

Local Production for Access to Medical Products: Developing a Framework to Improve Public Health



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IA
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Financing

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Local Production for Access to Medical Products: Developing a Framework to Improve Public Health



**World Health
Organization**

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

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Contents

Abbreviations	1
Acknowledgements	2
1. Introduction	3
2. Setting the context, background and definition of key concepts of local production, technology transfer and access to medical products in developing countries	5
2.1 Setting the context	5
2.2 Brief historical background	8
2.3 Definition and understanding of key concepts	9
2.3.1 "Access to medicines" and medical products	9
2.3.2 Essential medicines	10
2.3.3 Local production	11
2.3.4 Developing countries and definition by low to high income	13
2.3.5 Technology transfer	14
3. Overview of local production, technology transfer and access to medical products in developing countries	16
3.1 Arguments and evidence relating to local production and access to medical products	16
3.1.1 Overview	16
3.1.2 Barriers to local production are numerous and varied	17
3.1.3 Evidence from the literature on links between local production and access	18
3.1.4 Activities of Phase 1 of the project on improving access to medical products through local production	21
3.1.5 Discussion of common themes on local production, technology transfer and access to medical products	26
3.2 Common findings from Phase 1 actions on local production, technology transfer and access to medical products	32
3.2.1 Local production is growing in developing countries	32
3.2.2 Technology transfer is an important factor in coping with barriers to enable local production	33
3.2.3 Intellectual property rights are important for decisions on local production and technology transfer	33
3.2.4 Local production has the potential to improve access to medical products	34
4. The need for a policy framework for local production and access to medical products in developing countries	37
4.1 Why a policy framework for local production and access to medical products in developing countries is needed	38
4.2 The industrial policy perspective: Factors of relevance for local production	41
4.3 The health policy perspective: Key factors to ensure access to medical products	43
4.3.1 Universal access to medical products	44
4.3.2 Availability of essential medical products	45
4.3.3 Affordable prices	46
4.3.4 Quality assurance and regulatory support	47
4.3.5 Uninterrupted supply of medicines	49
4.3.6 Rational selection and rational use of medical products	49

5. Building a framework for government support for local production and access to medical products	50
5.1 The shared goals of industrial and health policies for local production and improvement in access to medical technology	50
5.1.1 <i>Policies to ensure strategic selection of essential medical products for local production.</i>50
5.1.2 <i>Policies to enable pricing of locally produced medical products that governments and people can afford</i>51
5.1.3 <i>Policies to ensure strict compliance to quality standards by manufacturers and effective national medicine regulatory authorities.</i>52
5.1.4 <i>Policies that ensure health security – an uninterrupted supply of essential medical products</i>52
5.1.5 <i>Innovation policies for development of formulations more suitable for local conditions</i>52
5.2 Government Support to local production for improving access to medical products	54
5.3 Direct government support to the local manufacturers of essential medical products.. . . .	54
5.3.1 <i>Policies that reduce the cost of manufacture</i>54
5.4 Indirect government support to the local manufacturers of essential medical products	55
5.4.1 <i>Invest in strengthening national medical products' regulation</i>55
5.4.2 <i>Develop national priority lists of medical products list.</i>55
5.4.3 <i>Improve the financing of health services for expanding the domestic market</i>55
5.4.4 <i>Facilitate access to foreign markets.</i>56
5.4.5 <i>Facilitate development of regional pooled procurement mechanisms</i>56
5.4.6 <i>Encourage regulatory harmonization</i>56
5.4.7 <i>Introduce appropriate pricing policies:</i>56
5.4.8 <i>Facilitate relevant transfer of technology</i>57
5.4.9 <i>Support incremental innovation and production:</i>57
5.4.10 <i>Develop appropriate intellectual property regimes</i>58
5.4.11 <i>Develop appropriate investment policies and facilitate joint ventures</i>59
5.4.12 <i>Facilitate international cooperation for local production</i>60
6. The way forward: Using the framework to advance industrial and health policy goals with regard to local production	61
6.1 Policy analysis for policy coherence	61
6.2 Development of global resources on local production, technology transfer and access to medical products	62
6.3 Advocacy for policy framework for local production and access to essential medical products	62
6.4 Capacity-building and technical assistance for local production of selected essential medical products	63
7. Conclusions	64
References	65

Abbreviations

AIDS	acquired immunodeficiency syndrome
API	active pharmaceutical ingredient
ARV	antiretroviral medicine
CIPHI	Commission on Intellectual Property Rights, Innovation and Public Health
DCVMN	Developing Countries Vaccine Manufacturers Network
DNDi	Drugs for Neglected Diseases Initiative
EPI	Expanded Programme on Immunization
GAVI	Global Alliance for Vaccines and Immunisation
GMP	good manufacturing practices
GNI	gross national income
GSPA-PHI	Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property
HIV	human immunodeficiency virus
ICTSD	International Centre for Trade and Sustainable Development
LDC	least-developed country
NGO	nongovernmental organization
PEPFAR	United States President's Emergency Plan for AIDS Relief
R&D	research and development
TB	tuberculosis
TRIPS	trade-related aspects of intellectual property rights
UN	United Nations
UNCTAD	United Nations Conference on Trade and Development
UNICEF	United Nations Children's Fund
UNIDO	United Nations Industrial Development Organization
WHO	World Health Organization
WTO	World Trade Organization

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1. Introduction

This paper is the output of work commissioned and undertaken by the World Health Organization (WHO), the United Nations Conference on Trade and Development (UNCTAD), the International Centre for Trade and Sustainable Development (ICTSD) and a range of stakeholders working in the fields of public health, industrial policy and development (United Nations, 2011a; WHO, 2011a,b,c,d,e).¹ It is supported by funding from the European Union.² The aim of this work was to develop a framework that could bring together and guide policy-makers and others from all these relevant fields. The framework presented here provides an entry point for supporting the local production of medicines, vaccines and diagnostics in a manner that should improve access to those medical products maximizing the potential to improve public health.

The definitions and assumptions that have been made are set out in section 2.

