in the knowledge-based, technologically advanced economies, economic growth has continued for nearly two centuries without running out of dynamism. Basic research alone is not enough – it must be translated into new products and processes that will stimulate, drive and create new markets. Investment in public and private R&D leads to new products and earns the revenue needed to maintain the investment, and also provide for the needs

117 Author's summary.

and wants of society A country's research base – both public and industrial – is a key engine that will drive and determine a country's economic success.

The third of the three inter-related mechanisms involved in economic growth is efficient allocation of resources, based on market competition (e.g. through international trade) and division of labour.

The underlying premise of this report is that the current global pattern of biopharmaceutical R&D is not sufficient and is not necessarily even efficiently allocated. In other words, more countries (and in particular some developing countries) could under clearly identifiable circumstances be major future participants in the biopharmaceutical sector. This report identifies, analyses and as far as possible prioritises the factors that will encourage the future development of private sector R&D for biopharmaceuticals within a country. The purpose is to provide a basic framework against which individual countries may assess their prospects of developing or attracting, and maintaining, a competitive research-based biopharmaceutical industry. It is not suggested that all countries could or should engage in biopharmaceutical R&D, but some are in a position to do more, to the mutual benefit of the country concerned and patients worldwide.

In particular, this study looks at the issues, prospects and barriers to certain developing countries – China or India for example – contributing more to the global effort in pharmaceutical R&D. What are the necessary conditions for such countries to develop domestic, private sector research-based industries, and what are the effective policy 'levers' that a country might use? Which individual countries have the structure, institutions, policies and human resources in place? The approach adopted leads to the identification of those best practices in public policy which encourage pharmaceutical innovation in the form of product- focused R&D – with the over-arching objectives of contributing to industrial development and economic growth and improving patient access to new medicines and health. The purpose of biopharmaceutical R&D is, ultimately, to find new medicines and vaccines to make people well and keep them healthy. It is not about economics, industrial development or job creation *per se* although these things are essential grist to the market economy of today. Market dynamics drive today's biopharmaceutical R&D and lie at the heart of this report. But the real and ultimate end point is, of course, the well being of individuals and of societies.

Some basic questions are first addressed. Do we really need more medicines or vaccines? Isn't there enough pharmaceutical R&D being undertaken already? Why would a country want to participate in this sector – why not be a "free-rider" on the investments of others? These are the topics of Chapter 1. The conclusion drawn is that there is considerable opportunity and need for more R&D in medicines and vaccines and that there would be a number of benefits to at least some developing countries becoming more involved. These benefits accrue to the countries concerned, to the private sector, and to patients worldwide.

In Chapter 2 the basics of pharmaceutical R&D are spelled out in what essentially describes the multinational model of today. The evidence presented in this Chapter shows that the research-based pharmaceutical industry is a knowledge-intensive industry requiring remarkably high investment. A large investment is currently dedicated to research in both public and private sectors, which has implications for companies and countries wishing to participate in knowledge-based industry – the “up-front” investment requirements can be very high. It is also concluded in Chapter 2 that alternative approaches to medicines R&D – for example government-sponsored R&D, or extensive use of public-private partnerships, is unlikely to make a broad contribution of innovative medicines (section 2.5). The natural questions therefore raised by Chapter 2 is: Given the enormous challenges and the costs of today’s pharma R&D and the size of today’s multinationals, “how can a country establish a successful, competitive industry”? Is it possible for new entrants to come in and be successful?

Chapter 3 starts to answer this question by looking at developments in science, technology and the practice of medicine. One clear conclusion is that no single company or government institution could hope to cover all areas, or be at the leading edge of all the interesting developments. Fragmentation and *de facto* outsourcing of individual components of the R&D process is offering increasing scope for new entrants to gain a foothold in the R&D chain, through specialisation. This opens up niches for focused, nimble, technology-based companies, and generics companies looking to evolve into research-based companies. These companies can concentrate on adding value through a disease/product or technology focus. For entities with limited R&D budgets, strategies for entry at particular points/specializations can reduce risk and greatly reduce the entry costs.

“Biotechnology” – products, services and research tools – represents an important opportunity, and the existence of special country resources in traditional medicines and population genetics should not be overlooked.

One further general conclusion is that all parties involved in medical R&D need each other, and have complementary positions in the biopharmaceutical sphere. Governments seeking to support domestic R&D should recognize the essential symbiosis of all players, and support them accordingly.

Chapter 4 considers the country conditions needed to develop and sustain a research-based industry. Three broad categories are identified: 1. National goals & objectives; 2. Country structures; and 3. Country resources. Underlying these are some 23 different factors, which vary in their importance. The five critically important factors without which a pharmaceutical R&D base cannot be established or maintained in any country are:

- Government support
- Essential services
- Existing industry
- Intellectual property protection
- Human resources including scientists, technicians, entrepreneurs etc.

A further group of five highly important factors are:

- Regulation
- Tax/fiscal incentives
- Government purchasing and pricing policies
- Education system
- Public research/institutions

It is difficult to imagine a research-based industry thriving in the absence of supportive conditions with respect to these five factors. A further 13 factors reviewed are of some importance.

Chapter 5 presents illustrations of country initiatives designed to encourage R&D investment, focusing particularly on the factors most important for biopharmaceutical R&D. One conclusion that can immediately be drawn from the examples is the profound power that governments have to create and shape a pro-innovative business environment.

Most developed countries seek to support their biopharmaceutical industries in some way. Globalisation of markets and businesses means that start-ups and multinationals can locate their R&D activities anywhere in the world if attracted by incentives and/or forced by adverse local conditions. The reality is that countries are competing with each other to attract and retain industrial R&D and any country that wants to develop a biopharmaceutical industry needs to be aware of this reality. At the same time it is clear that no one country provides the ideal situation for R&D to the exclusion of all others. One conclusion that may be drawn is that a country that has the determination to have biopharmaceutical R&D can achieve this, by giving due attention and support to the factors discussed in this report.

In the domain of R&D and technological innovation, the factors of government priority, intellectual property protection, and human resource development are recognized as crucial and receive strong support and recognition from many governments. The other factors identified as very important also receive considerable attention through regulation, financial support measures and a variety of special programmes. Although Chapter 5 has provided illustrations of only a selection of country initiatives, and focuses on the most important R&D factors, the relevance of all 23 R&D factors discussed in Chapter 4 must be emphasized. The precise combination of factors that country governments choose to support will depend on the local situation – and on the precise objectives with respect to biopharmaceutical R&D.

Chapter 6 draws together previous conclusions in a synthesis of general recommendations. Based on evidence presented, it is concluded that *under the right conditions*, countries such as China, India and Brazil, by encouraging biopharma R&D to be done in its own country, could make a substantial contribution, to the benefit of the country concerned, local industry and patients worldwide. From a practical perspective, the need for country audits to identify strengths and weaknesses, and R&D development strategies, is discussed.

*Jaffee (1986)*¹¹⁸

This paper quantifies the effects on the productivity of firms' R&D of exogenous variations in the state of technology (technological opportunity) and of the R&D of other firms (spillovers of R&D). The R&D productivity is increased by the R&D of "technological neighbors," though neighbors' R&D lowers the profits and market value of low-R&D-intensity firms. Firms are shown to adjust the technological composition of their R&D in response to technological opportunity.

*Juma et al. (2001)*¹¹⁹

In 2000, world leaders adopted the United Nations Millennium Declaration in which they pledged to halve, by 2015, the proportion of the world's people earning less than a dollar a day, suffering from hunger and unable to obtain safe drinking water. This paper argues that meeting these targets will entail concerted efforts to raise economic productivity in the developing world and to redirect research and development (R&D) in the industrialized countries to address problems that affect the developing countries. Doing this will require approaches that place science and technology at the centre of development policy in a world that is marked by extreme disparities in the creation of scientific and technical knowledge. Mobilizing this knowledge to meet the agricultural, health, communication and environmental needs of developing countries will continue to be one of the most important issues in international relations in the years to come. The paper identifies ways of using the world's scientific and technological knowledge to meet the needs of developing countries. More specifically, it examines linkages among science, technology and development; emerging trends in innovation systems; incentive measures for technological innovation; and how to make technology work for developing countries. The paper examines two categories of measures needed to promote the application of science and technology to development. The first includes measures adopted by developing countries themselves to promote scientific research and technological innovation as a key element in economic development policy. The second includes measures that can be adopted in the industrialized countries to contribute to solving problems in developing countries.

*Kaplan & Laing (2003)*¹²⁰

Fees charged by drug regulatory authorities (DRAs) may be used as a policy instrument to speed up regulatory approval, to encourage retention of quality staff and to stimulate introduction of generics versus new chemical entities. Often, the cost recovery function of these registration fees of various DRAs to indices of economic development – the GNP per capita and the total government health expenditure per capita.

118 Author's abstract.

119 Authors' summary.

120 Authors' abstract.

Based on the authors' analyses of 34 countries, most DRA registration fees for new drug applications for developing/non-OECD countries are less than the current GNP/capita of that country or are about US \$5000 for each \$1000 spent per capita on health care. At present, each \$1000 new drug registration fee for the developing/non-OECD countries analyzed corresponds to a total pharmaceutical market share of about \$85 million. Our analyses further suggest little relationship between DRA registration fees and drug approval times in developing countries.

The situation is complex, however, as policy tradeoffs are important to consider. Differential registration fees, presumably designed to encourage locally produced versus imported products, may violate international trade regulations. Moreover, certain DRA registration fees may provide perverse incentives for the pharmaceutical industry.

Developing countries should require that DRA registration fees be based on accurate accounting of the cost of services provided. At present levels, these fees could be increased without disincentive to the pharmaceutical industry. For new drug registration fees, the authors' analysis suggest that developing countries could charge between 1–5 times their GNP per capita or between \$17 000 and \$80 000 for each \$1000 spent per capita on healthcare.

KPMG (2005)¹²¹

India represents an economic opportunity on a massive scale: China and India are likely to be the world's two biggest economies by mid-century, and although India has underperformed in the first lap of the growth race, there was a strong possibility that India may well move ahead.

Although India is still seen by industrial investors as an economy where risk is higher and the business environment more problematic than in rival Asian investment locations, India also offers some advantages in the region. The legal framework that protects investment is one of the best in Asia. The economy offers an abundance of technical and managerial talent, often with international experience. Geopolitical risk is diminishing consistently, in contrast with some of India's emerging economy rivals in Asia. And above all, India has a demographic advantage that should see its working age population continue to grow well into the century, increasing wealth and reducing cost.

The political economy

India is changing from a command economy focused on self-sufficiency to becoming a key link in the global economic chain. But India's ambition to catch up with other high-growth Asian economies is not always matched by its ability to implement change.

Nation and state India is a federation of 29 states, and highly politicized. This means that an investment decision in India is quite likely to be affected by

121 Author's executive summary.

politics, and that needed changes in regulation and infrastructure development are often undermined by conflict and competition between state and federal governments. However, competition between states means that the total tax incentive package can be high.

Licensing, law, and reform Central government has succeeded in opening many sectors of the economy to foreign investment, while reserving others to state or local business. These continuing restrictions impose costs on manufacturers even though many manufacturing sectors (apart from strategic industries like defense and aerospace) are open for investment. According to the World Bank, the burden of licensing and bureaucratic administration has significantly reduced since 2000. In terms of companies' perception of the burden, India scores better than either China or Brazil on business regulation, better than either on the burden of tax and customs administration, and better than Brazil on the perceived level of corruption

Investment procedures Investments in some economic sectors are now given automatic approval by the Reserve Bank of India. In other sectors the government has attempted to streamline the process of approval through the Foreign Investment Promotion Board (FIPB). In practice companies report that decision-making can still appear arbitrary. Manufacturing investors can incorporate in India as Indian companies or foreign companies. Indian companies may be joint ventures or wholly owned subsidiaries, and foreign equity ownership can be up to 100 percent. However, foreign equity caps apply to several sectors.

Labor Some companies say that labor legislation remains a significant drag on business. Other companies point out that location tends to determine the quality of labor relations. Many complaints focus on the rigidity of firing regulations – only Mexico is considered equally restrictive. Nevertheless, the labor pool is exceptionally rich, with nine million new entrants a year. It takes on average fewer days to fill skilled job vacancies in India than in either China or Brazil; remuneration costs are also at the low end of the emerging economy scale. India is marginally more costly than China for most senior managers, such as directors of HR and manufacturing, and CFOs. But costs are significantly less than in other emerging economies such as Brazil and Mexico.

Taxation Corporate taxation is high compared to European and U.S. rates, but average in world terms, and has been significantly reduced in the last 15 years – the top basic rate fell from 48 percent to 35 percent in 2004. The indirect tax burden varies from state to state: the federal government has current plans to introduce a unified VAT at two lower rates of 4 percent and 12.5 percent; (20 of the 29 states have moved to the new VAT regime starting April 2005). Companies say this can bring a significant reduction in operational costs. Tax related industrial incentives include tax holidays, 100 percent deductible R&D and capital expenses, accelerated depreciation and exemptions or deferral of state sales taxes. The government is also committed to rapidly expanding the number of concessionary Special Economic Zones (SEZs) where tax is significantly reduced. A new SEZ bill was passed in Parliament in May 2005.

Location and market

In recent years almost all foreign direct investment in India went to a small privileged group of states and territories: according to the World Bank's *Investment Climate Report 2004*, over 80 percent of FDI in 2000-2003 went to Delhi, Maharashtra, Karnataka, Tamil Nadu, Chandigarh, Gujarat, and Andhra Pradesh. But investment patterns are changing, say companies, with many looking further afield to less congested and cheaper states.

Domestic markets The consumer market is remarkably undeveloped. Consumer goods penetration is very low compared to other emerging economies, partly because potential consumers are more difficult to reach. India has a lower proportion of urban households compared to Asian competitors: it is estimated that around 70 percent of Indians live in the countryside, compared to around 60 percent in China. Consumption patterns are also different: as Indians have grown richer, discretionary spending has become focused outside the home. Unlike other Asian consumers, Indians have tended not to greatly increase their spending on clothes, personal care, and household goods.

Infrastructure Infrastructure is top of the agenda for corporate planners in India. By far the most significant infrastructure constraint for manufacturing is the unreliability of power supply. On average a company can expect nearly 17 significant power outages per month, against one per month in Malaysia and fewer than five in China. At the same time costs are higher. Transport is also a constraint, and companies focus on the weakness of ports and the road network (the deterioration of the rail system means that companies have moved most of their distribution to road). However, new road investment is bringing significant improvements, and public-private partnerships are beginning to be struck in infrastructure development projects.

*Pefile et al. (2005)*¹²²

Developing Innovative Capacity in South Africa to Meet Health Needs, prepared by Sibongile Pefile

This paper reviews and discusses the current state of innovative capacity in South Africa. It identifies sets of policies at national and international level that have contributed to the promotion of innovative capacity in health R&D and establishes the indicators and drivers of innovative capacity. Policies that contribute to building a system of innovation to meet the health needs of developing countries are examined and proposals to improve the system of health innovation are presented.

The study begins with an overview of the health biotechnology sector in South Africa. It introduces key national strategies and identifies the main players in the biotechnology arena. Critical issues relating to biotechnology are reviewed and the constraints and strengths of the industry are discussed.

¹²² Authors' summary.

Before one can analyse the status of local innovation, it is important to understand the drivers of innovative capacity. Chapter one first focuses on examining what constitutes innovative capacity and then presents the various measures and approaches used to evaluate innovation.

Chapter two presents key data on the health industry and reports on existing local technical services and scientific and technological infrastructure that contribute to health innovation. The analysis is limited to understanding the dynamics of specific areas of biotechnology including R&D infrastructure, entrepreneurship, and manufacturing capacity.

Chapter three is an overview of the health innovation system and takes a closer look at the range of factors that contribute most to driving innovation and health outcomes. The impact of interventions aimed at promoting and stimulating biotechnology research and its development into marketable products is discussed. The broad policy areas reviewed in this chapter include Intellectual Property, Regulatory Controls, Government Funding, Business Affairs, Human Resources and Trade.

The role of regional and international partnerships and collaborations and their function in stimulating innovative capacity is addressed in chapter four. Here, the paper draws from local examples of South-South and North-South collaborations to determine their role in advancing policy, human capacity growth, and infrastructure development and funding.

The paper ends with brief concluding remarks and key recommendations from a health sector perspective.

**Developing Innovative Capacity in China to Meet Health Needs,
prepared by Zezhong Li, contributors Wen Ke and Chen Guang¹²³**

Broadly speaking, innovative capacity can be interpreted as “the potential for innovation and technological creativity”. Motivated by the swift development of technology and its profound impact on human life, innovative capacity, especially at the national level, has become a focal point for both academic and policy interests. In a recent study by Scott Stern, Michael Porter, and Jeffrey Furman, national innovative capacity is defined as “the ability of a country to produce and commercialize a flow of innovative technology over the long run” (Scott Stern etc, 2000). In the same article they also built an analytical framework for innovative capacity, which has been broadly used by many international organizations for the purpose of comparing national innovative capacity. This theoretical research, including its analytical framework, serves as a guideline for this paper as well.

The purpose of this paper is to present an empirical examination of the innovative capacity of the pharmaceutical industry in China, review its function in meeting local health needs, and draw some lessons from China’s experience for the international community, especially developing countries.

123 Author’s summary.

According to the analytical framework mentioned previously and the research guidelines, we divided the paper into six parts. The first is about the business environment, which includes three aspects: the disease burden, the health expenditure, and the market size. The second part is about China's regulatory environment, where we review the administration system, GMP practice, as well as the pricing policy. The third part focuses on IP management in China. The fourth part discusses the investment of innovation in China's pharmaceutical industry. We focus on government funding and other support to the industry. The emerging partnership between public and private sectors and China's promising biopharmaceutical and traditional medicine sectors are also reviewed here. The fifth part is on the human resources of the industry. The last section is on trade and trade-related issues. We examine the market structure in China, the joint ventures, China's international trade, and of course the medical access problem and the impact of WTO membership on China.

Developing Innovative Capacity in Brazil to Meet Health Needs, prepared by Claudia Ines Chamas¹²⁴

This work examines the policies, strategies and capabilities in the field of health innovation in Brazil. Brazil has a long tradition in biomedical oriented research, has developed policies for universal access to public health, has proved to be extremely active in international negotiations concerning intellectual property, offers excellent vaccinal coverage to its entire population, and has built a model of free antiretroviral therapy. Certain weaknesses curtail innovation in Brazil's health system; the most significant is its limited innovative capability which severely hinders fulfilling the population's requirements, especially those with low family incomes.

This work is composed of four parts, with the first providing an overall insight into the Brazilian health system, its capabilities in medicines, vaccines and biotechnology, as well as the main aspects of health research and innovation policies. The second part is from a commercial approach: the relationship between TRIPS and public health, pharmaceutical patents and Industrial Property Law, legal safeguards, the regulation of prices, and the Brazilian model of access to antiretroviral medicines. The third part studies regulations, funding for R&D, the business environment, and human resources. The final section advances recommendations for future policies.

Developing Innovative Capacity in India to Meet Health Needs, prepared by HR Bhojwani¹²⁵

Pharmaceuticals affect the very life and well-being of the people and cannot be priced as purely private goods. Thus the market, however perfect, may not be the right instrument for pricing of pharmaceutical products as the consumer (patient) does not have choice of the product. A social balance thus needs to be struck between the profitability of pharmaceutical companies and the equitable price for their products. Diverse social forms of price control are

124 Author's summary.

125 Concluding recommendations from author.

in vogue the world over. TRIPS does not debar such price controls. However for small nations, with limited bargaining or technological capacity, this may be difficult to do at the national level. It may be feasible to do so collectively by a few neighbouring countries on a sub-regional basis, for example Laos, Cambodia, Myanmar and Vietnam. It is thus suggested that a viable option for smaller and similarly placed sub-regional countries is to have a common social price control system. WHO could perhaps help stimulate and catalyze such sub-regional cooperation.

Even in India, despite a flourishing pharmaceutical industry, allopathic products do not reach a majority of the population. Similar conditions prevail in many other developing countries. However, a few FMCG [fast-moving consumer goods] MNCs [multinational corporations] have established distribution channels for their products to the remotest locations in such countries (e.g. Hindustan Lever Ltd. in India). In order to extend the reach of pharmaceutical products to such locations, public-private partnerships could be solicited to make available OTC and infectious disease therapeutics to the rural areas.

The only instrument that TRIPS provides the least-developed and developing countries to mitigate the monopolistic, albeit differential or even preferential, pricing by the patent holders is through compulsory licensing. It is an unused tool even for those countries like India that have had the tool in their patent kit for some time. Initiatives at WHO level need to be taken to develop capacity and skills among countries with low technological capacity to apply and use the tool judiciously, perhaps through the preparation of a manual and organizing applicable training programmes.

The present study has shown that the cost of pharmaceuticals, drugs, vaccines and healthcare delivery services like doctors' consultation, in-patient and out-patient costs are several-fold lower in India, Bangladesh, Thailand, etc. as compared to most other countries, even after applying the purchasing power parity factor. In order to have a more equitable and fair comparison of healthcare affordability by people in different countries, and thereby tacitly facilitate the MNCs to establish differential pricing of pharmaceutical products, a healthcare affordability index could be devised.

The emphasis in the present study is mainly to assess the innovative capacity developed in drugs, pharmaceuticals and biopharmaceutical sectors, which form an important aspect of curative and preventive healthcare. High-tech diagnostic services have come to play an equally important part in healthcare. The cost of these services is quite high, especially in developing countries. It may thus be useful to assess the innovative capacity developed for diagnostic kits, instruments, equipments and associated facilities as well.

The term "innovative capacity" is being interpreted as "the potential for innovation and technological capacity" along the lines of studies by Suarez-Villa, *inter alia*, on economic development, technology and patents. Thus, for the social sector of healthcare, the Suarez-Villa approach may not fully capture the spirit and the benefits of the new and effective (thus innovative) means, managerial systems, processes of delivery, and social and institutional

mechanisms devised to reach healthcare to the disadvantaged sections of the people. Defining innovative capacity for the healthcare sector may thus need to transcend mere technological capacity to encompass other relevant aspects as well.

