Pharmaceutical Production and Related Technology Transfer
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## Abbreviations

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<tr>
<th>Acronym</th>
<th>Full Form</th>
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<tr>
<td>AIDS</td>
<td>acquired immunodeficiency syndrome</td>
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<tr>
<td>API</td>
<td>active pharmaceutical ingredient</td>
</tr>
<tr>
<td>ARV</td>
<td>antiretroviral</td>
</tr>
<tr>
<td>AusAID</td>
<td>Australian Government Overseas Aid Program</td>
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<tr>
<td>BMZ</td>
<td>German Federal Ministry for Economic Cooperation and Development</td>
</tr>
<tr>
<td>BuZa</td>
<td>Ministerie van Buitenlandse Zaken (The Netherlands International Cooperation Agency)</td>
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<tr>
<td>cGMP</td>
<td>current good manufacturing practice</td>
</tr>
<tr>
<td>CIDA</td>
<td>Canadian International Development Agency</td>
</tr>
<tr>
<td>Danida</td>
<td>Danish International Development Agency</td>
</tr>
<tr>
<td>DEG</td>
<td>Deutsche Investitions- und Entwicklungsgesellschaft</td>
</tr>
<tr>
<td>DFID</td>
<td>United Kingdom Department for International Development</td>
</tr>
<tr>
<td>DNDi</td>
<td>Drugs for Neglected Diseases initiative</td>
</tr>
<tr>
<td>EAC</td>
<td>East African Community</td>
</tr>
<tr>
<td>ECOWAS</td>
<td>Economic Community of West African States</td>
</tr>
<tr>
<td>EMEA</td>
<td>European Medicines Agency</td>
</tr>
<tr>
<td>EU</td>
<td>European Union</td>
</tr>
<tr>
<td>FDC</td>
<td>fixed-dose combination</td>
</tr>
<tr>
<td>FIOCRUZ</td>
<td>Oswaldo Cruz Foundation</td>
</tr>
<tr>
<td>GFATM</td>
<td>Global Fund to Fight AIDS, TB and Malaria</td>
</tr>
<tr>
<td>G-FINDER</td>
<td>Global Funding of Innovation for Neglected Diseases</td>
</tr>
<tr>
<td>GCP</td>
<td>good clinical practice</td>
</tr>
<tr>
<td>GLP</td>
<td>good laboratory practice</td>
</tr>
<tr>
<td>GMP</td>
<td>good manufacturing practices</td>
</tr>
<tr>
<td>GNI</td>
<td>gross national income</td>
</tr>
<tr>
<td>GSK</td>
<td>GlaxoSmithKline</td>
</tr>
<tr>
<td>GSPAPHI</td>
<td>Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property</td>
</tr>
<tr>
<td>GIZ</td>
<td>Gesellschaft für Internationale Zusammenarbeit (Germany)</td>
</tr>
<tr>
<td>HIV</td>
<td>human immunodeficiency virus</td>
</tr>
<tr>
<td>ICH</td>
<td>International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use</td>
</tr>
<tr>
<td>ICTSD</td>
<td>International Centre for Trade and Sustainable Development</td>
</tr>
<tr>
<td>IFC</td>
<td>International Finance Corporation</td>
</tr>
<tr>
<td>Acronym</td>
<td>Full Form</td>
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<tr>
<td>---------</td>
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<tr>
<td>IFPMA</td>
<td>International Federation of Pharmaceutical Manufacturers and Associations</td>
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<tr>
<td>IoWH</td>
<td>Institute for OneWorld Health</td>
</tr>
<tr>
<td>IPC</td>
<td>Interagency Pharmaceutical Coordination Group</td>
</tr>
<tr>
<td>IPS</td>
<td>Aga Khan Fund for Economic Development-Industrial Promotion Services</td>
</tr>
<tr>
<td>JICA</td>
<td>Japanese International Cooperation Agency</td>
</tr>
<tr>
<td>LDC</td>
<td>least developed country</td>
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<tr>
<td>LIC</td>
<td>low-income country</td>
</tr>
<tr>
<td>MMV</td>
<td>Medicines for Malaria Venture</td>
</tr>
<tr>
<td>MSF</td>
<td>Médecins Sans Frontières</td>
</tr>
<tr>
<td>NGO</td>
<td>nongovernmental organization</td>
</tr>
<tr>
<td>Norad</td>
<td>Norwegian Agency for Development Cooperation</td>
</tr>
<tr>
<td>NIH</td>
<td>United States National Institutes of Health</td>
</tr>
<tr>
<td>OECD</td>
<td>Organisation for Economic Co-operation and Development</td>
</tr>
<tr>
<td>OTECII</td>
<td>Office Technique d’Études et de Coopération Internationale</td>
</tr>
<tr>
<td>PICS</td>
<td>Pharmaceutical Inspection Cooperation Scheme</td>
</tr>
<tr>
<td>R&amp;D</td>
<td>research and development</td>
</tr>
<tr>
<td>SACU</td>
<td>Southern African Customs Unit</td>
</tr>
<tr>
<td>SADC</td>
<td>Southern African Development Community</td>
</tr>
<tr>
<td>SAGMA</td>
<td>Southern African Generics Medicines Association</td>
</tr>
<tr>
<td>SIDA</td>
<td>Swedish International Development Agency</td>
</tr>
<tr>
<td>TB</td>
<td>tuberculosis</td>
</tr>
<tr>
<td>TRIPS</td>
<td>WTO Agreement on Trade-Related Aspects of Intellectual Property Rights</td>
</tr>
<tr>
<td>UN</td>
<td>United Nations</td>
</tr>
<tr>
<td>UNAIDS</td>
<td>United Nations Programme on HIV/AIDS</td>
</tr>
<tr>
<td>UNCTAD</td>
<td>United Nations Conference on Trade and Development</td>
</tr>
<tr>
<td>UNDP</td>
<td>United Nations Development Programme</td>
</tr>
<tr>
<td>UNFPA</td>
<td>United Nations Population Fund</td>
</tr>
<tr>
<td>UNICEF</td>
<td>United Nations Children’s Fund</td>
</tr>
<tr>
<td>UNIDO</td>
<td>United Nations Industrial Development Organization</td>
</tr>
<tr>
<td>USAID</td>
<td>United States Agency for International Development</td>
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<tr>
<td>WHO</td>
<td>World Health Organization</td>
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<tr>
<td>WIPO</td>
<td>World Intellectual Property Organization</td>
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<tr>
<td>WTO</td>
<td>World Trade Organization</td>
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</table>
Acknowledgments

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Executive summary

Introduction

The local production of drugs in developing countries has long been seen as a potential way to increase access to medicines and improve public health (1–4). At the same time, such production also held the possibility of supporting other policy goals such as economic development, industrialization and accelerated technological capacity. The potential importance of local production was recognized in the 2008 WHO Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA-PHI), which points to local production of pharmaceuticals as a key area for investment in Element 3 and focuses on health-related technology transfer in Element 4.

Renewed interest in local production arises against the context of increased interconnectedness and vulnerability to global health threats, a changed global intellectual property regime, growing capacity in key developing countries to produce and develop medicines, globalization of the pharmaceutical supply chain, the expansion of developing country pharmaceutical markets, and increased attention to the challenge of ensuring equitable access to medicines.

This landscaping study was conducted for the WHO Secretariat on Public Health, Innovation and Intellectual Property project “Improving access to medicines in developing countries through technology transfer related to medical products and local production”, which is funded by the European Commission. The purpose of the study is to provide:

• a description of the landscape of local production of drugs, relevant investment promotion and related transfer of technology;
• an outline of current and recent initiatives (taking place within the past 5–10 years);
• an identification of gaps and preliminary assessment of the initiatives.

This report provides a description of the current landscape related to the local production of drugs in developing countries and related technology transfer. The objective is to assist WHO in its support for Member States in implementing the GSPA-PHI, with particular reference to the promotion of capacity building for local production in developing countries.

Overall, the study offers a descriptive overview of trends in local production of drugs and related technology transfer and the key issues that arise. Vaccines and diagnostics are not covered in this study, due to important differences between pharmaceutical production and the development of vaccines and new diagnostics. These topics form the subject of separate reports in this series. It should be noted that this report is neither an exhaustive catalogue of all ongoing activities, nor an in-depth analysis of specific projects; there are important gaps in the coverage of the report due to data and feasibility constraints, as discussed further in Section 2. Rather, the intention is to provide some intuition on the scale, scope and key issues in the field as a whole, and
to offer some guidance for designing the next stage of work. Therefore, the findings should be interpreted with an appropriate degree of caution.

**Methods**

For the purposes of this study, “local” is defined as any production of drugs taking place in low-, lower-middle- and upper-middle-income countries, regardless of the ownership structure. “Production” is defined as any stage of the drug manufacturing process from production of active pharmaceutical ingredients (API), through formulation or packaging. Technology transfer is defined as “a series of processes for sharing ideas, knowledge, technology and skills with another individual or institution (e.g. a company, a university or a governmental body) and of acquisition by the other of such ideas, knowledge, technologies and skills” (5). In keeping with the focus of the study, the scope of examined initiatives was limited to those with the explicitly expressed intention to transfer technology or take other measures to improve capacity to produce drugs locally.

This report uses interchangeably the terms “developing country” and “low-or middle-income country” (World Bank classification1) and “south”. Where relevant, the United Nations (UN) categorization of “least developed country” (LDC) or a regional classification is specified. There is no publicly available uniform data source on initiatives for local production of drugs and relevant technology transfer, and the author is unaware of any such privately held data sources. Therefore, we searched a range of potential data sources from September to December 2009 in order to identify as many initiatives as possible (see Section 2).

**Overview of local production in developing countries**

According to the 2004 WHO World Medicines Situation report, pharmaceutical production remains concentrated in the high-income countries. In 1999, these countries accounted for 92.9% of world pharmaceutical production (by value). Based on a typology developed by Ballance et al. (6), ten countries1 were considered to have a “sophisticated industry” with “significant research” – none of which was a developing country. In addition, 16 countries were classified as having “innovative capability” – that is, “at least one new molecular entity was discovered and marketed by these countries from 1961–1990”. Of these, six are low- or middle-income countries: Argentina (7, 8), China, India, Mexico (8–10), the Russian Federation and the former state union of Serbia and Montenegro. A further 97 countries had some pharmaceutical production capacity, of which

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1 As defined by the World Bank. The World Banks country classifications are revised annually in July based on updated data. Economies are divided according to 2008 gross national income (GNI) per capita, calculated using the World Bank Atlas method. The groups are: low income, US$ 975 or less; lower-middle income, US$ 976-3855; upper-middle income, US$ 3856-11 905; and high income, US$ 11 906 or more.

2 The United States of America, the United Kingdom, France, Germany, Japan, Switzerland, Italy, Belgium, the Netherlands and Sweden.
84 only produced finished products from imported active ingredients, and 13 produced both active ingredients and finished products. Of these 13, 9 were low- or middle-income: Bolivia, Brazil (11–14), Bulgaria, Cuba (15), Egypt (16, 17), Indonesia, Poland, Romania and Turkey. An additional 42 countries were considered to have no pharmaceutical industry at all; this group comprised mostly developing countries. In addition to the countries listed in the World Medicines Situation report, the pharmaceutical industries of the following countries have attracted the interest of analysts as having substantial existing or potential capacity: Bangladesh (18–22), Ethiopia (23), Ghana (24), Iran (25), Jordan (26), Kenya (27), Nigeria (28), Rwanda (29), South Africa (30–32), the United Republic of Tanzania (33), Thailand (34–36), Tunisia (37–40), Uganda (41) and Viet Nam (42) have been noted in the literature. In summary, most low- and middle-income countries either have no pharmaceutical industry at all or are able to carry out only the relatively late-stage steps of formulation and packaging; a small number of countries produce a range of APIs, and an even smaller number conduct significant research and development (R&D). Of the developing countries listed above, India and China have by far the most advanced industries, in terms of both scale and level of technical sophistication.

Findings on initiatives for local production and technology transfer

Supporting the development of local pharmaceutical production capacity is a complex endeavour involving many types of activity. The initiatives identified by this study undertook a broad range of activities and varied widely along a number of dimensions, including the following:

- Type of technology transferors/transferees: private-to-private actors, public-to-private, private-to-public and public-to-public (note “public” denotes either a government or non-profit-making entity).
- Scale of projects: from individual consultants, to small nongovernmental organizations (NGOs), to small/medium-sized enterprises, to large multinational enterprises.
- Goals and interests of transferors and transferees (see Section 5).
- Complexity of transferred technology and technical capacities of transferees: from packaging to API production.
- Technical value of the transfer: from replicating existing knowledge (no gain for transferee) to providing valuable new technology.
- Economic value of transfer: from virtually nonexistent product markets to substantial market size.
- Scale and duration of transfer: from 3 weeks to 10 years.

Given the variance among the initiatives identified, generalizations should be taken with caution. The report very briefly outlines the major initiatives, which are summarized in Table 1 and further details of which can be found in Annex I.
Table 1  Summary of 30 identified technology transfer initiatives

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Type</th>
<th>Quantity (proportion)</th>
</tr>
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<tbody>
<tr>
<td>Development level of partner</td>
<td>North–south</td>
<td>20 (67%)</td>
</tr>
<tr>
<td></td>
<td>South–south</td>
<td>10 (33%)</td>
</tr>
<tr>
<td>Stage of production process</td>
<td>Packaging</td>
<td>1 (3%)</td>
</tr>
<tr>
<td></td>
<td>Formulation</td>
<td>20 (67%)</td>
</tr>
<tr>
<td></td>
<td>API</td>
<td>9 (30%)</td>
</tr>
<tr>
<td>Type of transferor/transferee</td>
<td>Private–private</td>
<td>15 (50%)</td>
</tr>
<tr>
<td></td>
<td>Public–private</td>
<td>10 (33%)</td>
</tr>
<tr>
<td></td>
<td>Public–public</td>
<td>1 (3%)</td>
</tr>
<tr>
<td></td>
<td>Private–public</td>
<td>1 (3%)</td>
</tr>
<tr>
<td></td>
<td>Mixed</td>
<td>3 (10%)</td>
</tr>
</tbody>
</table>

The study scope included initiatives encompassing all drugs and all diseases. However, the initiatives it identified generally focused on newer drugs (with a few exceptions) and also focused primarily on the four diseases that have received the most international attention and funding in recent years – human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS), tuberculosis (TB), malaria and pandemic flu.

This landscaping exercise uncovered initiatives for drugs that span a range of therapeutic areas. However, the findings also point to a notable absence of initiatives in certain areas: for example, there were almost no initiatives targeting products for type 1 diseases, such as diabetes or mental illnesses, except in the context of joint ventures or subsidiaries of the large multinational firms. In addition, we did not identify any initiatives for the production of biotechnology drugs (excluding vaccines). As one source from the Indian pharmaceutical industry commented, many Indian firms were already quite adept at producing small molecules but needed and would benefit from technology transfer for complex new biotechnology products. Finally, we found almost no initiatives focusing on traditional medicines (excluding artemisinin derivatives). However, due to the general unavailability of public information on private-to-private firm initiatives, it is not possible to conclude that no transfer is taking place in other therapeutic areas; for example, it is possible that significant technology transfer for production of type 1 disease-related drugs is taking place but did not appear in the information available to the author.

There is a wide range of actors transferring technology to local producers, ranging from individuals to non-profit-making institutions to multinational pharmaceutical companies to major public institutions. There is also wide variation in the scale and level of technical sophistication of technology transferees. Transferees include large firms with annual revenues hovering near US$ 1 billion, such as Cipla and Ranbaxy, and include all stages of production from API to finished products for both drugs and vaccines. India-based manufacturers of both drugs and vaccines were by far the most frequent

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3 Type 1 diseases are incident in both rich and poor countries, with large numbers of vulnerable populations in each. Type II diseases are incident in both rich and poor countries, but with a substantial proportion of the cases in poor countries. Type III diseases are those that are overwhelmingly or exclusively incident in developing countries.
participants of technology transfer initiatives, followed by China and Brazil. Technology was also transferred to less advanced generics firms in smaller or less-developed countries, with a wide distribution across sub-Saharan Africa, albeit with some concentration in east Africa (Kenya, United Republic of Tanzania, Uganda), particularly for antimalarials. Transfers to African firms usually involved formulation, packaging, good manufacturing practices (GMP) training and documentation support, and seldom included API production.

Joint ventures or subsidiaries of multinationals were also presumably frequent recipients of technology transfer for a broad range of products, as were contract manufacturers; however, a search through the web sites of the 20 largest pharmaceutical companies (ranked by 2008 revenue) uncovered only scarce information on production locations or contract manufacturing (with the exception of GlaxoSmithKline; GSK). From the information available, it appears that subsidiaries of multinationals for production (rather than for sales or distribution) are concentrated in India and China, with a few sites in Mexico (43–45).

In addition to technology transferors and transferees, local production initiatives often involve third parties or “facilitators”, who may play a variety of roles, including research, advocacy, coordination, funding, connecting or screening potential partners, brokering agreements, increasing absorptive capacity, advising, providing additional incentives and creating a conducive policy environment. Among the technology-receiving countries, government actors played a wide range of roles, and initiatives could involve ministries of health, the national drug regulatory authority, trade, industry, science and technology, and education – though in some cases, no government actor was involved at all. Since the 1970s, multilateral organizations and donor governments have played various facilitating roles in supporting the development of local pharmaceutical production capacity and relevant technology transfer. For example, the Interagency Pharmaceutical Coordination Group (IPC) was established in 1996 and convenes senior officials in the field of pharmaceuticals from WHO, the World Bank, the United Nations Programme on HIV/AIDS (UNAIDS; included in 2001), the United Nations Population Fund (UNFPA) and the United Nations Children's Fund (UNICEF) to coordinate technical and policy advice to countries. According to WHO, “these meetings, and many contacts in between, have lead to a much better exchange of information between the organizations, to more consistency of the technical advice given, and to the development of several joint policy documents and guidelines” (46). There is an IPC subgroup on local pharmaceutical production, which has also involved the United Nations Industrial Development Organization (UNIDO), UNCTAD, the United Nations Development Programme (UNDP) and other multilateral organizations relevant to local production and technology transfer such as the African Development Bank and the Global Fund to Fight AIDS, TB and Malaria (GFATM).

Three multilateral organizations provide “direct support” for local production: WHO, UNIDO and the International Finance Corporation of the World Bank Group (IFC). Direct support is defined here as those activities aimed specifically
at local producers, including technology transfer, training (e.g. quality assurance improvement) and financing. Seven multilateral organizations provide indirect support to local production efforts, such as policy advice, capacity building, institutional strengthening and analysis: UNIDO, UNCTAD, World Bank, UNDP, WHO, UNICEF and the African Union. Several governments from north and south – most notably Brazil, the European Union (EU), Germany, Thailand, the United Kingdom and the United States – have facilitated local production efforts in other countries, either directly through technology transfer, training or funding, or indirectly through analysis and policy advice. NGOs were also involved in technology transfer, training and funding to support local production, as well as conducting research, advocacy, analysis, policy advice and facilitating networking. Active NGOs included action medeor, Cordaid, ICTSD, InWent, Office Technique d’Études et de Coopération Internationale (OTECI), Médecins Sans Frontières (MSF) and Technoserve.

Generally, technology was transferred for one or more of three stages of pharmaceutical production for drugs: (i) packaging, (ii) formulation and (iii) API and/or raw material. Some initiatives also assisted manufacturers in upgrading or meeting quality standards (this does not include support to regulatory authorities). Of the 30 initiatives identified (see Annex I), most supported formulation (n=20), a fair number transferred technology for API (n=9), and only 1 provided support for packaging alone. Initiatives also often provided support for regulatory filings through access to data or documentation.

Generally, it appears that technology transfer initiatives, investments and voluntary licensing have increased since the mid-1990s, as demonstrated in Table 2.

Table 2 Trends in initiatives supporting local production and technology transfer

<table>
<thead>
<tr>
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<th>Start dates of initiatives</th>
</tr>
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<tbody>
<tr>
<td>Technology transfer initiatives</td>
<td>0</td>
</tr>
<tr>
<td>Investment initiatives</td>
<td>5</td>
</tr>
<tr>
<td>Voluntary licensing initiatives</td>
<td>0</td>
</tr>
</tbody>
</table>

Discussion and key issues

Why transfer? Reasons to transfer technology

Why does one party transfer technology, which is costly to generate or obtain, to another? As noted in the introduction, this study focuses largely on local production and technology transfer initiatives that were not purely commercial (due to data constraints). Nevertheless, even within this circumscribed set of initiatives, an important distinction emerges between technology transfer negotiated with profit-making entities (e.g. large multinational drug producers, small biotechnology companies) and those supported by public
or non-profit-making initiatives. The landscaping exercise uncovered a range of reasons that can roughly be divided into two categories: reasons for profit-making and non-profit-making/public entities.