The project itself is in two phases. Phase 1 of the project concentrated on identifying the main challenges and obstacles to local production and related technology transfer in developing and least-developed countries. The project involved commissioned literature reviews to describe the current landscape and historical and current trends; regional workshops with a broad range of stakeholders; and in-country work to investigate and describe a series of company-focused case studies from low- and middle-income countries. This document seeks to provide an overview of these findings in a style that is accessible to all readers and summarizes the issues at a high level. It is based on the ongoing work and wider evidence on the issues of local production and access to medical products from the wider literature available on the topic. For a more detailed discussion of the trends in local production, and the methods, analysis and findings from Phase 1, readers should be guided by the references throughout this document and the series of reports available for free download from the WHO web site.

In phase 2, the framework, as it develops, will be used to guide the actions of WHO and its partners in support of local production within developing and least developed countries.

Following the introduction, the main body of the paper is presented in six sections. Section 2 provides an historical overview and explores the definitions and assumptions associated with the debate surrounding local production and access to medicine and medical products. Section 3 provides an analysis of the feasibility arguments for and against the role of local production in improving access to medical technologies. It considers the barriers and challenges that exist to building local production capacity and ensuring access to good-quality affordable medical products. It presents the findings

1 The project is called "Improving access to medicines in developing countries through technology transfer and local production." Further information and all the reports associated with this project are available for free download at <http://www.who.int/phi/en/>

2 This is an action under a European Parliament Resolution to support pharmaceutical-related transfer of technology and capacity-building for local production of medicines in developing countries, especially in least developed countries (European Parliament, 2007).

of the project in the context of existing evidence and highlights cases from the in-country work where there are positive indications that local production capacity has the potential to meet domestic public health needs.

Section 4 attempts to bring these arguments together to identify where there are shared goals for industrial and health policy and concludes with identifying these in a common framework. In section 5, this framework is used as the basis to identify the role of governments in creating a coherent policy environment of incentives and regulation to support local production. Section 6 offers a potential way forward and section 7 provides some brief conclusions.

The findings presented here, coupled with the extensive experience of the organizations involved in the project, demonstrate that the links between local production and improved access to medical products may not materialize automatically. The authors are of the view, however, that it is possible for local production to contribute to increased access, provided that certain conditions are met and actively encouraged by governments and other stakeholders. To achieve this positive outcome, it is not simply a matter of “joining the dots”. Rather, a systematic approach, presented as a framework, is required in order to consider all of the issues that need to be addressed to create the best environment to improve both local production and public health.

Finally, this framework is offered as a contribution to the debate and is very much a work in progress. As we continue the development of the framework, we seek to bring attention to these issues with an inclusive approach, in a manner that is open to developing, adapting and building on these ideas to maximize the potential for local production to improve access to medical products.

2. Setting the context, background and definition of key concepts of local production, technology transfer and access to medical products in developing countries

2.1 Setting the context

Health is an established human right. In a review, 135 of 186 national constitutions (73%) include provisions on health or the right to health, and access to essential affordable medicines has been recognized as one part of that right to health (Hogerzeil et al., 2006; Perehudoff, 2008). Improving access to essential affordable medicine is also one part of the Millennium Development Goals.³ And yet access to medicines remains a challenge, as millions of poor people, especially in developing countries, are unable to obtain medicines when they need them the most. Medicine availability and prices in both the public and the private sector are key indicators of access to treatment. Surveys of medicine prices and availability, conducted using a standard methodology, have shown that poor medicine availability, particularly in the public sector, is a key barrier to access to medicines. For example, public-sector availability of a selection of generic medicines⁴ is less than 60% across WHO regions (WHO, 2011f).

Substantial production of generic medicines, vaccines and increasingly diagnostics already takes place in a number of low- and middle-income countries. India and China are major producers of generic pharmaceuticals, vaccines and biologicals, and active pharmaceutical ingredients (APIs), and their role has been critical to meeting public health needs in many low-income developing countries, especially in Africa. As an example of their significance, 80% of all donor-funded annual purchase volumes of antiretroviral medicines (ARVs) in 2008 were supplied by Indian manufacturers (Waning et al., 2010). Global API production has also been steadily concentrating in India, China and the Republic of Korea. Around 75% of API production from China and India is exported to the rest of the world (Bumpas & Betsch, 2009). More than half the world's children are immunized with vaccines produced in India (*The Economist*, 2011a; Serum Institute of India, 2011). There has also been an expansion in the manufacture of diagnostic devices in a number of developing countries (WHO, 2011g).

The global contributions from India and China are impressive, but the inherent size of their own economies and the development of their industry before

3 Millennium Development Goal Target 8.E: In cooperation with pharmaceutical companies, provide access to affordable essential drugs in developing countries. See <http://www.un.org/millenniumgoals/global.shtml>

4 WHO defines generic medicines as "Pharmaceutically equivalent or pharmaceutically alternative products that may or may not be therapeutically equivalent. Multisource pharmaceutical products that are therapeutically equivalent or interchangeable" (WHO, 2006a).

the Trade-Related Aspects of Intellectual Property Rights Agreement (TRIPS Agreement) coming into effect mean they are often considered as outliers in discussions about local production of medical products in developing countries. There are important lessons to be learnt from the experiences of India and China, some of which are highlighted in this report, they do not provide a readily transferable blueprint for other countries wishing to replicate their success.

Nevertheless, there are strong economic and political drivers to establish and enhance national capacity to manufacture medical products, particularly in the pharmaceutical sector, where the majority of the debate around local production and access has been centred. This has meant the development of many domestic, bilateral and international initiatives for local production of medical products. Over a period of time, a second tier of developing countries, mostly middle income, has also developed a considerable pharmaceutical and vaccine production capacity. Examples include, but are not limited to, Argentina, Brazil, Cuba, Indonesia, the Islamic Republic of Iran, Jordan, South Africa, the Republic of Korea and Thailand. Despite these noteworthy achievements, the fact remains that manufacturing capacity in most low-income countries is limited.

With a number of important initiatives to support local production (see below), and discussion in international fora such as the European Parliament Resolution and the World Health Assembly of WHO, there is now a desire to see that support for these initiatives improves access to medical products (European Parliament, 2007).⁵

Furthermore, trends in local production of medical products are continuing to change (Anderson, 2010; WHO, 2011a,b). In large developing countries, pharmaceutical companies and biotechnology companies are beginning to invest in research and development (R&D), pursuing patent protection for their products and aiming at markets in industrialized countries (Arora et al., 2009; Chaudhuri, 2010; Gehl Sampath, 2008).