*Thorsteinsdóttir et al. (2004)*¹²⁶

This supplement reports the results of a 3-year study of health biotechnology innovation systems in Brazil, China, Cuba, Egypt, India, South Africa and South Korea. When compared with industrially advanced nations, the seven countries in this study are each at a different stage of economic development, but they can generally be considered “innovating developing countries” (IDCs). Our objective was to identify and analyze the conditions encouraging successful development of health biotechnologies in developing countries. Ultimately, we want to identify lessons on how these countries have been able to build up capacity in health biotechnology. These lessons can potentially be put to use in other developing countries that so far have not succeeded in promoting biotechnology development, but may also be of relevance to industrially advanced nations.

This introduction addresses why it is important to study health biotechnology innovation systems in developing countries, who will probably be interested in the findings of the study, the conceptual framework of innovation systems used in the study, the study’s methods, the outline of the subsequent papers and the expected outcomes. The crux of the issue is the case studies of seven countries that follow. In a final paper, at the end of the supplement, we highlight our main findings, draw comparisons between the country case studies and outline lessons learned.

*Vestergaard (2006)*¹²⁷

This study proceeds from the World Bank’s assessment that Colombian innovation system could significantly contribute to the development of a knowledge-based economy, but its potential has not been fully realized. In the last decade, Columbia has made considerable efforts to improve its science base, yet investment in science has not translated into a high level of innovation in the private sector. The problem lies partly in weak interaction between research institutions and private firms. Weak industry-science linkages reduce economic benefits from public investments into science and technology and hamper the development of knowledge-based firms that are competitive in the global economy. The present study undertakes an analysis of the institutional framework for university interaction with industry within the context of the overall innovation system. The overarching objective of the study is to make policy recommendations that may assist the Colombian government in promoting science and technology driven economic development.

126 Sections of authors’ summary.

127 Author’s summary.

WHO (2002)

This edition of *State of the world's vaccines and immunization* highlights the immense strides made in global immunization since the mid-1990s. These include the near-eradication of polio worldwide and dramatic reductions in the incidence of measles and maternal and neonatal tetanus in some of the lowest-income countries. This report charts progress in the development and introduction of new life-saving vaccines that have the potential to save millions of lives every year. However, the report also points out that many children have yet to benefit from these achievements: although some low-income countries have made substantial progress in increasing immunization coverage, coverage in others is at its lowest for over a decade. In sub-Saharan Africa, for example, only about 50% of children are immunized during their first year of life. By contrast, the wealthier developed countries not only have far higher immunization rates but also provide access for children to a wider range of vaccines.

Part 1 of this report charts the growing divide in access to vaccines and immunization and warns of the global consequences of failure to sustain investments in immunization in developing countries. These include the re-emergence of diseases that were once under control, the spread of diseases to countries and continents where such disease had been eliminated, and the immense social costs of disease in the countries worst affected.

Part 2 outlines new initiatives launched in response to mounting international concern at low immunization coverage, the growing inequalities in immunization, and the unacceptable toll of infectious diseases in developing countries. The aim of these initiatives is to improve access to underused vaccines, accelerate the discovery and introduction of priority new vaccines, catalyse new sustainable financing, and raise both political commitment and public demand for immunization.

Part 3 looks at the impact of some vaccines already in use today and reviews progress in the R&D of high-priority new vaccines for developing countries.

Part 4 outlines some of the reasons why the world community should invest in immunization and looks at the promising future for vaccines and immunization.

WHO (2004)

To date, intellectual property rights have not been a significant obstacle to access to vaccines. However, for production of new vaccines and technologies in developing countries, intellectual property rights may assume a more significant role in the future. Institutions engaging in vaccine development often work on specific diseases with a limited number of methods to attain their research goals. Due to the unique nature of vaccine development, institutions cannot avoid obstacles posed by intellectual property rights by altering their approach to a research problem. As a result, many institutions encounter difficulties in accessing or licensing technology needed for R&D that are protected by intellectual property rights. Therefore, the rules on

patenting research tools may need to be examined in light of this problem. Additional impediments to access to vaccines in developing countries include increased regulatory review times, finances, long-term forecasting, increasing requirements for compliance with safety and efficacy standards, and increasing R&D costs.

WHO & Ethiopian Ministry of Health (2003)¹²⁸

The assessment of the pharmaceutical sector in Ethiopia was conducted from November–December 2002 by Pharmaceutical Administration and Supply Service in collaboration with the World Health Organization Country Office. The assessment was mainly based on a cross-sectional survey carried out in five national regional states (Tigray, Amahra, Oromia, SNNPR, Benishangul-Gumuz) and Addis Ababa. It involved 7 hospitals, 19 health centers, 85 health stations, 5 regional drug stores of PHARMID, 24 private pharmacies/drug shops and 490 households. This represents respective percentage sample sizes of 11.3%, 5.5%, 4.6% 71.4% and 5.4% of the hospitals, health centers, health stations, regional drug stores and private pharmacies/drug stores found in the surveyed regions.

The main objective of the study was to identify strengths and weaknesses in the pharmaceutical sector and give recommendations for improvement. Specifically, it was to see whether the target outcomes of the pharmaceutical sector (i.e. access, quality assurance and rational drug use) have been achieved and also determine whether Ethiopia has the necessary structures and mechanisms in place for improving its pharmaceutical sector.

The study has shown that the necessary structures and mechanisms required for the implementation of the National Drug Policy are more or less in place and a lot of achievements have been made. However, weaknesses in the implementation of the proclamation and some elements of the NDP were noted. For example, all manufacturers except one operate without having “certificate of competence” from the Drug Administration and Control Authority. Only drugs imported by the private sector are subjected to registration. The drug registration process is not linked to inspection of manufacturing sites abroad. The allocated drug budget was inadequate as revealed by a low per capita government drug budget of ETB 1.6 (US\$ 0.18), which is much lower than the target set in the Health Sector Development Program I (US\$ 1.25) and the WHO’s recommendation of US\$ 1.00. There is no proper stock management in health facilities as revealed by absence of stock control tools such as stock card in 60% of the surveyed health facilities.

Moreover, there is no specific NDP implementation plan that sets responsibilities, budget and time line although some elements of the NDP are incorporated in HSDPI. Monitoring and evaluation of the NDP was not included as an element of the policy itself. The results of the survey have also revealed the shortcomings in relation to achievement of the major outcome of the implementation of the policy ...

128 Sections of authors’ summary.

The study has shown both strengths and weaknesses in the pharmaceutical sector, which are related to policy/proclamation implementation and achievements of the target outcomes of the sector. To improve the situation, it is necessary to implement the interventions enumerated under the “recommendations” section of this report.

WHO & Ghanaian Ministry of Health (2003)¹²⁹

Monitoring, evaluating, and assessing the pharmaceutical situation in countries are important for determining if people have access to essential medicines that are safe, efficacious, and of good quality, and that these medicines are being used properly.

The World Health Organization in collaboration with Health Action International – Africa, supported the Ministry of Health in carrying out a baseline survey assessing the pharmaceutical situation based on Levels I and II indicators as described in the Operational Package for Monitoring and Assessing the Pharmaceutical Situation in Countries.

This survey was undertaken in 2002 to describe the current status of the pharmaceutical sector in Ghana in relation to the rational use of medicines, storage and management and people’s access to essential medicines.

The method was a cross sectional descriptive drug use indicator study covering both prescribing and dispensing practices on rational use of medicines and drug management, stock management and access to medicines in the community.

Using standard indicators, data were collected for the availability of key essential medicines, duration of stock-outs, rational use of medicines, household health care-seeking behaviour and access to prescribed medicines.

Four regions of the country were selected through a combination of purposive and random sampling based on their geographic and socioeconomic profiles. The study units comprised of public health facilities, pharmacies in the public and private sectors, public drug warehouses and households within 5km of a public health facility. These were surveyed at regional, district and sub-district levels.

The outcome measures were percentage of prescribing indicators, patient care indicators, facility indicators and access to medicines (including availability and affordability).

The median percentage availability of key medicines was 78.6% in public health facilities, and 82.2% in public sector warehouses. The median stock out duration of the basket of key medicines in public health facilities and district warehouses was found to be 78 days (~2.5 months) and 50.7 days (~1.5 months) respectively. The median antibiotic and injection use in public health facilities was found to be 43.3% and 30% respectively.

129 Authors’ summary.

The majority of the households sought healthcare from public health services, and 98% of the people surveyed could not obtain prescribed drugs due to economic and availability factors.

This baseline survey provides key information that will be used to plan and implement interventions to address under-performing areas identified in the assessment, which affect access, quality and rational use of essential medicines.

Although there have been tremendous improvement in the pharmaceutical sector over the past six years resulting from the activities of GNDP, there is still the need to emphasize the setting up of appropriate systems to monitor the pharmaceutical sector regularly. Greater efforts should be directed at drug management practices in public drug outlets to improve their efficiency. This survey provides a baseline for periodic review of work in the pharmaceuticals area so that adjustments may be made according to needs and performance.

WHO & Health Action International (2003)¹³⁰

Assessing the pharmaceutical situation in a country provides baseline information on whether its population has access to essential medicines that are of good quality, are efficacious and are being used properly. Results for such assessment can be used as a guide by policy makers and managers to develop and define the necessary changes and priority areas that require support for improved health for all. In the light of the above, WHO supported Kenya in April 2003 to carry out a baseline survey in the pharmaceutical sector to assess the current situation regarding access and use of quality medicines. The survey was carried out using the WHO Operational Package for Monitoring and Assessing the Pharmaceutical Situation in Countries (April 2003 version).

Kenya has the basic structures considered necessary for implementing a national medicine policy. However, no national assessment study has been conducted in the past to evaluate the impact of policy intervention.

Data obtained from this survey show that availability of essential medicines in public health facilities is more than 90% with 97% of public health facilities having greater than 75% availability. 45% of the households surveyed sought healthcare from public health facilities, and 6% of all households surveyed could not obtain all the prescribed medicines due to financial incapability. The cost of treatment of most common diseases in public health facilities demonstrated considerable variation ranging from an equivalent of a quarter of a day's lowest government salary for the treatment of child malaria in public health facilities to an equivalent of more than a day and a half's salary for the treatment of adult pneumonia in private pharmacy outlet.

More than 70% of the minimum criteria for adequate conservation conditions were met in only 30% of public health facilities.

130 Authors' summary.

There is a general tendency to over-prescribe medicines especially antibiotics. A national median of 78% patients received antibiotics. Irrational dispensing was also demonstrated – in 70% of public health facilities, more than three-quarters of dispensed medicines were inadequately labelled. In 27% of public health facilities, less than half of the respondents understood how to take their medicines. Performance measures suggest there is a considerable need to improve prescribing and dispensing practices in public health facilities.

Prescribers do not have access to key sources of therapeutic information they need in daily practice as Standard treatment guidelines (STG) were found in only 13% and the Essential Drugs Lists (EDL) was found in only 17% of public health facilities. Less than half public health facilities had more than 90% prescribing practice that conforms to the EDL. Only 29% of public health facilities used ORS, the recommended diarrhoea treatment, in greater than 90% of diarrhoea cases.

There is need to investigate the reasons for underperformance identified in the areas affecting access, quality and rational use of essential medicines.

WHO & Tanzanian Ministry of Health (2002)¹³¹

A survey on monitoring and assessing the pharmaceutical sector in Tanzania was carried out so as to know whether or not the population has access to essential drugs that are of good quality, efficacious and are being used properly. The survey also aimed at generating current information on the pharmaceutical situation in Tanzania. The information so gathered will form a basis for the review of the National Drug Policy (NDP) of 1991 and the Pharmaceutical Master Plan of 1992–2000.

This survey was carried out in October–November 2002 involving four purposely selected geographical areas, ie Mwanza, Kilimanjaro, Mbeya and the capital city, Dar es Salaam. From the four areas a total of 20 public health facilities were randomly selected (five from each study area). Around each of the health facilities visited, 15 households and one private pharmacy/drug outlet were surveyed.

Since the survey focused on monitoring and assessing the access, quality and rational use of medicines, the WHO level II core indicators were used. Face to face interviews, exit interviews plus retrospective record data were used to collect the required information. It has been noted in this survey that there are more areas of the pharmaceutical sector in Tanzania which have shown improvement than those which raise concern of every stakeholder of the sector. The evidence for this deduction is based upon the indicators which have shown positive results and these are: availability of key drugs in health facilities; stock out duration; affordability of key drugs in health facilities; adequacy of drug storage; patient knowledge; adequately labeled drugs; average number of drugs per encounter; percentage of prescribed drugs dispensed; patients

131 Authors' summary.

receiving injections; prescribing according to EDL [Essential Drugs List], [and] percentage of expired drugs.

The areas of concern as evidenced by those indicators which, showed negative trends are: tracer cases treated according to STGs; adherence to recommended treatment guidelines in treating diarrhoea in children; number of patients receiving antibiotics in one encounter and; availability of Guidelines, STG, EDL etc.

On the basis of the above results, the following conclusions and recommendations have been drawn: the availability of/and access to key drugs has improved in primary health facilities however, there is still room for the situation to be even better especially on the area of appropriate drug supply management; rational Use of Drugs is improving and again, efforts should be made to further raising the standards and sustain them accordingly; adherence to prescribing according to EDL is excellent and need to be encouraged and sustained/maintained; adherence to STG is low and the situation has some areas whose poor status has remained so for about ten (10) years! [The people concerned should institute corrective measures. The typical example here is the over usage of antibiotics]; prescribers and dispensers need further training and continuing education especially on areas of Rational Use of Drugs and Management of Drug Supply; preventive services need to be strengthened to improve the general sanitation in the community; the laboratory services need to be strengthened so as to support rational prescribing of drugs; the availability of STG, EDL and other National Guidelines is unacceptably low, efforts to improve the situation should be made which should include mounting of inspection exercises to health facilities for this purpose.

The general analysis of the survey data shows a considerable improvement in the performance of the pharmaceutical sector. The major recommendation is that, those indicators which, depicted unfavourable results should be addressed with new strategies of a revised NDP and the Pharmaceutical Master Plan.

WHO & Ugandan Ministry of Health (2002)¹³²

Monitoring, evaluating, and assessing the pharmaceutical situation in countries are important for determining if people have access to essential medicines that are safe, efficacious, and of good quality, and that are being used properly.

The World Health Organization in collaboration with Health Action International – Africa supported the Ministry of Health, Uganda in carrying out a baseline survey assessing the pharmaceutical situation based on Levels I and II indicators as described in the *Operational Package for Monitoring and Assessing the Pharmaceutical Situation in Countries*.

132 Authors' summary.

The assessment was carried out in four geographic and socio-economically representative districts with a study population of 20 randomly selected public health facilities, 20 public pharmacies, 20 private pharmacies/drug outlets, 5 central/district medicines warehouses, and 300 households.

Using standard indicators, data were collected for the availability of key essential medicines, duration of stock-outs, rational drug use, household health care-seeking behaviour and access to prescribed medicines.

The median percentage availability of key medicines was 75% in public health facilities, and 55% in district warehouses. The median stock out duration of the basket of key drugs in public health facilities and district warehouses was found to be 89.3 days (~3 months) and 182 days (~6 months) respectively. The median antibiotic and injection use in public health facilities was found to be 61.9% and 29.5% respectively.

The majority of the households sought healthcare from public health services, and 28 percent of the people could not obtain prescribed medicines due to economic and availability factors.

There was unacceptably high stock-out duration of key medicines and use of antibiotics and injections in public health facilities.

This baseline survey provides key information that will be used to plan and implement interventions to address under-performing areas identified in the assessment, which affect access, quality and rational use of essential medicines.

It also provides a baseline for periodic review of work in the pharmaceuticals area so that adjustments may be made according to needs and performance.

AI.2 Intellectual property rights and technology transfer generally

*Arora et al. (2001)*¹³³

Although market transactions for technologies, ideas, knowledge or information are limited by several well-known imperfections, there is evidence that they have become more common than in the past. In this paper [the authors] analyze how the presence of markets for technology conditions the technology and corporate strategy of firms. The first and most obvious implication is that markets for technology increase the strategy space: firms can choose to license in the technology instead of developing it in-house or they can choose to license out their technology instead of (or in addition to) investing in the downstream assets needed to manufacture and commercialize the goods. The implications for management include more proactive management of intellectual property, greater attention to external monitoring of technologies, and organizational changes to support technology licensing, joint-ventures and acquisition of external technology. For entrepreneurial startups, markets for technology make a focused business

133 Authors' abstract.

model more attractive. At the industry level, markets for technology may lower barriers to entry and increase competition, with important implications for the firms' broader strategy as well.

Arora et al. (2008)

This survey explains the ways in which patents assist the development of markets for technology in several ways. Patents enhance the ability of the licensor to extract rents from its innovation, reduce costs in trade of technology by forcing an increased codification of knowledge, and reduce information asymmetries, opportunistic behaviours and transaction costs. However, costs of patents include the cost of litigation and the problem of "anti-commons" (the cost of negotiating the large number of licences needed to commercialize the product is greater than the incremental value of the good itself). With regard to reductions in costs of technology trade, the direct costs of knowledge transfer are lowered when the knowledge is codified. Enhanced patent protection provides incentives to codify and organize new information in a way that others may use. Furthermore, stronger patent protection is likely to reduce information asymmetries that impose transaction costs on trade in technology. The anti-common problem may be illustrated in the case of genetic patenting: an increase in the patenting of gene fragments created a large number of patent holders whose consent is required to create a commercially useful genome product. In this situation, patent protection might hinder the market for technology because the costs of locating and negotiating with a large number of patent holders may be greater than the commercial value of the product itself.

*Barton (2007a)*¹³⁴

This paper describes how technology is today transferred to developing countries and the barriers that affect that transfer. It then identifies policy approaches that might overcome those barriers. It covers (1) the flow of human resources, as through international education, (2) the flow of public sector technology support, as through research and licensing by international organizations, and (3) the flow of private technology, as through the sale of consumer products (e.g. medicines) that may incorporate embodied technologies through licensing, and through foreign direct investment. After an introduction, the paper looks at these three areas in turn. It concentrates on policy approaches directly associated with technology transfer, thus avoiding issues of the overall investment, legal or political climate in specific developing nations ...

Today, because of free trade rules, an indigenous firm in the developing world may be less able to begin through a protected market, as did the US industrial firms of the early 19th century. And because of intellectual property (IP) protections in WTO Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), the firm may be less able to begin by imitating existing technologies, as did Japanese firms in the middle of the 20th century.

134 Sections of author's summary.

Moreover, technological flow has become strongly political, not only because of the global move towards IP but also because of technological protectionism.

Whether from basic research to applied technology or from one firm to another, the transfer of technology is fundamentally a matter of the flow of human knowledge from one human being to another. This can be through education, the scientific literature, or direct human contact. At the legal level, one thinks about licenses dealing with legal rights to use the particular technologies in the particular context – but it is the human level that dominates the managerial and economic reality. And the classic view of a flow from basic to applied technology is a great oversimplification – sometimes, for example, problems or insights arising at the production level give rise to new ideas that contribute to fundamental basic advance. At least in some sectors, close links between the basic researchers and the manufacturing experts, and even marketing personnel contribute to competitiveness and advance.

*Branstetter et al. (2006)*¹³⁵

This paper examines how technology transfer within U.S. multinational firms changes in response to a series of IPR reforms undertaken by 16 countries over the 1982–1999 period. Analysis of detailed firm-level data reveals that royalty payments for technology transferred to affiliates increase at the time of reforms, as do affiliate R&D expenditures and total levels of foreign patent applications. Increases in royalty payments and R&D expenditures are concentrated among affiliates of parent companies that use U.S. patents extensively prior to reform and are therefore expected to value IPR reform most. For this set of affiliates, increases in royalty payments exceed 30 percent. [The] results collectively imply that U.S. multinationals respond to changes in IPR regimes abroad by significantly increasing technology transfer to reforming countries.

*Briguglio (1998)*¹³⁶

This paper tests the hypothesis that small country size is associated with constraints relating to economies of scale in manufacturing. The study adopts a production function approach, utilizing data from 43 differently sized countries. The results, confirming the hypothesis, lend empirical support to the presumption that small countries face serious disadvantages in terms of production cost per unit in their manufacturing sectors, suggesting that such countries are, as a result, seriously disadvantaged in terms of international competitiveness in manufacturing trade ...

This paper presents the view that small country size is indeed disadvantageous since it imposes constraints with regard to economies of scale, and that therefore, the relatively good performance of some small countries has occurred in spite of, and not because of, small economic size.

This approach taken in this paper is based on the estimation of production function coefficients, including the returns to scale parameter, with data

135 Authors' abstract.

136 Author's summary and sections of introduction.

derived from the manufacturing across countries. Although the hypothesis that small countries experience economies of scale constraints in manufacturing has been discussed at a theoretical level in earlier work, the approach adopted in this study is innovative in that it lends empirical support to this hypothesis.

Brunetti et al. (1997)

The purpose of this survey was to better understand local investors' problems with uncertainties in dealing with their state. The survey enquired about investors' perceptions on the predictability of laws and policies, the reliability of the judiciary, corruption in bureaucracies and security of property rights. With regard to law and policy change, the results yielded that entrepreneurs fear policy surprises and unanticipated changes in rules that can seriously affect their businesses. Entrepreneurs in the Asian region have the most trust in announced government laws and policies, even more so than those in developed countries. Entrepreneurs in most regions of the world think that their problems with an unpredictable judiciary have increased over the past 10 years. Over 70% of entrepreneurs in less developed countries feel that judicial unpredictability causes significant problems for their business operations. When asked to select major obstacles, entrepreneurs in developed countries responded that tax regulations, labour regulations, safety and environmental regulations, regulations for starting a new business operation, and the general uncertainty surrounding the cost of complying with these regulations were major obstacles. Tax regulations/high taxes and inadequate supply of infrastructure were ranked as the two most significant hindrances to conducting business in South and South-East Asia. Entrepreneurs in the Middle East and North Africa claimed that the worst obstacle for business is the inadequate supply of infrastructure and tax regulations/high taxes. In central and eastern Europe, tax regulations/high taxes are considered a major obstacle.