**Profit-making entities**

- when a product is no longer of commercial interest;
- when a firm’s business model does not include high-volume/low-margin supply to developing countries, but rather focuses on high-margin supply to higher-income markets;
- when a firm needs access to increased production capacity to meet the volume of global demand;
- to meet corporate social responsibility commitments and strengthen the firm’s “social licence to operate”;
- to avert legal or regulatory action unfavourable to the firm, such as a compulsory licence or denial of a patent application;
- to enter a market (e.g. joint venture requirements).

These reasons are not mutually exclusive, and several may simultaneously influence a decision to transfer technology.

**Non-profit-making entities**

Reasons given by non-profit-making entities (governments, intergovernmental organizations, universities/research institutes, NGOs) to engage in technology transfer tend to be linked with organizational mission, and include the following:

- to improve public health and support access to medicines;
- to support industrial development;
- to reduce national reliance on imports;
- to disseminate knowledge;

**Why receive? Reasons to participate as transferees**

The most straightforward reason for a recipient firm to participate in a technology transfer initiative was to get access to new, useful technology for production. Such access can reduce the time and cost of developing the know-how in-house, increase the general skill level of employees, and create spillovers in other areas, including access to broader distribution networks and new business opportunities. For a smaller firm, partnering with a well-known multinational can also bring reputational benefits.

**Restrictions in technology transfer agreements**

Technology transfer agreements may come with a range of restrictions on the recipient, such as limitations on export markets, limits on further transfer of technology or know-how to third parties, the maintenance of trade secrets, preservation of patent monopolies for a certain period, price floors/ceilings and royalty payments.
**Intellectual property**

Among the initiatives reviewed, patents on pharmaceutical products had a variable impact on local production, depending on the therapeutic area, country of production, and level of technical capacity of the local pharmaceutical industry. Patents posed the largest barrier for firms based in non-LDCs interested in producing newer medicines, such as those for HIV/AIDS, pandemic flu or type 1 diseases. At the same time, the 2001 World Trade Organization (WTO) Declaration on the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) and Public Health (“the Doha Declaration”), which extended the deadline for LDC WTO Members to grant or enforce pharmaceutical patents until at least 2016, has also perhaps increased interest in exploring the possibilities for pharmaceutical production in LDCs (19, 20).

**Economic issues**

A full exploration of all the economic issues relevant to the complex topics of local production and technology transfer is beyond the scope of this landscaping exercise; however, an outline of the three main issues that have arisen most frequently in this overview of initiatives may be useful. First, and perhaps most important, is whether the price of a locally produced product will be competitive with the imported product (47). Closely related to this question is how much time will be required for local production to become competitive, which may depend on both the capacity of the producer itself and market conditions, such as growth of demand and economies of scale. Second, financing remains a challenge, as mobilizing the substantial amounts of capital required to invest in local production in developing countries can be quite difficult. Third, there are the sizeable economic challenges of inducing appropriate technology transfer, particularly if technology holders compete against technology-demandeurs: both face search costs to identify potentially appropriate technology transfer partners, as accurate information on the technological capacity of private enterprises is not usually made public. Even after potential technology suppliers have been identified, local producers may not be able to access the technology due to imbalances in bargaining power linked to information asymmetries.

**Utility of transfer**

There is wide variation in the reported utility of technology transfer initiatives for recipients. The extent to which a particular initiative is useful seems to depend on both the characteristics of the initiative itself (e.g. what is being offered, how effectively it is being transferred) and the level of technical skill of the recipient. For many Indian generic firms, which are some of the most advanced producers in the world, a particular package of technology transfer may be far less useful than for smaller or less technically sophisticated producers.
Timelines

The duration of technology transfer initiatives reviewed in this study varied widely from as short as 3 weeks to as long as 10 years. The amount of time required for an initiative may be quite lengthy, depending on the goal. For example, if the objective is to develop a strong local industry, it should be noted that the Indian industry took three decades to develop into the competitive industry it is today, and the Tunisian industry about two decades (38, 40, 48). Several interviewees and studies in the literature emphasized the importance of long-term cooperation between transferors and transferees to build trust, ensure successful transfer and allow recipients to advance through various stages of technological difficulty.

Quality assurance measures and other regulatory issues

Quality assurance measures were integral to the initiatives reviewed in this study. Technology holders often select transferees based in part on their existing or potential capacity to produce at international quality standards. Furthermore, training in GMP and producing the documentation required to meet regulatory standards is often a core part of local production initiatives. At the same time, regulatory standards can pose significant barriers to market entry by local producers or create delays in the availability of products (49). The difficult issues of how best to protect public safety while minimizing barriers to local production remain central questions requiring further research and analysis.

Defining success

A critical question discussed too rarely in the literature is how should “success” be defined for initiatives for local production and technology transfer? Given the wide range of technology transfer initiatives, each one is likely to have its own objectives and therefore differing definitions of “success”. At the project or country level, frequently used indicators of success may include price, quality standards, security of supply, sustainable production, increased human (employee) capacity, full mastery of the transferred technology, and increased firm capacity to produce more complex products. Although common criteria for success emerge from the country- or project-level perspective, it is much less clear how to define success from the perspective of the global health community. Is it enough if some technology is being transferred at all? Or if more technology is being transferred today than yesterday? Or if the proportion of global pharmaceutical production taking place in developing countries reaches a certain threshold, as UNIDO aimed to do in 1975? There is a need for further discussion regarding the following:

- What kind of, and how much, local production is desirable? What kind of, and how much, technology transfer is sufficient? To meet which public health or economic development objectives?
- How sufficient is the coverage of ongoing initiatives for local production and technology transfer?
- How well do the ongoing initiatives meet priority health needs?
- How effective are the ongoing initiatives at improving access to medicines?
- How effective are the ongoing initiatives at increasing local capacity and industrial development?
Summary and conclusions

The objective of this study was to provide a broad global overview of recent and ongoing initiatives. The evidence suggests that there is a significant amount of activity taking place to support local production and induce the relevant transfer of technology, both to countries with established pharmaceutical industries and to countries where capacity is nascent. However, despite the breadth and variety of activities, in the absence of clearly articulated international goals with respect to local production, there is no objective way to measure whether such efforts are sufficient or whether much greater efforts are needed. Given widespread interest in identifying long-term sustainable measures to improve access to essential drugs in developing countries, and renewed attention to local production strategies as one possible avenue to achieve this goal, this landscape study offers the following conclusions to inform ongoing debates:

• Information and research: There is a clear need for improved information about ongoing initiatives to provide a stronger evidence base for policy analysis and recommendations. In particular, a methodical, comprehensive, regularly updated and publicly accessible database of relevant initiatives is currently lacking but sorely needed in the current fragmented landscape.

• Drugs: Activities captured here have been concentrated in the areas of HIV/AIDS, TB, malaria and pandemic flu. There is ample opportunity and, arguably, a need to explore technology transfer for local production of a broader spectrum of products, including products for other therapeutic areas such as Type 1 diseases. For advanced local producers, the technologies available through existing transfer initiatives may offer little added value. Creative ways of inducing the transfer of more advanced technologies, such as for biotechnology products, should be explored. API production capacity in the developing world is largely concentrated in just two countries, India and China, which poses systemic risks to the stability of supply for countries whose local producers rely on Indian or Chinese APIs. Development banks should give serious consideration to investing in API production capacity in other countries, while keeping in mind the complexity and capital-intensive nature of such production.

• Intellectual property: There is renewed interest in the feasibility of pharmaceutical production in LDCs, perhaps due in part to the 2016 deadline for the granting and enforcement of pharmaceutical patents in LDC WTO Members. Given the long time horizons required to transfer technology and build local production capacity, the time period afforded by the 2016 deadline is likely to be too short. An additional extension of the deadline, perhaps to 2026 or later, may be required for LDC-based infant pharmaceutical industries to have the opportunity to develop and mature, particularly if they are striving to achieve international regulatory standards. In addition, it should be recognized that many developing countries will not be able to produce important medicines domestically, despite efforts to strengthen local production capacity. In light of concerns raised by several
developing countries regarding the practicability of the 30 August decision (see Section 1), WTO Members should ensure that trade rules do not hinder countries from importing sufficient quantities of medicines, including through the use of compulsory licensing.

- **Public policies for technology transfer**: Technology transfer may be very difficult to induce, particularly for products where technology holders and technology demandeurs are likely to be market competitors. In such cases, public or public-interest actors (such as foundations or NGOs) may need to play a stronger role in providing incentives for sharing, or alternative paths to, needed technologies. International actors can play an important role by connecting local producers to the relevant global networks, which may play a critical role in accessing the relevant technology in imperfect technology markets, and facilitating the development and further strengthening of such networks.

- **Capacity building**: There is widespread agreement that mid- to long-term investment in building the capacity of local manufacturers and national drug regulatory authorities is needed. For example, expanding opportunities for production staff to receive practical training would complement the theoretical training provided by academic institutions. This type of training is amenable to both north–south and south–south cooperation, since several developing countries are now home to advanced industries that could provide significant training opportunities to other developing country nationals. Finally, capacity building in how to negotiate effective technology transfer agreements may be useful, particularly for firms with limited experience in doing so. In addition to these specific areas, ongoing efforts in training national drug regulatory authorities and policy-makers on how to implement TRIPS in a manner that protects public health and expands the space for local production should be strongly supported and continued.

- **Tailored approach**: Local production capacities and relevant technology transfer needs vary widely across countries and product types, as do public health needs. International efforts to improve local production should be flexible enough that they allow tailoring initiatives to the specificities of each region, country or product.

- **Comprehensive targeted approach**: As noted above, this review of ongoing initiatives has found that most are specific to a particular product or disease area and that efforts are largely fragmented. There is a risk that ad hoc, piecemeal or small-scale initiatives will proliferate but collectively fail to capitalize on the potential to develop strong sustainable production capacity. Given the multifaceted nature of efforts required to promote local pharmaceutical production, a comprehensive approach may be needed to address simultaneously the many issues that require attention – for example, access to technology, strengthening absorptive capacity, access to capital, putting in place conducive policy measures, and measuring improved access to medicines. Concerned actors may consider jointly providing medium- to long-term comprehensive support to a few high-potential countries that have (or have strong potential to develop rapidly) the human resource base, infrastructure, regulatory capacity,
access to markets and strong governmental commitment required to develop a viable local pharmaceutical industry. However, currently lacking is an effective governance mechanism to ensure that the contributions of diverse actors interested in local production are channelled and targeted to have maximum impact. Such a mechanism would not necessarily imply formalized, centralized control, but rather institutional arrangements that would facilitate information sharing, collaboration and the identification of synergies to achieve jointly held goals.

- **Defining success in public health terms:** In a field in which public health and industrial considerations are deeply intertwined and where activities are currently quite fragmented, further debate among key stakeholders is urgently needed to clarify goals, define “successful” initiatives, and set broadly shared targets. Such goals would not necessarily have to be set at the global level as they were in the 1970s, but rather they could be agreed among the governments, multilateral agencies, firms, NGOs and other actors that have already expressed interest in or commitment to improving local production capacities. Such debates could take place at the global or regional level. Definitions of success should include public health goals. Whether and how local production improves access to medicines is likely to depend on the specificities of each context and may vary over time and by product. Local production can lead to improved access (defined as improved quality assurance, affordability, appropriateness of products or security of supply) – but it does not necessarily do so. Furthermore, some of these objectives may be more feasible to achieve than others in a given context, or there may be trade-offs between them. Stakeholders should engage in a deliberative process to define success in a given context, with considerations regarding access to medicines at the core.

- **Further research:** Further research is required, particularly in two areas: (i) measuring private-sector technology transfer flows; and (ii) understanding the conditions under which local production leads to improved access to medicines, and the pathways through which such improvements occur.

There is clearly strong interest in and demand from governments and local producers in the south for increased support, and particularly for technology transfer. Many technology holders – whether firms, experts or NGOs – have demonstrated a willingness to engage in technology transfer, albeit sometimes only under specific conditions. This enthusiasm offers an opportunity to launch more comprehensive, coherent and intensive efforts to encourage technology flows and upgrade local production capacity, with the ultimate aim of improving access to medicines in developing countries.
1. Introduction

The local production of drugs in developing countries has long been seen as a potential way to increase access to medicines and improve public health (1–4). At the same time, such production also held the possibility of supporting other policy goals such as economic development, industrialization and accelerated technological capacity. The potential importance of local production was recognized in the 2008 WHO Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA-PHI), which points to local production of pharmaceuticals as a key area for investment in Element 3 and focuses on health-related technology transfer in Element 4. The GSPA-PHI calls for investment, capacity building, identification of best practices, north–south and south–south cooperation, collaboration with the pharmaceutical industry and building up of absorptive capacity, among other recommendations (50).

Devising effective policies to implement the GSPA-PHI requires a solid understanding of the strengths and weaknesses of various approaches to supporting local production and relevant technology transfer from a public health perspective, as well as a clear picture of the scale and scope of ongoing initiatives.

Renewed interest in local production arises against the context of increased interconnectedness and vulnerability to global health threats, a changed global intellectual property regime, growing capacity in key developing countries to produce and develop medicines, globalization of the pharmaceutical supply chain, the expansion of developing country pharmaceutical markets, and increased attention to the challenge of ensuring equitable access to medicines. In particular, implementation of the World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) in all countries with well-developed pharmaceutical production capacity has raised a host of issues.

Furthermore, local production of pharmaceuticals is a relevant issue not only for the south but also for the north. With the globalization of trade, travel and pathogens, insufficient global production capacity for drugs can create shortages that affect all countries and reduce aggregate global capacity to respond to pressing health threats. Recent controversies around stockpiling of drugs and vaccines for pandemic flu (e.g. with respect to the H5N1 and H1N1 viruses) highlight the urgency of understanding current policies and practices around local production and technology transfer better (51).

There have been informative case studies of national experiences, theoretical modelling of the economic viability of local production (47), country-specific studies of the feasibility of local production (19, 22, 24, 29, 33), and broader international surveys of initiatives for the local production of drugs and vaccines (43, 52–58). There is also considerable ongoing activity, as described further in this report.

4 Much of the relevant academic literature provides case studies of individual technology transfer projects and offers lessons learned from specific initiatives. Relatively few studies draw generalizable conclusions from multiple cases. There is an important exception: Grace (43) compiled a broad range of examples of ongoing technology transfer initiatives and offered general conclusions regarding motivations for technology holders and technology recipients (this study is discussed and referred to in more detail in this report).
Yet, despite the importance of the topic, important questions remain unanswered. First, there is no clear consensus on if, how or under what conditions local production and technology transfer may improve access to drugs and vaccines in low- and middle-income countries. Improved access to medicines can be defined more specifically as improvements in:

- quality assurance;
- affordability;
- appropriateness (products adapted to local end-users’ needs);
- security of supply (availability in sufficient quantities, timely delivery, sustainable pricing).

Second, deeper understanding is necessary to build on cases in which local pharmaceutical production capacity has successfully been developed and has contributed to improved access to medicines. Specifically, it would be critical to understand the types of technology transfer policies that supported such development. Lessons on how to manage the tension that can easily arise between industrial and public health objectives are also needed.

Third, provisions that encourage or mandate technology transfer to developing countries are contained in many international agreements, particularly in the TRIPS Agreement and multilateral environmental agreements (61). Specifically, TRIPS Article 66.2 requires developed country Members to “provide incentives to enterprises and institutions in their territories for the purpose of promoting and encouraging technology transfer to least-developed country Members in order to enable them to create a sound and viable technological base”. However, analysts and developing country Members have raised concerns that implementation of Article 66.2 has fallen short, while the existing reporting system is insufficient to monitor compliance in a meaningful way (e.g. 62–65).

In general, information is insufficient regarding the extent to which support for local production and related technology transfer is taking place, which key lessons have been learned, and how these lessons can be applied to other contexts. This study aims to contribute to filling this knowledge gap by providing a broad overview of the landscape of ongoing and recent initiatives for local production and related technology transfer.

### 1.1 Purpose and scope

This landscaping study was conducted for the WHO Secretariat on Public Health, Innovation and Intellectual Property project “Improving access to medicines in developing countries through technology transfer related to medical products and local production”, which is funded by the European Commission. Research was primarily undertaken from September to December 2009, with updates incorporated in May 2010 and March 2011; therefore some

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5 According to WHO, “Quality assurance is a wide ranging concept covering all matters that individually or collectively influence the quality of a product. With regard to pharmaceuticals, quality assurance can be divided into four major areas: quality control, production, distribution, and inspections” (59).

6 Adapted from UNITAID Strategy 2010–2012 (60).
information may be out of date at the time of publication. The purpose of the study was to provide:

- a description of the landscape of local production of drugs, relevant investment promotion and related transfer of technology;
- an outline of current and recent initiatives (taking place within the past 5–10 years);
- an identification of gaps and preliminary assessment of the initiatives.

Overall, the study offers a descriptive overview of trends in local production of drugs and related technology transfer and the key issues that arise. (Ultimately it was decided not to include vaccines in this study, due to important differences between drugs and vaccines.) This landscaping exercise complements other arms of the research project: a set of in-depth case studies, an assessment of stakeholder views through interviews and a survey, and regional workshops of key stakeholders in sub-Saharan Africa, Latin America and Asia. It should be noted that this report is neither an exhaustive catalogue of all ongoing activities, nor an in-depth analysis of specific projects; there are important gaps in the coverage of the report due to data and feasibility constraints, as discussed further in Section 2. Rather, the intention is to provide some intuition on the scale, scope and key issues in the field as a whole, and to offer some guidance for designing the next stage of work. Therefore, the findings should be interpreted with an appropriate degree of caution.

1.2 Overview

Section 1.3 provides a brief historical background on local production and technology transfer, and outlines the key questions that arise in the literature. Section 2 describes the methodology used to collect data, including definitions for key terms. Section 3 provides a global overview of the current state of local pharmaceutical production. Section 4 describes initiatives for local production and relevant technology transfer (major initiatives are very briefly described here, with details available in Annex I). Section 5 discusses the key issues that arise in these initiatives. Section 6 offers conclusions and recommendations. The annexes provide further detail regarding initiatives for technology transfer, investment, voluntary licensing, and the list of people interviewed to supplement information found in written documents. References follow.

1.3 Background on local production and related technology transfer

Access to essential medicines is a critical component of meeting the human right to the highest attainable standard of health (66, 67). However, developing countries have long faced difficulties in ensuring such access for their populations. In 1975 the World Health Assembly asked WHO “to assist member states in selecting and procuring essential medicines, assuring good quality and reasonable cost”, which led to the publication 2 years later of the first WHO Essential Drugs List. The Essential Drugs List not only helped countries with the selection of medicines, but also drew their attention to the access issue. Although not its main purpose, simply by prioritizing certain medicines over others, the Essential Drugs List also helped to set
priorities for which medicines should be candidates for local production. Since the 1960s, international debates had also been taking place generally regarding technology transfer and how to remedy north–south disparities in levels of technological development, and regarding local production of pharmaceuticals in particular, as a means to achieve improved public health and industrial development.

These intersecting concerns on access to medicines, technology transfer and local production resulted in growing political attention to the possibility of international cooperation to enhance all three: access, technology and production. Local production of pharmaceuticals was identified as a top priority among developing countries at high-level meetings of the Group of 77 and the Non-Aligned Movement. In the mid-1970s, it was estimated that developing countries produced about 11% of world pharmaceutical output (by value). Determined to increase local production capacity in low- and middle-income countries, the United Nations Industrial Development Organization (UNIDO) Second General Conference in 1975 set the goal of achieving 25% of world pharmaceutical production in the developing world by 2000 (68). Reflecting the mix of health, trade and industrial concerns raised by the issue of local production, it became the subject of collaborative work between the United Nations Conference on Trade and Development (UNCTAD), UNIDO, WHO and the United Nations Development Programme (UNDP). However, by the early 1980s initiatives on local production and the push for greater technology transfer were losing steam. For example, multi-year negotiations over an International Code of Conduct for Technology Transfer, which developing countries had supported, collapsed in the early 1980s due to major disagreements between north and south (61).