A number of countries are investing in innovation strategies, and the second-tier countries are in competition to supply their own branded generic medicines to the global market (e.g. see United Nations, 2011).

There has also been a role for supporting local production via the transfer of technology, both north–south and south–south, especially in the cases of vaccines and diagnostics. A number of examples are highlighted in this document and the accompanying reports.

5 World Health Assembly Resolution WHA 59.24 requested the WHO Director-General to convene an intergovernmental working group to draw up a global strategy and plan of action aimed at, inter alia, securing an enhanced and sustainable basis for needs-driven essential health research and development relevant to diseases that disproportionately affect developing countries. The group completed its work in May 2008, when the Sixty-First World Health Assembly adopted Resolution WHA 61.21: Global strategy and plan of action on public health, innovation and intellectual property.

As local companies grow and become established, they are becoming attractive assets for acquisition. There is a discernable trend that pharmaceutical companies from high-income countries are strategically expanding their hold in emerging markets, and there are examples of their buying up established generic manufacturers in developing countries (Chaudhuri et al., 2010a). Consolidation is occurring in the global diagnostics industry, where, for example, a company based in the United States of America has acquired over 30 independent producers within 5 years, including companies operating in low- and middle-income countries. In the pharmaceutical sector, developing country firms have also been under increased pressure, leading to several mergers and acquisitions, as observed over the past few years in the Indian pharmaceutical market (Arora et al., 2009; Chaudhuri, 2010; Gehl Sampath, 2008). Recent examples of such transactions include Daiichi Sankyo's acquisition of Ranbaxy, Abbott's acquisition of Piramal, and GlaxoSmithKline's acquisition of South Africa's Aspen Pharmaceuticals.

These developments are against a backdrop of a changing intellectual property rights regime, with an increasingly uniform approach to intellectual property under the TRIPS Agreement, coupled with TRIPS-plus provisions in free trade agreements that may well limit the freedom of countries to manufacture generic medicines and other medical products (e.g. see Fink & Reichenmiller, 2005; Roffe & Spennemann, 2006; United Nations, 2011b). TRIPS establishes uniform minimum standards on intellectual property rights to which all World Trade Organization (WTO) Members must adhere. In 2001, the Doha Declaration on TRIPS and Public Health extended the period for least-developed countries (LDCs) to comply with provisions on pharmaceutical product patents to 2016. LDCs also benefit from a general transition period until 2013 exempting them from substantial obligations under the TRIPS Agreement. There is an expectation that this general transition period will be extended as Bangladesh has filed a request in this regard on behalf of the LDC Group at the WTO TRIPS Council in November 2011⁶, if WTO Members do not manage to agree on the extension on either of these transition periods these countries would have to comply with the TRIPS Agreement standards for protection of pharmaceuticals after 2016 (WTO, 2011). The TRIPS Council is expected to decide on the extension of the 2013 transition period in 2012. In other words, in the absence of a further exemption, the production of generic medicines would be made difficult in LDCs. In this context, the next 5 years (i.e. until the current exemption expires) are critically important for strengthening local production capacities. This situation is coupled with the open question of whether, due to changes in law and industry in India, India will continue to be a sustainable global supplier of affordable medicines. Such a potential threat to health security adds more weight to any decision to support local and regional manufacturing capacity from a strategic point of view – an argument well made, for example, in the case of the United Republic of Tanzania (Chaudhuri et al., 2010b). Even as local production is being actively pursued in a number of developing countries, however, a causal link between local

6 Elements Paper On The Extension Of The Transition Period Under Article 66.1 Of The Trips Agreement, Communication from Bangladesh on behalf of the LDC Group, IP/C/W/566.

production and improved access to high-quality medical products remains implicit in most cases. The evidence that is published to date can neither support nor refute these assumptions. Even within India, a large producer of medical products, the link between Indian domestic production and access of the Indian population to these products is not well established (Chaudhuri, 2007).

Yet the growth of local production is indisputable, and the future scenarios for the availability of good-quality affordable medical products will no doubt be affected by this reality. Therefore, the degree to which existing local production for medical products and the new investments in this area in developing countries can be aligned with those countries' public health needs is an important question that forms the basis for this project.

2.2 Brief historical background

Local production appeared for the first time in WHO discussions in 1978 during the International Conference on Primary Health Care (WHO, 1978). In the following decades, the issue of local or domestic production was promoted by United Nations (UN) agencies through the acquisition of technologies by technology transfer and local production capacity (UNCTAD, 2002) and assistance to build domestic production capacities at the firm and sector level (United Nations Industrial Development Organization (UNIDO)).

From 1995, with the establishment of WTO and adoption of the TRIPS Agreement, the discussion about stronger, longer and more uniform application of intellectual property protection and its impact on access to medicines in developing countries became important. While intellectual property rights provide important incentives for the development of new pharmaceutical products, concerns were raised about already underserved public health needs in developing countries due to (1) delays in the introduction of generic medicines because of the new intellectual property regime, (2) the impact on generic manufacturers in large developing countries in terms of restrictions to reverse-engineer the product-patented medicines and make available generic medicines, (3) the practice of "evergreening"⁷ patent protection, and (4) the tendency among manufacturers in some of these countries to turn their investment attention to the development and production of medicines for developed country markets (European Commission, 2009).⁸

The Fifty-Sixth World Health Assembly established the Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH) in May 2003. The aims of CIPIH were to "review the interfaces and linkages between intellectual property rights, innovation and public health" and to "examine in

7 According to the WHO Commission on Intellectual Property Rights, Innovation and Public Health, "ever-greening occurs when, in the absence of any apparent additional therapeutic benefits, patent-holders use various strategies to extend the length of their exclusivity beyond the 20-year patent term" (WHO 2006b).

8 See also, for example, the 2011 Economic Partnership Agreement between India and Japan, which contains a clause promoting trade in generic medicines between the two countries.

depth how to stimulate the creation of new medicines and other products for diseases that mainly affect developing countries” (CIPIH, 2011). In 2006 CIPIH produced a report in which it discussed local production as a means of reducing the prices of medicines and enhancing the bargaining position of developing countries for compulsory licences (WHO, 2006b: pp. 100, 120–123, 127). The report also identified some input-related barriers to local production and offered general solutions for these barriers (WHO, 2006b: pp. 151–153).