Carr et al. (2004)¹³⁷

As is often observed, there is a strong tendency for those concerned about the effects of globalization to see multinational enterprises as primarily drawn to low wage labor-abundant countries. It is easy to find anecdotes to support this view. The purpose of this paper is to see whether or not this characterization holds up in a relatively comprehensive data set.

A casual look at data in the *World Investment Report* makes it clear that the poorest countries of the world receive very little investment. It is not clear whether this is due to poor labor skills, poor infrastructure, or bad governance. Thus, we construct a data set of U.S. outward-affiliate activities and try to explain the cross-country variation by a set of host-country characteristics including size, labor-force composition, investment barriers, trade costs, and physical infrastructure. We use a full sample of all host countries and a subsample using only developing countries. Unfortunately, the data exclude all of the world's poorest countries, and, since these get almost no inward

137 Authors' summary.

investment, we are losing many of the observations that we would most like to explain.

The general conclusion is that U.S. outward investment seeks large, skilled-labor-abundant countries. In the full sample, outward investment seems to be unskilled-labor seeking for small markets, a conclusion that holds up in the developing-country subsample, which includes mainly less skilled-labor-abundant countries.

The preponderance of results suggests that increases in investment costs or investment barriers discourage inward investment and affiliate activity. Higher trade costs seem to encourage investment, but this result is weak, especially in the developing-country sample. Finally, higher-quality infrastructure seems to encourage investment and affiliate sales in most of our specifications. This result is in evidence sufficiently enough that it would be worthwhile to develop a more comprehensive infrastructure index and to incorporate many more countries into the analysis.

Turning to production for local sales versus exports, the data reveal the unexpected result that the share of production sold locally is in fact a bit lower in the full sample than in the developing-country sample. The characterization that MNE enter developing countries primarily to produce for export is another view that is not supported by the analysis in this paper. Overall, we reach the following conclusions from comparing the local sales and export-sales regressions.

First, affiliates in developing countries are not more export oriented than affiliates in the full sample of countries; local market sales are over 60 percent of the total in developing countries. Second, affiliate production is more income elastic the more similar the host country is to the United States in labor-force composition. Third, production for local sale is more income elastic than production for export sale. Fourth, production activities for both local sales and exports are generally skilled-labor seeking, but which type of flow is more skilled-labor seeking differs between the full sample and the developing-country sample. It is interesting that activity in the developing countries appears to be more responsive to an increase in local skill endowments than in the full sample, at least according to the weighted least squares regressions. Fifth, production for export sale is more sensitive to investment costs and infrastructure quality than is production for local sale. However, these last two results are not robust to estimation technique. Note that our regressions perform worst in explaining production for export sales in developing countries, indicating that missing explanatory variables likely are important.

All of these results fit reasonably well with both formal theories of the MNE and informal conjectures about the role of infrastructure. These results and the related theory do not lend support to view that MNEs exploit and impoverish developing countries. Indeed, the theories to which the empirical results lend support suggest that inward investments are of substantial benefit to host

countries, both in terms of overall income and in terms of promoting labor-skills upgrading. Finally, we note again the absence of data on the poorest of the developing countries. It would be useful to extend this research to include determinants of activity in those nations.

*Correa (2007)*¹³⁸

The production structure in least developed countries (LDCs) is dominated by agriculture and petty service activities. Agriculture contributes a large part of value added (33 per cent), with little diversification of primary commodity exports. While, some industrial activities are becoming slowly more important for the LDC group as a whole, the share of manufacturing activities in GDP is low (11 per cent), the main types of activities are technologically unsophisticated and the productivity gap with other developing countries is important and widening. Services make the largest contribution to GDP, but most of the LDCs have a very weak specialization in advanced commerce-support services. This general characterization, however, obscures important differences in the production structure of various LDCs.

The technological infrastructure in LDCs is extremely weak. Some indicators of technological effort are revealing: Gross expenditure in R&D in 2003 was 0.2 per cent of GDP, that is, about ten times less than in developed countries; the number of researchers and scientists engaged in R&D activities per million population in 2003 is 2 per cent the level in developed countries; between 1991 and 2004, only 20 US patents were granted to applicants from LDCs (compared with 1.8 million granted to applicants from developed countries).

Given the serious shortcomings of the scientific and technological infrastructure in LDCs and, particularly, the absence of firms that could absorb existing technologies and innovate thereon, the use of the concept of “systems of innovation” – well accepted in the literature on economics of innovation – may be inappropriate in the context of such countries. UNCTAD has suggested to use rather the broader notion of “domestic knowledge systems” in order to understand LDCs’ current situation and design suitable policies. This notion assumes that the entrepreneurial capabilities that are necessary to innovate on the basis of R&D and linkages with different actors of the innovation system are missing.

Technological learning and technical change in the LDCs take place primarily by exploiting and improving mature technologies already in the public domain, obtained by various channels, mainly of an informal nature, from developed or other developing countries. A crucial policy challenge for LDCs is to build productive capacities through improving the mechanisms of technology transfer and strengthening technological learning capacities in production at firm level. This will require, inter alia, to increase the knowledge component of their productive processes and to enhance their human capital formation and knowledge base.

138 Author’s introduction.

This paper briefly characterizes, first, the importance of different modes of technology transfer and dissemination in LDCs. Second, it examines the possible role of intellectual property rights (IPRs) in learning and knowledge accumulation in such countries. Third, it explores the possible use of utility models as a means of encouraging local innovation. Fourth, the implications of the TRIPS Agreement are examined, including the extent to which the implementation of article 66.2 of said Agreement may contribute to the creation of a viable technological base in LDCs. Fifth, the possible role of technical assistance and other modalities of technology transfer is discussed. Finally, the main conclusions and a set of recommendations are presented.

*Evenson (1990)*¹³⁹

Will developing countries benefit economically from strengthening their protection of intellectual property? They have been repeatedly urged to do so by developed nations, most recently in the ongoing Uruguay Round of Multilateral Trade Negotiations. In search of the answer to these questions the authors have reviewed a substantial body of economic literature, theoretical and empirical, covering the economics of patents and other instruments of intellectual property. The vast majority of studies conducted to date have focused on industrial economies. This important body of research suggests that increases in intellectual property protection generate research and development activity sufficient to offset the social cost of the limited monopoly granted to patentees, copyright holders, and other owners of intellectual property. For developing countries, unfortunately, similar research is lacking. The paper proposes a research agenda that includes an assessment of intellectual property protection in developing countries, the incentive effects on local R&D, foreign direct investment and technology licensing, and the potential benefit to developing countries of “petty patents” and plant breeders’ rights.

*Ferranti et al. (2003)*¹⁴⁰

One of the abiding mysteries in developing economics has been why poor countries have not aggressively exploited the immense global stock of knowledge to accelerate growth. Increasingly the literature focuses on shortcomings in national innovative capacity. High levels of human capital and exposure to foreign technologies – for instance through trade, FDI, licensing, and the international circulation of skilled workers – are critical not only in their own right, but also vitally in how they complement each other. As countries seek to accelerate the pace of technological progress, ensuring that the right human capital is available and coordinated, effectively with technological policies becomes central.

The evidence clearly shows that the higher-performing countries that made a transition to full partners in global innovation – Israel, Finland, Korea, for example – have dramatically increased both their level of human capital

139 Author’s abstract.

140 Authors’ summary of the introductory chapter.

and their investments and policies for innovation in a concerted fashion. In addition to getting the basics right in terms of plugging in to the global knowledge economy, they also came to terms with two fundamental issues affecting every country following in their footsteps.

First, knowledge as a commodity is plagued with extraordinary market failures and hence the market will not generate the optimal level of innovation. To repeat, serious analysts argue that the United States should probably increase its R&D by a factor of 4 and we offer evidence that Latin America and Caribbean (LAC) is also even further below optimal. Furthermore, the institutions created to resolve market failures – universities, government laboratories, intellectual property rights – lie, by definition, outside the market and hence are not coordinated by the price mechanism.

Second, a critical aspect of the process of development is that firms, and the country as a whole, “learn to learn.” In particular, increasing the technological absorptive capacity of the firm as required a supportive set of policies and institutions ranging from well-designated fiscal incentives and subsidies to the active promotion of collaboration through incubators, technological parks, and clusters; to the creation and coordination of industrial consortia that share the costs and risks of R&D and skill upgrading and serve as learning laboratories for less advanced firms; and to establish antennas for identifying ideas from abroad.

Both considerations demand an integrated approach and a coordinative and even leading role for government. At a minimum the state needs to ensure a consistent and coherent set of incentives to ensure that the institutions created to address market failures collaborate fruitfully with firms. In the highly successful countries, governments have not been shy about financing and undertaking R&D that has broad spillovers.

Not all countries are at a stage where undertaking such policies is feasible. It probably does not make sense to contemplate broad government financing of R&D if the economy remains closed, if basic institutional integrity is in doubt, or as the report has stressed, if the required human capital is absent. That said, the successful countries have consistently taken an active approach to integration in the world economy – upgrading the learning and training capacity of firms, selectively financing private R&D, encouraging the licensing of foreign technologies, protecting intellectual property rights, stimulating the development and access to ICT and progressively deepening and running up their National Innovation systems rather than passively waiting for multinational corporations or imports to transfer technology. Thus engagement in the long process of undertaking the necessary institutional reforms needs to start early in the development process.

Though arguments for traditional “industrial policy” have largely been discredited, a government’s role in providing the necessary innovation and skill upgrading-related complements to previous reforms provides a challenging policy agenda over the next decades. An active and efficient

“innovation policy” is required, and though many of its components and institutions should be neutral across sectors, some need to be tailored to support emerging innovation clusters in particular sectors. As this report will show, most countries in the Latin America and the Caribbean region lag in almost every dimension of educational and technological achievement. As a region, to rephrase Pasteur’s quote, our collective mind is not yet prepared to take advantage of the unpredictable technological opportunities that the new millennia will present us.

Foray (2009)¹⁴¹

This study draws on the abundant empirical literature produced over recent decades that addresses the issues of technology transfer (TT) between countries with very different development levels in an age of stronger intellectual property (IP) regimes.

The key findings of this study are that, in the case of least developed countries (LDCs), the number, scale and domains of TT cannot depend alone on general economic operations, such as foreign direct investment (FDI) or infrastructure construction; neither can they only take the form of market transactions (licences). In all these cases, the particular circumstances and conditions that prevail in LDCs imply a suboptimal level of TT in relation to these countries’ needs.

There is therefore an obvious economic rationality for specific projects in which the TT is the primary product (an economic project in itself, not linked with another economic operation) but entails a low expected private profitability for the technology-owning firm. Such a prospect would involve acknowledging the existence of TT operations with far smaller commercial returns or no commercial return at all and finding operational mechanisms to incentivise these firms to sink costs in these operations. Such a strategy requires the provision of additional incentives from governments of developed countries.

Incentivising foreign firms to enter such transactions is a clear opportunity for developed country governments to properly fulfil their obligations contained in Article 66.2 of the World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS). The following recommendations are applicable to developed countries’ TRIPS obligations: the transfer of technology should form the subject of a principal economic operation (and not be a *joint product* or *by-product*; i.e. contingent on other operations); the locus of decision-making regarding modes of learning and areas for focus must shift away from foreign bodies to local agents and authorities; in providing additional incentives to the technology-owning firms, governments should seek effectiveness and efficiency. To achieve effectiveness and efficiency: governments should provide incentives in an effective way by only assisting projects that are socially beneficial but not very profitable for the firms that own and could transfer the technology;

141 Author’s summary.

and conditions for the efficiency of the TT operations involve the choice of relevant partners both on supply and demand sides, selection of the right area for focus (related to a clearly expressed local demand for technology) and the creation of organizational forms that will favour the consolidation of the transfer (absorption, adaptation and subsequent spillovers), as well as the related entrepreneurial dynamic. Additionally, governments should make as much use as possible of public-private partnerships (PPPs) as a mechanism for ensuring both the effectiveness of the intervention and the efficiency of the TT operation.

Technology transfers have to be operated in many domains (including export-oriented industry). But they must be particularly supported in those domains that correspond to the model of innovation central to economic growth in LDCs: that is, entrepreneurial activities meeting needs in local markets that are likely to generate domestic spillovers. In other words, TTs must offer a positive supply response to a demand for technology stemming from local entrepreneurs. Two factors are relevant here: These domains are potentially important for growth because the spillovers generated in the course of such projects are likely to be captured by the local economy; and These domains *need* additional incentives so the donor's intervention will be effective and respond fully to the TRIPS provision, which is not necessarily the case of export-oriented sectors in which the market incentives alone are sufficiently strong to motivate firms in rich countries to operate TTs.

The other areas – for instance the export goods-oriented manufacturing and processing sectors – are also important but they will in any case be served through TTs operating as *joint products* of FDI. As such, they should not be listed as part of the efforts made by the developed countries to comply with Article 66.2 of the TRIPS Agreement.

*Fosfuri (2000)*¹⁴²

This paper analyzes a model in which a firm endowed with a new technology can choose between exports, licensing and direct investment as entry modes in a foreign market. [The author] endogenizes the vintage of the transferred technology and allows for imitation by the licensee. Subsidiary production and exports circumvent imitation but involve higher costs for the innovating firm. The firm can strategically use the vintage of the technology to deter imitation by the licensee. As a result, transfers to affiliates might be of later vintage than technologies sold to outsiders. Through modification of the imitation costs, the host country's system of patent protection influences the mode of technology transfers which in turn affect the welfare of the recipient country.

*Helleiner (1975)*¹⁴³

Multinational corporations sell technology – both for production and for consumption – on highly imperfect international markets to less developed countries. The buyers must concern themselves both with appropriateness and

142 Author's abstract.

143 Author's summary.

with price. Despite some experience to the contrary, multinational firms may increasingly be prepared to sell more labor-intensive technologies and more essential-intensive products. Political influences upon the governments of less developed countries make it likely that the role of multinational corporations in the future sale of more appropriate technologies will be concentrated in manufacturing for export.

*Hoekman et al. (2005)*¹⁴⁴

This paper analyzes national and international policy options to encourage the international transfer of technology, distinguishing between four major channels of such transfer: trade in products, trade in knowledge, direct foreign investment and intra-national and international movement of people. A typology of country "types" and appropriate policy rules of thumb is developed as a guide to both national policymakers and rule making in the WTO. We argue that policies should differentiate between countries. The policy recommendations made illustrate the more general need for such differentiation in the application of special and differential treatment of developing countries in the WTO.

*Keller (2002)*¹⁴⁵

Convergence in per capita income across countries turns on whether technological knowledge spillover are global or local. This paper estimates the amount of spillover from R&D expenditures in major industrialized countries on a geographic basis. A new data set is used which encompasses most of the world's innovative activity at the industry-level between the years 1970 and 1995. First, [the author] find[s] that technological knowledge is to a substantial degree local, not global, as the benefits from foreign spillover are declining with distance: on average, a 10% higher distance to a major technology-producing country such as the U.S. is associated with a 0.15% lower level of productivity. Second, technological knowledge has become more global over the sample period. As a determinant of productivity, foreign R&D has significantly gained in importance relative to domestic R&D, and the extent to which knowledge spillover decline with distance has fallen by 20%. The finding of a falling but still high degree of localization has important implications for macroeconomics and growth, trade, and regional economics.

Maskus (1998)

The need for effective transfer of technology to developing countries has acquired renewed urgency in recent years as production becomes increasingly knowledge-intensive and competition is determined more and more by the ability of enterprises to learn, to acquire and use knowledge, and to innovate. Access to knowledge has become key to economic success in the marketplace.

This article remarks on the global trend towards stronger intellectual property protection, and suggests that globalization tends to reward creative and technically skilled workers. One such channel through which globalization

144 Authors' abstract.

145 Author's abstract.

affects economics includes FDI. The author asserts that FDI, as the establishment or acquisition of production subsidiaries abroad by multinational enterprises, is a significant channel of globalization because it is a source of capital and knowledge about production techniques. A review of data on FDI reveals that FDI flows have risen sharply for both developing and developed countries in the past 10 years. Strong intellectual property protection standing alone does not sufficiently create strong incentives for a firm to invest in a country. It is posited that with respect to encouraging FDI, intellectual property rights should take on different levels of importance in different sectors. For example, goods and services that depend less on the strength of intellectual property rights include textiles, electronic assembly, distribution and hotels.

In countries with weak intellectual property rights, licensing is viewed as insecure in comparison with investment in the high-technology services. The best argument for a developing country to adopt stronger intellectual property protection is that stronger intellectual property rights increase the possibility that advanced technologies will be transferred. Therefore, as a developing country increases its ability to develop and absorb more sophisticated innovations, it should develop an interest in improving its intellectual property rights system. As intellectual property rights become stronger, firms tend to prefer joint ventures and technology licensing over FDI.

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*Maskus (2004)*¹⁴⁶

International technology transfer (ITT) is a comprehensive term covering mechanisms for shifting information across borders and its effective diffusion into recipient economies. Thus, it refers to numerous complex processes, ranging from innovation and international marketing of technology to its absorption and imitation. Included in these processes are technology, trade, and investment policies that can affect the terms of access to knowledge. Policy making in this area is especially complex and needs careful consideration, both by individual countries and at the multilateral level. Markets for exchanging technologies are inherently subject to failure due to appropriability problems, spillovers, asymmetric information, and market power. Thus, there is strong justification for public intervention. However, interests in shaping such intervention are not uniform. Technology developers are interested in reducing the costs and uncertainty of making transfers, along with protecting their rights to profit from such transfers. They argue that effective protection and policy supports for markets are necessary to increase the willingness of innovative firms to provide knowledge of their production processes to firms in developing countries. Technology importers are interested in acquiring knowledge at minimal cost. Some observers argue that this objective is best met by refusing to protect the rights of foreign firms to profit from such transfers, or at least to restrict sharply their exclusive rights to exploit technology.

There is scope for mutually advantageous changes in policy regimes within these extremes. The Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) within the WTO reflects an important multilateral effort to address these fundamental tradeoffs. However, the Agreement is widely criticized as being overly protective of the needs of technology developers and insensitive to the needs of developing countries. In fact, TRIPS does not address itself in practical ways to issues of ITT, confining its language to general statements.

There are numerous channels through which technology may be transferred across international boundaries. One major channel is trade in goods, especially capital goods and technological inputs. A second is foreign direct investment (FDI), which may be expected generally to transfer technological information that is newer or more productive than that of local firms. A third is technology licensing, which may be done either within firms or between unrelated firms at arm's-length. Licenses typically involve the purchase of production or distribution rights (protected by some intellectual property right) and the technical information and know-how required to make effective

146 Author's summary.

the exercise of those rights. In this regard patents, trade secrets, copyrights, and trademarks serve as direct means of information transfer.

There are also important non-market channels of ITT. Perhaps most significant is the process of imitation through product inspection, reverse engineering, decompilation of software, and even simple trial and error. Imitation can be a costly process. A related form of learning is for technical and managerial personnel to leave the firm and start a rival firm. Yet another means is to study available information about those technologies. Patent applications are available for this purpose. Thus, patents provide both a direct source of technology transfer, through FDI and licensing, and an indirect form through inspection. However, there is much debate over whether such patent disclosures provide sufficient information for rival engineers to understand the technologies.

Finally, much technology appears to be transferred through the temporary migration of students, scientists, and managerial and technical personnel to universities, laboratories, and conferences located mainly in the developed economies. Note that in-depth training in science and engineering may be gained this way, suggesting that it is a particularly longlasting form of ITT. Further, information may be available within the public domain, making it free for taking, although not necessarily absorbed at low cost.

A major reason for protecting IPRs is that they can serve as an important support for markets in technology, including ITT. Without protection from leakage of new technical information, firms would be less willing to provide it on open technology markets. Further, patents and trade secrets provide the legal basis for revealing the proprietary characteristics of technologies to subsidiaries and licensees, supporting the formation of contracts.

However, the idea that weak IPRs reduce inward ITT is not certain and is not accepted by all observers. Limited patent protection and weak trade secrets offer local firms some scope for imitating foreign technologies and reverse engineering products. With intellectual property protection foreign firms may choose not to have any physical presence in a country, preferring to satisfy a market through exports. Similarly, strengthened IPRs provide foreign inventors greater market power in setting licensing terms.

Thus, the question is really empirical. A crude summary of the available evidence is as follows: There is strong evidence that patent applications serve as a conduit for learning among OECD economies. Thus, "trade in ideas" is a major factor in world economic growth. Patent citations reflect "knowledge flows" across borders in the sense that local inventors learn from them. There is a strongly positive impact of knowledge flows on international innovation, at least among developed regions. Stronger patent rights may be expected to raise considerably the rents earned by international firms as patents become more valuable, obliging developing countries to pay more for the average inward protected technology. International trade flows, especially in patent-sensitive industries, respond positively to increases in patent rights among middle-income and large developing countries. However, trade flows to poor

countries are not responsive to patent rights. The evidence on patents and inward FDI is mixed but recent studies find positive impacts among middle-income and large developing countries. Again, poor countries with stronger patents do not attract FDI on this basis. There is an identifiable “internalisation effect” whereby strengthening of patent rights shifts ITT from exports and FDI toward licensing.

Further, the sophistication of technologies transferred rises with the strength of intellectual property protection. Whatever the role of IPRs, they are only one of a list of factors that influence ITT.

Important factors include the investment climate, efficient governance, market size and growth, proximity to suppliers and demanders, and infrastructure.

In addition to econometric studies one can look at the histories of such recent developers as Japan and the Republic of Korea. Both pursued IPR policies that favoured local use of international technologies, licensing, and incremental innovation as they moved from being crude imitators to creative imitators and then knowledge-intensive innovators. Developing countries today have much to learn from these histories. However, TRIPS has narrowed the avenues such countries may take toward technological learning and adaptation from foreign technologies.