Only a few years later, in 1986, the Uruguay Round of world trade negotiations was launched, one result of which was the 1994 WTO TRIPS Agreement. TRIPS mandated minimum standards of intellectual property protection in all WTO Members. Because TRIPS strengthened the property rights of technology holders, who were predominantly based in the north, it raised concerns among developing countries regarding access to technology in general, and access to medicines in particular (2, 69, 70). There is a rich literature on the impact of TRIPS on medicines prices and its possible effects on technology transfer (e.g. 62, 71–78); however, there is relatively less literature on the impact of TRIPS specifically on local production of medicines and related technology transfer, with the important exception of the Indian case (29, 36, 48, 76, 79–82).

In response to concerns that TRIPS would increase the price of medicines in many developing countries, WTO Members meeting at Doha adopted the 2001 Declaration on TRIPS and Public Health. The Doha Declaration clarified the right of countries to make use of legal safeguards such as compulsory licensing to protect public health and extended the deadline for least developed countries (LDCs) to grant or enforce pharmaceutical patents until at least 2016. The Declaration also recognized the problem that countries with insufficient local manufacturing capacity would have difficulty making use of compulsory licensing, as TRIPS Article 31(f) restricts exports of products
manufactured under compulsory licence. In 2003, WTO Members agreed on the “30 August Decision” to address this problem. However, developing country Members have raised concerns in the WTO TRIPS Council regarding the practicability of the 30 August decision, which has been used only once since its adoption in 2003 (64, 83). Ongoing concerns regarding the 30 August system may increase developing countries’ interest in strengthening local production capacity.

Indeed, with growing concerns regarding access to medicines over the past decade, the issue of local production is again attracting increased attention on the international agenda. The key questions that arise from the literature and policy debates fall into three broad categories: (i) Will local production provide the anticipated benefits for public health or economic development? (ii) If so, how can local production best be supported? (iii) What should international actors do? The specific questions that arise within these three categories are detailed in Box 1.

The list of questions in Box 1 is provided to highlight the complex, multifaceted nature of the issues surrounding local pharmaceutical production and relevant technology transfer. However, this study does not purport to answer all of these questions, many of which are broad, complex issues addressed elsewhere or requiring additional research (47, 84).
Box 1 *Key questions on local production and relevant technology transfer*

Benefits

Benefits from local pharmaceutical production are expected to accrue in two distinct domains: health and economic development:

- **Health:** Can local production improve access to medicines through improvements in:
  - quality assurance (e.g. reduced risk of substandard medicines);
  - affordability (e.g. lower prices);
  - appropriateness (e.g. products adapted to local end-users’ needs);
  - security of supply (e.g. availability in sufficient quantities, timely delivery, sustainable pricing)?

- **Economic development:** Can local production help meet other industrial or economic goals, particularly:
  - retaining greater proportion of donor funds in the domestic economy;
  - savings on foreign exchange or reduced currency-related risk;
  - building potential new export industries;
  - job creation, particularly skilled positions to retain highly educated nationals;
  - building technological capacity;
  - inducing increased technology transfer?

Supportive policies

If local production can indeed deliver at least some of these benefits, how can it best be supported? Within this area, issues can be divided into three subcategories: technological capacity, economic factors and legal frameworks:

- Technological capacity:
  - **Technology:** How can access to/transfer of appropriate technology be improved?
  - **Capacity:** How can capacity to absorb new knowledge and technologies be strengthened?

- Economic factors:
  - How can timely access to sufficient investment capital be secured?
  - What kinds of procurement policy will best support local industry?
  - What kinds of taxes, tariffs or trade policies should be implemented?
  - What types of subsidy, if any, should be provided?
  - How long should local industries be protected/granted preferential status through such policies?
  - More generally, how should trade-offs between price and local industrial development be balanced?
• What type of infrastructure is required?
• Legal frameworks:
  • What types of intellectual property policy should be adopted?
  • What regulatory requirements should apply? What regulatory capacity is required?

**Role of international actors**

Naturally following from the previous two categories is the question of what international actors – whether multilateral agencies, bilateral donors, foundations, investors or NGOs – should do to support local production and related technology transfer. Key questions include the following:

• In which countries or regions should local production be supported? What criteria should be used to decide, and how can they be measured?
• What incentives can international actors provide to induce technology transfer?
• What training or other activities can be provided to improve absorptive capacity? Regulatory capacity?
• What kinds of financing should be provided, to whom and upon which criteria?
• What types of policy analysis and advice – on procurement, taxes, intellectual property or regulatory standards – should international actors provide?
• What types of regional initiative (e.g. regulatory harmonization) should be facilitated, and how?
2. Methods

2.1 Definitions of “local production” and “technology transfer”

First, it is critical to clarify how this study interpreted and applied the terms “local production” and “technology transfer”, since there are no explicit, widely accepted definitions of either term. As Kaplan & Laing (84) point out, “local” can refer to a wide range of firm types, from small companies wholly owned by nationals of a developing country to subsidiaries of large multinational firms. For the purposes of this study, “local” is defined as any production of drugs taking place in low-, lower-middle- and upper-middle-income countries, regardless of the ownership structure. "Production" is defined as any stage of the drug manufacturing process from production of active pharmaceutical ingredients (APIs) to formulation or packaging.

The term “technology transfer” has been notoriously difficult to define precisely. The World Intellectual Property Organization (WIPO) provides a broad definition of technology transfer as “a series of processes for sharing ideas, knowledge, technology and skills with another individual or institution (e.g. a company, a university or a governmental body) and of acquisition by the other of such ideas, knowledge, technologies and skills” (5). In keeping with the focus of the study, the scope of examined initiatives was limited to those with the explicitly expressed intention to transfer technology or take other measures to improve capacity to produce drugs locally. Included in the study were direct transfer of “software” (e.g. information, data, know-how) and “hardware” (e.g. machinery) required for production, and education and training initiatives specifically targeted at drug or vaccine production. The study excluded research and development (R&D) activities that did not include end-product manufacturing (e.g. clinical trials, university-to-private sector licensing), and general education and training not directly linked to production (e.g. scholarships for higher education in the life sciences). Although these types of activity may certainly be considered as various

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7 There is some disagreement regarding the impact of ownership structure on technology transfer and local production capacity. Although this topic is beyond the scope of this study, a brief overview of the key arguments may be useful: On the one hand, multinational firms may be more likely to transfer technology to a wholly owned subsidiary or joint venture in a developing country rather than to a non-affiliated firm that is a potential competitor. Such an ownership structure is likely to afford the transferor with greater control over dissemination of valuable technology; local employees learn valuable technology and skills, and in the long run may leave the firm to start their own locally owned enterprises and thereby capture more of the benefits of the technology. On the other hand, policies such as transfer pricing (when a multinational charges above-market prices for inputs to subsidiaries) extract higher costs from the host country and reduce the potential benefits of local production; in some cases, locally owned firms may be more aligned with the interests of the developing country public and are therefore a preferable form of ownership (8). Such an ownership structure may also offer greater freedom to access technologies from multiple firms.

8 We exclude the very early phase of raw materials and intermediates production because of lack of available data and the difficulty of differentiating commerce in raw materials intended for pharmaceutical production from those intended for other end-products. An important exception is the case of Botanical Extracts EPZ Ltd (Kenya), which produces pharmaceutical-grade artemisinin; this case is discussed in further detail throughout this report and also summarized in Annex I. For a detailed description of the various phases of pharmaceutical production, see pages 3–7 of Kaplan & Laing (84).
means of enhancing absorptive capacity for technology transfer for local production, they were excluded in order to keep the focus on the initiatives most immediately relevant for production. Finally, voluntary licences that did not include a technology transfer for production component were considered in a separate category (see Box 2 for further discussion).

2.2 Definition of “developing” and other countries

This report uses interchangeably the terms “developing country” and “low- or middle-income” country (World Bank classification9) and “south”. The term “middle-income country” refers to both lower-middle- and upper-middle-income countries. Where relevant, the United Nations (UN) categorization of “least developed country” or a regional classification is specified. The report also uses interchangeably the terms “high-income country” and “north” but avoids use of the term “industrialized country” due to lack of specificity.

2.3 Data sources

There is no publicly available, uniform data source on initiatives for local production of drugs and relevant technology transfer, and the author is unaware of any such privately held data sources. Therefore, we searched a range of potential data sources from September to December 2009 in order to identify as many initiatives as possible. Consulted data sources include the following:

- academic literature: economic, public health, medical, social sciences;
- multilateral agency web sites, e.g. World Bank, WHO, Organisation for Economic Co-operation and Development (OECD), UNIDO, UNCTAD;
- bilateral donor web sites, e.g. Australian Government Overseas Aid Program (AusAID), Ministerie van Buitenlandse Zaken (The Netherlands International Cooperation Agency; BuZA), Canadian International Development Agency (CIDA), Danish International Development Agency (Danida), United Kingdom Department for International Development (DFID), European Commission, European Medicines Agency (EMEA), Gesellschaft für Technische Zusammenarbeit (GTZ), Japanese International Cooperation Agency (JICA), Norwegian Agency for Development Cooperation (Norad), Swedish International Development Cooperation Agency (SIDA), United States Agency for International Development (USAID), United States Food and Drug Administration (FDA);
- government web sites of developing countries with established pharmaceutical industries as potential transferors, e.g. Brazil, China, India, Thailand, South Africa (14, 82);
- pharmaceutical company and industry web sites, e.g. Top 20 multinational firms, International Federation of Pharmaceutical Manufacturers and Associations (IFPMA);

9 As defined by the World Bank. The World Bank’s country classifications are revised annually in July based on updated data. Economies are divided according to 2008 GNI per capita, calculated using the World Bank Atlas method. The groups are: low income, US$ 975 or less; lower-middle income, US$ 976–3855; upper-middle income, US$ 3856–11 905; and high income, US$ 11 906 or more.
• public–private product development partnerships, e.g. Drugs for Neglected Diseases Initiative (DNDi), Aeras, Medicines for Malaria Venture (MMV), Institute for OneWorld Health (IoWH);
• mainstream international and regional media through LexisNexis;
• reports of high-income WTO Members to the TRIPS Council on compliance with TRIPS Article 66.2;
• United States Department of Commerce statistics;
• selected interviews and personal referrals.

Not all data sources revealed substantive information on initiatives. Furthermore, in some cases, planned initiatives were announced publicly but no further information was found in the public domain several years later; such initiatives were excluded from the study because of lack of data, and it is possible they have not yet been implemented or were cancelled.

2.4 Strengths and weaknesses of the methodology

The strengths of the methodology are that the range of sources consulted is quite comprehensive and, through the searches of mainstream and regional media, it was possible to include recent publications. Weaknesses of the methodology are the lack of a uniform data source and a potential English-language bias in the sources consulted (searches included French, Spanish and Portuguese sources, but excluded other western and non-western languages such as Mandarin Chinese, Japanese and Thai). Therefore, it is impossible to guarantee that all existing initiatives have been uncovered by this research.

Furthermore, since the study examined “initiatives” – that is, organized efforts intended to support local production and relevant technology transfer – it did not capture the technology transfer that often occurs informally or unintentionally, for example through technology spillovers that occur as a side-effect of other projects, know-how gained through trade in goods and services, the migration of skilled personnel, or reverse engineering and imitation.

Perhaps most importantly, it was not possible to include initiatives for which there was little to no publicly available information, such as technology transactions largely taking place between private actors. This omission is significant because much technology transfer takes place through intra-firm transfers, contract manufacturing or private agreements between firms to buy or sell technology in an international marketplace.

Rather, many of the initiatives described in this study involve technology transfer that takes place outside standard market mechanisms, in which public actors or public interest play a significant role. This aspect of the methodology suggests that the study underreports on the transfer of technology to the more advanced pharmaceutical industries (e.g. those in India and China) where the market plays a stronger role in inducing technology transfer; in contrast, the study's coverage is probably more comprehensive of the transfer of technology to less advanced industries, for which third-party intervention may be
required to induce transfer (e.g. from advanced firms to LDCs (85). Finally, as the focus of the study was on north–south and south–south initiatives – that is, international initiatives – the study did not examine national government policies for local production that did not include an international actor.

The omission of these various potential modes of technology transfer may bias the conclusions of this report, and they should be interpreted with caution.

In light of the increasing level of interest in local production and relevant technology transfer, a unified publicly accessible data source of initiatives would be a valuable analytical resource and practical tool. Such a database could establish a more reliable baseline and measure progress in the development of local pharmaceutical production capacity and relevant technology transfer initiatives, aid the monitoring of compliance with obligations in international agreements (such as TRIPS) with respect to technology transfer, and facilitate collaboration between potential transferors and transferees of technology in a field that is currently quite fragmented. It could also enable more evidence-based analysis of policies intended to support local production and technology transfer – a subject area where further data are sorely needed (84). Precedent for establishing such a centralized data source exists in the Initiative for Public–Private Partnerships for Health (which is unfortunately no longer operating) and the Global Funding of Innovation for Neglected Diseases (G-FINDER) project, which tracks global investment in neglected disease R&D based on a survey of over 200 organizations worldwide (86).

3. Overview of local production of drugs in low- and middle-income countries

In the 1970s, pharmaceutical production was dominated by high-income countries, particularly the United States, Japan and Germany. Among the developing countries, a handful of the more advanced economies supplied two-thirds of (developing country) production: Argentina, Brazil, Egypt, India, Mexico and the Republic of Korea (8). In terms of the north–south distribution of production capacity and share of world markets, the situation remains largely unchanged, as reflected in a 1992 study (6) and an update of that study in 2004 (87): according to the 2004 WHO World Medicines Situation report,¹⁰ pharmaceutical production remains concentrated in the high-income countries. In 1985, these countries accounted for 89.1% of world pharmaceutical production (by value), a share that increased to 90.5% in 1990 and 92.9% in 1999. The five countries that are home to the large multinational pharmaceutical companies – the United States, the United Kingdom, France, Germany and Japan – accounted for 67% of pharmaceutical production (by value) in 1999, followed closely by Switzerland and Italy.

¹⁰ At the time of writing, it is likely that the 2004 WHO World Medicines Situation report is out of date; however, the report remains the most recent comprehensive assessment of global production capacity and is therefore referenced here.
Based on a typology developed by Ballance et al. (6), ten countries11 were considered to have a “sophisticated industry” with “significant research” – none of which was a developing country. In addition, 16 countries were classified as having “innovative capability” – that is, “at least one new molecular entity was discovered and marketed by these countries from 1961–1990”. Of these, six are low- or middle-income countries: Argentina (7, 8), China, India, Mexico (8–10), the Russian Federation and the former state union of Serbia and Montenegro.12 A further 97 countries had some pharmaceutical production capacity, of which 84 produced only finished products from imported active ingredients, and 13 produced both active ingredients and finished products. Of these 13, 9 were low- or middle-income: Bolivia, Brazil (11–14), Bulgaria, Cuba (15), Egypt (16, 17), Indonesia, Poland, Romania and Turkey. An additional 42 countries were considered to have no pharmaceutical industry at all, and this group was comprised mostly of developing countries. In addition to the countries listed in the World Medicines Situation report, the pharmaceutical industries of the following countries have been noted in the literature as having substantial existing or potential capacity: Bangladesh (18–22), Ethiopia (23), Ghana (24), Iran (25), Jordan (26), Kenya (27), Nigeria (28), Rwanda (29), South Africa (30–32), the United Republic of Tanzania (33), Thailand (34–36), Tunisia (37–40), Uganda (41) and Viet Nam (42).

In summary, most low- and middle-income countries either have no pharmaceutical industry at all or are able to carry out only the relatively late-stage steps of formulation and packaging (see Figure 1). A small number of countries produce a range of APIs, and an even smaller number conduct significant R&D.

Of the developing countries listed above, India and China have by far the most advanced industries, in terms of both scale and level of technical sophistication. Not surprisingly, these two countries have attracted the most scholarly analysis and commercial interest (e.g. 14, 52, 54, 70, 76, 80–81, 88–96).

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11 The United States, the United Kingdom, France, Germany, Japan, Switzerland, Italy, Belgium, the Netherlands and Sweden.

12 The 2004 World Medicines Situation report based its assessment of this category on data up until 1990, when Yugoslavia was a state.
Nevertheless, in comparison with the situation in the 1970s or 1990s, recent years have witnessed several notable new trends in local production. First, several countries that currently do not have strong API production capacity are interested in developing it, recognizing that this value-added step of the production process may be critical to enable firms to compete at an international level. For example, the Government of Bangladesh has approved the creation of an “API Park” to support its domestic industry, which currently primarily carries out formulation and packaging of imported APIs. Industry sources in Tunisia, South Africa, Argentina and Brazil also mentioned interest in upgrading their API production capacity. Second, some of the larger generics firms are developing into multinationals, with production sites in multiple countries. For example, India-based Ranbaxy has production sites in China, Ireland, India, Malaysia, Nigeria, Viet Nam and the United States. Third, the more advanced generics firms are spending increasing and substantial percentages of revenue on R&D for new formulations, new drug-delivery systems and new chemical entities. Finally, northern-based multinationals are acquiring or partnering with southern-based firms; in recent years, for example, Japan’s Daiichi-Sankyo has acquired India’s Ranbaxy, United States-based generics giant Mylan now owns India’s Matrix Laboratories, and United Kingdom-based GlaxoSmithKline (GSK) has taken a 19% ownership stake in South Africa’s Aspen. Thus, in some cases, “local producers” may be multinational and technically sophisticated and carry out significant amounts of research in addition to production.
4. Findings on initiatives for local production and technology transfer

4.1 Overview

Supporting the development of local pharmaceutical production capacity is a complex endeavour involving many types of activity. The initiatives identified by this study undertook a broad range of activities and varied widely along a number of dimensions, including the following:

- Type of technology transferors/transferees: private-to-private actors, public-to-private, private-to-public and public-to-public (note “public” here denotes a government or non-profit-making entity).
- Scale of projects: from individual consultants, to small NGOs, to small/medium-sized enterprises, to large multinational enterprises.
- Goals and interests of transferors and transferees: see Sections 5.1 and 5.2.
- Complexity of transferred technology and technical capacities of transferees: from packaging to API production.
- Technical value of the transfer: from replicating existing knowledge to providing valuable new technology.
- Economic value of transfer: from virtually nonexistent product markets to substantial market size.
- Scale and duration of transfer: from 3 weeks to 10 years.

To gain a clearer impression of the landscape of recent and ongoing activities, this study categorized initiatives into four types:

- transfer of technology for production \((n=30)\);
- investment initiatives \((n=27)\);
- voluntary licensing initiatives \((n=14)\);
- facilitating production, including support to national drug regulatory authorities, industrial policy advice, intellectual property advice, networking and strategy planning (see Sections 4.8 and 4.9).