The recommendations of the CIPIH report became the basis for negotiations between WHO Member States, and in 2008 the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA-PHI) was adopted. GSPA-PHI has brought a new emphasis to local production as a means of contributing to the overall goals of promoting technology transfer, innovation, capacity-building and improving access.⁹ It is the implementation of this strategy that brings together the organizations associated with this project.

2.3 Definition and understanding of key concepts

2.3.1 “Access to medicines” and medical products

The term “access to medicines” describes the various factors that interplay to determine the degree of access of patients to a wide range of medical products and services. In the context of this report, the focus is on local production and access to medical products. The term “medical products” is used in this report as a collective term to cover pharmaceuticals, vaccines and diagnostics and does not include medical devices and other health services.

Defining access is a construct that encompasses various dimensions distinguished by sets of specific relationships and market forces that differ for different medical products. For example, the diagnostics market is largely profit-driven, with little public-sector influence on price; for vaccines, however, the public sector plays a key role in setting prices and in procurement, for example with global purchase schemes administered by the United Nations Children’s Fund (UNICEF) and the Global Alliance for Vaccines and Immunisation (GAVI). The WHO 2004 Framework on access to medicines describes four key areas to ensure access: (1) A rational selection of medicines, (2) adequate financing, (3) affordable prices and (4) reliable supply systems (WHO, 2004a). There is also ongoing work to expand the conceptualization of access and prioritized policy research (Alliance for Health Policy and Systems Research, 2011). Combining this work, we can describe five dimensions of access to which medical products are subject:

⁹ Element 3 of GSPA-PHI, on building and improving innovative capacity, highlights key areas for investment, including capacities related to science and technology, local production of pharmaceuticals, clinical trials, regulation, intellectual property and traditional medicines. Element 4 of GSPA-PHI (promoting transfer of technology and the production of health products in developing countries) on transfer of technology emphasizes north–south and south–south development cooperation, partnerships and networks to build and improve transfer of technology related to health innovation.

- **Physical availability:** Defined by the relationship between the type and quantity of product or service needed, and the type and quantity of product or service provided.
- **Affordability:** Defined by the relationship between the prices of the products or services, and the user's ability to pay for them.
- **Geographical accessibility:** Defined by the relationship between the location of the product or service, and the location of the eventual user of the product or service.
- **Acceptability (or satisfaction):** Defined by the relationship between the user's attitudes and expectations about the products and services, and the actual characteristics of the products and services. This includes both the rational selection of medical products, for example through the creation of a national essential medicines list (see below), and measures to ensure the appropriate or rational use of those medicines or products within the health system (WHO, 2011h,i,j).¹⁰
- **Quality:** Defined by the product being assured by a regulatory body to meet national or international standards, for example pharmacopoeial specifications for pharmaceuticals (WHO, 2011k)¹¹ or the WHO Technical Report Series for vaccines and good manufacturing practice (GMP) (WHO, 2011l). Quality assurance ensures a product's safety and efficacy. It is an essential component of access that cuts across all the other dimensions (Management Sciences for Health, 2000).

These dimensions interact; for example, a medicine may be available within the private sector but may not be accessible to poor people if the price is too high. Similarly, there is an interdependence of products and services, such that medicines may be available within a country but access is denied if the person does not have access to diagnosis or screening.

2.3.2 Essential medicines

It is important to consider that a measure of access is related to the degree to which the product meets the health needs of the patient population. WHO has identified "essential medicines" – that is, medicines it considers to meet high-priority health-care needs of the population. Essential medicines are selected with due regard to public health relevance, evidence on efficacy and safety, and comparative cost-effectiveness (WHO, 2010a). Essential medicines are intended to be available within the context of functioning health systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality and adequate information, and at a price the individual and the community can afford.

10 In 2007, WHO, in collaboration with the Government of the Netherlands, launched the Priority Medical Devices project. The aim of the project was to bring medical devices to the attention of policy-makers and to help guide both industry and government on public health spending.

11 The International Pharmacopoeia comprises a collection of quality specifications for pharmaceutical substances (active ingredients and excipients) and dosage forms, together with supporting general methods of analysis, and is intended to serve as source material for reference or adaptation by any WHO Member State wishing to establish pharmaceutical requirements.

The WHO Model List of Essential Medicines, reviewed every 2 years, is a guide for the development of national and institutional essential medicine lists. The current Model List is the seventeenth revised version of the list and was prepared by the WHO Expert Committee in March 2011. For the past 30 years the Model List has led to a global acceptance of the concept of essential medicines as a powerful means to promote health equity. Most countries have national lists, and some countries also have provincial or state lists. National lists of essential medicines usually relate closely to national guidelines for clinical health-care practice used for the training and supervision of health workers. WHO now also maintains a model list of essential medicines for children, currently in its third edition (WHO, 2011f,m).

2.3.3 Local production

There are two important ways of understanding local production. One is with respect to the production's territorial location and consequently the jurisdiction under which it operates. This is often used to imply production outside of an industrialized country and is usually a shorthand term to mean production in a developing or least-developed country. A second way of understanding local production is by defining ownership. For example, manufacturing taking place within a country and subject to a national jurisdiction may be considered "local production", regardless of whether nationals or foreigners own the business; from another perspective, however, it is felt that if nationals do not have more than a majority ownership, then the business may not be called "local production". For the purposes of Phase 1 of this project, the territorial/ jurisdictional basis of describing production has been used, as the objective in this phase was to explore the wide variation of local production that currently occurs in developing countries. Such production often occurs within firms that are locally controlled, either entirely or partly, or through foreign companies that are located there. Phase 1 showed that although medicines are produced in a range of countries and situations, access to medicines is not always the paramount consideration, regardless of the ownership issue. A distinction can be drawn between some cases of locally owned local production (e.g. production of ARVs in Uganda and vaccines in Thailand) and production that occurs locally through a wholly owned subsidiary company of a multinational enterprise (as illustrated by the case study for Indonesia).