TRIPS recognizes in Article 7 that the transfer and dissemination of technology is a fundamental objective of the global IPR system. However, most provisions of TRIPS offer little direct assurance that there will be a rise in ITT to poor countries. Thus the negotiators included Article 66.2, which obligates developed countries to offer positive incentives to its firms and institutions to transfer technologies to the least developed countries. Article 67 obligates the developed countries to providing technical and financial assistance to help induce more ITT.

Article 66.2 is not likely on its own merits to achieve significant increases in ITT. There are two essential difficulties. For one, ITT largely relies on private market incentives and this article does little to redress the basic problems mentioned above. Second, even if governments in developed countries were willing to offer substantial incentives they would face domestic political opposition in doing so.

In this regard, the following set of policy recommendations should provide a framework for improving the environment for ITT. I organize them in terms of host-country policies, source country policies and issues for the global system.

*Maskus & Reichman (2005)*¹⁴⁷

Global trade and investment have become increasingly liberalized in recent decades. This liberalization has lately been accompanied by substantive new requirements for strong minimum standards of intellectual property (IP) protection, which moves the world economy toward harmonized private

147 Authors' abstract.

rights in knowledge goods. While this trend may have beneficial impacts in terms of innovation and technology diffusion, such impacts would not be evenly distributed across countries. Deep questions also arise about whether such globalization of rights to information will raise roadblocks to the national and international provision of such public goods as environmental protection, public health, education, and scientific advance. This article argues that the globalized IP regime will strongly affect prospects for technology transfer and competition in developing countries. In turn, these nations must determine how to implement such standards in a pro-competitive manner and foster innovation and competition in their own markets. Developing countries may need to take the lead in policy experimentation and IP innovation in order to offset overly protectionist tendencies in the rich countries and to maintain the supply of global public goods in an emerging transnational system of innovation.

Matsui (1977)

This paper focuses on specific problems and a solution that is workable to protect the interests of developing countries in the rapid transfer of technology, while simultaneously protecting the legitimate industrial property rights of the inventors of that technology. The author does not believe that the weakening of patent protection in developing countries will facilitate the transfer of technology to developing countries. Rather, the author asserts that inventions must be protected by patents in developing countries because this provides an incentive to foreigners for investment and technology export. The author acknowledges that, both economically and technically, an unworked patent is inferior to a patent that is worked. However, sanction to work patents beyond a limited extent would not encourage the transfer of technology. The type of technology transferred to developing countries without significant industrial activity of any kind must be transferred in a hierarchical sequence: transfer of the most basic level of technology must precede the transfer of highly sophisticated inventions.

To facilitate the transfer of technology, the author proposes the introduction of a system that protects “peti”-inventions; inventions related to improvements in the existing technology or conversions of the latter technology to a different application. The author also suggests the establishment of an International Technology Transfer Fund, the purpose of which would be to assist in the payment of remuneration to the sellers or licensors of technology. An International Technology Transfer Fund would allow developing countries to import technologies they could not import otherwise.

Nordqvist & Nilsson (2001)¹⁴⁸

China is the world’s leading cement producer and the second largest emitter of greenhouse gases. Due to widespread use of outdated technology, energy efficiency in Chinese cement production is generally poor, despite a reduction in national energy intensity during the past two decades.

148 Authors’ abstract.

For reasons not including climate concern, a process of structural transformation of China's cement industry has been initiated through policy statements and regulatory measures. If successful, the reform will bring substantial reductions of greenhouse gas emissions, but competing objectives and other impediments will make progress slow. A future framework such as the clean development mechanism, which creates market-based incentives for foreign private actors to invest in technology transfer, may catalyse the transformation. Dual objectives of climate change mitigation and third world development could be combined.

Various barriers in China threaten to deter climate-change driven, privately funded technology transfer. Based on literature studies and on-site interviews, this paper touches upon the reasons for this situation and ways to address it. Systems of innovation, capacity building, industrial behaviour, and market change exemplify focal areas of the analysis.

*OECD (2004)*¹⁴⁹

Patented inventions are increasingly present throughout the economy and their influences on innovation and economic performance is pervasive. Over the past two decades the number of patent applications filed each year in major patent offices has grown at a rapid pace, especially in new areas such as information and communication technologies (ICT) and biotechnology. Increased inventiveness and growing investment in research explain part of the growth in patenting, but changes in patent regimes that have expanded in the realm of patent protection and strengthened rights of patent holders together with a more strategic behavior of patentees, have also played a role. Ensuring that the patent system continues to serve its dual role of providing incentives to invention and facilitating diffusion of technology in this new environment will require increased vigilance by policy makers and robust empirical evidence for measuring the effects of patents on innovation and economic performance.

Ministers in charge of science and technology policy from all OECD Countries concluded at the January 2004 meeting of the OECD Committee for Scientific and Technological Policy at Ministerial level that "patent regimes play an increasingly complex role in encouraging innovation, diffusing scientific and technical knowledge, and enhancing market entry and firm creation. As such, they should be subject to closer scrutiny by science, technology and innovation policy makers."

The OECD Conference on Intellectual Property Rights, Innovation and Economic Performance, held in Paris on 28–29 August 2003, foreshadowed this need by providing policy makers with factual evidence and analysis that shed light on the policy debate about patents and by setting out implications for the development of IPR regimes that contribute more efficiently to innovation and economic performance. Organized at the initiative of the OECD Directorate of Science, Technology and Industry, as part of a broader project on IPR,

149 Book's executive summary.

the conference was designed as a forum for discussion among researchers, stakeholders and policy makers. A number of policy-oriented empirical studies undertaken by economists and legal experts, in most part especially prepared for the project, were presented and discussed at the conference. Results and conclusions from those studies were tested against the views of policy makers and practitioners from the business community and patent offices. Discussions were organized around a number of themes, including the link between patents and economic performance, recent changes in patent regimes, the impact of patents on entrepreneurship and technology diffusion, and the protection of intellectual property in software and services.

The presentations and discussions led to the conclusion that the strengthening and extension of the patent system corresponded to broader changes in the economy, notably the transition to increasingly global knowledge-based economies characterized by growing innovation and heightened dependence on intellectual assets as a key source of economic value and competitive advantage. Broad generalizations about the effects of patenting on innovation and economic performance are difficult to make, as the effectiveness of patents seems to vary considerably by industry sector and technological field. For example, whereas most participants agreed that patents provide incentives to innovate in the pharmaceuticals sector, opinions were divided as regards software. Nevertheless, discussions reflected that the expansion of patent protection has certainly influenced industrial structure by, for example, facilitating the breakdown of vertically integrated industries (e.g. semiconductors and pharmaceuticals) and creating opportunities for small firms that by virtue of their intellectual property can attract capital and integrate themselves into the global value chains (e.g. biotechnology). At the same time, participants identified several areas for which additional attention is needed in order to ensure that patents continue to both protect inventions and encourage disclosure: (1) enhancing the diffusion of patented technology; (2) ensuring thorough examination and high-quality of issued patents; and (3) improving international coordination.

Participants raised concerns about the possible effects of patenting on diffusion of knowledge and on access to patented knowledge for follow-on research, especially in new technological fields. Two main areas of interest were identified regarding policy directions to improve the diffusion of knowledge and follow-on innovation:

- *Exemptions for research use of patented inventions.* Participants indicated a need for better monitoring the evolution of exceptions for research use of patented inventions. Research exemptions allow research institutions when the purpose is non-commercial. Recent court decisions in the United States have narrowed the scope of application of the exception and the definition and status of research exemptions in other regions is heterogeneous and sometimes uncertain.
- *Markets for technology,* notably patent licensing agreements, play an increasingly important role in the economy, especially as innovation becomes more co-operative. They contribute to the diffusion of technology

in an era characterized by greater patent protection and favor the creation of science based SMEs. On the basis of improved understanding of such markets, governments might consider the policy measures to remove obstacles to their development.

Key to an effective patent system is ensuring quality of patents. Low quality patents include those that are overly broad or for which inventiveness is weak. Such patents contribute to congestion in the patent system and give patent holders more protection than might be warranted, reducing the net benefit of patents to society. However, ensuring high-quality standards for patents can be costly. Participants identified two areas in need of attention.

- *New areas of patent protection*, notably biotechnology, software and business methods, have raised new issues that the patent system have had difficulties in addressing. There is need for developing the capability to rapidly build up expertise in new areas and learn how best to apply basic patenting principles and ensure the granting of high quality patents. More policy-oriented studies based on empirical evidence have to be undertaken to face future challenges.
- *Patent administration*. Concerns regarding the quality of patents are not limited to new areas. Growing workloads at patent offices make it more difficult to maintain the quality of all issued patents. Participants noted that post-grant measures, such as opposition systems, can help off-set such problems. They also identified a need for a better assessment of the issue of patent quality, including definitions and measurement, and for imposing existing solutions.

International issues were also high on the conference participants' agenda. The question if patent administration and enforcement in developing countries was hotly debated. Even among OECD countries, business representatives highlighted the challenges of protecting inventions across multiple jurisdictions, and patent officials identified a need for greater co-operation.

- *Developing countries* are currently strengthening their patent systems, mainly under pressure from developed countries but also with the view of encouraging indigenous inventions. The level of development of a country, notably its innovative capability, determined its ability to use efficiently a patent system. As a result, it might not be in the interest of all developing countries to adopt patent systems as strong as in developed countries in all aspects. More economic analysis distinguishing between the poorest and middle income among the less developed countries is need in the domain.
- Reinforced *international co-operation* among patent authorities was seen as a priority by many participants, especially as relates to patentability criteria and prior art searches. This could not only reduce the administrative burden on patent offices, but provide a more consistent IPR framework for firms and other inventors that exploit their IP globally.

These proceedings summarize the presentations and discussions held at the conference and include a compilation of written contributions prepared by a number of participants. The publication is organized into five parts

that roughly follow the conference structure. The first part explores the links between patenting, innovation and economic performance. The second describes recent changes in patent regimes. The third analyses the impact of patents on entrepreneurship and diffusion of technology. The fourth part looks at the protection of intellectual property in software and services and the impact of patents on diffusion of knowledge in this area. The last part concludes with the views of patent officials, policy makers and experts on current and future challenges for patent policy, including issues related to adapting patent systems to developing countries.

*Patel et al. (2000)*¹⁵⁰

The need for effective transfer of technology to developing countries has acquired renewed urgency in recent years as production becomes increasingly knowledge-intensive and competition is determined more and more by the ability of enterprises to learn, to acquire and use knowledge, and to innovate. Access to knowledge has become key to economic success in the marketplace.

This book discusses the background, objectives, approaches and progress achieved in the decade-long negotiations on an International Code of Conduct on the Transfer of Technology which took place under the aegis of UNCTAD. It examines the impact and continued relevance of the Code negotiations to subsequent policy and legislative instruments on international technology transfer, both at domestic and international levels, and identifies and examines emerging trends and negotiating agendas that will help to shape the future of international technological cooperation.

The central question posed by the initiators of the Draft Code of Conduct is still relevant today – how can we facilitate a just and mutually beneficial system of technology flow in a world of rapid change and increasing gaps in the technological capability of developed and developing countries?

The need for marginalized countries to access knowledge in order to learn, adjust and integrate effectively into the world economic system must be balanced with the vital need to reward inventors and innovators to ensure the continued generation of knowledge. It is these issues that will continue to dominate any future discussion on the international transfer of technology.

Radosevic (1999)

The purpose of this book was to assess emerging technology transfer issues for developing countries in the context of a globalized economy. The first conclusion the author arrives at is that the characteristics of the host country and its domestic absorptive capacity are significant determining factors of technology transfer. The absorptive capacity and structural characteristics of the receiving country are factors that determine the extent and quality of technology transfer. The second conclusion is that the technology transfer cannot be treated as an isolated process. Rather, there is a broad set of factors that must be dealt with to understand the circumstances under which

¹⁵⁰ Authors' description.

technology transfer facilitates economic growth and development. Markets are social institutions and, as such, the deregulation of trade and investments is causing concern in areas such as intellectual property rights, domestic competition rules, and labour and environmental standards. Therefore, the third conclusion is that the liberalization of trade and investments is not resulting in a borderless, free-market global economy.

The final section in the book identifies the main directions for further research on technology transfer. The main problem of technology transfer policy is how innovative and productive sectors attract high-in-value in-bound transnational corporation activity, creating a “virtuous circle” of asset accumulation and clustering. This issue must be dealt with in a dynamic and evolutionary framework, as opposed to a static framework of costs and benefits. The author suggests that the factors of linkages that arise from FDI may be identified by looking at the relationship between domestic and technology transfer factors and their outcomes with regard to “vicious”/“virtuous” circles.

Roffe & Tesfachew (2002)

A working group has been established by the Ministerial Conference at WTO to analyse the relationship between trade and technology and to address the debate on transfer of technology to developing countries. The authors remark that the subject of transfer of technology to developing countries has surfaced at multilateral discussions in recent years. For instance, multilateral environmental agreements regularly include the issue of the transfer of environmentally sound technologies to developing countries. The TRIPS Agreement also incorporates a general statement about the importance of technology transfer in Article 7. In Article 67 of TRIPS, developed countries are encouraged to provide financial and technical cooperation in favour of developing countries and LDCs. The authors stress the importance of domestic absorptive and adaptation capacity, stating that the evolution of the process of technology transfer has taught us that attention must be paid to the processes of adaptation and domestic technology mastery.

The multiple factors that impact on technology transfer, including property rights, know-how, trade and technology policies, competition policies and investment flows, must be taken into consideration at the multilateral level. Successful transfer of technology from a developed country to a developing country requires both the home and host country policy measures to stimulate the transfer and local adaptation of technology. Therefore, efforts to facilitate the transfer of technology to developing countries at the multilateral level must integrate flexibility in the design of national technology policy to encourage the development of competitive productive sector, establish conditions conducive to facilitating transfer of technologies by international firms whose collaboration is essential to make it effective, devise a mechanism for effective implementation of existing technology-related provisions in WTO Agreements, and encourage opportunities for international cooperation in R&D aimed at enhancing trade from developing countries.

Sathaye & Holt (2005)

The authors of this paper, recognizing the important role governments undertake in providing funding for R&D programmes and government sponsorship of a range of R&D that may underpin private-sector investments in developing new technologies, examine several types of transfer technology pathway for government-funded R&D programmes in the United States, the Republic of Korea, Canada and the United Kingdom.

The authors select the Lawrence Berkeley National Laboratory, a laboratory managed by the University of California for the United States Department of Energy, to illustrate two ways in which industry can access technologies funded by the United States Government. The first method is to seek licences to technologies that were developed at the laboratory, and the second is to conduct research jointly with the laboratory in a public-private partnership.

With the enactment of the Technology Transfer Facilitation Law in 2000, all intellectual property management systems for public research organizations in the Republic of Korea are unified into one system. Subsequent amendments to the law require public research organizations to make use of the technology it patents or license it to another entity. In addition, public universities became legal entities in their own right, which enabled them to claim intellectual property rights to the invention and also to appropriate licence fees. The authors proceed to describe the implications of these laws on R&D and technology transfer, concluding that although the organizational structure differed from that of the United States, the Government of the Republic of Korea is using public funds to facilitate innovation among its private and public sectors.

In Canada, the rights to intellectual property developed by its federal laboratories, which are owned and operated by the Canadian Government, belong to the Government. In collaborative projects where other entities such as universities, private companies or other governments are involved, intellectual property rights are negotiated on a project-by-project basis. There is a range of mechanisms for Government-sponsored research, including departmental programmes to non-profit-making organizations established by the Government.

Public research organizations in the United Kingdom own the intellectual property rights to the intellectual property generated by publicly funded research. Most public sector research is conducted at Research Council Institutes. Because university control of transfer of technology is relatively new in the United Kingdom, the Treasury conducted a survey in 2003 to determine why academic quality of science and technology base is high and yet commercializing the knowledge generated at universities is relatively unsuccessful. Uncertainty about intellectual property ownership is one of the primary barriers to effective technology transfer and research collaboration.

*Wheeler & Mody (1992)*¹⁵¹

In international “location tournaments”, governments compete for foreign investment with tax and other short-run incentives. Such tournaments can be won if agglomeration economies are sufficiently powerful to overcome investors’ desire to spread investments as a hedge against risk. [The authors] focus on manufacturing investments by U.S. multinationals in the 1980s. [The authors’] econometric results suggest that agglomeration economies are indeed the dominant influence on investor calculations. Paradoxically, short-run incentives have limited apparent impact on location choice. [The authors] conclude that high-cost tournament play is unnecessary for countries with good infrastructure development, specialized input suppliers and an expanding domestic market.

AI.3 Technology transfer and climate change

Abbott (2009)

This paper examines issues surrounding the development and transfer of technologies for addressing the problem of climate change based on the experience of developing countries in addressing problems of innovation and access in the field of medicines.

It looks at alternative energy resources (AERs) and climate-change-mitigation technologies (MTs), at the forms of intellectual property rights used to promote and protect innovation, and at the ways these intellectual property rights may have different effects and implications for AERs/MTs as compared with pharmaceutical technologies. It is generally assumed that the originator pharmaceutical sector is highly dependent on strong patent protection, mainly because of the high cost involved in developing novel drug therapies and the low cost of reverse engineering these new drugs. Preliminary research suggests that most AERs/MTs industries may be less dependent on strong patent protection, or that patents are less likely to cause significant bottlenecks in the development and transfer of AERs/MTs. Although it is premature to come to a definitive conclusion because researchers are only now focusing on the evidence, there is some basis for anticipating that intellectual property rights will present fewer risks for developing countries in the context of climate change than for public health.

Developing country negotiators understood that the General Agreement on Tariffs and Trade (GATT) Uruguay Round negotiations on trade-related aspects of intellectual property rights would affect access to medicines. The resulting WTO TRIPS Agreement did, in fact, present serious risks to public health. These risks were addressed through negotiation of the Doha Declaration on the TRIPS Agreement and Public Health, the Article 31bis amendment and the WHO Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property. The “Doha Declaration process” broadly speaking has resulted in some positive movement.

151 Authors’ abstract.

There are a number of lessons that can be drawn from the public health-related negotiations, at the WTO and other forums, that may be useful to developing country negotiators addressing intellectual property rights and climate change. Some of these lessons are relatively straightforward: economic and political power substantially influences the outcome of negotiations; the involvement of NGOs and other stakeholders is essential; and it is important to shape public opinion through effective communication. Other lessons may be somewhat less evident.

Public health negotiations suggest that zero-sum bargaining is unlikely to be productive from the standpoint of developing countries, and that appeal to “equity” as the basis for demanding concessions is not enough.

The private sector in the developed countries controls most pharmaceutical technology and AERs/MTs. Governments in developed countries are unlikely to “order” that technology be transferred by the private sector. Developing countries therefore might usefully focus on establishing frameworks for mutually beneficial joint venture economic arrangements between developed and developing country enterprises that will stimulate innovation and concrete transfers of technology to address climate change.

To the extent possible, technology transfer commitments resulting from climate change negotiations should be specific and concrete. “Soft” commitments on transfer of technology typically do not bear fruit.

A number of developing countries and NGOs have proposed that a declaration comparable to the Doha Declaration on the TRIPS Agreement and public health be adopted with respect to intellectual property rights and climate change. Even if current multilateral intellectual property rights rules incorporate flexibilities and exceptions adequate to address most foreseeable obstacles to technology transfer, a declaration may be useful in the progressive development of international law so that it properly balances the rights of innovators and access by the public to the benefits arising from new technologies.

*Barton (2007b)*¹⁵²

As part of the world’s move to combat global warming, developing nations are likely to seek to reduce their emissions of greenhouse gases, and particularly of carbon dioxide (CO₂). They may have to obtain new technologies in order to do so. This paper explores whether there will be barriers, particularly intellectual property (IP) barriers, to access those technologies. To do so, it examines the industrial structure of three sectors, photo-voltaic (PV), bio-mass and wind energy. It concentrates on the more scientifically advanced developing countries such as Brazil, China, and India.

There are several modes of technology transfer. One is to provide products incorporating the technology, e.g. ozone-layer-safe coolant compounds or

152 Author’s executive summary.

photovoltaic panels for off-grid electrical supply. Another is to license the capability to produce such products, perhaps to an indigenous firm or perhaps to a joint venture. And a final one is to support developing national capability to research and produce the products independent of a licensor (or at least in a relatively equal position with the licensor).

Intellectual property (IP) protection generally plays a quite different role in the renewable energy industries than it does in the pharmaceutical sector, the source of many developing nation perspectives on IP. In general, in the pharmaceutical sector, an individual patent may have a very substantial impact because a specific drug may not have any substitutes. In such circumstances, the patent holder is in a very strong market position and may be able to charge a price well above production cost. In contrast, in the three renewable sectors considered here (and in many other industrial sectors), the basic approaches to solving the specific technological problems have long been off-patent. What are usually patented are specific improvements or features. Thus, there is competition between a number of patented products – and the normal result of competition is to bring prices down to a point at which royalties and the price increases available with a monopoly are reduced. This will be particularly the case for the products considered here, where there is competition not only between the firms in the specific sector but also between the sectors and alternate sources of fuel or electricity. In effect the benefit of the technologies is shared with the ultimate customers.

There are several different markets for renewable energy capabilities for developing nations. The most obvious one is the market for enabling the nation itself to reduce its CO₂ emissions (not currently required by international law but possibly required in the future). The second is the market for providing carbon offsets under the clean development mechanism (CDM) system of the Kyoto accord. And the third is the market for exporting renewable products, such as biofuel (or conceivably electricity), and equipment, such as wind turbines, in which the developing-world industry becomes integrated into the global industry as a supplier.

It is clear that some of the renewable energy technologies, particularly PV technologies, are not yet inexpensive enough to be used for general application. Because of this, economics firms have been hesitant to invest in substantial research on their own, save where there are significant subsidies, as in the current ethanol boom in the United States. Hence, much of the research in these areas is funded by the government. At least in the case of the United States, such subsidised research will almost certainly end up protected by patent rights. And when such research is licensed, certain favouritism is, by law, to be shown to US manufacturers.