Some initiatives carried out more than one type of activity and therefore may be counted more than once. The initiatives are listed with available details in Annexes I–III and summarized in Table 3. The quantification of initiatives should be interpreted with caution, however, as the initiatives varied widely in the number of drugs or companies covered, duration, scale, monetary value and other salient characteristics. For example, if Firm A transferred the same technology to five recipient firms under the same conditions, this was counted as one initiative; if, however, Firm A offered one type of technology to Firm B and another type of technology to Firm C or on significantly different terms, this was counted as two initiatives. Because of the conceptual challenges of quantifying initiatives, Table 3 provides alternative ways of quantifying ongoing activities, for example by technology transferor, transferee, facilitators and recipient countries. Finally, these figures should be interpreted with caution, as it was not to include all relevant activities worldwide due to lack of public information, and many initiatives are therefore not included here (see Section 2 for further discussion).
### Table 3 Summary of initiatives for local production and technology transfer

<table>
<thead>
<tr>
<th>Type</th>
<th>Quantity</th>
<th>Entities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Private-sector technology transferors</td>
<td>12</td>
<td>Berlin Pharmaceuticals (Thailand), Bristol-Myers Squibb (United States), Boehringer Ingelheim (Germany), Cadila (India), Cipla (India), Eli Lilly (United States), Gilead (USA), GlaxoSmithKline (United Kingdom), Jin Wan &amp; China Associates (China), Merck (United States), Roche (Switzerland), Tibotec (Belgium/United States)</td>
</tr>
<tr>
<td>Private-sector technology transferees (Artepal participant firms excluded for reasons of confidentiality)</td>
<td>33</td>
<td>JB Chemicals (India), Advanced Bio Extracts (Kenya), Alkem (India), Aspen Pharmacare (South Africa), Aurobindo (India), Baz International (Afghanistan), Bethlehem (Ethiopia), Beximco (Bangladesh), Cadila Ethiopia, Cosmos (Kenya), East African Pharmaceuticals (Ethiopia), Emcure (India), FDC (India), Gland Pharma (India), Hetero (India), Hisun (China), Gabon producer, Jordanian Association of Pharmaceutical Manufacturers (Jordan), Matrix (India), Medchem (India), Mozambique state firm, Pharmakina (Democratic Republic of the Congo), Quality Chemicals (Uganda), Radiant (Bangladesh), Ranbaxy (India), Shanghai Desano (China), Shasun (India), SIA International/Biocom (Russia), Sino-Ethiop (Ethiopia), Strides Arcolab (India), Tanzanian Pharmaceutical Industries (United Republic of Tanzania), Universal (Kenya), Usine Malienne de Produits Pharmaceutiques (Mali)</td>
</tr>
<tr>
<td>Public-sector direct supporters (transfer technology, train, or finance local production)</td>
<td>7</td>
<td>BMZ/GTZ (Germany), Oswaldo Cruz Foundation (FIOCRUZ, Brazil), Harbin Institute of Technology (China), IFC, Thai Ministry of Foreign Affairs, UNIDO, USAID, WHO</td>
</tr>
<tr>
<td>Public-sector Facilitators</td>
<td>10</td>
<td>BMZ/GTZ (Germany), DFID (UK), EU, UNCTAD, UNDP, UNICEF, UNIDO, World Bank, WHO</td>
</tr>
<tr>
<td>Public-sector technology transferees</td>
<td>8</td>
<td>Centre Hospitalier Aristide le Dantec (Senegal), Centre Hospitalier National Pediatrique, Charles de Gaulle (Burkina Faso), Government of Brazil/Lafepe, Government of Brazil (FIOCRUZ), Institut National de la Sante Public (Burundi), Muhimbili University of Health and Allied Sciences (United Republic of Tanzania), MUSALAC (Burundi), Royal Victoria Teaching Hospital (Gambia)</td>
</tr>
<tr>
<td>NGO direct supporters (transfer technology, train, or finance local production)</td>
<td>8</td>
<td>Action medeor, Business Humanitarian Forum, Cordaid, DNDi, IoWH, Krisana Kraisintu, OTECI, Technoserve</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Type</th>
<th>Quantity</th>
<th>Entities</th>
</tr>
</thead>
<tbody>
<tr>
<td>NGO facilitators</td>
<td>3</td>
<td>ICTSD, InWent, MSF</td>
</tr>
<tr>
<td>Specific diseases (excludes initiatives for general drug production)</td>
<td>6</td>
<td>Chagas disease, HIV/AIDS, malaria, multidrug-resistant TB, pandemic flu, visceral leishmaniasis</td>
</tr>
<tr>
<td>Specific drugs (excludes initiatives targeting general essential drugs production)</td>
<td>22</td>
<td>Artesunate, artesunate/amodiaquine FDC, atazanavir, benznidazole, capreomycin, cycloserine, darunavir, didanosine, efavirenz, lamivudine, lamivudine/zidovudine FDC, nelfinavir, nevirapine, oseltamivir, paramomycin IM, saquinavir, stavudine, stavudine/lamivudine/nevirapine FDC, tenofovir, tenofovir/emtricitabine FDC, tenofovir/lamivudine/efavirenz FDC, zidovudine</td>
</tr>
<tr>
<td>Private-sector investment recipients</td>
<td>26</td>
<td>ABOLOmed (Russian Federation), Advanced Bio Extracts (Kenya), Aldaph SPA (Algeria), Alkaloid A.D. Skopje (former Yugoslav Republic of Macedonia), APIDC Biotechnology Venture Fund (India), BioVeda China Fund LP (China), Bosnalijek d.d. Sarajevo (Bosnia and Herzegovina), Botanical Extracts EPZ Ltd (Kenya), Core Pharmasons (Uzbekistan), Corporacion Drokasa S.A. (Peru), Dabur Pharma (India), Dar al Shifa Pharmaceuticals (West Bank and Gaza Strip), Dishman (India), Distribuidora Cesar Guerero (Nicaragua), Granules India Limited (India), Hikal Limited (India), Hikma Investment Company (Jordan), Investment Fund for Health in Africa, Kampala Pharmaceutical Industries (Uganda), Orchid Pharmaceuticals (India), Productos Gutis (Costa Rica), Sekem Holdings (Egypt), Shanghai Fosun (China), SRF Ltd (India), Tecnoquimicas (Colombia)</td>
</tr>
<tr>
<td>Countries (technology transfer or investment recipients)</td>
<td>40 (AFR, 20; SEAR 5; WPR 1; AMR 5; EMR 5; EUR 4)¹³</td>
<td>Afghanistan, Algeria, Bangladesh, Benin, Bosnia and Herzegovina, Brazil, Burkina Faso, Burundi, Cambodia, China, Colombia, Costa Rica, Democratic Republic of the Congo, Egypt, Eritrea, Ethiopia, Gabon, Gambia, Ghana, India, Jordan, Kenya, former Yugoslav Republic of Macedonia, Madagascar, Mali, Morocco, Mozambique, Nepal, Nicaragua, Peru, Russian Federation, Senegal, South Africa, United Republic of Tanzania, Uganda, Uzbekistan, Vietnam, West Bank and Gaza Strip, Zambia, Zimbabwe</td>
</tr>
</tbody>
</table>

FDC, fixed-dose combination; IM, intramuscular.

Given the variance among the initiatives identified, generalizations should be taken with caution. The following sections very briefly outline the major initiatives, further details of which can be found in Annex I.

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¹³ The six WHO regions are the African Region (AFR), the Region of the Americas (AMR), the South-East Asia Region (SEAR), the European Region (EUR), the Eastern Mediterranean Region (EMR) and the Western Pacific Region (WPR).
4.2 Therapeutic areas: drugs

The study scope included initiatives encompassing all drugs and all diseases. However, the initiatives it identified generally focused on newer drugs (with a few exceptions) and also focused primarily on the four diseases that have received the most international attention and funding in recent years – HIV/AIDS, TB, malaria and pandemic flu.

4.2.1 HIV/AIDS

For HIV/AIDS, initiatives targeted first- and second-line antiretrovirals (ARVs) and included voluntary licences from patent holders with technology transfer for production of single-dose and fixed-dose combinations (FDCs) for adults (for example, Gilead for emtricitabine, tenofovir and related FDCs with technology transfer; and Roche for nelfinavir and saquinavir with technology transfer (45); see Box 2 for further discussion of voluntary licences with and without technology transfer for production). Dr Krisana Kraisintu, formerly head of R&D of the Government Pharmaceutical Organization, Thailand, has also transferred technology to formulate the fixed-dose combination of stavudine/lamivudine/nevirapine to two firms in the United Republic of Tanzania and the Democratic Republic of the Congo. In addition, German NGO action medeor has been working in a project cofinanced by Gesellschaft für Technische Zusammenarbeit (GTZ) and located at Muhimbili University of Health and Allied Sciences (MUHA), United Republic of Tanzania, to develop a once-daily fixed-dose combination formulation of tenofovir, lamivudine and efavirenz; after this has been fully developed, the technology is to be transferred to interested local manufacturers free of charge. In addition, Indian pharmaceutical company Cipla has transferred technology to Shanghai Desano (China) and Quality Chemicals (Uganda) for the production of a range of ARVs (98). Finally, the Government of Brazil is cofinancing and transferring technology through the Oswaldo Cruz Foundation (FIOCRUZ) to the Government of Mozambique to construct a new pharmaceutical manufacturing plant with an initial focus on ARVs (99).

4.2.2 Tuberculosis

For TB, the major initiative is Eli Lilly’s project to transfer technology for the production of two drugs to treat multidrug-resistant TB, capreomycin and cycloserine.14 The technology transfer project is one part of a broader multidrug-resistant TB initiative that Lilly launched in 2002, after Médecins Sans Frontières (MSF) raised concerns about access to the drugs in 2001.15 Lilly has transferred the technology to produce capreomycin and cycloserine to seven recipients, including four firms based in low- or middle-income countries: Shasun (India), Hisun (China), Aspen (South Africa), BioCom (Russian

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14 Grace (43) identified a project in the late 1980s in which a Japanese firm transferred technology for the production of a first-line TB drug to a state-owned producer in Nepal. However, as it seems production is not ongoing and the initiative ended some time ago, this case is not discussed further here.

15 Since then, Lilly has provided capreomycin and cycloserine at concessionary prices to the Green Light Committee of WHO.
Box 2 Voluntary licensing

Voluntary licensing has primarily been used in the area of ARVs for HIV/AIDS and has been increasingly adopted over the past 5–7 years (100). Voluntary licensing initiatives are considered in a separate category in this report, since such licences provide the legal right to produce a patented drug locally but do not necessarily support a producer’s capacity to do so. In other words, the mere right to produce is not considered to constitute a local production or technology transfer initiative. Some voluntary licence agreements do include technology transfer components, and these have been included in this study as technology transfer initiatives (see Annex I); such licences include those for tenofovir and emtricitabine (Gilead), saquinavir and nelfinavir (Roche), atazanavir (Bristol-Myers Squibb) and darunavir (packaging only, Tibotec). In contrast, licences for abacavir, lamivudine and zidovudine (GSK), efavirenz (Merck), nevirapine (Boehringer Ingelheim) and stavudine and didanosine (Bristol-Myers Squibb) did not appear to include an explicit technology transfer component. (Voluntary licence agreements are generally confidential, but the most salient terms and conditions may be announced publicly or reported by the media.)

Although voluntary licences may broaden the legal space for local firms to produce a patented product, a number of critiques have also been raised regarding the terms and conditions of some licences, particularly restrictions on their geographical scope that constrain economies of scale, high royalty rates, and restrictions on sourcing API (100). In cases where a patent application is pending for a product (i.e. where a patent has not yet been granted), a licence may even restrict the legal space for production if the terms block the licensee from challenging the grant of the patent (100). All voluntary licences identified by this study, whether or not they include an explicit technology transfer component, are listed in Annex IV.

Federation). The technology to produce the API for capreomycin has been transferred to Hisun, and for cycloserine to Shasun; all other transfers are for formulation. Lilly’s objective is that its technology transferees will take over supplying the global market once they have obtained WHO prequalification, which has been achieved for cycloserine and is in process for capreomycin.
4.2.3 Malaria

For malaria, there have been several different types of project promoting local production of the newer artemisinin derivatives. One of the largest is Kenya-based Botanical Extracts EPZ Ltd, a holding company that owns Advanced Bio Extracts and three artemisinin producers in Kenya, the United Republic of Tanzania and Uganda. Botanical Extracts contracts with over 5000 smallholder farmers in east Africa to grow *Artemisia annua* and processes the raw material into pharmaceutical-grade artemisinin. Botanical Extracts faced a difficult period during 2004–2006 when global artemisinin prices were particularly volatile and demand forecasts were proven inaccurate; however, by 2007 Botanical Extracts had secured financing and opened a new processing plant in the export zone at Athi River, Kenya, which produced artemisinin raw material for 22 million artemisinin-based combination therapies that year. Botanical Extracts has helped to establish east Africa as an important additional supplier to producers in China and Viet Nam (101).

Another significant initiative is the Artepal project, which was funded by the European Commission and supported by the Office Technique d'Études et de Coopération Internationale (OTECI), a French association of retired executives from the pharmaceutical and other industries. Artepal focused on transferring technology for the more efficient cultivation of *Artemisia annua* and subsequent extraction of artemisinin. Working with firms in nine countries in sub-Saharan Africa, five countries in Asia and two countries in Europe, Artepal provided support for the production of raw materials through APIs and recently began working on formulation.

The German NGO action medeor has also partnered with Dr Kraisintu to provide technology transfer to Tanzania Pharmaceutical Industries for the production of artesunate. Partnering with a research laboratory at Graz University, Austria, action medeor has also developed a less environmentally harmful method of producing artesunate, which it plans to test and potentially transfer to interested recipient firms. Furthermore, in her personal capacity and sometimes with the support of the Thai Ministry of Foreign Affairs, Dr Kraisintu has carried out numerous technology transfer projects for the small-scale production of artemisinin-based drugs in west, central and east Africa.

Finally, DNDi has developed two new ACT FDCs which are both produced in the south: artesunate and mefloquine was jointly developed with Brazil’s FIOCRUZ and is being produced by Farmanguinhos, with an agreement in 2008 to transfer technology to Cipla to supply the Asian market (102). Artesunate and amodiaquine was jointly developed with sanofi-aventis in 2007 and is being produced at a Sanofi manufacturing plant in Morocco (103).

4.2.4 Pandemic flu

In response to concerns regarding the H5N1 and H1N1 flu viruses, a number of countries announced plans to produce the antiviral drug oseltamivir locally, either in territories where patents on the drug did not exist or where governments had granted compulsory licences or issued government use...
orders. In 2005, the patent holder Roche granted a voluntary licence to Indian firm Hetero to produce the drug for government stockpiles in India and Africa; it has since also granted licences to Shanghai Pharmaceuticals and HEC in China and Aspen Pharmacare in South Africa (104).

4.2.5 Other diseases

The study also identified two further initiatives for “neglected diseases”: IoWH, a public–private product development partnership, worked with India-based Gland Pharma to produce injectable paramomycin for the treatment of visceral leishmaniasis. In addition, Roche transferred the technology to produce benznidazole to the government of Brazil for the treatment of Chagas disease; benznidazole is currently being produced by the Pharmaceutical Laboratory of Pernambuco (Lafepe), including a new paediatric formulation developed in partnership with DNDi (105).

4.3 Therapeutic areas not covered

This landscaping exercise uncovered initiatives for drugs that span a range of therapeutic areas. However, the findings also point to a notable absence of initiatives in certain areas; for example, there were almost no initiatives targeting products for type 1 diseases,16 such as diabetes and mental illnesses, except in the context of joint ventures or subsidiaries of the large multinational firms. In addition, we did not identify any initiatives for the production of biotechnology drugs (excluding vaccines). As one source from the Indian pharmaceutical industry commented, many Indian firms were already quite adept at producing small molecules but needed and would benefit from technology transfer for complex new biotechnology products. Finally, we found almost no initiatives focusing on traditional medicines (excluding artemisinin derivatives). However, due to the general unavailability of public information on private-to-private firm initiatives, it is not possible to conclude that no transfer is taking place in other therapeutic areas; for example, it is possible that significant technology transfer for production of type 1 disease-related drugs is taking place but did not appear in the information available to the author.

4.4 Who transfers technology?

As noted in Section 4.1, there is a wide range of actors transferring technology to local producers. At one end of the scale are Dr Kraisintu’s initiatives, which have been funded variously by action medeor, the Thai Ministry of Foreign Affairs, several Thai embassies in Africa, and – when other funding is unavailable – from her personal finances. At the other end of the scale are multiyear initiatives of large multinational pharmaceutical companies, such as the Lilly multidrug-resistant TB initiative or joint ventures. In between are a range of mid-size actors, including public actors such as the United States

16 Type 1 diseases are incident in both rich and poor countries, with large numbers of vulnerable populations in each. Type II diseases are incident in both rich and poor countries, but with a substantial proportion of the cases in poor countries. Type III diseases are those that are overwhelmingly or exclusively incident in developing countries.
National Institutes of Health (NIH) (106), universities; public–private product development partnerships such as DNDi, and NGOs such as action medeor and OTECI.

Of the 30 technology transfer initiatives identified, 20 were north–south transfers and 10 were south–south transfers.

4.5 Who receives technology?

The scale and level of technical sophistication of transferees also varies widely. Transferees include large firms with annual revenues hovering near US$ 1 billion, such as Cipla and Ranbaxy, and include all stages of production from API to finished products. India-based manufacturers were by far the most frequent participants of technology transfer initiatives, followed by China and Brazil. Technology was also transferred to less advanced generics firms in smaller or less-developed countries, with a wide distribution across sub-Saharan Africa, albeit with some concentration in east Africa (Kenya, United Republic of Tanzania, Uganda), particularly for antimalarials. Transfers to African firms usually involved formulation, packaging, GMP training and documentation support, and seldom included API production.

Joint ventures or subsidiaries of multinationals were also presumably frequent recipients of technology transfer for a broad range of products, as were contract manufacturers. GSK reports that it has 46 manufacturing sites outside of Europe and North America: for the domestic market (Algeria, Bangladesh, Hungary, Morocco, Nigeria, Sri Lanka and Turkey), for domestic and export markets (Argentina, Brazil, Costa Rica, Egypt, India, Indonesia, Kenya, Malaysia, Mexico, Pakistan, Panama, the Philippines and South Africa) and joint ventures (two in Tianjin, China) (44). However, a search through the web sites of the 20 largest pharmaceutical companies (ranked by 2008 revenue) uncovered only scarce information on production locations or contract manufacturing (with the exception of GSK). From the available information, it appears that subsidiaries of multinationals for production (rather than for sales or distribution) are concentrated in India and China, with a few sites in Mexico (43–45).

Finally, universities and research institutes with a focus on pharmaceutical sciences have been recipients of technology transfer for education, training and small-scale laboratory production of drugs.

4.6 Who facilitates local production and technology transfer?

In addition to technology transferors and transferees, local production initiatives often involve third parties, or “facilitators”, who may play a variety of roles, including research, advocacy, coordination, funding, connecting or screening potential partners, brokering agreements, increasing absorptive capacity, advising, providing additional incentives and creating a conducive policy environment.
Among the countries receiving technology, the government actors most often involved were the ministries of health, the national drug regulatory authority, trade, industry, science and technology, and education – although in some cases no government actor was involved at all. Government actors played a wide range of roles. For example, in Bangladesh and Uganda, the government invested in the development of infrastructure and facilities to upgrade local production (19, 98). In Ethiopia, the government provided up to 70% of the investment capital at a below-market interest rate with an extended repayment period (through its development bank), a 20% margin advantage for local producers competing with imports for government tenders, and a 30% advance payment for government purchases (23). In other cases, initiatives were arranged between transferors, transferees and third parties without any significant government involvement.

Finally, some interviewees noted that governments could hamper technology transfer initiatives by imposing undue delays on approving projects, processing drug registration applications or taxing imports of inputs (e.g. APIs or machinery).

The specific facilitating contributions of multilateral organizations and donor governments are detailed in the Section 4.7.

### 4.7 Multilateral organizations and donor governments

Since the 1970s, multilateral organizations and donor governments have played various facilitating roles in supporting the development of local pharmaceutical production capacity and relevant technology transfer. Recent efforts from the past 5–10 years are described below.

#### 4.7.1 Coordination

The Interagency Pharmaceutical Coordination Group (IPC) was established in 1996 and convenes senior officials in the field of pharmaceuticals from WHO, the World Bank, UNAIDS (included in 2001), UNFPA and UNICEF to coordinate technical and policy advice to countries. According to WHO, “these meetings, and many contacts in between, have lead to a much better exchange of information between the organizations, to more consistency of the technical advice given, and to the development of several joint policy documents and guidelines” (46). There is an IPC subgroup on Local Pharmaceutical Production, which has also involved UNIDO, UNCTAD, UNDP and other multilateral organizations relevant to local production and technology transfer such as the African Development Bank and the Global Fund to Fight AIDS, TB and Malaria (GFATM).

#### 4.7.2 Multilateral organizations

Three multilateral organizations provide direct support for local production: WHO, UNIDO and the International Finance Corporation (IFC) of the World Bank Group. Direct support is defined here as those activities aimed specifically at

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17 This section draws heavily from the results of a survey conducted by the IPC, as summarized by Juergen Reinhardt of UNIDO.
local producers, including technology transfer, training (e.g. quality assurance improvement) and financing.

UNIDO’s work to support local production is managed by its Industrial Policy and Private Sector Development Branch. Since 2006, UNIDO has run a project jointly funded by Germany to “support the establishment and/or expansion and upgrading of SMEs [small and medium enterprises] in 3–4 (L)DCs for the local manufacturing of essential generic drugs,” taking advantage of the extension until at least 2016 for pharmaceutical patent enforcement in LDCs. The project focuses on HIV/AIDS, malaria, TB and neglected tropical diseases. UNIDO carries out a range of interventions, including policy advice on how to improve the business environment for production, facilitating public–private dialogue to formulate pharmaceutical sector strategies, and raising awareness and supporting networking through national or regional workshops (107). The project also supports the development of pharmaceutical manufacturers associations such as the Southern African Generics Medicines Association (SAGMA), strengthening of national drug regulatory authorities, and regional harmonization efforts to reduce barriers to trade. Finally, at the individual firm level, UNIDO has provided technical and managerial assistance on business plans, plant assessments and achieving international GMP standards, and assisted firms in identifying potential partners for access to capital or technology.