Therefore, the debate of whether local production should be defined in either a territorial or an ownership-based manner misses the point. The lesson for phase 2 of this project is that, from a public health perspective, local production should in any event have the explicit intention of improving access to medical products for populations in such countries.

Three different manufacturing stages define the level of production:

- **Tertiary manufacturing** is the packaging of already formulated products and may involve some small-scale production. It is the most common form of local production found in low-income countries and LDCs.

- **Secondary manufacturing** involves the mixing of raw materials and production of different dosage formulations. Much of the manufacturing that takes place in middle-income countries is of this type.
- **Primary manufacturing** is the manufacturing of APIs, intermediaries and excipients. Primary manufacturing takes place in industrialized countries and large developing countries such as India and China. Generally, primary manufacturing countries have all three manufacturing processes vertically integrated within the company, although the manufacture may be spread over many locations (Bennett et al., 1997).

It is recognized that these categories are generalizations and increasingly becoming outmoded, with a number of low-income countries and LDCs able to demonstrate growing capacity in tertiary, secondary and even limited primary manufacture. Also, within a company different product lines may demonstrate these different manufacturing levels.

According to the WHO *World medicines situation*, primary medicine production is highly concentrated in industrialized countries; just five countries – the United States of America, Japan, Germany, France and the United Kingdom of Great Britain and Northern Ireland – account for two-thirds of the value of all medicines produced. Large-volume production of lower-price medicines exists in the highly competitive domestic markets of China and India. In 2004, WHO undertook a classification of countries, according to their medicines production capability, updating the work carried out by UNCTAD in 2002. Of 188 countries classified, 10 industrialized countries had “sophisticated industry with significant research”; a further 16 countries, including India and China, were grouped as having “innovative capability”, with India described as having a rapidly growing pharmaceuticals biotechnology market. Ninety-seven countries had a domestic medicines industry based on reproducer firms, manufacturing branded or generics; although the majority (84) of these countries manufacture finished products from imported ingredients, 13 countries (including Brazil, Egypt, Norway, Turkey and Indonesia) were considered to have industries that make both active ingredients and finished products (WHO, 2004b).¹²

Local production of vaccines in most developing countries is less common than that of pharmaceuticals and is more situated within the public sector. Developing country manufacturers with WHO prequalified vaccines on the market include Brazil, Bulgaria, Cuba, India, Indonesia, the Republic of Korea, the Russian Federation, Senegal and Thailand.

Manufacturers from 14 countries (Argentina, Brazil, Cuba, Egypt, India, Indonesia, the Islamic Republic of Iran, Mexico, China, the Republic of Korea, Romania, South Africa, Thailand, Viet Nam) have formed the Developing Countries Vaccine Manufacturers Network (DCVMN). This is a voluntary public health-driven alliance of vaccine manufacturers from developing countries that aims to make a consistent supply of good-quality vaccines accessible

¹² Please note the third edition is now available (WHO, 2011f).

to developing countries, especially the vaccines used in the WHO Expanded Programme on Immunization (EPI) (Jadhav et al., 2008). Two of every three children born in the world are immunized with at least one vaccine from a DCVMN manufacturer.

The situation for diagnostics is more complex. Manufacturers of diagnostic tests range in size and scope, from large multinational corporations to small local companies employing a handful of people. The market is less dominated by large multinational corporations compared with other medical product sectors, with an estimated 42% share of global revenues being taken by small companies in 2008. Diagnostics developed by large multinational companies are targeted primarily at developed country markets, and most make their way to developing countries through donor programmes. There is often segmentation of the market due to the presence in the market of large numbers of small companies. Complexities of manufacture, due to non-availability of complex technologies, or due to difficulties in technological upgrading, restrict production of some products, and the focus of most developing country manufacturers is on simple technologies. In the diagnostics sector a lack of regulation and quality assurance has allowed a flourishing market of substandard and copycat tests to emerge in parts of the developing world (Blacksell et al., 2006; Morris, 2011; WHO, 2010b). Where local production of quality-assured diagnostic products has been achieved, it often struggles or cannot even attempt to compete against these substandard products that do not have to include the cost of quality control in their production costs (e.g. see WHO & Special Programme for Research and Training in Tropical Diseases, 2011).

2.3.4 Developing countries and definition by low to high income

One approach to the grouping of countries has been established by the World Bank and is on the basis of gross national income (GNI) per capita – low income, middle income (subdivided into lower middle and upper middle) and high income.¹³ The low- and middle-income economies are also referred to as “developing economies”. Among low-income countries are a group of 48 countries (in 2009) called LDCs, which are the weakest and poorest among developing countries. Of the 48 LDCs, 33 are in Africa, 14 in Asia and the Pacific, and 1 in Latin America (United Nations Office of the High Representative for the Least Developed Countries).

Such income-based classification does not correspond to the pharmaceutical production capacity of the countries. For example, China and India, each with a population over 1 billion, are lower-middle-income economies but are the largest producers by volume of pharmaceuticals, including APIs. At the other end of the spectrum are the LDCs, many of which have little or no pharmaceutical production capacity. Even in this latter group, however, there are important exceptions, including Bangladesh, Cambodia, Ethiopia, the

¹³ Economies are divided according to 2009 GNI per capita, calculated using the World Bank Atlas method. The groups are: low-income – GNI US\$ 995 or less; lower middle-income – US\$ 996–3945; upper middle-income – US\$3 946–12 195; and high-income – US\$ 12 196 or more.

United Republic of Tanzania, the Sudan, Uganda and Yemen. All of these LDCs are at various levels of basic pharmaceutical production. In between these two poles are a large number of developing countries belonging to various income groups and having varying levels of development in pharmaceutical production. Among upper-middle-income developing countries, important producers of medical products include Brazil, Cuba, the Islamic Republic of Iran, South Africa and the Russian Federation. Among lower-middle-income developing countries (apart from India and China), Indonesia, Egypt, Jordan, Morocco, Nigeria, Pakistan, the Philippines, the Syrian Arab Republic, Thailand, Tunisia and Viet Nam are known to have sizeable pharmaceutical industries. High-income countries in the Gulf, especially the United Arab Emirates and Saudi Arabia, are also increasingly developing their pharmaceutical industries. The Republic of Korea in this income group has emerged as a major supplier of APIs and, increasingly, finished medical products.