In the PV sector, the developing nations are facing an oligopoly structure. But it is a somewhat loose oligopoly with lots of entrants. Thus, the benefits of the basic (silicon-slice) technology are likely to be available to developing nations even in the face of patents. But, even if they face patent issues in entering the field as producers, they are likely to be able to obtain licenses on reasonable

terms, because of the large number of firms in the sector. The possibility of entry is demonstrated by Tata-BP Solar, an Indian firm, based on a joint venture, and Suntech, a Chinese firm, based on a combination of its own technologies and of purchases of developed world firms.

At this time, it appears as if developing nations also have good access to the current generation of biofuel technology. The technologies are quite traditional, and there are many firms interested in bringing the technologies to developing nations. The harder question is with future biofuel technologies. It is likely that methods, or enzymes, or new micro-organisms for breaking down lignin will be patented. It is also likely that the holders of these patents will be willing to license their technology for use everywhere, and the licensing fees for these technologies are unlikely to be very high for very long. Thus, the key barriers are not likely to be associated with patents but rather associated with the tariffs and other restrictions related to the international sugar and ethanol markets.

The wind sector is competitive enough that developing nations will be able to build wind farms with equipment from the global market without enormous IP costs. However, it is much more difficult for developing nations to enter the global market for wind turbines; the existing industrial leaders are strong and hesitant to share their leading technology out of fear of creating new competitors. Moreover, a new firm that seeks to create its own technology must face the pricing problem of recovering its research and development costs. Initially, new firms are likely to have a smaller number of sales than their global competitors. In spite of these barriers, two developing nations, China and India, have succeeded in building important firms over the last 10 years.

With respect to access to the benefits of the technology, i.e. for the markets for reducing CO₂ emissions or for providing emission offsets to developed nations, there seem to be insignificant IP barriers to developing nation access. For the exporting markets, including PV cells, ethanol (or other renewable fuel) or wind engines, the picture is slightly more mixed. Certainly, for ethanol, the key concerns will be tariff and similar barriers, not IP barriers. For PV, the IP system is still unlikely to be a significant barrier. For wind energy, the issue is slightly less clear, but there will still probably be little IP problem. However, because of the global concentration in some of the industries, all countries should be alert to the risks of cartel behaviour.

There are other questions of importance to developing nations exploring these industries. Should developing nations strengthen their IP protection in order to make foreign investors more willing to transfer technology? The evidence suggests a possibility that stronger IP will help in the more scientifically-advanced developing nations, and offers little indication of risk associated with such strengthening. The answer may be different in poorer nations.

Are local trade barriers proving helpful or harmful in developing these industries? A confident analysis here requires much more detailed economic data, but the data here suggests that the argument against such tariffs is more

likely to win. The available evidence is agnostic on the benefit of nationally-funded research programmes oriented toward helping national firms gain the technology needed to compete globally. Clearly, there have been major benefits of such research in the developed world, but the success of the developing-world programmes is less clear.

For lenders and donors, a group of key issues arises in the “software” area – i.e. in designing the subsidies or legal requirements needed to make renewable energy economical. It is important to ensure that these subsidies, and particularly research subsidies, take developing-nation needs into account.

Of particular importance in this sector is public support of technologies. Developed nation governments are likely to seek to ensure that patents are gained on the results of the research and then seek to ensure that national firms are favoured in the licensing process. In essence, part of the political basis for the technology support is the hope of helping national manufacturers. It is possible to resolve this problem by asking developed nations to agree to forego their national favouritism in licensing publicly-funded inventions, at least with respect to technologies of global environmental importance. This is quite similar to the “humanitarian clauses” being considered in the medical and agricultural areas.

It would be far better for developed nations to go even further and commit themselves to devote a portion of their technology development to the special needs of developing nations. They could also ensure that firms in developing nations have an opportunity to participate in such efforts. In any such arrangement it is crucial that the various research programmes leave space for many different strategies to bloom. An arrangement could be negotiated in either of two ways. One would be as part of climate change negotiations, in which the commitment to make the technology more readily available would be included, perhaps as a quid-pro-quo for stronger environmental constraints upon developing nations. This would require a stronger commitment than has been typical of global environmental agreements. The other approach would be as part of a stand-alone technology arrangement, with the quid-pro-quo based on reciprocity among research funders. This is envisioned in the proposed Treaty on a Global Scientific and Technological Commons.

Almost certainly the most important need is to remove unnecessary barriers to trade in the area, such as those that restrict Brazilian ethanol. In a sector such as renewable energy, it is economically wise to maintain some subsidies for the sake of the global environment (assuming the world does not move toward a carbon-tax or its economic equivalent). Although the subsidies serve environmental goals, they are often designed in response to domestic concerns, particularly domestic agricultural concerns, and may end up discriminating against developing countries. It would be ideal to design the subsidies in ways that do not distort trade or discriminate against developing nation firms. This would be a very difficult negotiation, but an extremely valuable goal to seek.

*Barton (2007c)*¹⁵³

This paper explores methods for encouraging the diffusion of new environmental technologies to and within China and the European Union (EU), and considers the role of intellectual property (IP) in encouraging and discouraging that diffusion. It is organized according to the various forms of technology encouragement and of standardization. For each of the areas, the paper describes the intended role of the encouragement or standard, the ways that it might encourage innovation and diffusion of technology, the way IP affects that encouragement, and finally ways, such as licenses and pools, to deal with any IP problems. The paper uses a series of historical examples as case studies, and attempts to apply the findings to current issues. To the extent possible, the examples are taken from the contemporary climate change/energy context; in some cases earlier examples of other technologies have proven more illuminating. The paper explores diffusion and adoption of new climate change technologies in both the EU and China. Clearly, its findings must be viewed as provisional; the historical examples often raise controversies on their own, and application to future issues is necessarily tentative.

The paper is written for the benefit of legislators and regulators seeking to encourage environmental innovation in both the European Union and China. It is particularly concerned with helping to assist and implement the 2005 EU and China Partnership on Climate Change as well as China's National Climate Change Programme of June 2007. The EU-China initiative is focused on the development of zero-emissions coal technology, and on the deployment and dissemination of other key technologies designed to slow climate change. The UK is leading the first phase of the zero-emissions coal project. It is, of course, also hoped that the analysis of the paper will be beneficial to others as well, such as those involved in international lending in the environmental area, those structuring global markets and institutions, and those involved in other programs of international environmental research cooperation.

*Barton (2008)*¹⁵⁴

This paper discusses climate change technologies that affect the transport sector by examining various intellectual property (IP) and technology diffusion issues surrounding new fuel technologies, automobiles, and other forms of transport.

[Barton offers several] key recommendations to encourage technology diffusion and transfer in the biofuel and automotive parts of the transport sector, including (1) to impose strong, ideally globally uniform, technology-forcing standards and regulations to require the use of low-emissions automobiles, even in the developing world, (2) to support genuine global free trade in biofuels, again with global standards, (3) to subsidize research and development on new biofuels including those based on feedstocks

153 Author's introduction.

154 Author's summary, with minor adaptations.

from developing nations, (4) to use antitrust law to prevent the emergence of technological monopolies or unfair practices in either sector, (5) to encourage cooperation among governmental technology sponsors in ensuring development and diffusion in the advanced technology sectors, and (6), possibly to authorize a global compulsory licenses of fuel or automotive technologies, through a mechanism similar to that of the U.S. CAA compulsory license. The need for this last point is not clear and the approach should be used, if at all, only when the technology is of particular importance and proves otherwise unavailable.

[Barton states that] it is clear that there should be further thinking on these issues, and that a major portion of the thought should be on a sectoral basis. There is certainly a link between the fuel issues and the automobile industry; but most of the issues are significantly different as between the two sectors. Individual sector discussions can reasonably explore the design of the standards needed, and can consider the specific technology transfer and antitrust issues as well as the tasks of interrelating different national and regional research programs. There will be need to integrate industry into these discussions, but the history of regulatory tension with the automobile industry (at least in the United States) should be taken into account, as should be the obvious competition concerns.

This suggests a key role for groups like, say, the International Energy Agency, although industry groups such as the World Business Council for Sustainable Development might play a supporting role, especially in the biofuels area and in consideration of the trade barrier questions. Entities like the Asia-Pacific Partnership on Clean Development and Climate might also be helpful, but it should be noted that this entity does not include Europe (important to both vehicles and fuel) or Brazil (important to fuel). But the initial steps are almost certainly to examine and evaluate specific approaches to freeing trade in biofuels, to defining standards for those fuels, and to defining technology-forcing standards for automobiles. In the first instance these require technological expertise and careful economics, and may well be best achieved by think-tank type efforts, or by groups like the California Air Resources Board or the Intergovernmental Panel on Climate Change. Political and economic interests are strong; the initial need is to develop proposals that take such concerns into account but are not dominated by them; then the proposals can be negotiated in broader fora.

*Maskus (2010)*¹⁵⁵

Designing global policies to combat climate change through technological innovation and diffusion is a complex task. Parts of the negotiations at interim meetings of the UNFCCC leading up to the Copenhagen meeting in December have focused on reforms in the global intellectual property rights (IPR) system for this purpose. Positions seem to be hardening; the U.S. Congress has issued a directive that any new climate treaty cannot limit the scope or exercise of American IP rights while some developing countries continue

155 Author's summary.

to push for strong language on compulsory licensing or even exclusion of environmentally-sound technologies (EST) from patentability.

It is fair to say that neither of these positions is well informed with respect to the economics of intellectual property. Patent rights can support market power and refusals to license, though the evidence to date of this happening in ESTs is anecdotal. More generally, quantitative and qualitative analysis finds that patents have not yet mounted to a significant barrier to access in developing countries. Indeed, econometric evidence of general licensing behavior finds that multinational firms tend to increase the availability of new technologies when patent rights are strengthened, at least as regards transactions with partners in the middle-income and larger developing countries. In this context, caution should be exercised in advocating changes that would weaken the IP system, though countries should remain vigilant to the potential need for competition policy in cases of demonstrated abuse. For this purpose TRIPS is already sufficiently flexible and any access gains that might emerge from its reform are likely to be outweighed by the risks from reduced incentives to invest in the development and transfer of new technologies.

This report addresses the question of whether particular changes in patent rules, which would require legislative changes in key countries, would be effective in inducing innovation and diffusion of ESTs to address climate change. Following is a summary view.

Patent term extensions: (1) If extensions are provided to compensate for regulatory delays in approving patents, they are warranted. (2) *Ex post* term extensions to extend life at the end of an existing patent offer little innovative benefits and are a costly means of incentivizing future innovation; (3) the promise of short extensions to protect a useful modification or adaptation offers some useful *ex ante* incentives but may need to be tied to a commitment to transfer the technologies.

Patent standards and eligibility: (1) There is little argument to be made for excluding ESTs generally from patent eligibility; (2) It is likely impossible to reach an international agreement on harmonization of patent rules across countries because practices, standards and limitations are quite variable. It is not advisable to seek such harmonization if it focuses on the low-quality standards in some jurisdictions, such as the United States; (3) There is scope for expediting patent examinations in ESTs and to employ differentiated fee structures upon initial examination and renewal periods for purposes of incentivizing more investment and technology transfer; (4) For such a proposal to be effective, many patent offices would need to invest more resources in examination capacity. This cost could be reduced, and global patenting made more efficient through greater coordination among authorities with respect to relying on earlier examination results.

Wild-card patents: (1) There are some potential advantages in a transparent wild-card system available under well-defined and limited circumstances. It could provide useful incentives for investing in secondary (from the firms standpoint) technologies to meet specific needs in poor nations; (2) Calibration

of such patents and their scope and duration is bureaucratically difficult. Even more problematic is the fact that the beneficiaries likely would reside in the countries in which the secondary technologies are implemented while the costs would be borne by technology users and consumers in the countries where the original invention is patented.

Compulsory licenses: (1) Countries already have resort to compulsory licenses and government use licenses in their own legislation and under terms of the TRIPS Agreement; (2) Widespread use of compulsory licenses is likely to be deterrent to inward technology transfer in new ESTs; (3) Compulsory licensing has generally not been effective in forcing technology transfer to developing countries. It cannot mandate the transfer of know-how for example, which may be critical in learning how to use the technology. It is of no use in countries where patents are not registered; (4) Excessive focus on extensive global compulsory licensing regime in climate change negotiations would tend to distract attention from more important agenda items.

Competition policy: (1) Competition authorities should remain vigilant to potential licensing abuses in cases where an international firm has a dominant market position.; (2) It would be useful for authorities in developed economies to provide technical assistance in building competition policy competency in poor countries, including consultation on best practices in particular cases.

Patent landscaping: Investments in the development of publicly available patent landscapes would be valuable to patent examiners and potential licensors and licensees.

Voluntary patent pools and licensing: (1) There are good reasons to facilitate the development of voluntary patent pools for ESTs in which there are multiple patents on complementary components and inputs; (2) The willingness of firms to place IP into voluntary pools for licensing at agreed royalty rates depends on a variety of factors, including the reduction of transaction costs. There is an argument for public subsidization of royalties paid by institutions in developing countries in order to increase participation incentives.

Border tax adjustments and trade restrictions: (1) There is emerging interest among developed economies to offset the perceived competitiveness burdens imposed on their firms by emissions regulations through restricting imports from countries with weaker regulation.; (2) Such adjustments would be counter-productive for many reasons and would likely reduce incentives to transfer technologies. The net effect would be less reduction of GHGs [greenhouse gases] and sustained high-cost production of carbon-intensive goods; (3) Resort to such restrictions may also reduce the willingness of developing countries to participate in climate-change negotiations.

Fiscal supports: (1) As is common in any situation involving global public goods that externalities and market failures inherent in GHGs emissions and innovation may imply that too-little investments are being made. Public funds collected on a global basis but largely from the developed economies could

be used to incentivize R&D and technology transfers; (2) There are a number of means of financing such funds. Most sustainable and least distorting would be the use of carbon-tax revenues or returns from auctioning emission rights under a cap-and-trade system.

Maskus & Okediji (2009)¹⁵⁶

For developing and least-developed countries (DCs/LDCs), access to new technologies, including environmentally sound technologies (ESTs), is integrally linked to long-standing development priorities now compounded by anticipated significant shifts in resource endowments due to existing and expected effects of climate change. Disagreement between these countries and the leading technology producers over the relevance and role of intellectual property (IP) protection in addressing the complex challenges of inducing optimal levels of innovation, dissemination, and deployment of ESTs has emerged as a significant fault line in negotiations for a global climate change treaty. This paper addresses the prospects and limits of intellectual property rights (IPRs) as the classic legal mechanism of choice to incentivise innovation and dissemination of “green technologies” and related policy considerations. We focus on three principal questions: 1) Do the economics of climate change alter the gains traditionally associated with the role of IPRs in international technology transfer (ITT)? 2) In what ways does a globalised IP regime affect the policy options available to DCs and LDCs in climate-change mitigation and adaptation efforts? 3) Are there useful changes in the global IPRs system that would yield development gains with respect to the costs of access to ESTs or is this objective more efficiently approached through general fiscal supports?

We view compliance with climate change policies as a public good. Reducing the costs of access to ESTs is particularly important to induce compliance with greenhouse gas (GHG) emissions targets for countries that least value climate-change mitigation, including those that can least afford the preconditions for effective technology transfer. Generalized IPR reforms are less likely to affect measurable benefits for innovation in ESTs, while entailing high political cost to DCs and LDCs. Nevertheless, there is some value in targeted IPR reforms to support access to new technical knowledge necessary to assist mitigation and adaptation efforts, improve prospects for domestic innovation in DCs and LDCs, while also facilitating a more balanced global regime. We argue, however, that IPR reform to stimulate access to and diffusion of ESTs should be coordinated with other policy initiatives to supply a range of incentives to firms to develop, use, and transfer ESTs. Further, alternative incentive models must be considered to address particular problems such as small markets where IPRs are unlikely to induce innovation, the differentiated adaptation costs for ESTs in developing and least-developed economies, and the need for sustainable long-term investments in research and development (R&D) to ensure the development of technologies that can meet emerging threats to the environment.

156 Authors' abstract.

*OECD Environment Directorate & International Energy Agency (2004)*¹⁵⁷

This paper is the last in an AIXG [Annex I Expert Group] series that looks at international collaboration, particularly for energy technologies, in the context of climate change mitigation. The papers and case studies point out that there is little information to indicate that technology collaboration alone leads to emission reductions on the scale needed to limit growth in greenhouse gas emissions. For many energy production and consumption activities, technology change is a slow process. So to improve the environmental performance of energy technologies and accelerate their uptake, governments need a portfolio approach that includes technology and complementary economic and social policies that provide an adequate framework for essential private sector investment.

As the papers and case studies show, international collaboration can help in the quest by speeding momentum, sharing risks, exchanging knowledge and resources, sharing learning investments and harmonising standards. The incentives for collaboration include the need to “learn” from technical and operational solutions and failed approaches of others, to improve the reliability of tools and techniques, to develop standards across market areas and to foster technical expertise for regulatory and standard setting processes. Technology collaboration can also provide a framework for long-term co-operation on climate change and energy challenges in which Annex I and Non-Annex I Parties can participate.

The rationale for governments to engage in international collaboration is considered in the second part of this paper including the benefits and possible drawbacks of co-operative endeavours. Long-term and large scale transformative energy technologies and systems that entail significant costs and risks are well suited for broad collaboration, as illustrated in the examples of hydrogen-fuel cells and fusion power (see annex [not reproduced here]) and carbon capture and storage. As new technologies progress towards commercialisation, the scope for collaborative research, development, and demonstration becomes more limited. However, there is ample range for international co-operation in market deployment efforts, information dissemination and standards development.

Government collaboration related to energy technology and climate change is carried out in a variety of forms. The formal enabling mechanisms are surveyed here with examples of current initiatives and, where available, evidence of their results. All of the mechanisms considered here are based on common objectives, voluntary participation and a shared view that collaboration can provide benefits additional to an independent pursuit. Beyond those elements, the characteristics of collaborative mechanisms vary widely and range from pronouncements of “good intentions” to legal contracts with non-compliance provisions. Some approaches include centralised management, defined milestones, cost-sharing, monitoring and evaluation provisions; while others function on a dispersed basis and are largely for data and information exchange. There is not one model that accommodates the various modes in

157 Authors’ executive summary.

which governments pursue co-operative international energy technology development. What is important in designing effective joint activities is flexibility in the nature of the collaboration, the participants and the scope of the programme.

The form of an approach for near-market collaborative activities, for example an energy efficiency labelling scheme for refrigerators, is most likely to be distinct from co-operative research on nanotechnologies. Joint research consortia for large-scale energy technology innovation tend to have a structured framework, significant duration and a diversity of players. The design features that need to be considered for developing an effective collaboration dealing with new energy technologies and systems – from setting goals to sharing results – are summarised in the last section.

*Rockwell D et al. (2007)*¹⁵⁸

This report supports the commencement of Phase II of the UK–India collaborative study on low carbon technology transfer. It provides a review of some of the literature on intellectual property rights (IPRs) in relation to low carbon technology transfer to developing countries and attempts to organise this in such a way as to highlight significant findings and provide a contextual basis upon which to proceed with further desk based and field research on this theme. Based on the findings of the Phase I UK–India study, I also set out an important consideration which, based on current understanding of the IPR debate, is central to informing whether or not IPRs might be considered as representing a barrier to low carbon technology transfer. This relates to the extent to which we are primarily concerned with rapid deployment of low carbon technologies for greenhouse gas mitigation or with the long term technological development of developing countries.

*Tata Energy Research Institute, India (2003)*¹⁵⁹

[This] technical paper was prepared on the basis of the terms of reference recommended by the EGTT at its second meeting held on 20–21 October 2002 in New Delhi, India. Its focus is on the enabling environments created for the enhancement of technology transfer activities under Article 4.5 of the Convention and as defined in the aforementioned technology framework,¹ as well as analyses provided in the Intergovernmental Panel on Climate Change (IPCC) special report *Methodological and Technological Issues in Technology Transfer*, the UNFCCC [United Nations Framework Convention on Climate Change] Technical Paper “Barriers and opportunities related to the transfer of technology” (FCCC/TP/1998/1), the IPCC Third Assessment Report, and numerous case studies. It also uses information generated from the ongoing work of the World Trade Organization (WTO) and the United Nations Conference on Trade and Development (UNCTAD) relating to international technology transfer in general. Information from recent national

158 Authors’ scope of report.

159 Author’s scope of paper.

communications from Parties included in Annex I to the Convention (Annex I Parties) and non-Annex I Parties have also been used.

This paper has three goals: (a) To highlight the issues surrounding the enabling environments topic; (b) To analyse progress on the creation of domestic and international environments and to synthesize success and, to the extent possible, failure stories in both international transfer, and international support for diffusion of adaptation and mitigation technologies under the Convention; (c) To present some cross-cutting conclusions and suggest steps that may be taken for further analysis on the subject.

Chapter II describes the principal challenges surrounding this topic; reviews the various references to barriers and enabling environments in multilateral forums; and categorizes some important facets of domestic as well as international environments, as learned from an overview of current literature. Chapter III provides a sector-wise analysis, with more depth on the specific policies, institutions, regulatory frameworks, and financing mechanisms that have been deployed. Brief case studies are provided in Chapter IV with a summary of lessons learned. A summary of major conclusions is given in chapter V.

UNEP-UNCTAD (2007)¹⁶⁰

The critical role technology plays in reducing and controlling pollution, treating waste, managing natural resources, monitoring the state of the environment, and predicting environmental change has long been recognized by the international community. Agenda 21, adopted at the Earth Summit in 1992, highlighted the importance of technology in achieving environmental goals, and the need to make this technology accessible, by calling for favourable access to and transfer of environmentally sound technologies to developing countries. This call is reflected in a number of Multilateral Environmental Agreements (MEAs), which include provisions related to identifying appropriate technology as well as facilitating access to and encouraging the transfer of technology.