Through its Prequalification Programme, WHO supports local producers, clinical research organizations, national drug regulatory authorities and quality control laboratories in achieving the production of quality-assured medicines. This support is provided through trainings (e.g. on GMP, prequalification requirements and bioequivalence), technical assistance (e.g. provision of expert consultants on GMP, good clinical practice (GCP) or good laboratory practice (GLP), and preparation of regulatory dossiers) and the provision of information and standards. The Programme also trains national drug regulatory authority staff by inviting them to attend GMP audits in their respective countries and to participate in the assessment of dossiers.18 In addition, the multiyear intergovernmental negotiations that led to the adoption of the GSPA-PHI by the 2008 World Health Assembly (Resolution 61.21) underscore the important institutional role of WHO in securing a place for local production and technology transfer on the international agenda.

IFC provides financing through loans, equity investments or guarantees for viable pharmaceutical production enterprises. Such financing projects may incorporate elements of technology transfer, but IFC does not have any special programmes in place to encourage technology transfer relevant to local pharmaceutical industry development. From 1997 to 2009, IFC provided financing to 26 projects supporting local pharmaceutical production in low- or middle-income countries (see Annex III). During this period, IFC committed up to approximately US$ 280 million. Of these 26 investments, 15 (58%) went to lower-middle-income countries (of which 9 investments were in India), 8 (31%) went to upper-middle-income countries, and only 3 (12%) investments went to low-income countries.

18 I thank Elodie Jambert for bringing this point to my attention.
Seven multilateral organizations provide indirect support to local production efforts, such as policy advice, capacity building, institutional strengthening and analysis: UNIDO, UNCTAD, World Bank, UNDP, WHO, UNICEF and the African Union.

In 2005, UNCTAD’s Commission on Investment, Technology and Related Financial Issues recommended that “UNCTAD should ... assess ways in which developing countries can develop their domestic productive capability in the supply of essential drugs in cooperation with pharmaceutical companies” (Paragraph 9(c)) (108). UNCTAD is developing a “Stakeholders’ reference guide to IP and related policies”, which is intended to “provide concise and practical information on ways to promote local pharmaceutical production and improve access to medicines through a variety of policy tools, focusing on the flexibilities provided under TRIPS, and the interfaces between IP, trade and investment, drugs regulation and procurement strategies” (109). UNCTAD and UNIDO have both carried out intellectual property and pharmaceutical sector studies in various countries, primarily in the African (AFR) and South-East Asia Region (SEAR) regions.

UNCTAD and WHO are also collaborating on the European Commission-funded project, of which this study is one part (see Section 1). WHO is also supporting regulatory harmonization efforts in the Southern African Development Community (SADC) and the East African Community (EAC), and similar efforts are also under way within the Economic Community of West African States (ECOWAS) (24).

The World Bank has published studies of local production that have contributed important data and analyses to ongoing debates (in particular, see 21, 84, 110, 111).

UNDP and UNCTAD provide technical advice to countries on TRIPS and intellectual property policies. UNDP is also undertaking analytical work on local production with an emphasis on south–south cooperation, including a recently completed study on Brazil (“Technical, economic and legal assessment of the Brazilian antiretroviral production capacity,” jointly with the Ministry of Health/National AIDS Programme and UNAIDS Brazil), a study on the Indian pharmaceutical industry and the impact of recently adopted laws (forthcoming), and a planned study on the South African pharmaceutical industry.19

UNICEF carries out GMP audits of local producers for potential procurement purposes, which can help to upgrade the skills of manufacturers.

In addition, in 2007 the African Union agreed upon a Pharmaceutical Manufacturing Plan for Africa, placing local production and technology transfer firmly on the regional agenda (112).

19 Tenu Avafia, United Nations Development Programme, personal communication, 8 March 2010.
Finally, multilateral organizations influence the environment for local production as major purchasers of medicines in developing countries, by setting norms and standards, and through their procurement policies and policy advice. The most relevant are WHO (setting norms and standards such as GMP, GLP and GDP; and assessing the quality, safety and efficacy of drugs through GMP audits and dossier assessment), GFATM, UNICEF, UNFPA, World Bank and UNDP.

4.7.3 Donor governments

Several governments from north and south have facilitated local production efforts, either directly through technology transfer, training and funding, or indirectly through analysis and policy advice.

Brazil

The Government of Brazil, through FIOCRUZ is transferring technology for the production of ARVs and other drugs (antibiotics, antimalarials, anti-TB drugs) to a new pharmaceutical production facility in Mozambique as part of a bilateral agreement. The first phase is expected to cost US$ 9 million, of which the Mozambican Government is contributing US$ 2 million and the Brazilian Government the remaining US$ 7 million (99). As noted above, FIOCRUZ is also transferring technology for the production of the fixed-dose combination of the antimalarial artesunate and mefloquine, which was jointly developed with DNDi, to the Indian generic producer Cipla (102).

European Union

The EU has supported local production and relevant technology transfer through its initiative Aid for Poverty-Related Diseases (HIV/AIDS, Tuberculosis and Malaria). In particular, the EU funded the Artepal project, which provided technical assistance to producers of artemisinin raw material and formulations in Asia and Africa (see Section 4.2.3). The EU has also cofinanced with Tanzanian Pharmaceutical Industries and action medeor the construction of a new factory to produce ARVs at GMP standards. Finally, the EU is funding the study of which this report is one part, “Improving access to medicines in developing countries through technology transfer related to medical products and local production” (see Section 1), involving WHO, UNCTAD and ICTSD.

Germany

The German Government is one of the most active supporters of local production and relevant technology transfer in LDCs, channelling its support primarily through GTZ or the German Federal Ministry for Economic Cooperation and Development (BMZ), and often in partnership with UNIDO and UNCTAD. From 2004 to 2008, GTZ supported the improvement of quality standards in eight pharmaceutical manufacturers in Syria that were deemed to have the capacity to produce at Pharmaceutical Inspection Cooperation Scheme (PICS) GMP standards. The project increased awareness of quality assurance within the industry and strengthened political support for companies, according to GTZ,
and publicity around the project attracted interest from producers based in Kenya and the United Republic of Tanzania (113).

GTZ also commissioned studies of the viability of local production in Bangladesh, Ghana, Rwanda and the United Republic of Tanzania, including analysis of economic factors and legal and regulatory frameworks (22, 24, 29, 33). In addition, GTZ has hosted regional workshops on local production, provided financial support for local production in Kenya, the United Republic of Tanzania and the Democratic Republic of the Congo and provided technical assistance and training in quality management for firms and regulators in Ethiopia and EAC Member States, including a training programme for industrial pharmacists at St Luke’s Foundation in Moshi, United Republic of Tanzania (114). (GTZ’s support for the development of a pharmaceutical industry in Ethiopia is the subject of an in-depth case study (see Section 1) and is not described in further detail here.) GTZ is supporting a 2-year project (2008–2010) of the EAC to “strengthen the EAC Secretariat’s capacity to utilize WTO TRIPS flexibilities and develop pharmaceutical production in the region” (115). The project is to support development of a regional protocol on intellectual property rights harmonization and a regional pharmaceutical manufacturing plan, and to establish a regional pharmaceutical manufacturers’ association.

GTZ also announced in 2007 a pilot project to support the development of a “pharma cluster” of small and medium-sized enterprises in Hyderabad, India. GTZ support was to include training in current good manufacturing practice (cGMP) and waste management (including construction of an effluent treatment plant), and facilitating access to credit and export markets (116).

Finally, through its investment arm Deutsche Investitions- und Entwicklungsgesellschaft (DEG), Germany has provided a long-term loan of 3.2 million euros to Botanical Extracts EPZ Ltd (formerly Advanced Bio Extracts) for the production of artemisinin in east Africa (117).

Thailand

The Thai Ministry of Foreign Affairs has provided support to Dr Krisana Kraisintu, former head of R&D at the Thai Government Pharmaceutical Organization, in her various training and technology transfer projects in sub-Saharan Africa.

United Kingdom

The United Kingdom Department for International Development (DFID) has commissioned a number of analytical reports directly relevant to local production, which have provided valuable data and analysis to inform ongoing debates (in particular, see 43, 47, 96).

United States

Through the United States Agency for International Development (USAID) Jordan Economic Development Program, USAID has supported the Jordanian Association of Pharmaceutical Manufacturers “to develop and upgrade
the pharmaceutical industry in Jordan into world-class standards” by strengthening capacity of regulators and contract research organizations to conduct bioequivalence studies according to GCP and GLP standards, and to meet international regulatory requirements in order to access export markets (118). The project has also supported a regional meeting with United States Pharmacopeia to support good-quality manufacturing and national meetings to improve packaging/printing and documentation of manufacturing. Finally, USAID has funded the NGO Technoserve to support Tanzanian farmers in growing *Artemisia annua* for sale to Advanced Bio Extracts/Botanical Extracts Ltd (see Section 4.2.3) (119).

### 4.8 Nongovernmental organizations

NGOs were involved in technology transfer, training and funding to support local production, and conducting research, advocacy, analysis, policy advice and facilitating networking. Active NGOs included action medeor, Cordaid, ICTSD, InWent, OTECI, MSF and Technoserve. As described in further detail in Annex I, action medeor carries out various projects supporting the technical and quality assurance capacities of local producers, training for students of industrial pharmacy, research for a less environmentally harmful production process for artemisinin, and research for a fixed-dose combination of tenofovir, lamivudine and efavirenz, and has provided funding to support expansion of production capacity in the United Republic of Tanzania. Cordaid, a Dutch foundation, provided funding to Advanced Bio-Extracts in 2007 to expand its capacity to produce pharmaceutical-grade artemisinin. InWent, a capacity-building organization, provides policy support to developing country governments through the project Support to Developing Countries in Utilising Flexibilities Resulting from the TRIPS Agreement (115). OTECI was involved in the Artepals project (see Annex I). Finally, MSF carries out research and advocacy on the use of TRIPS flexibilities and carries out GMP audits of local producers for potential supply to its medical projects.

Overall, many different types of organization have played a facilitating role in the various local production and technology transfer initiatives identified by the study.

### 4.9 What kind of technology is transferred?

Generally, technology was transferred for one or more of three stages of pharmaceutical production (for drugs):

- packaging;
- formulation;
- API or raw material.

Some initiatives also assisted manufacturers in upgrading or meeting quality standards (this does not include support to regulatory authorities). Of the 30 initiatives identified (see Table 5 and Annex I), 20 supported formulation, 9 transferred technology for API and only 1 provided support for packaging alone. Initiatives also often provided support for regulatory filings through access to data or documentation.
Table 5  Summary of 30 identified technology transfer initiatives

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Type</th>
<th>Quantity (proportion)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Development level of partner</td>
<td>North–south</td>
<td>20  (67%)</td>
</tr>
<tr>
<td></td>
<td>South–south</td>
<td>10  (33%)</td>
</tr>
<tr>
<td>Stage of production process</td>
<td>Packaging</td>
<td>1  (3%)</td>
</tr>
<tr>
<td></td>
<td>Formulation</td>
<td>20  (67%)</td>
</tr>
<tr>
<td></td>
<td>API</td>
<td>9  (30%)</td>
</tr>
<tr>
<td>Type of transferor/transferee</td>
<td>Private–private</td>
<td>15  (50%)</td>
</tr>
<tr>
<td></td>
<td>Public–private</td>
<td>12  (33%)</td>
</tr>
<tr>
<td></td>
<td>Public–public</td>
<td>1  (3%)</td>
</tr>
<tr>
<td></td>
<td>Private–public</td>
<td>1  (3%)</td>
</tr>
<tr>
<td></td>
<td>Mixed</td>
<td>3  (10%)</td>
</tr>
</tbody>
</table>

4.10 What are the trends?

Generally, it appears that technology transfer initiatives, investments and voluntary licensing have increased since the mid-1990s (see Table 6).

Table 6  Trends in initiatives supporting local production and technology transfer

<table>
<thead>
<tr>
<th></th>
<th>Start dates of initiatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technology transfer initiatives</td>
<td>0</td>
</tr>
<tr>
<td>Investment initiatives</td>
<td>5</td>
</tr>
<tr>
<td>Voluntary licensing initiatives</td>
<td>0</td>
</tr>
</tbody>
</table>
5. Discussion and key issues

This landscaping exercise has highlighted the great variety and broad range of activities taking place to support local production and related technology transfer. This section discusses key issues that arise regarding the incentives, scope and potential shortcomings of such initiatives.

5.1 Why transfer? Reasons to transfer technology

Why does one party transfer technology, which is costly to generate or obtain, to another? As noted in Section 1, this study largely focuses on local production and technology transfer initiatives that were not purely commercial (due to data constraints). Nevertheless, even within this circumscribed set of initiatives, an important distinction emerges between technology transfer negotiated with profit-making entities (e.g. large multinational drug producers and small biotechnology companies) and those supported by public or non-profit-making initiatives. The landscaping exercise uncovered a range of reasons that can roughly be divided into two categories: reasons for profit-making and non-profit-making/public entities.

5.1.1 Profit-making entities

For joint ventures or subsidiaries of multinational firms, there is a clear commercial reason to transfer technology: such transfer will benefit the technology holder directly. In addition, in market-based transactions we can assume that technology holders receive a sufficient price or other benefit to induce transfer. However, there are a number of reasons why technology holders would rather not transfer their technology to another party. In general, as Abbott & Reichman (74) have pointed out, “the evidence suggests that the wealthy OECD nations are little inclined to promote the development of world-class pharmaceutical producers in poor countries, which might eventually compete with the existing originators”. In other words, in the general case, a profit-making entity will not have the incentive to transfer a technology that will strengthen a competitor. If that is the case, what are the reasons that technology holders do transfer their knowledge to another party, outside of standard market-based transactions? In her 2004 study of technology transfer initiatives, Grace (43) found a broad range of technology transfer arrangements: at one end of the spectrum, multinational firms created subsidiaries in developing countries, maintained tight control over the relevant technology, and were driven primarily by commercial considerations (e.g. market access, lower production and R&D costs, regulatory goodwill). In addition, some large multinational firms may pursue a “B-generic strategy” in which they transfer technology or license patent rights to a developing country firm for supply of generic drugs to the local market while simultaneously withdrawing the A-brand product from the market; if the A-brand product is priced significantly less in the south, such a strategy can reduce the risk that products will be diverted from lower-priced to higher-priced markets in the north.20 Finally, some research-based firms are facing a “patent cliff”, with

20 I thank Wilbert Bannenberg for calling my attention to this strategy.
many lucrative products going off patent and few new patented products to replace them \((120)\); these firms may seek to bolster revenue through increased sales of branded generics in emerging markets and may transfer technology to local subsidiaries as a result. The research firm IMS Health has predicted that the developed markets in the United States and Europe will grow by just 3–6\% per year from 2010 to 2014, while the emerging markets – especially China, India and the Russian Federation – will grow by 14–17\% per year \((121)\). (IMS Health has defined the “pharmerging” markets as Brazil, China, India, the Russian Federation, Turkey, Mexico, the Republic of Korea, Argentina, Poland, Venezuela, Viet Nam, South Africa, Thailand, Indonesia, Romania, Egypt, Pakistan and Ukraine.)

At the other end of the spectrum, multinational firms freely provide their technology to developing country producers, motivated by a mix of commercial and social considerations, such as freeing up limited production capacity, transferring know-how for products of little commercial value in high-income markets, and expanding access to products needed only in developing country markets \((43)\). Whether as transferors or transferees, Grace \((43)\) emphasized that in nearly all the initiatives she examined, there was a “business case” for the involvement of private firms. Among the initiatives reviewed in this report, reasons for private firms to transfer technology include:

- when a product is no longer of commercial interest \(\text{(e.g. capreomycin and cycloserine for Lilly, and benznidazole and saquinavir for Roche)}\);
- when a firm’s business model does not include high-volume/low-margin supply to developing countries, but rather focuses on high-margin supply to higher-income markets \(\text{(e.g. tenofovir and emtricitabine voluntary licences for Gilead)}\);
- when a firm needs access to increased production capacity to meet the volume of global demand \(\text{(e.g. oseltamivir for Roche)}\);
- to meet corporate social responsibility commitments and strengthen the firm’s “social licence to operate” \(\text{（nearly all technology transfer initiatives were publicized by the transferring firm and pharmaceutical industry association （45））}}\);
- to avert legal or regulatory action unfavourable to the firm, such as a compulsory licence or denial of a patent application \(\text{(e.g. voluntary licences in response to South African Competition Commission findings of anticompetitive practice （122））}}\);
- to enter a market \(\text{(e.g. some governments, such as that of China, required joint ventures for firms seeking to enter the market）}}\).

These reasons are not mutually exclusive, and several may simultaneously influence a decision to transfer technology.

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\(21\) I thank Elodie Jambert for bringing this point to my attention.
5.1.2 Non-profit-making entities

Reasons given by non-profit-making entities (governments, intergovernmental organizations, universities/research institutes and NGOs) to engage in technology transfer tend to be linked with organizational mission, and include:

- to improve public health and support access to medicines (i.e. improve affordability, access to improved formulations or products and security of supply, and remove barriers to adoption of newer medicines);
- to support industrial development;
- to reduce national reliance on imports;
- to disseminate knowledge (e.g. NIH (106)).

This overview of reasons for commercial and noncommercial entities to engage in technology transfer suggests that transfer from private firms is likely to take place only when there is, indeed, a business case. If so, such transfer is likely to be ad hoc and limited to a few products and therefore may not provide the type of sustained and broad-ranging technology transfer required for the development of a vibrant local pharmaceutical industry. Although public or non-profit-making entities may have different reasons to transfer technology, the type of support such entities provide is likely to depend on their organizational mission and may also be product-specific or of an ad hoc nature.

5.2 Why receive? Reasons to participate as transferees

The most straightforward reason for a recipient firm to participate in a technology transfer initiative was to get access to new, useful technology for production. Such access can reduce the time and cost of developing the know-how in-house, increase the general skill level of employees, and create spillovers in other areas, including access to broader distribution networks and new business opportunities. For a smaller firm, partnering with a well-known multinational can also bring reputational benefits.

5.3 Restrictions in technology transfer agreements

Technology transfer agreements may come with a range of restrictions on the recipient. For example, limitations on export markets may be required to restrict competition from the transferee. Limits on further transfer of technology or know-how to third parties, the maintenance of trade secrets, preservation of patent monopolies for a certain period, price floors/ceilings, royalty payments and other terms may all be included in transfer agreements. Whether the two parties reach mutually agreeable and beneficial terms is likely to depend on the negotiating leverage of the technology recipient, which may often be in

22 One of the original motivations behind the Artepal project was to find a way to overcome the political resistance of local manufacturers of older antimalarials (e.g. chloroquine and quinine) to the adoption of the newer, more effective artemisinin-based combination therapies. The project’s founders hypothesized that if local producers were also able to produce artemisinin-based combination therapies, they would perceive the adoption of these in national malaria treatment protocols as an opportunity rather than a threat, and then put their political support behind protocol change.
a weaker position as the technology “demandeur”. Excessive restrictions may undermine the economic viability of a particular product or producer and are more likely to be an issue when firms are current or potential competitors.

5.4 Intellectual property management

5.4.1 Patents

Among the initiatives reviewed, patents on pharmaceutical products had a variable impact on local production, depending on the therapeutic area, country of production and level of technical capacity of the local pharmaceutical industry. Patents posed the largest barrier for firms based in non-LDCs interested in producing newer medicines, such as those for HIV/AIDS, pandemic flu or type 1 diseases. There is a rich and growing literature analysing the impact of full TRIPS implementation in India (48, 70, 80, 123); it is apparent that the space to produce newer drugs for which patents have been applied or granted is rapidly narrowing, with serious consequences for public health in India and the many developing countries to which Indian firms export generic drugs (124, 125).

At the same time, the 2001 Doha Declaration has also perhaps increased interest in exploring the possibilities for pharmaceutical production in LDCs (19, 20). The Doha Declaration extended the deadline for LDCs to grant or enforce pharmaceutical patents until at least 2016, and possibly later if WTO Members agree on additional extensions (73). Much interest has centred on Bangladesh, which has a burgeoning pharmaceutical industry and a sizeable domestic market, and could perhaps play a key role as a generics exporter; plans for an “API Park” have also been discussed by the Bangladeshi Government and outside funders (19–22). Increased attention to production potential in sub-Saharan African LDCs, such as Uganda and Ethiopia, is also at least partially attributable to the 2016 LDC waiver. Despite this potential, many LDCs have not taken full advantage of the 2016 extension to create the clear legal space for local pharmaceutical producers to make drugs widely patented elsewhere (19, 126).