Such a range of manufacturing situations throughout countries at different stages of development means that if the conditions to establish the right environment can be identified and appropriately supported, then the level of economic development is not a barrier per se to establishing a manufacturing base for medical products.

2.3.5 Technology transfer

Although technology transfer has been a key issue in international forums for a long time, no single widely accepted definition of technology transfer exists (e.g. see Maskus & Reichman, 2005; Patel et al., 2000). The UNCTAD Draft International Code on the Transfer of Technology is one of the earliest efforts to define technology transfer as the “transfer of systematic knowledge for the manufacture of a product, for the application of a process or for the rendering of a service, which does not extend to the transactions involving the mere sale or mere lease of goods” (UNCTAD, 1985: Chapter 1, Para. 1.2).

Throughout this project, and in this document, “transfer of technology” is understood as the transfer of technical information, tacit know-how and performance skills, technical materials or equipment, jointly or as individual elements, with the intent of enabling the technological or manufacturing capacity of the recipients. Such transfer can take place within a variety of configurations, including public and private, institutional and individual, formal and informal, through partnerships and joint ventures, and within and across national borders. Specifically in the context of medical products, activities related to the transfer of technology may include the explicit aim of bringing together those that either own the technology or possess the know-how (where a technology is free from property rights) and the intended recipients of technology to interact in a mutually beneficial manner, while promoting public health objectives. It must be noted that transfer of technology only implies incorporation of appropriate measures to ensure the quality of products produced, and such quality assurance has to be locally enforced through regulation. Technology transfer remains a top priority for developing countries, and intellectual property protection is often seen as a tool to control access to technology and maintain strategic dominance in

the market. The TRIPS Agreement on the one hand has set higher standards of patent protection, but on the other hand in Article 7 WTO Members have agreed that “the protection and enforcement of intellectual property rights should contribute to the promotion of technological innovation and to the transfer and dissemination of technology, to the mutual advantage of the producers and users of technological knowledge and in a manner conducive to social and economic welfare, and to a balance of rights and obligations.” In Article 66.2, developed countries are asked to provide incentives to their enterprises and institutions to encourage technology transfer to LDCs to enable them to create a sound and viable technological base.

Although technology transfer remains an important component of the TRIPS Agreement, in 2003 the TRIPS Council decided that developed country Members must submit full reports on activities undertaken to meet these obligations every 3 years. A recent analysis of such reporting has shown that only 21 countries and the European Union have submitted a report since 2003. The analysis has found little evidence that TRIPS Article 66.2 has resulted in significant additional incentives beyond “business as usual” for transferring technology to LDC Members, and no case of transfer of pharmaceutical technology (Moon, 2011).

However, on a broader scale, the case studies point to several examples where developing country firms have transferred pharmaceutical or vaccine technology to other developing countries. Technology transfer also takes place through collaboration between researching and generic companies, including through the increasing number of voluntary license agreements (WHO, 2011b]. It is difficult to quantify the extent of such technology transfer, however, as these transactions are not covered by the TRIPS Article 66.2 reporting requirements, and may not always include transfer to LDCs.

3. Overview of local production, technology transfer and access to medical products in developing countries

3.1 Arguments and evidence relating to local production and access to medical products

3.1.1 Overview

The International Conference on Primary Health Care, held in Alma-Ata in 1978, stated:

In developing a supply system, consideration has to be given both to cost and to national and local production as part of overall development. For example, it may be cheaper to buy certain items abroad, but economically more productive in the long run to produce them within the country. This principle may also apply to the alternatives of national purchasing and local production.

Industrial and innovation policy advocates argue that static costs of developing production capacity can be offset by the dynamic gains that accrue from reasonably priced products that are locally produced in the mid- or long term, provided countries ensure a policy environment that secures increasing financial returns to local enterprises over time. Other arguments in favour of local production in small developing countries include reliability of supply, foreign import savings, and the potential impact on the global market by increased competitive pricing. The need for government support, however, is also emphasized in these arguments. The indirect benefits of promoting local production on national economies have also been identified as including employment generation, foreign export earnings through export of medical products, and spill-over effects in other sectors of the economy (Gehl Sampath, 2010; United Nations, 2011c: Chapter 2).

To establish themselves as economically viable in the short to medium term, local producers, particularly those based in low-income countries, have to address one or all of a number of major challenges. These challenges may include weak physical infrastructure; scarcity of appropriately trained technical staff; dependence on import of raw materials, including essential APIs; lack of economies of scale; high import duties and taxes; lack of a conducive policy environment and policy coherence across sectors; weak and uncertain markets; weak quality control and regulation measures; proliferation of patents on minor changes in health products; and, where recognized, data exclusivity rules that make the authorization of generic medicines more timely and costly. The extent of these respective problems necessarily differs from country to country, however, and requires a country-by-country analysis.

Overcoming these challenges can inflate the cost of production, which means the final product is often available for a higher price, making the end product relatively non-competitive with potentially cheaper imports. This difficulty

in being competitive at start-up can reduce the economic feasibility of local production in the short term. According to Kaplan & Laing (2005), “local production of medicines at higher cost than equivalent imports may have no impact whatsoever on patient access to needed medicines”.

Such a focus on assessing economic feasibility from a static short-term perspective tends to ignore public health factors and the strategic long-term benefits, highlighted in the Alma-Ata Declaration, of establishing regional or national capacity to ensure access into the future. From the research published to date (see below), there is no clear method for assessing this long-term benefit to balance the short-term economic disadvantages. It is also not clear how an assessment of whether public health needs and objectives of improving access to medicines are to be factored in. For some neglected diseases, no satisfactory diagnostics or medicines are currently available, and local innovation for development and production may be the only option to fill the needs gap.