The international trade community also reflected the potential for technology to support environmental objectives in the WTO Doha Ministerial Declaration, which calls for negotiations on the reduction or elimination of tariff and non-tariff barriers on environmental goods and services as a means of enhancing the mutual supportiveness of trade and the environment. The negotiations, however, are currently at an impasse as negotiators struggle to agree on what constitutes “environmental goods.”

Created through the process of multilateral negotiation and consensus building, MEAs provide a baseline of widely agreed upon environmental objectives. MEA Secretariats and their Parties have been engaged for a number of years in identifying relevant technology and promoting technology transfer as a step towards achieving these environmental goals. This paper examines this experience with a view to enriching WTO negotiations on the liberalization of trade in environmental goods and services.

¹⁶⁰ Author’s executive summary.

The paper provides a summary of provisions related to technology found in five of the major MEAs, including the Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and their Disposal, the Convention on Biological Diversity, the Convention on International Trade in Endangered Species of Wild Fauna and Flora, the Montreal Protocol on Substances that Deplete the Ozone Layer, and the Stockholm Convention on Persistent Organic Pollutants. The paper also provides an overview of the activities undertaken by the respective MEA Secretariats and their Parties in identifying technology and facilitating its transfer.

This analysis led to the identification of a number of commonalities related to technology identification and transfer across MEAs that may be relevant to the WTO negotiations. For example, the paper finds that MEAs and their Parties generally adopt a dynamic mechanism for technology identification; designed to respond to the changing nature of environmental challenges, scientific discoveries, technological development, as well as changing economic, social and cultural circumstances. The paper also notes that MEA Secretariats and Parties often adopt a “package” approach to technology and technology transfer, where the transfer of the technology is complemented by capacity building, technical assistance, training of personnel, sharing of know-how, and exchange of information.

These conclusions are presented as take-away lessons from the MEA experience, and serve as a foundation from which further research can be conducted. The paper suggests a number of areas where further analysis may be warranted, including: (1) identification of specific technologies or groups of technologies that support MEA implementation; (2) analysis of the impact of tariffs and non-tariff barriers on the flow of MEA-related technologies and to what extent further liberalization would increase this flow; (3) further examination of the role of technology in MEA implementation at the national level; and (4) examination of the current challenges to increased MEA technology transfer.

*Watson et al. (2000)*¹⁶¹

Coal plays a central role in the Chinese economy. It has accounted for 75% of annual energy use throughout the 1990s. Whilst it is cheap and plentiful, the environmental and health effects of coal use are becoming more and more severe as the economy continues to grow at a rapid rate. There is an increasing need to find ways of limiting pollution of the air and water through the use of cleaner technologies and more efficient processes. Clean coal technologies have the potential to reduce emissions of the gases which cause urban smog and acid rain, they can limit the effects of coal extraction on rivers and lakes, and they can make a contribution to global efforts to tackle climate change.

This preliminary report to the Trade and Environment Working Group summarises the work completed so far on the international inputs to the study of Clean Coal Technology Transfer to China. The main focus of our work to date

161 Authors' introduction.

has been the extent to which real knowledge and skills have been transferred from international companies to their Chinese counterparts.

We have focused on the apparent tension between the wish of international firms to forge closer alliances with Chinese equipment suppliers, and their need to maintain their technological and commercial position in the world market. Whilst clean coal technology transfer is often discussed in terms of the export of hardware (e.g. power station boilers or flue gas desulphurisation units), previous studies have shown that such exports are not sufficient on their own for successful technology transfer to occur.

Without access to training, technological knowledge and new management skills (e.g. through joint ventures or licensing arrangements with foreign firms), Chinese companies will find it much more difficult to develop their own clean coal capabilities. The development of such capabilities is essential so that Chinese firms are able to maintain new and existing hardware, and to make incremental improvements to it.

At the outset, it is important to recognise that this work is of a preliminary nature. It is based on a review of relevant research work which is being conducted elsewhere, and a small number of interviews with companies, Government representatives and consultants in the UK and USA. Since the amount of work carried out so far is small, it is not possible to provide any definite policy recommendations to the China Council at this stage. Further research will be required in order to establish how Chinese policies may be modified to maximize technology transfer in the future.

The report is composed of five different sections. The first three sections provide a context for the study – the first summarises position of coal in the Chinese energy system, the second explores China's capability in cleaner coal technologies, and the third gives a brief overview of Chinese policies for trade, investment and environmental protection. The fourth section is more specific. Through a number of short case studies, it looks at the experience of international companies which are involved in transferring cleaner coal technologies to China. This experience is then used as the basis of a fifth section which contains some tentative conclusions and makes the case for further work by the international team.

Annex II: Medicines research and development and transfer of technology programmes not specifically linked to production¹⁶²

AII.1 Research and development and technical support programmes and initiatives

A substantial portion of technology transfer-related programmes focus on R&D relating to treatment or prevention of HIV/AIDS, malaria and TB, and there is a considerable focus on tropical diseases (including neglected tropical diseases, such as sleeping sickness and Chagas disease). A number of the programmes contributing to technology transfer for R&D are focused on upgrading facilities, improving clinical practices, and education and training of researchers for conducting clinical trials.

Aeras Global TB Vaccine Foundation

Aeras Global TB Vaccine Foundation (Aeras) is a “non-profit product development partnership (PDP) dedicated to the development of effective TB vaccine regimens that will prevent tuberculosis in all age groups and will be affordable, available and adopted worldwide”.¹⁶³ Aeras promotes and encourages capacity building and transfer of knowledge to build sustainable R&D for TB drug development in developing countries. Many of Aeras’s programmes are performed jointly with regional partners to bolster local capacity in administering clinical trials on vaccine candidates. Aeras has partnered with local research organizations to increase local capacity in health systems by funding and building staff capacity and facilities in countries where TB is highly prevalent. In partnership with the Cambodian Health Committee, Aeras will contribute staff to plan and increase capacity of a clinical field trial site in the Svey Rieng province of Cambodia.¹⁶⁴

In partnership with the European and Developing Countries Clinical Trials Partnership (EDCTP), Aeras started a research initiative in 2008 to ensure there are four distinct clinical trial sites for phase II and phase III clinical trials in sub-Saharan Africa. The initiative works with sites in Kenya, Mozambique, South Africa and Uganda to increase each site’s infrastructural capacity for conducting large-scale clinical trials of new TB vaccines.¹⁶⁵ In Kenya and Uganda, Aeras provides training to the field site staff and aids the renovation

¹⁶² The author acknowledges valuable research assistance by Rene Casey Larkin and Maegan McCann in the preparation of this annex.

¹⁶³ Aeras. *Annual Report 2008*. Rockville, MD Aeras Global TB Vaccine, 2008 Foundation(<http://www.aeras.org/newscenter/headlines.php>).

¹⁶⁴ Ibid.

¹⁶⁵ Ibid.

of diagnostic laboratory facilities in Kenya, with possible construction of a TB diagnostics laboratory in Uganda.¹⁶⁶

African Comprehensive HIV/AIDS Partnerships

The African Comprehensive HIV/AIDS Partnerships (ACHAP) is a country-led, public–private development partnership between the Government of Botswana, the Bill & Melinda Gates Foundation, and the Merck Company Foundation/Merck & Co., Inc., dedicated to supporting and enhancing Botswana’s national response to HIV/AIDS.¹⁶⁷ The programme’s main focus is building the capacity of the health infrastructure within Botswana. One aspect of the programme has led to an increase in diagnostic capacity for HIV in Botswana. ACHAP has procured and donated equipment to update four laboratory facilities with CD4 cell count and viral load equipment and HIV rapid diagnosis tests to assist the efforts of local health clinics in providing efficient diagnostics.¹⁶⁸

Centro Internacional de Entrenamiento e Investigaciones Medicas

Centro Internacional de Entrenamiento e Investigaciones Medicas (CIDEIM), based in Colombia, “is a non-profit, non-governmental organization dedicated to biomedical research in infectious diseases and the development of research capability”.¹⁶⁹ CIDEIM focuses its research on malaria, TB, leishmaniasis, vector control and bacterial resistance.¹⁷⁰ CIDEIM also conducts a training programme for researchers from around the world who are pursuing their PhD, Master’s or undergraduate degrees. Through this programme, the organization “seeks to strengthen the country’s capability to train researchers by using the scientific and technological infrastructure available in CIDEIM”.¹⁷¹

European and Developing Countries Clinical Trials Partnership

EDCTP “aims to accelerate the development of new or improved drugs, vaccines and microbicides against HIV/AIDS, malaria and tuberculosis, with a focus on phase II and III clinical trials in sub-Saharan Africa”.¹⁷² The Partnership does this by offering an extensive grant programme, supporting regional initiatives for

166 Ibid.

167 Merck. *African comprehensive HIV/AIDS partnerships*. Merck, (<http://www.merck.com/corporate-responsibility/access/access-hiv-aids/access-hiv-aids-ACHAP-botswana/approach.html>).

168 Merck. *Health care capacity-building in the developing world*. Merck (<http://www.merck.com/corporate-responsibility/access/health-care-capacity/initiatives.html>).

169 CIDEIM. *Welcome to CIDEIM*. Cali, Centro Internacional de Entrenamiento e Investigaciones Medicas, 2011 (http://www.cideim.org.co/site/index.php?option=com_content&task=view&id=1&Itemid=1).

170 CIDEIM. *Research: Subject areas*. Cali, Centro Internacional de Entrenamiento e Investigaciones Medicas, 2011 (http://www.cideim.org.co/site/index.php?option=com_content&task=view&id=10&Itemid=16).

171 CIDEIM. *Training*. Cali, Centro Internacional de Entrenamiento e Investigaciones Medicas, 2011 (http://www.cideim.org.co/site/index.php?option=com_content&task=view&id=14&Itemid=30).

172 EDCTP. *About EDCTP*. The Hague, European and Developing Countries Clinical Trials Partnership (http://www.edctp.org/About_EDCTP.2.0.html).

improving the conditions of facilities, and teaching and implementing good clinical practices in conducting research.

The grant programme has four areas of focus: integrated projects for clinical trials, senior fellowships, ethics review and joint programme activities.¹⁷³ EDCTP's integrated project for clinical trials places a large emphasis on enabling developing countries to take the lead in conducting clinical trials, thereby building sustainable capacity through the partnerships.¹⁷⁴ In 2008, EDCTP issued eight grants for integrated projects, each for the purpose of increasing clinical trial capacity for HIV/AIDS, malaria and TB. The African countries receiving the 2008 grants in partnership with European Member States were Gambia, Uganda, Zambia, the United Republic of Tanzania, South Africa, Mozambique, Burkina Faso, Kenya, Gabon, Malawi and Mali.¹⁷⁵

European Malaria Vaccine Initiative

This is an initiative by the European Community to stimulate R&D of a malaria vaccine. The initiative takes part in the EDCTP clinical trials, partnering with African countries to conduct trials for candidate malaria vaccines.¹⁷⁶

Foundation for Innovative New Diagnostics

The Foundation for Innovative New Diagnostics (FIND)¹⁷⁷ is a product development partnership founded in 2003 with the objective of creating new diagnostic tests for the detection of diseases prevalent in developing countries. FIND is seeking to take advantage of the latest developments in technology to develop products that are suitable for use in less affluent settings, are low cost, work rapidly and produce reliable results. FIND has a full-time staff of about 40 professionals, and works with an extensive group of noncommercial, commercial and government partners to develop and implement its programmes. Initial and continuing funding for FIND has come from the Bill & Melinda Gates Foundation. Funding has also come more recently from the Netherlands, the United Kingdom Department for International Development (DFID), Irish Aid, the EU and private sources such as UBS. In 2008, FIND, together with the Global Laboratory Initiative and the Global Drug Facility from the Stop TB Department of WHO, spent over US\$ 25 million on R&D activities. FIND has been awarded contracts from UNITAID totalling US\$ 86 million to scale up and provide diagnostic tests in developing countries.

173 EDCTP. *Annual Report 2008*. The Hague, European and Developing Countries Clinical Trial Partnership, 2008 (http://www.edctp.org/fileadmin/documents/ANNUAL_REPORT_2008_ENGLISH_FINAL_pdf.PDF).

174 Ibid.

175 Ibid.

176 European Malaria Vaccine Initiative. *Annual report 2008*. Heidelberg, European Malaria Vaccine Initiative, 2008 (http://www.euvaccine.eu/sites/default/files/uploads/docs/annual_reports/EMVI_Annual_Report_2008.pdf).

177 FIND. *Annual report 2008*. Geneva, Foundation for Innovative New Diagnostics, 2008 (http://www.finddiagnostics.org/export/sites/default/resource-centre/annual_reports/2008_Annual_Report.pdf).

FIND initially focused on diagnostic tests for TB, but it expanded its scope of activities to human African trypanosomiasis and malaria, and then other neglected diseases such as leishmaniasis, Buruli and Chagas disease. The emergence of multidrug-resistant TB and extremely drug-resistant TB has stimulated interest and demand for effective rapid diagnostic testing.

Since its inception, FIND has developed four diagnostic technologies that have been approved by WHO, including a molecular diagnostic test for TB.

FIND has worked closely with private-sector partners, including Becton, Dickinson (United States), Eiken Chemical (Japan), Hain Lifescience (Germany), TAUNS Laboratories (Japan), Zeiss (Germany) and Cephiad (United States). In its collaborations, FIND has worked successfully with a model that ensures the availability of low-cost products for patients in developing country, while permitting its private-sector partners to market products in developed countries.

FIND is strongly committed to building up and taking advantage of capacity in developing countries. It has established offices in India and Uganda. It has signed memorandums of understanding and is working closely with a number of governments in Africa (including Ethiopia, Lesotho, South Africa, the United Republic of Tanzania and Uganda) to improve the capacity of local laboratories to perform diagnostic testing of various types. FIND is working closely with academic institutions throughout Africa on R&D projects.

Global Alliance for TB Drug Development

Global Alliance for TB Drug Development (TB Alliance) is a product development partnership that advocates and works for discovery and production of new TB drugs. A recent challenge for TB Alliance was coordinating large-scale phase III clinical trials around the world for the TB drug ReMoxTB. TB Alliance instigated an assessment of clinical trial sites to ensure all sites used in the study met modern regulatory standards required for clinical trials and participating sites had the capacity to take part in multiple, concurrent trials. This assessment led to a continued effort to improve the capacity and infrastructure of the local communities where the clinical trial sites are located.¹⁷⁸

Global Health Committee

Global Health Committee (GHC) is part of the Cambodian Health Committee, a local non-profit-making organization that created GHC in an effort to share information learned in Cambodia about treating AIDS and TB with other nations, specifically those in Africa.¹⁷⁹ GHC's programmes are aimed at increasing Cambodian capacity for clinical trials. GHC's Comprehensive International Program for Research on AIDS (CIPRA) received a grant from the United States' National Institutes of Health (NIH) to improve CIPRA's

178 TB Alliance. *Annual report 2009*. New York, Global Alliance for TB Drug Development, 2009 (<http://new.tballiance.org/downloads/publications/TBA%20Annual%202009.pdf>).

179 Cambodian Health Committee. *Our mission*. Phnom Penh, Cambodian Health Committee Global Health Committee, 2011 (http://www.cambodianhealthcommittee.org/mission_mission.html).

facilities for conducting clinical trials.¹⁸⁰ Cambodian Early vs. Late Introduction of Antiretrovirals (CAMELIA) is a programme within CIPRA that studies the effective timing for treatment for people with AIDS who are also being treated for TB.¹⁸¹

Global HIV Vaccine Enterprise

This “is an alliance of independent organizations around the world dedicated to accelerating the development of a preventive HIV vaccine.”¹⁸² The organization seeks to collaborate the activities of stakeholders and researchers around the world, creating a strategic plan to encourage a united effort in R&D of a preventive HIV vaccine.¹⁸³

Harvard University Office of Technology Development

Harvard University Office of Technology Development issued a press release on 9 November 2009 in collaboration with Yale University, Brown University, Boston University, the University of Pennsylvania, Oregon Health & Science University and the Association of University Technology Managers (AUTM) adopting principles to increase technology transfer to improve access to medicines in developing countries.¹⁸⁴ The agreement proposed strategies to ensure that intellectual property is not a barrier to improving access to affordable medicines. The universities’ commitments include developing effective licensing strategies, exerting control over patent rights to make products available to the developing world, and supporting development of new technologies that will address the diseases that most affect the developing world.¹⁸⁵

Harvard has partnerships with organizations working in developing countries to promote R&D of effective and affordable treatments for diseases common in developing countries. Harvard has partnered with the Cambodian Health Committee in efforts to study effective treatments for HIV/AIDS and TB.¹⁸⁶ Harvard also participates in the Lilly MDR-TB Partnership in efforts to discover and develop effective treatments for multidrug-resistant TB.¹⁸⁷

180 Cambodian Health Committee. *Research*. Phnom Penh, Cambodian Health Committee Global Health Committee, 2011 (<http://www.cambodianhealthcommittee.org/research.html>).

181 Ibid.

182 Global HIV Vaccine Enterprise. *About the enterprise*. New York, Global HIV Vaccine Enterprise, 2010 (<http://www.hivvaccineenterprise.org/content/about-enterprise-secretariat>).

183 Global HIV Vaccine Enterprise. *Scientific strategic plan*. New York, Global HIV Vaccine Enterprise, 2010 (<http://www.hivvaccineenterprise.org/scientific-strategic-plan>).

184 Harvard University Office of Technology Development. *Six universities adopt new technology transfer principles designed to speed access to affordable medicines in the developing world*. Cambridge, MA, Harvard University Office of Technology Development, 9 November 2009 (<http://www.techtransfer.harvard.edu/mediacenter/pr/release/20091109-01.php>).

185 Ibid.

186 Cambodian Health Committee. *Research*. Phnom Penh, Cambodian Health Committee Global Health Committee (<http://www.cambodianhealthcommittee.org/research.html>).

187 Lilly MDR-TB Partnership. *Activities*. Geneva, Lilly MDR-TB Partnership, 2010 (<http://www.lillymdr-tb.com/activities.html>).

Institute for OneWorld Health

This is a non-profit-making pharmaceutical company focusing solely on discovery and R&D of drugs needed to treat diseases common in the developing world, including malaria, visceral leishmaniasis, diarrhoeal disease and soil-transmitted helminthiasis.¹⁸⁸ The Institute partners with organizations, hospitals, institutions and governments around the world, including in India, Bangladesh, the United States, Switzerland and the United Kingdom.¹⁸⁹

The Institute conducted clinical trials in 2004 on the drug paromomycin for the treatment of visceral leishmaniasis in Bihar, India. The trials were conducted in partnership with the Kala-azar Medical Research Centre and the Kal-azar Research Centre in Muzzafarpur and the Kal-azar Research Centre and the Rajendra Memorial Research Institute in Patna. Gland Pharma Ltd., in Hyderabad, India, the Institute for OneWorld Health and the IDA Foundation will be the manufacturing facilities for paromomycin.¹⁹⁰

The Institute for OneWorld Health received a grant from the Bill & Melinda Gates Foundation for improvement of diarrhoeal treatments by identifying gaps in current diarrhoeal treatments and developing treatments to fill those gaps.

The Institute for OneWorld Health has also partnered with Roche, which allowed the Institute to survey Roche's molecular library for potential candidates for treating diarrhoeal diseases. A similar partnership was formed with Novartis for development of potential drug candidates for preclinical testing.¹⁹¹

In efforts to combat malaria, by creating a secondary source of artemisinin, the Institute for OneWorld Health has started the Artemisinin Project and is collaborating with the California Institute of Quantitative Biomedical Research (QB3) at the University of California, Berkeley, Amyris and sanofi-aventis.¹⁹²

International AIDS Vaccine Initiative

The International AIDS Vaccine Initiative (IAVI) is a public-private product development partnership formed to advocate for and develop an affordable AIDS vaccine. IAVI works from the discovery phase through the clinical trials of candidate HIV/AIDS vaccines. The organization works closely with local governments in developing countries to ensure effective and transparent

188 Institute for OneWorld Health. *Project pipeline*. San Francisco, CA, Institute for OneWorld Health, 2011 (<http://www.oneworldhealth.org/Pipeline>).

189 Institute for OneWorld Health. *Partnerships*. San Francisco, CA, Institute for OneWorld Health, 2011 (<http://www.oneworldhealth.org/partnerships>).

190 Institute for OneWorld Health. *Visceral leishmaniasis: Drug program*. San Francisco, CA, Institute for OneWorld Health, 2011 (http://www.oneworldhealth.org/drug_program).

191 Institute for OneWorld Health. *Diarrheal disease*. San Francisco, CA, Institute for OneWorld Health, 2011 (http://www.oneworldhealth.org/diarrheal_disease).

192 Institute for OneWorld Health. San Francisco, CA, Institute for OneWorld Health, 2011 *Malaria*. (<http://www.oneworldhealth.org/malaria>).

clinical trials. One of its main goals is to establish a sustainable clinical trial programme in countries most heavily affected by HIV.¹⁹³

International Trachoma Institute

The International Trachoma Institute (ITI) was initially established as a private–public partnership with the goal of eradicating trachoma, but it has recently moved to work against neglected tropical diseases that are prevalent in developing countries. In 2006, ITI received a grant from the Bill & Melinda Gates Foundation to study the “effectiveness of integrating treatment of trachoma with another neglected tropical disease, lymphatic filariasis”. ITI began conducting clinical studies in Mali and most recently in Ethiopia.¹⁹⁴

International Vaccine Institute

The International Vaccine Institute (IVI) was created by UNDP and is based in the Republic of Korea.¹⁹⁵ IVI conducts R&D for vaccine candidates suitable for developing countries’ needs and practical restrictions. IVI’s goal is to make effective vaccines for developing countries that can also be developed and produced in developing countries so as to decrease the costs of the end-product, making the vaccines more accessible to people who need them most. The Cholera Vaccine Program, largely funded by the Bill & Melinda Gates Foundation, works to develop and field-test low-cost cholera vaccines. In collaboration with the Vaccine Product and Technology Transfer Department at IVI, the Cholera Vaccine Program “assist[s] with the transfer of the production technology for this vaccine to high-quality producers in developing countries”.¹⁹⁶ IVI’s Division of Laboratory Services has developed three new or improved vaccines against typhoid fever and cholera and is transferring technology for the production of the vaccines to vaccine producers in developing countries.¹⁹⁷

Kenya Medical Research Institute

Kenya Medical Research Institute (KEMRI) is a public research institute responsible for carrying out health research in Kenya. KEMRI partners with global and regional institutions and foreign governments to conduct local clinical studies. Currently it is partnering with the United States Centers for Disease Control and Prevention to conduct TB vaccine clinical trials in Kenya.¹⁹⁸

193 IAVI. *2008 annual progress report*. New York, International Aids Vaccine Initiative, 2009 (<http://www.iavi.org/publications-resources/pages/publicationdetail.aspx?pubid=2b9e821b-6800-43ef-8ccb-8ab57e2e8123>).