Finally, for a number of products, patents seem to be neither a significant barrier nor an incentive, either because they are older drugs off patent (e.g. capreomycin, cycloserine, benznidazole, artesunate), because voluntary licences or non-assert clauses (agreements not to sue for infringement) have been granted (see Box 1), because the products were not eligible for patents (e.g. with plant extracts in some countries), or because patents were not applied for or granted in certain territories (e.g. oseltamivir).

5.4.2 Data

Data exclusivity provisions create a period of time during which generic producers may not rely on clinical data submitted by the originator to demonstrate the safety and efficacy of the product. In practice, this means that generic firms must either carry out new clinical trials for the product, which can be very costly and potentially unethical, or wait until the period...
of exclusivity ends (often a period of 5–6 years). Effectively, data exclusivity creates a regulatory barrier for the approval and marketing of generic drugs. Developing countries have been advised that data exclusivity is not required by TRIPS, and that for public health reasons it should not be included in their national laws (127). However, some developing countries have adopted data exclusivity provisions in their national regulatory systems, while others are in the process of negotiating the possibility of such provisions in the course of bilateral or regional free trade agreements (128, 129).23 If technology transfer agreements do not include either access to the data or the right to refer to the data (in countries with data exclusivity provisions), local production may be delayed. In the technology transfer initiatives reviewed here, access to data did not appear to be an issue, suggesting that suitable arrangements were made to address this potential barrier. Nevertheless, efforts to support local production should ensure that data exclusivity provisions do not pose additional barriers to the marketing of generic medicines.

5.5 Environmental protection

The vast majority of initiatives reviewed by the study did not include any special additional measures for environmental protection. Rather, the common practice appeared to be to abide by national environmental regulations. According to one interviewee24 carrying out hands-on transfer activities, national environmental standards in the south were often comparable to or even more stringent than those in the north. Manufacturer compliance and enforcement by the authorities were cited as bigger issues than the level of the standards themselves. Standards will vary by country.

Nevertheless, local production initiatives may have explicit environmental objectives, as demonstrated by the research collaboration between action medeor and a laboratory at Graz University, Austria. This project has developed a less environmentally harmful derivatization process for artesunate that eliminates a toxic chemical from the process; if the process proves itself on an industrial scale, this technology could potentially be transferred to interested producers in the south. In addition, Merck KGaA and GTZ announced in December 2009 a new initiative “to improve laboratory chemicals waste management” in Thailand, Indonesia and the Philippines (laboratories at pharmaceutical production sites could potentially be included, although such details were not reported).

5.6 Economic issues

Local production and technology transfer are complex topics encompassing a broad range of economic issues. A full exploration of all relevant economic issues is beyond the scope of this landscaping exercise; however, an outline of the issues that have arisen most frequently in this overview of initiatives may be useful. The three main areas in which issues arise are financing of

23 See a list of provisions at http://www.cptech.org/ip/health/dataexcl/.
24 Personal communication, October 2009. As a general rule, interviewees have not been identified in connection with specific statements throughout this report.
investment into local production, economic feasibility of local production, and the economic challenges of inducing appropriate technology transfer.

5.6.1 Financing investment into local production

Mobilizing the substantial amounts of capital required to invest in local production in developing countries can be quite difficult. First, capital markets often do not function well in resource-poor settings, which leads to insufficient capital or high costs. Second, the long time horizons and significant risks associated with local production make attracting sufficient investment difficult. For example, the time needed to obtain regulatory approval and the difficulty of accurately forecasting demand both add significant uncertainty to local production ventures, as demonstrated in the case of Botanical Extracts (see Section 4.2.3). Third, the amount of financing required will be nontrivial for firms seeking to achieve economies of scale through large-scale production or aiming to tap into international markets. IFC has invested significant amounts of capital in local pharmaceutical producers but has invested a very small proportion of these funds in low-income countries (see Section 4.7.2). Other sources or terms of financing may be required for enterprises in the earlier and more risky stages of development and in less-developed economies.

5.6.2 Economic feasibility of local production

Perhaps the most important question raised with respect to the economic feasibility of local production is whether the price of the locally produced product is competitive with that of the imported product (47). However, for the vast majority of initiatives reviewed in this study, information on product prices was not provided or available. A related question that is raised less often is how much time will be required for local production to become competitive, which may depend on both the capacity of the producer itself and the market conditions, such as growth of demand. For several years, Eli Lilly supplied the multidrug-resistant TB drug cycloserine to the WHO Green Light Committee at a concessionary price of US$ 0.14 per unit (2007 price) – or about US$ 256 per treatment course (130). At the same time, Lilly launched an initiative to transfer the technology to produce this drug to three generic firms. However, after the transfer was completed and the transferees obtained WHO prequalification, the generic price jumped to US$ 931 in 2008 – 264% greater than Lilly’s 2007 price (Lilly no longer supplies the Green Light Committee). The global market for this drug is relatively small and uncertain but has been growing significantly in recent years; therefore, it is possible that producers will achieve economies of scale and drop their prices in the medium term. However, the growth of the market depends on the capacity of countries to scale up access to multidrug-resistant TB treatment, which has proven difficult.

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25 Based on an average case scenario of 750 mg/day for 20 months.
26 Management Sciences for Health (MSH) international drug price indicator guide: http://erc.msh.org/dmpguide/resultsdetail.cfm?language=english&code=CYS5250T&s_year=2008&year=2008&str=250%20mg&desc=Cycloserine&pack=new&frm=TAB%2DCAP&rte=PO&class_code=06%2E2%2E4%2E&supplement=&class_name=%2806%2E2%2E4%2E29%29Antituberculosis%20medicines%3Cbr%3E.
27 I thank Elodie Jambert for drawing this example to my attention and pointing me to the relevant price data.
to predict in the past. The cycloserine example illustrates the complexity and difficulty of predicting prices and competitiveness in the context of uncertain or volatile global markets.

Second, will the product market size be sufficient to enable sustainable production by the transferee? This concern has arisen, for example, with respect to Roche’s transfer of technology for saquinavir to over ten firms. The global market for saquinavir is quite small, as it is an infrequently used ARV with little prospect for growth (it is not among the preferred drugs included in the 2010 WHO ARV treatment guidelines (131)). Market size is also a concern for local producers based in small countries, which may have to rely on regional exports to become economically viable. Regional markets may be fragmented by differing regulatory requirements, patent situations or other national policies that create barriers to entering a national market.

Finally, given that economies of scale are important for drug production, will the terms of the technology transfer enable local producers to achieve such scale? Since the volumes required to achieve scale will vary product by product, and many factors can influence price and market size, it is likely that initiatives will require case-by-case analysis to determine economic feasibility.

5.6.3 Economic challenges of inducing appropriate technology transfer

As noted earlier, getting access to the technologies needed to support the development of local production capacity is subject to a number of potential market failures, particularly if technology holders compete against technology demandeurs. First, timely, accurate information on the technological capacity of private enterprises is not usually made public, since technology is often costly to obtain and revealing it risks a loss of competitive advantage or loss of the ability to derive value from selling the technology. As a result, technology holders are likely to face difficulty identifying precisely who is interested in purchasing their technology, while technology demandeurs face a similar challenge in finding entities willing to transfer their knowledge. The resulting information asymmetries create search costs – that is, firms incur costs to identify potentially appropriate technology transfer partners. Even after potential technology suppliers have been identified, local producers may not be able to access the technology due to imbalances in bargaining power: by definition, technology holders are likely to have more information about their technology than demandeurs, an information asymmetry that weakens the demandeur’s negotiating position; in addition, technology demandeurs may be unable to afford the price that the technology holder requires to induce transfer.

Homma & Moreira (132) suggest that the Brazilian Government’s purchasing power and relatively large population have strengthened its ability to negotiate technology transfer agreements with large multinational vaccine producers. However, if population size and income are prerequisites for technology transfer agreements on commercial terms, smaller, lower-income

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28 I thank Padmashree Gehl Sampath for raising these issues.
countries are unlikely to benefit from such transfer without some type of external public or donor support. These power imbalances and the many risks of market failure suggest that public or public-interest actors have a critical role to play in facilitating access to technology through improved information, networking and other measures to reduce search costs.

5.7 Utility of transfer

There is wide variation in the reported utility of technology transfer initiatives for recipients. For example, sources in the Indian pharmaceutical industry have critiqued the technology transfer offered by Gilead for tenofovir as being of little additional value to information already publicly disclosed in the relevant patent applications, and remarked that significant additional R&D was required to produce tenofovir generically (100). On the other hand, several transferees in other countries stated that they benefited significantly from transfer initiatives, which enabled them to improve their GMP compliance, learn to produce complex formulations, and save time and money in producing documents for regulatory approval. The extent to which a particular initiative is useful seems to depend on both the characteristics of the initiative itself (e.g. what is being offered and how effectively it is being transferred) and the level of technical skill of the recipient. For many Indian generic firms, which are some of the most advanced producers in the world, a particular package of technology transfer may be far less useful than for smaller or less technically sophisticated producers. Nevertheless, Agarwal et al. (133) argue that even in India access to technology remains problematic, and they call for revised government policies to improve access to the technologies needed to realize the country’s innovative potential. Sources in the Indian pharmaceutical industry remarked that although the industry’s capacity to produce small-molecule drugs was quite advanced, it would benefit greatly from technology transfer to produce newer, more complex biotechnology products.

5.8 Timelines

As noted in Section 4.1, the duration of technology transfer initiatives reviewed in this study varied widely from as short as 3 weeks to as long as 10 years. The amount of time required for an initiative may be quite lengthy, depending on the goal.

For example, if the objective is to develop a strong local industry, it should be noted that the Indian industry took three decades to develop into the competitive industry it is today and the Tunisian industry about two decades (38, 40, 48). Furthermore, technology transfer and local production capacity develop gradually and progressively. For example, nascent drug industries often begin with the least technically demanding steps of packaging and formulation, and then gradually move back up the production process to manufacture APIs (8). Progressing through these stages requires sufficient and significant amounts of time.
Even to achieve a much more specific goal, such as approval by a stringent drug regulatory authority for all transferees (as in the case of the Lilly initiative), several years may be required. Pharmaceutical production is a long-term process, even with technology transfer, as it may encompass API R&D, formulation R&D, stability studies, additional clinical trials and other elements of the registration process.

Several interviewees and studies in the literature emphasized the importance of long-term cooperation between transferors and transferees to build trust, ensure successful transfer, and allow recipients to advance through various stages of technological difficulty. It is important to develop a clearer understanding of the timescales required for effective transfer and to devise policies that ensure sustained support for the requisite period of time.

Finally, in some cases an initiative may be extended for commercial rather than technical reasons. For example, a government could offer a fixed-term purchase guarantee to the technology holder as an incentive to transfer the technology to a local producer; although such an arrangement facilitates access to the technology, it may also artificially lengthen the amount of time required to complete the transfer.

5.9 Quality assurance measures and other regulatory issues

Quality assurance measures were integral to the initiatives reviewed in this study. Technology holders often select transferees based in part on their existing or potential capacity to produce at international quality standards. Furthermore, training in GMP and producing the documentation required to meet regulatory standards is often a core part of local production initiatives. In addition, one interviewee commented that effective enforcement by national regulatory authorities was essential to providing local producers with the incentive to comply with higher quality standards; in the absence of fair, effective regulation, a firm adhering to costly quality standards would be at a competitive disadvantage. Finally, achieving a certain quality standard may be a central indicator of the “success” of an initiative (see further discussions of defining success in Section 5.10).

At the same time, regulatory standards can pose significant barriers to market entry by local producers or create delays in the availability of products (49). For example, Dr Kraisintu commented that she felt an African firm she was working with had the human resources capacity to produce at international standards but would have had to build an entirely new factory in order to obtain WHO prequalification; the firm was unable to find the capital to do so, and the opportunity to build local production capacity was missed. Only a relatively small number of local drug producers have received WHO prequalification; among the manufacturers of the 352 products (for HIV/AIDS, influenza, malaria, reproductive health and TB) on the WHO Prequalified Drug Product list as of 20 March 2011, only 7 developing countries were represented: China, India, Morocco, Pakistan, South Africa, Uganda and Zimbabwe. The small number of producers that have obtained WHO prequalification raises concerns
regarding market concentration, sufficiency of supply and the economic feasibility of widespread local production and technology transfer initiatives. Similar concerns may arise if more developing countries adopt the regulatory standards developed by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), which are based on the regulatory standards of the United States, the EU and Japan.29

In addition, there is disagreement on how important it is for local producers to meet international regulatory standards. For those firms interested in tapping into the substantial donor-funded markets for ARVs and antimalarials, for example, obtaining WHO prequalification or United States FDA approval is very important. For those interested in producing products primarily purchased by national governments or out of pocket by consumers, such standards had less of an impact on business viability. As one participant at a December 2009 workshop on local production in Africa pointed out, even the strongest developing country industry does not necessarily produce to stringent international standards – the majority of Indian firms produce at India's national standards, not at international standards.

Finally, delays for local production may arise if national drug regulatory authorities require new information regarding older drugs in order to meet more recent regulatory standards, as has occurred with respect to capreomycin. In addition, local producers may be dissuaded from supplying small markets if the cost of registering a product (in time or money) exceeds the product’s profit potential; this leaves smaller markets with limited competition among suppliers or sometimes with no supply at all.

The difficult issues of how best to protect public safety while minimizing barriers to local production remain central questions requiring further research and analysis.

5.10 Defining success

A critical question discussed too rarely in the literature is: how should “success” be defined for initiatives for local production and technology transfer? Given the wide range of technology transfer initiatives, each one is likely to have its own objectives and therefore differing definitions of “success”.

At the project or country level, frequently used indicators of success may include some or all of the following:

• competitive or more affordable price;
• achievement of agreed quality standard;
• improved security of local supply;
• ongoing, sustainable production;

29 The ICH aims to “make recommendations towards achieving greater harmonisation in the interpretation and application of technical guidelines and requirements for pharmaceutical product registration” and has regularly convened the regulatory authorities of the United States, the EU and Japan for this purpose (134).
• increased human (employee) capacity;
• full mastery of the transferred technology;
• increased firm capacity to produce newer, more complex products.

For example, in the case of its multidrug-resistant TB initiative, Lilly considers the transfer to be complete only when a sufficient number of firms have received WHO prequalification and are supplying the Green Light Committee. Lilly considers that this goal has been reached for cycloserine, for which there are two WHO prequalified producers; as a result, Lilly no longer produces this drug.

Although common criteria for success emerge from the country- or project-level perspective, it is much less clear how to define success from the perspective of the global health community. Is it enough if some technology is being transferred at all? Or if more technology is being transferred today than yesterday? Or if the proportion of global pharmaceutical production taking place in developing countries reaches a certain threshold, as UNIDO aimed to do in 1975? There is a need for further discussion regarding the following questions:

• What kind of, and how much, local production is desirable? Based on which criteria? What kind of, and how much, technology transfer is sufficient? To meet which public health or economic development objectives?
• How sufficient is the coverage of ongoing initiatives for local production and technology transfer?
• How well do the initiatives meet priority health needs?
• How effective are the initiatives at improving access to medicines?
• How effective are the initiatives at increasing local capacity and industrial development?

Further policy debate on these questions may bring greater clarity to international efforts to support local production and relevant technology transfer.
6. Recommendations and conclusions

The objective of this study was to provide a broad global overview of recent and ongoing initiatives for local production of drugs and relevant technology transfer. Although the study aimed to be as comprehensive as possible based on publicly available data sources, it is not exhaustive. Therefore, the recommendations and conclusions drawn here should be taken as preliminary and interpreted with an appropriate degree of caution.

Drug production capacity in the developing world has advanced in the past several decades, with a few developing countries having achieved notable success in developing local pharmaceutical industries with the ability to export to stringently regulated markets and to compete globally. However, production capacity – particularly for APIs – remains concentrated in a handful of countries. The evidence suggests that there is a significant amount of activity taking place to support local production and induce the relevant transfer of technology, both to countries with established pharmaceutical industries and to countries where capacity is nascent. The initiatives vary dramatically with respect to the objectives, underlying rationale and geographical location of transferors and transferees; the scale, scope, duration, targeted disease/product area, and restrictions on and technical complexity of the transfer; and varying ways of defining success. Initiatives also differ in terms of the impact of patents or other forms of intellectual property protection, the economic viability of the transferred product, the utility of the transfer for the recipient, and the impact of regulatory standards. However, despite the breadth and variety of activities, in the absence of clearly articulated international goals with respect to local production, there is no objective way to measure whether such efforts are sufficient or whether much greater efforts are needed.

Given widespread interest in identifying long-term, sustainable measures to improve access to essential drugs and vaccines in developing countries, and renewed attention to local production strategies as one possible avenue to achieve this goal, this landscape study offers the following conclusions to inform ongoing debates:

6.1 Information

There is a clear need for improved information about ongoing initiatives to provide a stronger evidence base for policy analysis and recommendations, and to aid in the monitoring of compliance with obligations in international agreements (such as TRIPS) with respect to technology transfer. In particular, a methodical, comprehensive, regularly updated and publicly accessible database of relevant initiatives is currently lacking but sorely needed. The current landscape of initiatives is quite fragmented. Such a data source not only would be critical for measuring progress but also could help globally dispersed actors with shared interests in local production to network, gain access to resources (e.g. technology or financing) and identify opportunities to collaborate.
6.2 Drugs

Activities captured here have been concentrated in the areas of HIV/AIDS, TB, malaria and pandemic flu, and many initiatives are product-specific. There is ample opportunity and, arguably, a need to explore technology transfer for local production of a broader spectrum of products, including products for other therapeutic areas such as type 1 chronic diseases.

For the advanced local producers, the technologies available through existing transfer initiatives may offer little added value. Creative ways of inducing the transfer of more advanced technologies, such as for biotechnology products, should be explored.

API production capacity in the developing world is largely concentrated in just two countries, India and China. This concentration poses systemic risks to the stability of supply for countries whose local producers rely on Indian or Chinese API sources: for example, if a patent is granted on Medicine X in both of these countries, API supply for Medicine X would be seriously threatened, even to countries where there was no patent on the drug. Development banks should give serious consideration to investing in API production capacity in other countries, while keeping in mind the complexity and capital-intensive nature of such production.

6.3 Intellectual property

6.3.1 Least developed countries

There is renewed interest in the feasibility of pharmaceutical production in LDCs, perhaps due in part to the 2016 deadline for the granting and enforcement of pharmaceutical patents in LDC WTO Members. Given the long time horizons required to transfer technology and build local production capacity, the time period afforded by the 2016 deadline is likely to be too short. An additional extension of the deadline, perhaps to 2026 or later, may be required for LDC-based infant pharmaceutical industries to have the opportunity to develop and mature, particularly if they are striving to achieve international regulatory standards. Nevertheless, as noted above, no LDC currently has significant API production capacity, and building such capacity will take time. Therefore, international strategies to support local production should not invest solely in the LDCs but rather should also support intellectual property and industrial policies in the non-LDCs that will ensure the sustained supply of both API and newer finished products to developing countries.

6.3.2 “30 August decision”

Many developing countries will not be able to produce important medicines domestically, despite efforts to strengthen local production capacity. In light of concerns raised by several developing countries regarding the practicability of the 30 August decision (see Section 1), WTO Members should ensure that trade rules do not hinder countries from importing sufficient quantities of affordable medicines, including through the use of compulsory licensing.
6.4 Public policies for technology transfer

Public and private entities have diverse and differing sets of reasons to engage in technology transfer initiatives. Technology transfer may be very difficult to induce, particularly for products where technology holders and demandeurs are likely to be market competitors. In such cases, public or public-interest actors (such as foundations or NGOs) may need to play a stronger role in providing incentives for sharing or alternative paths to needed technologies. In addition, given the many market failures in international markets for technology, networks may play a critical role in accessing the expertise and information required to identify the types of technology required to strengthen local production capacity. International actors can play an important role by connecting local producers to the relevant global networks, and facilitating the development and further strengthening of such networks. Finally, TRIPS Article 66.2 mandates that developed countries provide incentives to their enterprises and institutions to encourage technology transfer to LDC WTO Members (135); however, in practice, implementation of this obligation seems to be quite weak (63). Putting in place new technology transfer incentives for local pharmaceutical production in the LDCs is one significant way in which developed countries could demonstrate their implementation of Article 66.2.