3.1.2 Barriers to local production are numerous and varied

As mentioned above, local production and related technology transfer in low- and middle-income countries often operate in a difficult environment. Although the same challenges are not equally present in all countries, the following issues have been identified as commonly occurring:

- **Human resource constraints:** Human resources include trained and licensed pharmacists; people with expertise in chemistry, pharmacology, and physical, chemical and biological sciences; technicians and engineers who can use and repair precision scientific equipment; and business managers. The three LDC case studies (Bangladesh, Ethiopia, Uganda) show that the national universities in these countries have made significant efforts to strengthen their faculties in the sciences, but other countries, particularly those within sub-Saharan Africa, are lagging far behind. There are also limited opportunities for entrepreneurs and business managers to receive training or professional support and mentoring.
- **Poor infrastructure:** Poor roads, poor communication infrastructure, lack of transport, and unreliable basic services such as water and electricity result in high operating costs. Firms do not operate in favourable environments such as cluster technology parks or special economic zones. These unfavourable environments increase their basic operational costs.
- **Lack of collaborative linkages:** Frequently, ambiguous policies and lack of policy coordination between various relevant ministries, departments and institutions, especially between those for trade, science, technology and innovation on the one hand and health on the other hand, are a major barrier to meaningful and sustainable local production. Competing agendas of organizations for science, technology and innovation, lack of a collaborative culture among academics and industry practitioners, lack of access to knowledge, and lack of incentives that reward modes of collaborative conduct contribute to a lack of collaborations, which impacts upon the process of interactive learning.

- **High cost of finance:** Production and innovation processes are associated with their own range of technological and market-related uncertainties. Start-ups may be seen as high risk; as such, interest rates and the cost of capitalizing a manufacturing plant may be very high and the loan periods too short to realistically allow a manufacturer to generate the return to repay the loan.¹⁴
- **Lack of economies of scale:** A combination of weak production capacity and uncertain markets results in limited economies of operation and weak feasibility. For example, sub-Saharan African manufacturers generally produce certain products at a cost disadvantage to the large Asian generic manufacturers. Political, legal and regulatory barriers often make it difficult for local producers to exploit regional economies of scale.
- **Low production quality standards:** Weak adherence by manufacturers to GMP standards and weak medicine regulatory authorities result in products of non-assured quality. Local producers find it difficult to meet regulatory standards, including those for WHO prequalification, and medicine regulatory authorities in Africa are not considered to be meeting their own national or international standards.¹⁵

This is not an exhaustive list; neither do all of these factors operate at the same time in each country. In the following section we summarize the work that was undertaken and commissioned in Phase 1 of this project. The common findings suggest that although the challenges are considerable, there are examples, from within this study and elsewhere, that show how efforts can be made to overcome these barriers with a coherent approach to industrial and health policy.

3.1.3 Evidence from the literature on links between local production and access

A detailed literature survey was conducted for the purposes of this project to summarize existing theoretical and empirical work on the local production of biomedical products and its potential impact on access to medicines in low- and middle-income countries (WHO, 2011e). The literature review was conducted to capture as many different aspects of the issue as possible. Along with peer-reviewed literature, the “grey literature” (e.g. reports, white papers, news articles) was also analysed.

¹⁴ See, for example, the pharmaceutical sector profiles of UNIDO for Zimbabwe, Nigeria, Uganda and Kenya at <http://www.unido.org/index.php?id=1001014>.

¹⁵ WHO runs the UN prequalification programme in close cooperation with national regulatory agencies and partner organizations. The prequalification programme aims to make high-quality priority medicines available for the benefit of people in need through its evaluation and inspection activities, and by building national capacity for sustainable manufacturing and monitoring of quality medicines. The list of prequalified medicinal products used for HIV/AIDS, malaria, TB and reproductive health produced by the programme is used principally by UN agencies, including UNAIDS and UNICEF, to guide their procurement decisions. The list has also become a vital tool for any agency or organization involved in bulk purchasing of medicines, whether at the country or international level, as demonstrated by the Global Fund to Fight AIDS, Tuberculosis and Malaria.

The objectives of the literature search were:

- to assess the extent to which existing studies and scholarly work explore the links between local production and access;
- to critically analyse whether the methods used in the literature are sufficient to suggest a robust relationship (positive or negative) between local production and access;
- to evaluate whether the results obtained could be directly applied to local production conditions in developing and least developed country contexts.

Additionally, a large amount of literature was reviewed that compared multinational companies and local firms on the determinants of local production in various countries with regard to, for example, finances, foreign direct investment and labour productivity, which span various sectors.

Local production is not an “economic” term in the strict sense, so further searching was done for literature on comparative economics between domestic and foreign firms in terms of their relative performance indicators, including exports, competitiveness, and ability to withstand foreign entry into the local market.

Various databases were searched using combinations of terms such as “comparison”, “foreign”, “multinational”, “domestic”, “local”, “performance”, “price”, “pharmaceutical” and “emerging markets”. The literature was further split into categories according to the type of study (e.g. case study, econometric model, survey) and the subject matter (e.g. access, intellectual property rights, innovation and supply chains).

A large number of studies and papers on the topic assume a particular causal relationship between local production and access, positive or negative, with a lack of, for example, econometric and time-series studies to justify their findings. The business and economic literature is concentrated on the upstream side (e.g. supply side, industrial policy, knowledge spill-over, innovation), with seemingly little information on the downstream issues of local production and access to medicines. At the same time, the public health literature on the subject of local production is directed predominantly at the issue of intellectual property rights and access to medicines. Many of the available pricing surveys do not distinguish the prices of local and foreign producers on a product-by-product basis, thereby offering no basis for deducing the competitiveness of local products, even in the short term.

This literature search attempted to list the putative benefits of local production and to find evidence from the studies. It concluded that the methods used in the literature to date are insufficient to demonstrate the relationship between local production and access. There are mixed messages from various studies, and although the studies may correctly depict specific situations in specific countries with reference to specific products, such evidence cannot be generalized. This suggests that there is a paucity of studies that have looked specifically at the link between local production and access to medical products; it also demonstrates the methodological limitations of the studies.

It is important not to draw any definitive conclusions from the evidence available and to bear in mind that the absence of evidence is not evidence of absence of a causal link – that is, negative evidence.

From the published literature, caution must therefore be exercised in drawing any general conclusions for or against local production and how it impacts on access. The literature search indicates the need for more thorough studies, which, using reliable methods, should look specifically at this relationship. This work will inform future research that is undertaken under phase 2 of this project.

Table 1 summarizes the direction of the available evidence gathered in this literature search with reference to putative benefits of local production.