194 ITI. *10th anniversary report 1998–2008*. Decatur, GA, International Trachoma Institute, 2008 (<http://www.trachoma.org/special-iti-tenth-anniversary-report>).

195 IVI. *Annual report 2008*. Seoul, International Vaccine Institute, 2008 (http://www.ivi.int/publication/annual_report.html).

196 Ibid.

197 Ibid.

198 KEMRI. *Highlights*. Nairobi, Kenya Medical Research Institute, 2011 (<http://www.kemri.org/#>).

KNCV Tuberculosis Foundation

This is a Dutch organization that works to control TB. The Foundation conducts research on effective control strategies for TB and provides assistance to governments and health workers in 42 countries around the world, helping provide effective TB treatment and control.¹⁹⁹ The Foundation works to improve the capacity of its partners in developing countries by improving the capabilities of the laboratories for diagnosis, treatment and research.²⁰⁰

Makerere University Walter Reed Project

Makerere University Walter Reed Project (MUWRP) is a partnership between the Henry M. Jackson Foundation of the United States and Makerere University in Uganda. "The primary mission of MUWRP is HIV vaccine development and building of vaccine testing capability in Uganda."²⁰¹ The partnership includes development of infrastructure, acquisition of the necessary equipment, and building clinical trial capacity for the university to be able to conduct phase III clinical trials.²⁰²

Medical Research Council

The Medical Research Council (MRC) is a biomedical research organization funded by the United Kingdom Government. MRC participates in EDCTP and conducts many clinical trials in sub-Saharan Africa. MRC has committed to working with developing countries by empowering governments and research institutions in building capacity for sustainable health research.²⁰³

Medicines for Malaria Venture

Medicines for Malaria Venture (MMV) is a non-profit-making public-private partnership "dedicated to reducing the burden of malaria in disease-endemic countries by discovering, developing and facilitating delivery of new, high-quality, affordable antimalarial drugs through public-private partnerships."²⁰⁴ MMV partners with a broad range of stakeholders, from pharmaceutical companies to local governments in developing countries, to encourage the discovery, development and testing of antimalarial drugs.

199 KNCV Tuberculosis Foundation. *Annual report 2008*. The Hague, KNCV Tuberculosis Foundation, 2008 (<http://www.kncvtbc.nl/Site/Components/SitePageCP/ShowPage.aspx?ItemID=c2739d3a-8f52-482b-8d01-b55e09edf2ed&SelectedMenuItemID=2588b0df-6a8f-4c37-9a96-4e6811c834c4>).

200 Ibid.

201 Makerere University Walter Reed Project. *Mission*. Nakasero, Makerere University Walter Reed Project (http://www.muwrp.org/?page_id=273).

202 Makerere University Walter Reed Project. *About us*. Nakasero, Makerere University Walter Reed Project (<http://www.muwrp.org/about.php>).

203 MRC. *Strategic aim three: Global health*. London, Medical Research Council, 2009 (<http://www.mrc.ac.uk/About/Strategy/StrategicPlan2009-2014/StrategicAim3/Globalhealth/index.htm>).

204 MMV. *MMV at a glance 2009-2010*. Geneva, Medicines for Malaria Venture, 2010 (http://www.mmv.org/rubrique.php3?id_rubrique=20).

Medicine in Need

Medicine in Need (MEND) is a non-profit-making research organization with offices and facilities in Cambridge, MA, Pretoria and Paris. MEND's research and collaborations focus on HIV/AIDS, malaria and TB. The organization divides its work between two departments, MEND Biotechnology Department and MEND Innovation and Translation Alliance Management (MITAM).²⁰⁵ The Biotechnology Department conducts research for innovative approaches to diagnose and treat HIV/AIDS, malaria and TB.²⁰⁶ MITAM's "primary mission is to provide a nexus where the most promising advanced technologies can be vetted against the most daunting issues confronting vaccine and drug candidates for diseases of poverty, and yield solutions to allow real products to get to market."²⁰⁷ MITAM seeks to maintain a large network of scientists, engineers and other interested stakeholders to address these issues.²⁰⁸

National Institutes of Health Office of Technology Transfer

The NIH Office of Technology Transfer (OTT) "is working to address global health challenges by facilitating the transfer of technologies to people around the world."²⁰⁹ NIH OTT moves technology from the public to the private sector for the purposes of improving public health. NIH OTT has licensed over 300 of its technologies internationally.²¹⁰ To improve the capacity for management of technology transfer, NIH OTT has created the International Technology Transfer Training Program to train professionals in intellectual property management and other issues related to technology transfer. This training programme currently operates with institutions in China, India, Brazil, South Africa and Hungary, but with potential to expand to other countries.²¹¹

Netherlands Development Cooperation

This is the Dutch arm of the Ministry of Foreign Affairs for international foreign aid. The agency contributes a substantial amount of money to national governments and organizations for the purpose of improving infrastructure and meeting urgent needs of developing countries.²¹² A majority of the agency's financial contributions are made through grant programmes for

205 MEND. *About us*. Cambridge, MA, Medicine in Need, 2008 (<http://www.medicineinneed.org/who-we-are.html>).

206 MEND. *MEND biotechnology department*. Cambridge, MA, Medicine in Need, 2008 (<http://www.medicineinneed.org/mend-biotech-development.html>).

207 MEND. *MEND Innovation & Translation Alliance Management (MITAM)*. Cambridge, MA, Medicine in Need, 2008 (<http://www.medicineinneed.org/mend-innovation-translation.html>).

208 Ibid.

209 NIH OTT. *International technology transfer*. Rockville, MD, National Institutes of Health Office of Technology Transfer (http://ott.od.nih.gov/about_nih/intl_tt.aspx).

210 Ibid.

211 Ibid.

212 Netherlands Development Cooperation. *Development cooperation*. The Hague, Netherlands Development Cooperation, 2007 (http://www.minbuza.nl/en/Key_Topics/Development_Cooperation).

international NGOs and product development partnerships focused on R&D for medicines treating AIDS, TB and malaria.²¹³

Netherlands Vaccine Institute

Netherlands Vaccine Institute (NVI) is a Dutch Government-based organization that has been in operation since 2003, when the Dutch Government's vaccine production unit and vaccine unit merged. The Institute has both research and production capabilities, providing needed vaccines for the Dutch population.²¹⁴ NVI also collaborates with other nations and international organizations such as WHO to share expertise in vaccine development. For example, "NVI functions as a training centre within the WHO Global Training Network on Vaccine Quality and the WHO Collaborating Centre for Smallpox Vaccine".²¹⁵ Additionally, in 2008 NVI made a 5-year agreement with WHO to develop an "in house egg-based pilot seasonal influenza vaccine production process suitable for up scaling, training and technology transfer to manufacture in lower and middle income countries".²¹⁶ NVI also partners with other companies and government health ministries to provide technology suitable for producing vaccines in developing countries. One example is the Serum Institute in India, which has developed a vaccine against *Haemophilus influenzae* type b (Hib) using a pilot process and technology know-how developed and licensed by NIV. NIV has similar partnerships with Bio Farma in Indonesia and Biological E. Limited in India.²¹⁷

Norwegian Agency for Development Cooperation

The Norwegian Agency for Development Cooperation (NORAD) is Norway's international aid agency. The agency partners with national governments and provides financial contributions to international organizations for the improvement of health-care systems in developing countries. Norway is a substantial contributor to the Global Alliance for Vaccines and Immunisation (GAVI), through direct support, the International Finance Facility for Immunisation and advance market commitment.²¹⁸

PATH

This international non-profit-making organization is devoted to developing health technology designed for improving access to medicines in the developing world. A few of PATH's notable projects facilitate the transfer of technology for development of vaccines to developing countries. One of PATH's projects is to design affordable vaccines that can be manufactured in

213 Netherlands Development Cooperation. *Grant programs*. The Hague, Netherlands Development Cooperation, 2007 (http://www.minbuza.nl/en/Key_Topics/Development_Cooperation/Grant_Programmes).

214 NVI. *Home*. Bilthoven, Netherlands Vaccine Institute, 2011 (<http://www.nvi-vaccin.nl>).

215 Ibid.

216 NVI. Bilthoven, Netherlands Vaccine Institute (http://flusecure.eu/Technology_Transfer_Influenza_Vaccines). WORKING URL: http://flusecure.eu/Technology_Transfer_of_Influenza_Vaccines

217 NVI. *Home*. Bilthoven, Netherlands Vaccine Institute, 2011 (<http://www.nvi-vaccin.nl>).

218 GAVI. *Donor contributions and commitments*. Geneva, Global Alliance for Vaccines and Immunisation, 2011 (<http://www.gavialliance.org/support/donors/index.php>).

developing countries.²¹⁹ PATH has created a freeze-stabilization technology to protect vaccines from being harmed by cooling agents in transit. The technology was placed in the public domain, accessible for use in the production of vaccines.²²⁰ A third PATH project, in partnership with Chengdu Institute of Biological Products, increased China's vaccine manufacturing capacity by building a new manufacturing facility for production of a vaccine to treat Japanese encephalitis.²²¹

Royal Tropical Institute

The Royal Tropical Institute (KIT) is a non-profit-making organization based in Amsterdam. It "operates internationally through development projects, scientific research and training, and also provides consultancy and information services".²²² One of KIT's research projects is to develop rapid diagnostic tests for malaria; the research is being conducted in Burkina Faso, Nigeria, the United Republic of Tanzania, Belgium and the United Kingdom.²²³

South African Tuberculosis Vaccine Initiative

The South African Tuberculosis Vaccine Initiative (SATVI) is a research group located in the Institute of Infectious Disease and Molecular Medicine of the University of Cape Town. The group has conducted several clinical studies and phase I and II trials of novel TB vaccines.²²⁴ To enhance capacity for clinical studies, SATVI also invests in training and education of individuals by offering PhD and Master's programmes, capacity development through individual professional development, and a number of other education and training programmes.²²⁵

South East Asia Infectious Disease Clinical Research Network

The South East Asia Infectious Disease Clinical Research Network (SEAIRC�) is a partnership of hospitals and research institutions that focuses on clinical research studies of infectious diseases that are important in the region. SEAIRC�'s goals are to increase collaboration and enhance capacity of institutions to meet international standards for clinical research.²²⁶ In efforts to increase capacity of clinical trial sites within the region, SEAIRC� participated

219 PATH. *Where solutions start: Annual report 2008*. Seattle, WA, PATH, 2009 (<http://www.path.org/annual-report/2008/message-from-president-and-board-chair.htm>).

220 Ibid.

221 Ibid.

222 KIT. *Organization*. Amsterdam, Royal Tropical Institute, 2011 (<http://www.kit.nl/smartsite.shtml?ch=KIT&id=52934>).

223 KIT. *2008 annual report*. Amsterdam, Royal Tropical Institute, 2008 (<http://www.kit.nl/annualreport2008/magazine.html#/z/9/>).

224 SATVI. *About us*. Cape Town, South African Tuberculosis Vaccine Initiative (<http://www.satvi.uct.ac.za/index.php/201011092/About-us.html>).

225 SATVI. *Training activities*. Cape Town, South African Tuberculosis Vaccine Initiative (<http://www.satvi.uct.ac.za/training/satvi-training-activities.html>).

226 SEAIRC�. *Profile*. Jakarta, South East Asia Infectious Disease Clinical Research Network (http://www.seaicrn.org/index.php?option=com_content&task=view&id=45&Itemid=114).

in a building renovation to update and equip a facility with the necessary technology to be used as a tropical disease bioequivalence study site.²²⁷

Special Programme for Research and Training in Tropical Diseases

The Special Programme for Research and Training in Tropical Diseases (TDR) is a UN-based organization created to aid developing nations to combat tropical diseases. TDR conducts R&D for new medicines, technologies and diagnostics to increase access to essential medicines and treatment in developing nations. One of TDR's new initiatives, the African Network for Drugs and Diagnostics Innovation (ANDI), "operates to bring together researchers, research organizations, policy makers and manufacturers in a coordinated manner that promotes and sustains African-led product R&D innovation and capacity building".²²⁸ TDR has constructed facilities for clinical trial research in Liberia and the Democratic Republic of the Congo, which are to be used for African-led studies.²²⁹

Swedish International Development Cooperation Agency

The Swedish International Development Cooperation Agency (SIDA) is the principal Swedish agency for international aid. It channels most of its funds through international NGOs, EU, UN and the World Bank.²³⁰ A key focus for SIDA is investing in programmes to improve knowledge, health and social development, finding "a strong link between investments in social development and reduced poverty".²³¹ Sweden is one of the original donors to GAVI, to which it continues to provide financial support through direct support and through the International Finance Facility for Immunisation.²³²

University of Notre Dame

The University of Notre Dame was granted a US\$20 million dollar grant from the Bill & Melinda Gates Foundation for a 5-year research programme on malaria control. "The research effort will include partners in Indonesia, Tanzania, Kenya, Uganda and Zambia, as well as researchers from the Swiss Tropical Institute, the U.S. Centers for Disease Control, the London School of Tropical Medicine and Hygiene, and Durham University."²³³

227 SEACIRN. The Mahidol University Faculty of Tropical Medicine Hospital for Tropical Diseases' Bioequivalence Ward. *South East Asia Infectious Disease Clinical Research Network Newsletter*, August 2009. (http://www.seaicrn.org/index.php?option=com_content&task=view&id=74&Itemid=151).

228 TDR. *Innovation for health: Research that makes a difference*. Geneva, Special Programme for Research and Training in Tropical Diseases, 2008 (http://apps.who.int/tdr/publications/about-tdr/annual-reports/biennial-report-07-08/pdf/TDR_19th_Progress_Report_part3.pdf).

229 Ibid.

230 SIDA. *Swedish development cooperation: This is how it works*. Stockholm, Swedish International Development Cooperation Agency (http://www.sida.se/Global/About%20Sida/S%C3%A5%20arbetar%20vi/SIDA4848en_web.pdf).

231 Ibid.

232 GAVI. *Donor contributions and commitments*. Geneva, Global Alliance for Vaccines and Immunisation, 2011 (<http://www.gavialliance.org/support/donors/index.php>).

233 Gilroy WD. Gates Foundation grant to support malaria control research. *Notre Dame News*, 19 September 2007 (<http://newsinfo.nd.edu/news/9022-gates-foundation-grant-to-support-malaria-control-research>).

University of Washington, Department of Global Health

University of Washington, Department of Global Health is home to five centres and institutes that work in the developing world to improve access to medicines and health care. Two of these facilitate the transfer of know-how for HIV/AIDS research between the university and clinical research sites located in developing countries. The Center for AIDS Research offers assistance to national and international researchers. The Center for AIDS Research is part of a network of AIDS clinical researchers funded by the NIH and works with researchers in Kenya, Peru, Uganda, Mozambique and China.²³⁴ The International Clinical Research Center conducts “multiple clinical trials throughout Africa related to the prevention of HIV with thousands of research participants at sites in Botswana, Kenya, Rwanda, South Africa, Tanzania, Uganda, and Zambia”.²³⁵

AII.2 Financing and support programmes and initiatives

Bill & Melinda Gates Foundation

This is one of the largest financers for global health initiatives. The Foundation partners with global, regional and local health initiatives to increase access to medicines, promote education for common diseases afflicting developing nations, and encourage discovery and R&D of new medicines. Some of the partners and grantee recipients from the Foundation include GAVI, MMV, Malaria Control and Evaluation Partnership in Africa, Avahan, ACHAP, Aeras, DNDi, FIND, PATH and UNICEF.²³⁶

Department for International Development

DFID is a United Kingdom Government agency that provides funding and participates in programmes supporting development in impoverished nations. Global health and access to medicines is a major issue that the agency addresses by working through partnerships with governments in developing countries, NGOs and global coalitions and organizations. DFID also provides a significant amount of funding to international organizations and partnerships that work to increase access to medicines and conduct R&D for new medicines. Organizations and partnerships that DFID financially supports include the Global Fund to Fight AIDS, Tuberculosis and Malaria, GAVI, MMV, Roll Back Malaria Partnership, STOP TB Partnership, International Aids Vaccine Initiative and DNDi.²³⁷

234 University of Washington Department of Global Health. *Center for AIDS Research*. Seattle, WA, University of Washington Department of Global Health (http://globalhealth.washington.edu/centers_institutes/cfar.php).

235 University of Washington Department of Global Health. *International Clinical Research Center*. Seattle, WA, University of Washington Department of Global Health (http://globalhealth.washington.edu/centers_institutes/icrc.php).

236 Bill & Melinda Gates Foundation. *Global health program fact sheet*. Seattle, WA, Bill & Melinda Gates Foundation, 2009 (<http://www.gatesfoundation.org/global-health/Documents/global-health-fact-sheet-english-version.pdf>).

237 DFID. *Access to medicines fact sheet*. London, Department of International Development, 2006 (<http://www.dfid.gov.uk/Documents/publications/atm-factsheet0106.pdf>).

Federal Ministry for Economic Cooperation and Development

The Federal Ministry for Economic Cooperation and Development (BMZ) is the responsible ministry of the German Government for development cooperation. Development cooperation is seen as global structural and peace policy. BMZ aims to help resolve crises and conflicts in a peaceful manner, ensure that scarce resources are shared more equitably and that the environment is preserved for coming generations, and reduce global poverty. The rationale of the German Government's approach to intellectual property rights and health is to foster local/regional pharmaceutical R&D and production in developing countries by using TRIPS flexibilities, helping countries and private enterprises use the TRIPS flexibilities, and providing sustainable investments in R&D and production of essential medicines. The objectives are to improve access to low-cost, high-quality medicines, to foster innovation, and to develop local/regional pharmaceutical industries in developing countries. Germany channels its development cooperation through bilateral agencies such as GTZ and Inwent, through the Bank DEG (an affiliate of KfW), and through multilateral projects of the UN system.

Global Alliance for Vaccines and Immunisation

GAVI is a global health partnership established to promote the use of and access to vaccines in developing countries. GAVI's milestones include facilitating access to rotavirus and pneumococcal vaccines for developing countries and aiding countries in introducing underused vaccines.²³⁸

Global Fund to Fight AIDS, TB and Malaria

The Global Fund to Fight AIDS, TB and Malaria is a global public-private partnership that provides funds for treatment and prevention of AIDS, TB and malaria. The Fund plays a large role in funding initiatives and projects to increase the capacity of health-care systems in developing countries. The Fund is the largest international financier for malaria and TB and plays a significant role in funding HIV/AIDS research. Most of its grants go to projects in low-income and middle- to low-income countries.²³⁹

Grand Challenges for Global Health Explorations

This is a grant programme for ideas that potentially could lead to effective preventive medicines, diagnostics and medicines for diseases affecting the developing world. In a recent round of grants, the proposals focused on HIV/AIDS, TB, malaria, diarrhoeal vaccines and typhoid fever. Notably, a few of the grants were issued to researchers in Thailand and India with proposals of increasing efficacy of vaccines, and diagnostics for malaria and TB.²⁴⁰

238 GAVI. *Saving lives & protecting health: Results and opportunities*. Geneva, Global Alliance for Vaccines and Immunisation, 2010. (<http://www.gavialliance.org/>).

239 Global Fund to Fight Aids, TB and Malaria. *Annual report 2009*. Geneva, Global Fund to Fight Aids, TB and Malaria, 2010 (<http://www.theglobalfund.org/en/media/?lang=en>).

240 Grand Challenges in Global Health Explorations. *Grants*. Grand Challenges in Global Health Explorations (<http://www.grandchallenges.org/explorations/Pages/GrantsAwarded.aspx?Round=3>).

Irish Aid

This is the Irish Government's aid agency, providing aid for development in foreign countries. Irish Aid has committed to investing in health research for diseases common in developing countries, partnering Irish research and academic institutions and international organizations for collaboration on research for medicines and technological advances.²⁴¹

Médecins Sans Frontières

Médecins Sans Frontières (MSF) is an international humanitarian organization that provides medical assistance in countries with broken or nonexistent health-care systems. The organization works to raise awareness and advocate for improvement of the health-care systems in the countries in which it operates.²⁴² MSF started the campaign Access to Medicines in 2001, advocating for needed medicines to treat diseases in developing countries. MSF has also partnered with DNDi to combat sleeping sickness and other neglected diseases²⁴³ and gives significant financial support to DNDi.

Rockefeller Foundation

The Rockefeller Foundation is based in the United States and participates as an advocate in partnership and financially with initiatives that help disadvantaged individuals and communities to gain access to health care.²⁴⁴ An initiative currently undertaken by the Foundation is the Disease Surveillance Network Initiative, which seeks to increase capacity and coordination of disease surveillance systems to improve and increase efficiency of global responses.²⁴⁵

Tuberculosis Vaccine Initiative

Tuberculosis Vaccine Initiative (TBVI) is a non-profit-making European organization that partners with a network of universities, initiatives and institutions with the goal of creating accessible and affordable vaccines.²⁴⁶ TBVI funds discovery and research for new vaccines and biomarkers, and assists and advises ongoing research programmes.²⁴⁷

241 Irish Aid. *Improving health to reduce poverty*. Limerick, Irish Aid (<http://www.irishaid.gov.ie/article.asp?article=977>).

242 MSF. *About MSF*. Geneva, Médecins Sans Frontières (http://www.msf.org/msf/about-msf/about-msf_home.cfm).

243 MSF. *Annual Report 2008*. Geneva, Médecins Sans Frontières, 2008 (http://www.msf.org/source/actrep/2008annual/MSF_IAR2008.pdf).