6.5 Capacity building

There is widespread agreement that mid- to long-term investment in building the capacity of local manufacturers and national drug regulatory authorities is needed to strengthen local production in general and increase absorptive capacity for technology transfer in particular. For example, expanding opportunities for production staff to receive practical training would complement the theoretical training provided by academic institutions. This type of training is amenable to both north–south and south–south cooperation, since several developing countries are now home to advanced industries that could provide significant training opportunities to other developing country nationals. Finally, capacity building in how to negotiate effective technology transfer agreements may be useful, particularly for firms with limited experience in doing so. In addition to these specific areas, ongoing efforts in training national drug regulatory authorities and policy-makers on how to implement TRIPS in a manner that protects public health and expands the space for local production should be strongly supported and continued.

6.6 Tailored approach

Local production capacities and relevant technology transfer needs vary widely across countries and product types, as do public health needs. International efforts to improve local production should be flexible enough that they allow tailoring of initiatives to the specificities of each region, country or product. Regional approaches may be useful, particularly where significant regional similarities exist in technical industrial capacity, business environment (including financing, language and business culture), regulatory capacity and epidemiological patterns.
6.7 Comprehensive targeted approach

As noted above, this review of ongoing initiatives has found that most initiatives are specific to a particular product or disease area, and that efforts are largely fragmented. For example, regulatory capacity may be strengthened in Country A, while technology is transferred in Country B, investment is provided in Country C, policy analysis and advice is provided to Country D, and regional harmonization initiatives are supported around Country E. Although such initiatives often provide valuable benefits to recipients, there is a risk that ad hoc, piecemeal or small-scale initiatives will proliferate but collectively fail to capitalize on the potential to develop strong, sustainable production capacity. Given the multifaceted nature of efforts required to promote local pharmaceutical production, a comprehensive approach may be needed to address simultaneously the many issues that require attention – for example, access to technology, strengthening absorptive capacity, access to capital, putting in place conducive policy measures, and measuring improved access to medicines. The complexity of developing local production capacity suggests that there are important roles and contributions for multiple actors to play, and this is reflected in the wide range of actors already involved in such initiatives (see Table 3).

Concerned actors may consider jointly providing medium- to long-term comprehensive support to a few high-potential countries that have (or have strong potential to develop rapidly) the human resource base, infrastructure, regulatory capacity, access to markets, and strong governmental commitment required to develop a viable local pharmaceutical industry. However, currently lacking is an effective governance mechanism to ensure that the contributions of diverse actors interested in local production are channelled and targeted to have maximum impact. Such a mechanism would not necessarily imply formalized, centralized control but rather institutional arrangements that would facilitate information sharing, collaboration and the identification of synergies to achieve jointly held goals.

6.8 Defining success in public health terms

In a field in which public health and industrial considerations are deeply intertwined and where activities are currently quite fragmented, further debate among key stakeholders is urgently needed to clarify goals, define “successful” initiatives and set broadly shared targets. Such goals would not necessarily have to be set at the global level as they were in the 1970s, but rather they could be agreed among the governments, multilateral agencies, firms, NGOs and other actors that have already expressed interest in or commitment to improving local production capacities. Such debates could take place at the global or regional level.

Definitions of success should include public health goals. Whether and how local production improves access to medicines is likely to depend on the specificities of each context and may vary over time and by product. Local production can lead to improved access (defined as improved quality
assurance, affordability, appropriateness of products or security of supply), but it does not necessarily do so. Furthermore, some of these objectives may be more feasible to achieve than others in a given context, or there may be trade-offs between them. Stakeholders should engage in a deliberative process to define success in a given context, with access to medicines considerations at the core.

6.9 Further research

Further research is required, particularly in two areas: (i) measuring private-sector technology transfer flows, and (ii) understanding the conditions under which local production leads to improved access to medicines, and the pathways through which such improvements occur.

There is clearly strong interest in and demand from governments and local producers in the south for increased support, and particularly for technology transfer. Many technology holders – whether firms, experts or NGOs – have demonstrated a willingness to engage in technology transfer, albeit sometimes only under specific conditions. This enthusiasm offers an opportunity to launch more comprehensive, coherent and intensive efforts to encourage technology flows and upgrade local production capacity, with the ultimate aim of improving access to medicines in developing countries.
References


106. Salicrup LA, Rohrbaugh ML. Partnerships in technology transfer: An innovative program to enhance biomedical research and global health. International Microbiology, 2005, 8:1–3.


# Annex I Technology transfer projects for local production

<table>
<thead>
<tr>
<th>Drug (International non-proprietary name)</th>
<th>Indication</th>
<th>Technology transferor (or facilitator)</th>
<th>Transferee</th>
<th>Producing country</th>
<th>Year start</th>
<th>Production stage*</th>
<th>Terms, conditions and notes</th>
<th>North to/from South</th>
<th>Public to/from private</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stavudine/lamivudine/nevirapine; artesunate</td>
<td>HIV/AIDS, malaria</td>
<td>action medeor with Krisana Kraisintu</td>
<td>TPI</td>
<td>United Republic of Tanzania (Arusha)</td>
<td>2001</td>
<td>2</td>
<td>For stavudine/lamivudine/nevirapine and artesunate, technology transfer for formulation, adults and paediatric dry syrup. action medeor carries out GMP audits. TPI 40% owned by government, 60% private</td>
<td>North–south</td>
<td>Public–private</td>
</tr>
<tr>
<td>Antiretrovirals</td>
<td>HIV/AIDS</td>
<td>Cipla</td>
<td>Shanghai Desano</td>
<td>China</td>
<td>2002</td>
<td>3</td>
<td>Desano received ARV manufacturing know-how from Cipla. Cipla now owns a 20% share in Desano</td>
<td>South–south</td>
<td>Private–private</td>
</tr>
<tr>
<td>Pharmaceutical-grade artemisinin</td>
<td>Malaria</td>
<td>action medeor, GTZ, IFC, IPS, Cordaid, Technoserve (USAID-funded), Novartis (purchaser)</td>
<td>Advanced Bio Extracts (ABE) (Botanical Extracts as of 2008)</td>
<td>Kenya (Nairobi), Uganda, United Republic of Tanzania</td>
<td>2002</td>
<td>3</td>
<td>ABE supports small-scale cultivation of <em>Artemisia annua</em> and carries out the extraction and purification process for pharmaceutical-grade artemisinin in Kenya. In 2008, the entity was restructured such that Botanical Extracts (BE) became the holding company for ABE and three subsidiaries in Kenya, Uganda and the United Republic of Tanzania. BE is also involved in the development of a less environmentally harmful artesunate extraction process, in collaboration with action medeor and Graz University, Austria. Technoserve, funded by USAID, has supported Tanzanian farmers growing <em>Artemisia annua</em> for sale to ABE</td>
<td>North–south</td>
<td>Public–private</td>
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<tr>
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<th>Year start</th>
<th>Production stage*</th>
<th>Terms, conditions and notes</th>
<th>North to/from south</th>
<th>Public to/from</th>
<th>Private to/from</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capreomycin</td>
<td>Multidrug-resistant TB</td>
<td>Eli Lilly</td>
<td>Hisun Pharmaceuticals</td>
<td>China</td>
<td>2003</td>
<td>3</td>
<td>Technology transfer for API</td>
<td>North–south</td>
<td>Private–private</td>
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<tr>
<td>Cycloserine</td>
<td>Multidrug-resistant TB</td>
<td>Eli Lilly</td>
<td>Shasun Pharmaceuticals</td>
<td>India</td>
<td>2003</td>
<td>3</td>
<td>Technology transfer for API</td>
<td>North–south</td>
<td>Private–private</td>
<td></td>
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<tr>
<td>Capreomycin, cycloserine</td>
<td>Multidrug-resistant TB</td>
<td>Eli Lilly</td>
<td>SIA International/Biocom</td>
<td>Russian Federation</td>
<td>2003</td>
<td>2</td>
<td>Technology transfer for formulation, registration</td>
<td>North–south</td>
<td>Private–private</td>
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<td>Capreomycin, cycloserine</td>
<td>Multidrug-resistant TB</td>
<td>Eli Lilly</td>
<td>Aspen Pharmacare</td>
<td>South Africa</td>
<td>2003</td>
<td>2</td>
<td>Technology transfer for formulation, registration</td>
<td>North–south</td>
<td>Private–private</td>
<td></td>
</tr>
<tr>
<td>Capreomycin, cycloserine</td>
<td>AIDS, malaria, TB, other</td>
<td>Government of Brazil (FIOCRUZ)</td>
<td>Mozambique</td>
<td>Mozambique</td>
<td>2003</td>
<td>2</td>
<td>FIOCRUZ is transferring technology for the production of ARVs and other drugs (antibiotics, antimalarials, anti-TB drugs) to a new pharmaceutical production facility in Mozambique as part of a bilateral agreement. The first phase is expected to cost US$ 9 million, of which the Mozambican Government is contributing US$ 2 million and the Brazilian Government the remaining US$ 7 million; the plant was expected to be operational by end of 2009</td>
<td>South–south</td>
<td>Public–public</td>
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<th>Year start</th>
<th>Production stage*</th>
<th>Terms, conditions and notes</th>
<th>North to/from south</th>
<th>Public to/from private</th>
</tr>
</thead>
<tbody>
<tr>
<td>Artemisinin derivatives</td>
<td>Malaria</td>
<td>OTECI/Artepal project (also collaborating with Aedes and Epicentre)</td>
<td>14 plantations, 11 extraction firms, 8 API producers, 16 pharmaceutical companies (firm names are nonpublic information)</td>
<td>South Africa, Bangladesh, Cambodia, China, Eritrea, Gabon, Ghana, India, Kenya, Madagascar, Uganda, United Republic of Tanzania, Viet Nam, Zimbabwe</td>
<td>2004</td>
<td>2, 3</td>
<td>European Commission-funded technology-transfer project to improve production of artemisinin derivatives, primarily in Africa but also included Asia. Organizers currently seeking new funding</td>
<td>North–south</td>
<td>Public–private</td>
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<tr>
<td>Stavudine/lamivudine/nevirapine</td>
<td>HIV/AIDS</td>
<td>action medeor, GTZ with Krisana Kraisintu</td>
<td>Pharmakina</td>
<td>Democratic Republic of the Congo (Bukavu)</td>
<td>2004</td>
<td>2</td>
<td>Technology transfer for formulation</td>
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<td>Year start</td>
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<tr>
<td>Paramomycin IM injection</td>
<td>Visceral leishmaniasis</td>
<td>IoWH</td>
<td>Gland Pharma</td>
<td>India</td>
<td>2005</td>
<td>3</td>
<td>Partnership with public–private product development partnership PDP to supply clinical trial and market. Pfizer donated product dossier to IoWH, which transferred it to Gland. Gland had in-house production capacity and did not receive further technology transfer</td>
<td>North–south</td>
<td>Mixed</td>
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<tr>
<td>Tenofovir, tenofovir + emtricitabine</td>
<td>HIV/AIDS</td>
<td>Gilead</td>
<td>Aspen</td>
<td>South Africa</td>
<td>2005</td>
<td>2</td>
<td>Manufacture and market to Gilead “access countries” (n=97). Aspen to register in Africa where Gilead not yet registered</td>
<td>North–South</td>
<td>Private–private</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>action medeor</td>
<td>TPI</td>
<td>United Republic of Tanzania (Arusha)</td>
<td>2006</td>
<td>2</td>
<td>Building new factory to produce ARVs at GMP standards; cofinanced by TPI &amp; action medeor (715 000 euros) and European Commission (5 million euros)</td>
<td>North–south</td>
<td>Public–private</td>
<td></td>
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<tr>
<td>Artesunate suppositories</td>
<td>Malaria</td>
<td>Krisana Kraisintu with Royal Thai Government</td>
<td>Centre Hospitalier National Pediatrique, Charles de Gaulle (Burkina Faso); Royal Victoria Teaching Hospital (Gambia); Centre Hospitalier Aristide le Dantec (Senegal); Usine Malienne de Produits Pharmaceutiques (Mali), Zambia</td>
<td>Burkina Faso (Ouagadougou); Gambia (Banjul); Senegal (Dakar); Mali (Bamako), Zambia</td>
<td>2006</td>
<td>2</td>
<td>Technology transfer for hospital-based production of suppositories</td>
<td>South–south</td>
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<tr>
<th>Drug (International non-proprietary name)</th>
<th>Indication</th>
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<th>Producing country</th>
<th>Year start</th>
<th>Production stage*</th>
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<th>North to/from south</th>
<th>Public to/from private</th>
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<tbody>
<tr>
<td>5 products</td>
<td>N/A</td>
<td>Berlin Pharmaceuticals (Thailand)</td>
<td>TPI</td>
<td>Tanzania (Arusha)</td>
<td>2006</td>
<td>2</td>
<td>MoU for technical cooperation</td>
<td>South–south</td>
<td>Private–private</td>
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<tr>
<td>Antimalarials</td>
<td>Malaria</td>
<td>Krisana Kraisintu with Royal Thai Government</td>
<td>Bethlehem Pharmaceuticals</td>
<td>Ethiopia</td>
<td>2006</td>
<td>2</td>
<td>Technology transfer for formulation of antimalarials. Project stalled due to lack of working capital</td>
<td>South–south</td>
<td>Public–private</td>
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<tr>
<td>Atazanavir</td>
<td>HIV/AIDS</td>
<td>Bristol-Myers Squibb</td>
<td>Aspen</td>
<td>South Africa</td>
<td>2006</td>
<td>2</td>
<td>Transferred intellectual property and technical know-how related to manufacturing, testing, packaging, storage and handling of API and finished dosage form. Aspen and Emcure now working on regulatory submissions for sub-Saharan Africa and India. Licences are royalty-free</td>
<td>North–south</td>
<td>Private–private</td>
</tr>
<tr>
<td>Atazanavir</td>
<td>HIV/AIDS</td>
<td>Bristol-Myers Squibb</td>
<td>Emcure</td>
<td>India</td>
<td>2006</td>
<td>3</td>
<td>Transferred intellectual property and technical know-how related to manufacturing, testing, packaging, storage and handling of API and finished dosage form. Aspen and Emcure now working on regulatory submissions for sub-Saharan Africa and India. Licences are royalty-free</td>
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<td>Private–private</td>
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<tr>
<td>Tenofovir, tеноfovir + emtricitabine</td>
<td>HIV/AIDS</td>
<td>Gilead</td>
<td>Alkem, Aurobindo, FDC, JB Chemicals, Matrix, Medchem, Ranbaxy, Shasun, Emcure, Hetero, Strides Arcolab</td>
<td>India</td>
<td>2006</td>
<td>3</td>
<td>If licensed to produce API, may only sell API to other Gilead licensees. Eligible markets: Gilead “access countries” (n=97)</td>
<td>North–south</td>
<td>Private–private</td>
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<tr>
<td>Drug (International non-proprietary name)</td>
<td>Indication</td>
<td>Technology transferor (or facilitator)</td>
<td>Transferee</td>
<td>Producing country</td>
<td>Year start</td>
<td>Production stage</td>
<td>Terms, conditions and notes</td>
<td>North to/from south</td>
<td>Public to/from private</td>
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<td>Saquinavir, nelfinavir</td>
<td>HIV/AIDS</td>
<td>Roche</td>
<td>10 generic firms (Aspen, South Africa; Cosmos and Universal, Kenya; Beximco and Radiant, Bangladesh; Bethlehem, Ethiopia)</td>
<td>Bangladesh, Ethiopia, Kenya, South Africa, United Republic of Tanzania and Zimbabwe</td>
<td>2006</td>
<td>2</td>
<td>Royalty-free technology transfer; also started training seminars on GMP for African producers. Roche commits not to file new patents or enforce existing patents in LDCs (for ARVs, also all sub-Saharan Africa). Roche has announced withdrawal from HIV therapeutic area</td>
<td>North–south</td>
<td>Private–private</td>
</tr>
<tr>
<td>Benznidazole</td>
<td>Chagas disease</td>
<td>Roche</td>
<td>Government of Brazil/Lafepe</td>
<td>Brazil</td>
<td>2006</td>
<td>3</td>
<td>Roche licensed Government of Brazil in 2003 to produce benznidazole. Several years later, Roche transferred technology for benznidazole API to Lafepe, which is currently the world’s only producer of this drug. Lafa produces to other countries in Latin America where Chagas disease is endemic. Lafa partnered with DNDi in 2008 to develop the first paediatric formulation of benznidazole</td>
<td>North–south</td>
<td>Private–public</td>
</tr>
<tr>
<td>Artesunate + amodiaquine</td>
<td>Malaria</td>
<td>DNDi, sanofi-aventis HQ</td>
<td>sanofi-aventis Morocco</td>
<td>Morocco</td>
<td>2006</td>
<td>2</td>
<td>DNDi and its partner sanofi-aventis developed a fixed-dose combination antimalarial of artesunate and amodiaquine. This drug is now being produced in Morocco at a Sanofi facility. This initiative does not fit the typical definition of transfer, since Sanofi developed its own production</td>
<td>North–south</td>
<td>Mixed</td>
</tr>
<tr>
<td>Drug (International non-proprietary name)</td>
<td>Indication</td>
<td>Technology transferor (or facilitator)</td>
<td>Transferee</td>
<td>Producing country</td>
<td>Year start</td>
<td>Production stage*</td>
<td>Terms, conditions and notes</td>
<td>North to/from south</td>
<td>Public to/from private</td>
</tr>
<tr>
<td>-----------------------------------------</td>
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</tr>
<tr>
<td>HIV/AIDS</td>
<td>Cipla</td>
<td>Quality Chemicals</td>
<td>Uganda (Kampala)</td>
<td>2007</td>
<td>2</td>
<td>Ugandan Government investing to start-up firm, 5-year purchase guarantee for ARVs</td>
<td>South–south</td>
<td>Private–private</td>
<td></td>
</tr>
<tr>
<td>Artesunate/ amodiaquine</td>
<td>Malaria</td>
<td>Krisana Kraisintu with Royal Thai Government</td>
<td>Usine Malienne de Produits Pharmaceutiques, Benin</td>
<td>Mali (Bamako), Benin</td>
<td>2007</td>
<td>2</td>
<td>Technology transfer for artesunate/amodiaquine fixed-dose combination (direct compression, wet granulation)</td>
<td>South–south</td>
<td>Public–private</td>
</tr>
<tr>
<td>Darunavir</td>
<td>HIV/AIDS</td>
<td>Tibotec</td>
<td>Aspen</td>
<td>South Africa</td>
<td>2007</td>
<td>1</td>
<td>Aspen is packaging, received technology transfer for packaging and data; also managing distribution</td>
<td>North–south</td>
<td>Private–private</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cadila India</td>
<td>Cadila Ethiopia</td>
<td>Ethiopia</td>
<td>2008</td>
<td>Joint venture. Machines and all raw materials from India. GMP PICS scheduled for first quarter of 2010. Export to Djibouti, Kenya, United Republic of Tanzania, Rwanda.</td>
<td>South–south</td>
<td>Private–private</td>
</tr>
<tr>
<td>Artesunate + mefloquine</td>
<td>Malaria</td>
<td>FIOCRUZ with DNDi</td>
<td>Cipla</td>
<td>India</td>
<td>2008</td>
<td>2</td>
<td>FIOCRUZ and Farmanguinhos (public Brazilian pharmaceutical producer) developed a fixed-dose combination antimalarial of artesunate and mefloquine jointly with DNDi. This drug is now being produced in Brazil. FIOCRUZ agreed to transfer the technology to Cipla (India) to supply the Asian market</td>
<td>South–south</td>
<td>Public–private</td>
</tr>
</tbody>
</table>

Continues…
<table>
<thead>
<tr>
<th>Drug (International non-proprietary name)</th>
<th>Indication</th>
<th>Technology transferor (or facilitator)</th>
<th>Transferee</th>
<th>Producing country</th>
<th>Year start</th>
<th>Production stage*</th>
<th>Terms, conditions and notes</th>
<th>North to/from south</th>
<th>Public to/from private</th>
</tr>
</thead>
<tbody>
<tr>
<td>GTZ</td>
<td></td>
<td>GTZ and the Government of Ethiopia are engaging in a broad range of activities to support and develop a pharmaceutical industry, including quality assurance support, bioequivalence regulations, training of staff, establishment of a bioequivalence study centre, and advice to the drug regulatory authority and producers on PICS GMP</td>
<td>Ethiopia</td>
<td>2009</td>
<td>2</td>
<td>North–south</td>
<td>Public–private</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Production stage: 1, packaging; 2, formulation; 3, API.
API, active pharmaceutical ingredient; ARV, antiretroviral; DNDi, Drugs for Neglected Diseases initiative; FIOCRUZ, Oswaldo Cruz Foundation; GMP, good manufacturing practice; GTZ, Gesellschaft für Technische Zusammenarbeit; HIV, human immunodeficiency virus; HQ, headquarters; IFC, International Finance Corporation; IM, intramuscular; IoWH, Institute for OneWorld Health; IPS, Aga Khan Fund for Economic Development-Industrial Promotion Services; N/A, not applicable; LDC, least developed countries; OTECI, Office Technique d’Etudes et de Coopération Internationale; PICS, Pharmaceutical Inspection Cooperation Scheme; TB, tuberculosis; TPI, Tanzanian Pharmaceutical Industries; USAID, United States Agency for International Development.
## Annex II  Investment initiatives supporting local production

<table>
<thead>
<tr>
<th>Investment recipient</th>
<th>Producing country (2009 World Bank category)</th>
<th>Year</th>
<th>Investor</th>
<th>Amount</th>
<th>Description/notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kampala Pharmaceutical Industries</td>
<td>Uganda (LIC)</td>
<td>1996</td>
<td>Aga Khan Development Network</td>
<td>N/A</td>
<td>Aga Khan Fund for Economic Development’s Industrial Promotion Service’s group of companies focus on supporting economic development of local industry</td>
</tr>
<tr>
<td>Dar al Shifa Pharmaceuticals</td>
<td>West Bank and Gaza Strip (LMIC)</td>
<td>1997</td>
<td>IFC</td>
<td>US$ 0.5 million</td>
<td>Upgrade and expand production facilities</td>
</tr>
<tr>
<td>Core Pharmsanat</td>
<td>Uzbekistan (UC)</td>
<td>1998</td>
<td>IFC</td>
<td>US$ 7 million</td>
<td>Establish plant (joint project of India-based Core and Government of Uzbekistan)</td>
</tr>
<tr>
<td>Distribuidora Cesar Guerrero</td>
<td>Nicaragua (LMIC)</td>
<td>1999</td>
<td>IFC</td>
<td>US$ 1.3 million</td>
<td>Expand and modernize production facilities</td>
</tr>
<tr>
<td>Bosnalijek, d.d. Sarajevo</td>
<td>Bosnia and Herzegovina (UMIC)</td>
<td>1999</td>
<td>IFC</td>
<td>US$ 2.5 million</td>
<td>Reconstruction of facilities destroyed in war, modernization of existing facilities</td>
</tr>
<tr>
<td>Alkaloid A.D. Skopje</td>
<td>Former Yugoslav Republic of Macedonia (UMIC)</td>
<td>2000</td>
<td>IFC</td>
<td>US$ 8.9 million</td>
<td>Build new GMP-compliant facilities and upgrade existing facilities</td>
</tr>
<tr>
<td>Aldaph SPA</td>
<td>Algeria (UMIC)</td>
<td>2000</td>
<td>IFC</td>
<td>US$ 15 million</td>
<td>Build new production facility</td>
</tr>
<tr>
<td>Orchid Chemicals &amp; Pharmaceuticals Limited</td>
<td>India (LMIC)</td>
<td>2001</td>
<td>IFC</td>
<td>US$ 30 million</td>
<td>Expand and diversify product mix</td>
</tr>
<tr>
<td>Sekem Holdings (Atos Phyto-Pharmaceuticals)</td>
<td>Egypt (LMIC)</td>
<td>2002</td>
<td>IFC</td>
<td>Up to US$ 5 million</td>
<td>Expand, reorganize and financially restructure firms within Sekem Holdings</td>
</tr>
<tr>
<td>Hikma Investment Company</td>
<td>Jordan (LMIC)</td>
<td>2003</td>
<td>IFC</td>
<td>Up to US$ 15 million</td>
<td>Help Hikma to expand operations to Middle East, Portugal and Asia</td>
</tr>
<tr>
<td>Productos Gutis S.A.</td>
<td>Costa Rica (UMIC)</td>
<td>2004</td>
<td>IFC</td>
<td>US$ 7 million</td>
<td>Relocate operations to modernized facility, seek to obtain GMP standards</td>
</tr>
<tr>
<td>Corporacion Drokasa S.A.</td>
<td>Peru (UMIC)</td>
<td>2004</td>
<td>IFC</td>
<td>Partial guarantee of bond and commercial paper</td>
<td>To finance maintenance capital expenditure and refinance debt</td>
</tr>
<tr>
<td>SRF Ltd.</td>
<td>India (LMIC)</td>
<td>2005</td>
<td>IFC</td>
<td>US$ 20 million</td>
<td>To build new API plant (among other, non-pharma activities)</td>
</tr>
</tbody>
</table>

Continues…
<table>
<thead>
<tr>
<th>Investment recipient</th>
<th>Producing country (2009 World Bank category)</th>
<th>Year</th>
<th>Investor</th>
<th>Amount</th>
<th>Description/notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>APIDC Biotechnology Venture Fund</td>
<td>India (LMIC)</td>
<td>2005</td>
<td>IFC</td>
<td>US$ 4 million</td>
<td>Providing capital, strategic, financial, operational and technical expertise to 20–25 early-stage biotechnology companies at a time when early-stage venture capital is in short supply in India</td>
</tr>
<tr>
<td>ABOLmed</td>
<td>Russian Federation (UMIC)</td>
<td>2005</td>
<td>IFC</td>
<td>US$ 8 million</td>
<td>Build new facilities to expand product line and expand capacity</td>
</tr>
<tr>
<td>BioVeda China Fund L.P.</td>
<td>China (LMIC)</td>
<td>2005</td>
<td>IFC</td>
<td>Up to US$ 5 million</td>
<td>Provide venture capital and management expertise to Chinese biotechnology and life sciences companies</td>
</tr>
<tr>
<td>Bosnalijek, d.d. Sarajevo</td>
<td>Bosnia and Herzegovina (UMIC)</td>
<td>2005</td>
<td>IFC</td>
<td>7.5 million euros</td>
<td>Expand production capacity</td>
</tr>
<tr>
<td>Dabur Pharma</td>
<td>India (LMIC)</td>
<td>2005</td>
<td>IFC</td>
<td>US$ 15 million</td>
<td>Expand international market reach and commercialize new products</td>
</tr>
<tr>
<td>Bharat Biotech</td>
<td>India (LMIC)</td>
<td>2006</td>
<td>IFC</td>
<td>US$ 6 million</td>
<td>Upgrade and expand production facilities, increase contract manufacturing, increase R&amp;D</td>
</tr>
<tr>
<td>Shanghai Fosun Pharmaceutical Group Co. Ltd</td>
<td>China (LMIC)</td>
<td>2006</td>
<td>IFC</td>
<td>US$ 40 million</td>
<td>Various activities, including larger-scale antimalarials production</td>
</tr>
<tr>
<td>Granules India Limited</td>
<td>India (LMIC)</td>
<td>2007</td>
<td>IFC</td>
<td>Up to US$ 15 million</td>
<td>Expand capacity for finished products and API, develop and register new products</td>
</tr>
<tr>
<td>Advanced Bio Extracts (part of holding company Botanical Extracts EPZ Ltd)</td>
<td>Kenya, Uganda, United Republic of Tanzania (LICs)</td>
<td>2008</td>
<td>IFC, DEG (Germany), IPS (Aga Khan), Acumen Fund, Cordaid</td>
<td>US$ 30 million total</td>
<td>Establish manufacturing capacity to extract and purify crude artemisinin from leaves; conduct derivatization, establish raw material production equipment. IFC (US$ 9 million), DEG (3.4 million euros)</td>
</tr>
<tr>
<td>Hikal Limited</td>
<td>India (LMIC)</td>
<td>2008</td>
<td>IFC</td>
<td>Equity, debt</td>
<td>Expand capacity for existing and new products and API</td>
</tr>
<tr>
<td>Tecnoquimicas S.A.</td>
<td>Colombia (UMIC)</td>
<td>2009</td>
<td>IFC</td>
<td>Up to US$ 45 million</td>
<td>Expand and upgrade facilities, possibly acquire pharma companies or facilities in region</td>
</tr>
<tr>
<td>Dishman Pharmaceuticals and Chemicals Ltd</td>
<td>India (LMIC)</td>
<td>2009</td>
<td>IFC</td>
<td>Debt</td>
<td>Build new facilities in India and China, invest in overseas subsidiaries and joint ventures</td>
</tr>
<tr>
<td>Granules India Limited</td>
<td>India (LMIC)</td>
<td>2009</td>
<td>IFC</td>
<td>US$ 1 million</td>
<td>Improve energy and water efficiency of production plants, ultimately decrease prices</td>
</tr>
<tr>
<td>Investment Fund for Health in Africa B.V.</td>
<td>African region (mixed)</td>
<td>2009</td>
<td>IFC</td>
<td>Up to 10 million euros</td>
<td>Investment fund for health-related companies in Africa, including pharma production (investment pending approval)</td>
</tr>
</tbody>
</table>

DEG, Deutsche Investitions- und Entwicklungsgesellschaft; IFC, International Finance Corporation; IPS, Aga Khan Fund for Economic Development-Industrial Promotion Services; LIC, low-income country; LMIC, lower middle-income country; UMIC, upper middle-income country.
Annex III Voluntary licences for drugs (with and without technology transfer)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Abbreviation</th>
<th>Indication</th>
<th>Licensor</th>
<th>Licensee</th>
<th>Producing country</th>
<th>Year start</th>
<th>Technology transfer component?</th>
<th>Description, terms and conditions (sources)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamivudine, zidovudine, lamivudine + zidovudine</td>
<td>3TC, 3TC+AZT</td>
<td>HIV/AIDS</td>
<td>GSK</td>
<td>Aspen, Cipla-Medpro, Feza, Thembalami, Biotech Laboratories, Sonke</td>
<td>South Africa</td>
<td>2001</td>
<td>No</td>
<td>May produce and market to public and private sectors of SACU and SADC; 5% royalty on net sales. Original 2001 licenses were renegotiated after the Treatment Action Campaign and the AIDS Law Project brought a complaint to the South African Competition Commission alleging anticompetitive practice (100, 122, 136)</td>
</tr>
<tr>
<td>Nevirapine</td>
<td>NVP</td>
<td>HIV/AIDS</td>
<td>Boehringer Ingelheim</td>
<td>Aspen, Biotech Laboratories</td>
<td>South Africa</td>
<td>2003</td>
<td>No</td>
<td>May produce and market to public &amp; private sectors of SACU and SADC; 5% royalty on net sales. Licences responded to the Treatment Action Campaign and AIDS Law Project complaint to the South African Competition Commission alleging anticompetitive practice. Boehringer Ingelheim has since offered not to sue any WHO-prequalified generic producer of NVP supplying LDCs, LICs or sub-Saharan Africa (100, 136)</td>
</tr>
<tr>
<td>Zidovudine, lamivudine</td>
<td>AZT, 3TC</td>
<td>HIV/AIDS</td>
<td>GSK</td>
<td>Cosmos Pharmaceuticals</td>
<td>Kenya</td>
<td>2004</td>
<td>No</td>
<td>Eligible markets: east Africa (Kenya, Burundi, Uganda, Rwanda, United Republic of Tanzania), 5% royalty (27, 100)</td>
</tr>
<tr>
<td>Nevirapine</td>
<td>NVP</td>
<td>HIV/AIDS</td>
<td>Boehringer Ingelheim</td>
<td>Cosmos Pharmaceuticals</td>
<td>Kenya</td>
<td>2004</td>
<td>No</td>
<td>Eligible markets: east Africa (Kenya, Burundi, Uganda, Rwanda, United Republic of Tanzania), 5% royalty. Boehringer Ingelheim has since offered not to sue any WHO-prequalified generic producer of NVP supplying LDCs, LICs or sub-Saharan Africa (100, 136)</td>
</tr>
</tbody>
</table>

Continues…
<table>
<thead>
<tr>
<th>Drug</th>
<th>Abbreviation</th>
<th>Indication</th>
<th>Licensor</th>
<th>Licensee</th>
<th>Producing country</th>
<th>Year start</th>
<th>Technology transfer component?</th>
<th>Description, terms and conditions (sources)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nevirapine</td>
<td>NVP</td>
<td>HIV/AIDS</td>
<td>Boehringer-Ingelheim</td>
<td>Memphis</td>
<td>Egypt</td>
<td>2004</td>
<td>No</td>
<td>Eligible markets: Egypt and neighbouring countries. Boehringer Ingelheim has since offered not to sue any WHO-prequalified generic producer of NVP supplying LDCs, LICs or sub-Saharan Africa (100, 136)</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>EFV</td>
<td>HIV/AIDS</td>
<td>Merck</td>
<td>Thembalami, Aspen, Adcock Ingram</td>
<td>South Africa</td>
<td>2004</td>
<td>No</td>
<td>Eligible markets: public and private sectors in SADC. Treatment Action Campaign and AIDS Law Project filed a complaint in 2007 to the South African Competition Commission that the terms of the licence were overly restrictive because they exclude the lowest-cost suppliers and did not allow coformulation into fixed-dose combinations (100, 136, 137)</td>
</tr>
<tr>
<td>Tenofovir, tenofovir + emtricitabine</td>
<td>TDF, TDF+FTC</td>
<td>HIV/AIDS</td>
<td>Gilead</td>
<td>Aspen</td>
<td>South Africa</td>
<td>2005</td>
<td>Yes</td>
<td>Manufacture and market to Gilead “access countries” (n=97). Aspen to register in Africa where Gilead not yet registered. Aspen to sell at price agreed with Gilead (100, 136)</td>
</tr>
<tr>
<td>Oseltamivir</td>
<td></td>
<td>Pandemic flu</td>
<td>Roche</td>
<td>Hetero, Shanghai Pharma, HEC (China), Aspen</td>
<td>India</td>
<td>2005</td>
<td>No</td>
<td>Hetero licence is for production for government stockpiling in India and Africa. Roche has announced it will not enforce any oseltamivir patents in LDCs (100, 104)</td>
</tr>
<tr>
<td>Stavudine</td>
<td>d4T, ddl</td>
<td>HIV/AIDS</td>
<td>Bristol-Myers Squibb</td>
<td>Aurobindo</td>
<td>India</td>
<td>2006</td>
<td>No</td>
<td>Manufacture and market in South Africa and 49 other countries. Bristol-Myers Squibb has also committed not to enforce its patent rights for d4T and ddl in sub-Saharan Africa since 2001 (100, 136)</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Drug Abbreviation</th>
<th>Indication</th>
<th>Licensor</th>
<th>Licensee</th>
<th>Producing country</th>
<th>Year start</th>
<th>Technology transfer component?</th>
<th>Description, terms and conditions (sources)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATV</td>
<td>HIV/AIDS</td>
<td>Bristol-Myers Squibb</td>
<td>Aspen (formulation), Emcure (API and formulation)</td>
<td>South Africa</td>
<td>2006</td>
<td>Yes</td>
<td>Transferred intellectual property and technical know-how related to manufacturing, testing, packaging, storage, and handling of API and finished dosage-form. Aspen and Emcure are now working on regulatory submissions for sub-Saharan Africa and India. Licences are royalty-free (100, 136).</td>
</tr>
<tr>
<td>TDF, TDF+FTC</td>
<td>HIV/AIDS</td>
<td>Gilead</td>
<td>Alkem, FDC, Chemicals, Marco, Merck, Ranbaxy, Heptis, Hetero</td>
<td>India</td>
<td>2006</td>
<td>Yes</td>
<td>If licensed to produce API, may only sell API to other Gilead licensees; initially, Clause 5.2 suggested licensees could not challenge validity of patent. Eligible markets: Gilead “access countries” (n=97) (100, 136).</td>
</tr>
<tr>
<td>Saquinavir, nelfinavir</td>
<td>HIV/AIDS</td>
<td>Roche</td>
<td>10 generic firms (Aspen, South Africa; Cosmos and Universal, Kenya; Beximco and Radiant, Bangladesh; Bethlehem, Ethiopia)</td>
<td>Bangladesh, Ethiopia, Kenya, South Africa, United Republic of Tanzania and Zimbabwe</td>
<td>2006</td>
<td>Yes</td>
<td>Royalty-free technology transfer; also started training seminars on GMP for African producers. Roche commits not to file new patents or enforce existing patents in LDCs (for ARVs, also all sub-Saharan Africa). Roche has announced withdrawal from HIV therapeutic area (136).</td>
</tr>
<tr>
<td>DRV</td>
<td>HIV/AIDS</td>
<td>Tibotec</td>
<td>Aspen</td>
<td>South Africa</td>
<td>2007</td>
<td>Yes</td>
<td>Aspen is packaging and data; also managing distribution.</td>
</tr>
<tr>
<td>Darunavir</td>
<td>HIV/AIDS</td>
<td>GSK</td>
<td>Aspen</td>
<td>South Africa</td>
<td>2009</td>
<td>No</td>
<td>Nonexclusive royalty-free licence to Aspen. South African Competition Commission required GSK to grant voluntary licences for abacavir to other generic firms as a condition of approving the merger of GSK’S South Africa operations with Aspen (139, 140).</td>
</tr>
</tbody>
</table>

AIDS, acquired immunodeficiency syndrome; GSK, GlaxoSmithKline; HIV, human immunodeficiency virus; LIC, low-income country; LDC, least developing country; SACU, Southern African Customs Union; SADC, Southern African Development Community; WHO, World Health Organization.
Annex IV Interviewed individuals

Christoph Bonsmann, Action Medeor, Germany
Patrizia Carlevaro, Eli Lilly MDR TB Initiative, Switzerland
Tobias Dzangare, Varichem, Zimbabwe
Michael Gebbers, Pharmakina, Democratic Republic of the Congo
Yusuf Hamied, Cipla, India
Anand Iyer, Ranbaxy, India
Jean-Marie Kindermans, Artepal Project, Belgium
Krisana Kraisintu, independent consultant, Thailand
Morena Makhoana, BIOVAC Institute, South Africa
Stavros Nicolaou, Aspen Pharmacare, South Africa
Mohamed Rabie, Vacsera Holding Company, Egypt
Rabbur Reza, Beximco, Bangladesh
Iain Robertson, Eli Lilly MDR TB Initiative, United States
Nina Sautenkova, WHO-EURO, Denmark
Nasser Shahrear Zahedee, Radiant, Bangladesh
Five anonymous sources from the Indian pharmaceutical industry
Annex V Interview protocol

Interview methodology

All interviews were carried out by the author, primarily by telephone. Interviews were requested from October 2009 to December 2009 with individuals involved in the larger-scale technology transfer initiatives or with entities involved in more than one initiative. Given the infeasibility of interviewing representatives of all the initiatives, interviewees were selectively targeted to cover the different disease areas and the different regions, and to understand better the perspective of both transferors and transferees. However, interviews carried out were subject to the availability and willingness of individuals to be interviewed. Additional interviewees were identified through “snowballing” – that is, individuals recommended by initial interviewees and other stakeholders.

Semi-structured interviews were carried out based on the list of questions below. Upon request, the questions were provided in advance to interviewees. Given the potentially sensitive nature of some of the questions and information, all interviewees were given the option of remaining anonymous. Each interview lasted approximately 30–60 minutes. Additional questions were posed in response to new information provided throughout the interview.

Standard interview questions

1. Introduction of research project.

2. How would you like to be accredited in the report?
   (a) For attribution: your responses may be quoted and attributed to you.
   (b) Not for attribution: your name will be included on a list of interviewees, but no specific quote or information will be attributed to you.
   (c) Totally anonymous: no mention of your name in the report.

3. (For interviews on specific projects): How did the technology transfer collaboration first come about?

4. Who are the key actors involved (e.g. companies, government ministries, international agencies)? Are there any specific government policies that encouraged the technology transfer project?

5. What type of technology was transferred and how (i.e. know-how, in-person training, hardware, software, data/documentation, intellectual property rights)?

6. What specific stages of the production process were covered (e.g. raw materials, intermediates, API, formulation, packaging, other)?
7. What has been the impact of the technology transfer on price, quality and the security/stability of local supply?

8. How was intellectual property managed?

9. What environmental policies were linked to the technology transfer, if any (e.g. extra safeguards, limitations on inputs, additional requirements above business as usual)?

10. What were the main challenges and opportunities of the initiative(s)?

11. Additional questions specific to each initiative.