244 The Rockefeller Foundation. *2008 annual report*. New York, The Rockefeller Foundation, 2008 (http://www.rockefellerfoundation.org/uploads/files/901c639d-bf3f-43d2-9975-5d98d02d0be8-rfar_2008.pdf).

245 The Rockefeller Foundation. *Disease surveillance networks initiative*. New York, The Rockefeller Foundation (<http://www.rockefellerfoundation.org/uploads/files/d3588732-0562-4dad-9aa0-a080862bec05-dsn.pdf>).

246 TBVI. *Annual report 2008*. Lelystad, Tuberculosis Vaccine Initiative, 2008 (http://www.tbvi.eu/uploads/media/Annual_Report_2008_03.pdf).

247 Ibid.

UNITAID

UNITAID advocates for continued increase in access to treatment for HIV/AIDS, malaria and TB for infected individuals from low-income countries.²⁴⁸ UNITAID provides medicines and diagnostics mainly to developing countries and advocates for new and innovative medicines to meet the needs of developing countries.²⁴⁹

United States President's Emergency Fund for African Relief

The United States President's Emergency Fund for African Relief (PEPFAR) is a fund that the United States Congress has designated for international programmes focused on prevention, treatment and care of HIV/AIDS, TB and malaria.²⁵⁰ In 2008, PEPFAR's prevention efforts included a wide range of programmes, partnering with national governments and organizations in developing countries for programmes on HIV/AIDS education for young people and the general population, programmes to ensure a safe supply of blood, and promoting education and training for safety procedures for medical injections.²⁵¹ Treatment programmes supported by PEPFAR include building local capacity of clinics, hospitals and diagnostic laboratories to increase the availability and level of treatment for local communities in developing countries.²⁵² PEPFAR also funds programmes to offer care and holistic support – not only medical treatments – to people with HIV/AIDS, malaria or TB.²⁵³

Wellcome Trust

The Wellcome Trust is a charity based in the United Kingdom that funds innovative biomedical research. The Trust partners with other institutions and organizations worldwide to promote its research efforts. In India, the Trust partnered with the Indian Department of Biotechnology to “provide support and training for Indian research scientists – from newly qualified postdocs through senior researchers – enabling them to pursue excellent career paths and continue working in their home country”.²⁵⁴ In Africa, the Trust has invested in the African Institutions Initiative to build capacity for African-led clinical research conducted in African and developed countries.²⁵⁵ The Trust partnered

248 UNITAID. *Annual report 2008*. Geneva, UNITAID, 2008 (http://www.unitaid.eu/images/news/annual_report_2008_en.pdf).

249 Ibid.

250 PEPFAR. *About PEPFAR*. Washington, DC, United States President's Emergency Plan for AIDS Relief (<http://www.pepfar.gov/about/index.htm>).

251 PEPFAR. *Prevention*. Washington, DC, United States President's Emergency Plan for AIDS Relief (<http://www.pepfar.gov/about/c19387.htm>). See “Prevention programs for youth”, “Prevention of sexual transmission in the general population”, “Prevention of sexual transmission for people engaged in high-risk activity”, “Blood safety”, medical injection safety”, “Prevention of mother-to-child transmission” and “Male circumcision”.

252 PEPFAR. *Treatment*. Washington, DC, United States President's Emergency Plan for AIDS Relief (<http://www.pepfar.gov/about/c19384.htm>).

253 PEPFAR. *Care*. Washington, DC, United States President's Emergency Plan for AIDS Relief (<http://www.pepfar.gov/about/c19386.htm>).

254 Wellcome Trust. *Annual review 2008*. London, Wellcome Trust, 2008 (<http://www.wellcome.ac.uk/About-us/Publications/Annual-review/Previous/2008/index.htm>).

255 Ibid.

with the University of Oxford and Mahosot Hospital, Vientiane in Laos to build a diagnosis and treatment facility for infectious diseases.²⁵⁶

III.3 Private-sector programmes and initiatives

Abbott Laboratories

Abbott Laboratories, a global pharmaceutical company, is engaged in a variety of programmes for increasing access to medicines. Abbott has partnered with the Government of the United Republic of Tanzania in an effort to improve the Tanzanian health-care system. Abbott helped to modernize four regional laboratories, donated laboratory equipment and offered personnel training for the staff.²⁵⁷ Abbott has donated drugs to a variety of humanitarian causes and medical missions.²⁵⁸ Abbott also makes available its HIV/AIDS medicines to African and least-developed countries at preferential prices. In partnership with the Institute for OneWorld Health, Abbott donated the API for an R&D effort to lower the cost of artemisin-based antiretrovirals.²⁵⁹

AstraZeneca,²⁶⁰ Baxter Healthcare,²⁶¹ Crucell,²⁶² CSL, Inc.,²⁶³ Johnson & Johnson,²⁶⁴ Sinovac Biotech,²⁶⁵ Takeda²⁶⁶ and Watson Pharmaceuticals²⁶⁷

These pharmaceutical companies make drug donations for a variety of needs around the world. The companies donate their proprietary medicines to provide humanitarian assistance in areas affected by natural disasters, and in partnerships with NGOs or governments in developing countries.

256 Ibid.

257 Abbott Laboratories. *2008 global citizenship report*. Abbott Park, IL, Abbott Laboratories, 2009 (<http://nova-worldwide.com/dotnetnuke/LinkClick.aspx?fileticket=ikJ9Dy4MzWE%3d&tabid=75&mid=449>).

258 Ibid.

259 Ibid.

260 AstraZeneca. *Annual report 2008*. AstraZeneca, 2008 (<http://www.astrazeneca-annualreports.com/2008/>).

261 Baxter Healthcare. *Baxter Healthcare sustainability priorities report 2008*. Deerfield, IL, Baxter Healthcare, 2008 (<http://sustainability.baxter.com>).

262 Crucell. *Combating infectious diseases*. Leiden, Crucell, 2008 (http://www.crucell.com/annual_report_2008/csr/crucell_mission.html).

263 CSL. *CSL donates 3 million doses of pandemic H1N1 2009 vaccine to the World Health Organisation (WHO) for use in low-income countries in this region*. Melbourne, CSL 14 October 2009 (<http://www.csl.com.au/s1/cs/auhq/1187378853299/news/1253567369773/prdetail.htm>).

264 Johnson & Johnson. *Our giving*. New Brunswick, NJ, Johnson & Johnson, 2011 (<http://www.jnj.com/connect/caring/corporate-giving?contentIDR=eb99da0047b1a394b52af73e4cc71393&useDefaultText=1&useDefaultDesc=1>).

265 Sinovac Biotech. *Investor relations*. Beijing, Sinovac Biotech, 2011 (<http://www.sinovac.com/?optionid=444>).

266 Takeda. (<http://www.takeda.com/>).

267 Watson Pharmaceuticals. *Our community outreach efforts*. Corona, CA, Watson Pharmaceuticals, 2011 (<http://www.watson.com/about/community.asp>).

Bayer

Bayer has partnered with WHO to fight against Chagas disease, a widespread infectious disease in Latin America. WHO has received free supplies of drugs that have proven effective in treating the virus that causes Chagas disease.²⁶⁸ Bayer similarly partners with other international organizations to fight African sleeping sickness, malaria and TB.²⁶⁹ In addition, medicines on the WHO essential medicines list are made available by Bayer to developing countries on a preferential pricing plan to make the drugs more accessible and affordable.²⁷⁰

Boehringer Ingelheim

This is a global pharmaceutical company and patent holder on nevirapine, a non-nucleoside reverse transcriptase inhibitor used to treat HIV. Boehringer Ingelheim has committed to not enforce its patent on nevirapine and “offers interested manufacturers listed on the WHO prequalification list non-assert declarations, allowing them to supply nevirapine-containing medicines for eligible countries”.²⁷¹ Additionally, Boehringer Ingelheim donates Viamune (nevirapine) for the fight against mother-to-child transmission of HIV during birth. Viamune is donated to the countries most in need, including countries in Africa, Asia, Latin America and eastern Europe.²⁷²

Bristol-Myers Squibb

Bristol-Myers Squibb has a voluntary licensing agreement with Aspen Pharmaceuticals. In addition, it works with hepatitis awareness and vaccination efforts in Asia and HIV/AIDS in Africa.²⁷³ Secure the Future is a programme supported by Bristol-Myers Squibb working to develop sustainable solutions for people with and affected by HIV/AIDS in Africa, offering education, counselling, testing and referral for treatment.²⁷⁴ Bristol-Myers Squibb offers its ARV drugs through the Global Access programme to sub-Saharan Africa at non-profit-making prices and has implemented a differential pricing plan for other markets around the world.²⁷⁵

Genzyme

Genzyme is a biopharmaceutical company based in the United States. The company provides access to Genzyme’s proprietary medicines for preferential-

268 Bayer. *Sustainable development report 2008*. Leverkusen, Bayer, 2008 (<http://www.bayer.com/en/Sustainable-Development-Report.aspx>).

269 Ibid.

270 Ibid.

271 Boehringer Ingelheim. *Combating HIV/AIDS*. Ingelheim am Rhein, Boehringer Ingelheim, 2010 (http://www.neufrankfurt-digital.de/wecare/content/subpages/Combating_HIV_AIDS.php?nid=1&subid=1).

272 Boehringer Ingelheim. *Viamune donation program*. Ingelheim am Rhein, Boehringer Ingelheim, 2011 (<http://www.pmtctdonations.org/en/welcome/Default.aspx>).

273 Bristol-Myers Squibb. *Bristol-Myers Squibb Foundation and corporate philanthropy*. New York, Bristol-Myers Squibb, 2010 (<http://www.bms.com/news/publications/Pages/default.aspx>).

274 Ibid.

275 Ibid.

pricing, at-cost or donated.²⁷⁶ Genzyme has initiated Humanitarian Assistance for Neglected Disease (HAND), a programme to address the long-term needs of humanitarian assistance. "Genzyme is partnering with academic and non-profit organizations on focused research collaborations. Genzyme and the Drugs for Neglected Diseases initiative (DNDi) are working together to advance a treatment for African sleeping sickness. Genzyme and the Broad Institute are collaborating on the discovery of new therapeutic candidates for malaria. If a successful new drug is developed through these research collaborations, Genzyme will grant the rights and intellectual property for use to non-profit organizations with no commercial interest for Genzyme related to neglected diseases."²⁷⁷

Novartis Institute for Tropical Disease

Novartis Institute for Tropical Disease (NITD) was established in Singapore in 2003 by Novartis to work with local and international researchers and Novartis research centres to develop medicines for combating dengue fever, malaria and TB. NITD provides any drugs discovered by the institute at cost to patients in countries that most need them.²⁷⁸ One of the initiatives of NITD is a joint clinical research initiative between the Indonesian Eijkman Institute and Hasanuddin University "that expands the research capabilities of NITD to conduct research for dengue, tuberculosis and malaria."²⁷⁹

Novartis Vaccines Institute for Global Health

Novartis Vaccines Institute for Global Health (NVGH), founded by Novartis, partners with a variety of organizations and institutions for the development of vaccines to address unmet needs in the developing world. NVGH is based in Italy and shares the resources of Novartis' vaccine headquarters. "NVGH bridges an existing gap between the discovery of promising vaccine candidates in academic and research institutes and the manufacturing and distribution of vaccines by providing the facilities and expertise for scale vaccine production and human proof of concept studies."²⁸⁰

Pfizer

Pfizer is a global pharmaceutical company that donates many of its drugs in partnership with other organizations. Pfizer donates Zithromax, an antibiotic,

276 Genzyme. *Free drug programs*. Cambridge, MA, Genzyme, 2011 (http://www.genzyme.com/commitment/patients/free_programs.asp).

277 Genzyme. *Humanitarian programs*. Cambridge, MA, Genzyme, (http://www.genzyme.com/commitment/patients/humanitarian_programs.asp).

278 Novartis. *Corporate citizenship review*. Novartis, 2007 (<http://www.corporatecitizenship.novartis.com/managing-cc/governance/code-policies-guidelines.shtml>).

279 Novartis Institute for Tropical Diseases. *About NITD*. Cambridge, MA, Novartis Institute for Tropical Diseases, 2011 (<http://www.novartis.com/research/nitd/about/nehcri-initiative.shtml>).

280 Novartis Vaccines Institute for Global Health. *NVGH fact sheet*. Novartis, 2008 (<http://www.novartis.com/research/corporate-research/nvgh.shtml>).

to ITI for use in eradicating trachoma in developing countries.²⁸¹ Pfizer created a partnership in 2000, donating Diflucan, a drug used to treat common infections in people with HIV/AIDS, to NGOs and governments in developing countries.²⁸² In partnership with the Infectious Diseases Institute, Pfizer has committed to training researchers and building necessary facilities to increase Kampala's research and training capacity for the study of HIV/AIDS.²⁸³

sanofi-aventis

sanofi-aventis, a global pharmaceutical company, works to promote access and education for five diseases: malaria, sleeping sickness, TB, leishmaniasis and epilepsy. sanofi-aventis has a three-pronged approach, offering preferential pricing of essential medicines, improvement of existing drugs, and promotion of information, education and communication.²⁸⁴ Impact Malaria Initiative was started by sanofi-aventis in 2001; the initiative "aims to mobilize the company's expertise and resources to join the fight against malaria".²⁸⁵ Impact Malaria Initiative collaborates with research institutions to promote discovery of new antimalarial drugs and new combinations of therapies.²⁸⁶ sanofi-aventis renewed its partnership with WHO in 2006 to contribute funds, expertise and medicines for ongoing efforts to train, screen and treat sleeping sickness.²⁸⁷ sanofi-aventis has also committed to preferential pricing for treatment of medicines that treat leishmaniasis and partners with WHO by providing funds to support education and treatment of the disease.²⁸⁸

Sanofi Pasteur

Sanofi Pasteur, the vaccine division of sanofi-aventis, partners with GAVI and aids in GAVI's efforts "to improve the infrastructures required for proper vaccine administration and to encourage research and development programs focused on diseases that predominantly affect developing countries, and has historically practiced a policy of tiered pricing to facilitate access to vaccines in GAVI Alliance countries". Sanofi Pasteur is a part of the Global Polio Eradication Initiative (GPEI), which it supplies with needed vaccines, and supports the immunization of children in Angola, Liberia, Sierra Leone and southern Sudan.²⁸⁹

281 Pfizer. *Partnership to end blinding trachoma through the International Trachoma Initiative International Trachoma Initiative*. New York, Pfizer, 2011 (http://www.pfizer.com/responsibility/global_health/international_trachoma_initiative.jsp).

282 Pfizer. *Diflucan partnership*. New York, Pfizer, 2000 (http://www.pfizer.com/responsibility/global_health/diflucan_partnership_program.jsp).

283 Pfizer. *Infectious Diseases Institute in partnership with Accordia Global Health Foundation*. New York, Pfizer, 2001 (http://www.pfizer.com/responsibility/global_health/infectious_diseases_institute.jsp).

284 sanofi-aventis. *Access to medicines*. Paris, sanofi-aventis, 2007 (http://en.sanofi-aventis.com/binaries/brochure_aam_en_tcm28-18133.pdf).

285 Ibid.

286 Ibid.

287 Ibid.

288 Ibid.

289 Sanofi Pasteur. *Access to vaccines*. Lyon, Sanofi Pasteur, 2009 (http://www.sanofipasteur.com/sanofi-pasteur2/front/index.jsp?siteCode=SP_CORP&codeRubrique=26).

AII.4 Advocacy and coordination organizations

AIDS Vaccine Advocacy Coalition

AIDS Vaccine Advocacy Coalition (AVAC) is an international non-profit-making organization that builds partnerships and collaborations, encourages R&D and supports clinical trials for AIDS vaccines and new HIV-prevention options. One of AVAC's programmes is participating on a community level where clinical trials of interest take place. In November 2007 AVAC, together with the United Nations Programme on HIV/AIDS (UNAIDS), published *Good participatory practice guidelines for biomedical HIV prevention trials*, which established a guideline for people conducting clinical trials around the world.²⁹⁰ The programme conducted by AVAC, based on these published guidelines, "is raising awareness about the GPP guidelines, assist[ing] trial sites and communities to begin using them, and encouraging the adoption of systematic ways for trials sites conducting biomedical HIV prevention research to collaborate with local communities in positive ways worldwide".²⁹¹

Global Business Coalition on HIV/AIDS, Tuberculosis and Malaria

This is an NGO comprised of businesses from around the world. The Coalition "bring(s) the private sector's special capabilities and drive for measurable results to the fight against HIV/AIDS, tuberculosis and malaria".²⁹² Members partner with other NGOs, international organizations such as UNAIDS, and the governments of the United States, Kenya and China to make collaborative efforts in fighting HIV/AIDS, TB and malaria.²⁹³

Health Action International

Health Action International (HAI) is a Dutch civil society NGO. It has a coordinating office in Amsterdam and partner regional offices in Africa (Nairobi), Asia Pacific (Colombo), Latin America (Lima) and Europe (Amsterdam). "Although primarily a Dutch organization, HAI is recognized for its global medicines policy expertise and as a non-profit, independent, worldwide network of over 200 members including consumer groups, public interest NGOs, health care providers, academics, media and individuals in more than 70 countries."²⁹⁴

Knowledge Ecology International

Knowledge Ecology International (KEI) is an NGO that advocates for access to medicines for developing countries by engaging in global public health policy

290 UNAIDS, AVAC. *Good participatory practice guidelines for biomedical HIV prevention trials*. Geneva, United Nations Programme on HIV/AIDS and AIDS Vaccine Advocacy Coalition, 2007 (<http://www.avac.org/ht/a/GetDocumentAction/i/2824>).

291 AVAC. *AVAC programs*. New York, AIDS Vaccine Advocacy Coalition, (<http://www.avac.org/ht/d/sp/i/479/pid/479>).

292 Merriman V. *Collaboration, coordination and collective action that will end disease faster*. Global Business Coalition on HIV/AIDS, Tuberculosis, and Malaria, 2008 (<http://www.gbciimpact.org/about-gbc>).

293 Ibid.

294 HAI. *Health Action International*. Amsterdam, Health Action International <http://www.haiweb.org/>.

in issues such as intellectual property, drug pricing, procurement and other issues regarding R&D of new medicines.²⁹⁵

Malaria Consortium

Malaria Consortium “works in partnership with communities, health systems, government and non-government agencies, academic institutions and local and international organisations to ensure good evidence supports delivery of effective services”.²⁹⁶ Malaria Consortium helps to build capacity for health-care systems in developing countries by providing training resources for health-care workers, and assisting in development of long-term policy at a national level.²⁹⁷

MSF Campaign for Access to Essential Medicines

This was started in 1999 by MSF in response to a lack of essential medicines in developing countries. The Campaign advocates for lower prices on essential medicines and encourages R&D for medicines, vaccines and diagnostics for diseases including malaria, TB and sleeping sickness.²⁹⁸

Neglected Tropical Diseases Initiative

Neglected Tropical Diseases Initiative is a USAID programme. The Initiative was created in 2006 and pools together donated drugs from pharmaceutical companies and drugs procured through organizations for distribution to developing countries.²⁹⁹

Oxfam

Oxfam is an international organization composed of NGOs around the world that work together to reduce poverty and promote justice through advocacy, coordination for collaborative programmes, and policy research.³⁰⁰ One of the organization’s main issues is global health and education and providing affordable health care access around the world.³⁰¹ In 2007, Oxfam began the campaign Health and Education for All, which encouraged developing countries to devote more resources to improve the infrastructure of their

295 KEI. *About KEI*. Washington, DC, Knowledge Ecology International, 2009 (<http://www.keionline.org/about>).

296 Malaria Consortium. *What we do*. London, Malaria Consortium, 2011 (http://www.malariaconsortium.org/pages/what_we_do.htm).

297 Malaria Consortium. *Capacity building*. London, Malaria Consortium, 2011 (<http://www.malariaconsortium.org/page.php?id=106>).

298 Campaign for Access to Medicines. *About us*. Geneva, Campaign for Access to Medicines (<http://www.msfaaccess.org/about-us/>).

299 USAID NTD Program. *About the Neglected Tropical Disease Program*. Washington, DC, United States Agency for International Development Neglected Tropical Diseases Program, 2009 (<http://www.neglecteddiseases.gov/about/index.html>).

300 Oxfam International. *Oxfam International's mission statement*. Ottawa, Oxfam International, 1996 (<http://www.oxfam.org/en/about/what/mission>).

301 Oxfam International. *Health*. Oxfam International, 2011 (<http://www.oxfam.org/en/about/issues/health>).

health systems, while advocating for rich countries to donate resources to support efforts made by developing countries.³⁰²

Roll Back Malaria Partnership

This is a partnership between WHO and a number of stakeholders invested in combating malaria. The Partnership developed the Global Malaria Action Plan, a “global strategy [to] (1) control malaria to reduce the current burden and sustain control as long as necessary, (2) eliminate malaria over time country by country and (3) research new tools and approaches to support global control and elimination efforts.”³⁰³ The Global Malaria Action Plan aids governments and international initiatives, providing guidance and collaborative goals in the combat against malaria.³⁰⁴

Task Force for Global Health

This is a non-profit-making organization that “facilitates consensus and implements programs to support better global health in the areas of infectious diseases. ... [It] also helps public health organizations develop and implement information systems that support improved health and well-being in communities.”³⁰⁵

302 Oxfam International. *Annual report 2007*. Oxfam International, 2007 (<http://www.oxfam.org/sites/www.oxfam.org/files/OI-annual-report-2007-en.pdf>).

303 Roll Back Malaria. *Global malaria action plan 2008*. Geneva, Roll Back Malaria, 2008 (<http://www.rollbackmalaria.org/gmap/index.html>).

304 Ibid.

305 Task Force for Global Health. *About us*. Decatur, GA, Task Force for Global Health, 2011 (<http://www.taskforce.org/about-us>).



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ISBN 978 92 4 150234 4



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