Table 1 Summary of published evidence of the potential impacts of local production (WHO, 2011e)

Potential benefit of local production	Countries with positive benefit	Countries with unclear or negative impact
Potential cost savings	Some locally produced medicines are less expensive than foreign-made counterparts (e.g. Bangladesh, India, West Bank and Gaza Strip)	Some locally produced medicines are more expensive than foreign-made counterparts (e.g. Brazil, Jordan, Turkey, Malaysia, United Republic of Tanzania, Viet Nam)
Reliability of supply	No direct evidence available from literature review	No direct evidence available from literature review
Improved quality standards	A benefit in countries with suitable medicines regulatory authorities (Cuba, India, Jordan, Uganda, South Africa)	Little direct evidence in low- and middle-income countries
Foreign import savings	Little direct evidence from literature search on positive benefit	Little direct evidence from literature search on negative impact
Increased local innovation capacity	Vast literature on “knowledge spill-over” in high-income/ emerging market countries especially, but also in South-East Asia (Thailand); the term “innovation” is not clearly defined	Little evidence from low- and middle-income countries; the term “innovation” is often not clearly defined, as it could encompass incremental changes (e.g. small but significant changes) or breakthrough (e.g. introduces an existing technology into a new market or a new technology into an existing market, or changes the way the offering is delivered)

Potential benefit of local production	Countries with positive benefit	Countries with unclear or negative impact
Development of export capacity	Chinese, Indian and South African companies are exporters of ARVs; Cuba, Egypt, Ghana, Jordan and other countries export their medicines	So far, little clear evidence from most of sub-Saharan Africa of any benefit to developing export capacity
Development of human capital	Essential skills for R&D and manufacturing capacity already developed in India, Brazil, Jordan, Egypt, South Africa, China and other countries	Little evidence overall; in Tanzanian firms producers, there is a preponderance of expatriate technical and managerial staff

3.1.4 Activities of Phase 1 of the project on improving access to medical products through local production

In addition to the literature review, WHO, UNCTAD and ICTSD implemented a number of activities between 2009 and 2011 to generate evidence and information on which recommendations on local production and related technology transfer could be based (United Nations, 2011a; WHO, 2011a,b,c,d,e). The approach used the following different methods:

- a trends survey examining overall patterns in local production of pharmaceuticals and related technology transfer;
- a landscape report on the current status of local pharmaceutical production;
- a series of regional stakeholder workshops involving local manufacturers and other stakeholders in developing countries to ascertain the challenges they currently face;
- firm-level case studies of pharmaceutical production and technology transfer in developing and least developed countries;
- an exercise to gauge the current status of the local production of vaccines in developing countries;
- an exercise to gauge the current status of the local production of diagnostics in developing countries.

The data, research and information collected through these activities form a large compilation of the complex interface of local production, technology transfer and its implications on access to medicines (United Nations, 2011a). A series of reports that accompany and provide greater detail on the methods, analysis and references used to inform the development of this framework are summarized below and are available for free download from the WHO web site.

“Trends in local production of medicines and related technology transfer”

This report focused on identifying the current state of the global pharmaceutical production sector, with an emphasis on the interests of developing countries (WHO, 2011a). The aim was to identify elements necessary for the successful establishment of local production facilities, including through transfer of technology.

The research methodology included interviews with stakeholders in the pharmaceutical industry (generic and originator), product development partnerships, governments (including public health and industrial development agencies), access-oriented nongovernmental organizations (NGOs), generic and originator industry groups, universities and research institutions, and multilateral and regional organizations. The report presents the views on local production of various stakeholders representing varied interests and perspectives at workshops conducted in Africa, Asia and Latin America. Research for the report included canvassing of available literature addressing local production of medicine and related technology transfer, and Internet-based identification of existing projects and programmes aimed at supporting local production.

The report notes that there may be a difference between industrial policy and public health objectives for undertaking local production of medicines, and that the WHO mandate suggests that its efforts in this area should focus on promoting public health objectives. The report also notes that stakeholders identified a largely consistent set of factors or elements necessary for the successful development and implementation of local pharmaceutical production, including availability of skilled personnel, access to investment capital, adequate infrastructure development, adequate regulatory environment, access to relevant technologies, availability of suitable input materials, and achieving economies of scale. The report makes a number of recommendations regarding means by which WHO can support local production efforts, and suggests an initial geographical focus.¹⁶

“Pharmaceutical production and related technology transfer: Landscape report”

The purpose of this report was to provide a description of the landscape of local production of medicines and vaccines, relevant investment promotion and related transfer of technology, an outline of current and recent initiatives (in the past 5–10 years), and identification of gaps and preliminary assessment of the initiatives (WHO, 2011b). A range of potential data sources was consulted to identify as many initiatives as possible; this was supplemented

¹⁶ One element of the research involved the development and administration of a detailed Internet-based survey of a wide range of stakeholders regarding their views on local production and technology transfer, and R&D on new medicines relevant to developing countries. The results of this survey, although interesting, are not included in this document because the response rate was deemed insufficient to generate results sufficiently robust to guide policy.

with selected interviews and personal referrals. The 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.
- **Drugs:** The activities reviewed in this report concentrated on the areas of human immunodeficiency virus (HIV) and acquired immunodeficiency virus (AIDS), tuberculosis (TB), malaria and pandemic flu, suggesting a need to explore technology transfer for local production of a broader spectrum of products, including products for other therapeutic areas.
- **Intellectual property:** 2016 is the 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. The WTO TRIPS Council is expected to decide on the extension of the general transition period for LDCs beyond 2013 in 2012.
- **Public policies for technology transfer:** Technology transfer may be very difficult to induce, particularly for products where technology holders and technology demanders are likely to be market competitors. In such cases, public or public-interest actors (such as foundations and NGOs) may need to play a stronger role in providing incentives for sharing, or alternative paths to, needed technologies.
- **Capacity-building:** Mid- to long-term investment in building the capacity of local manufacturers and national drug regulatory authorities is needed.
- **Tailored approaches:** Local production capacities and relevant technology transfer needs vary widely across countries and product types, as do public health needs.
- **Comprehensive targeted approach:** 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.
- **Defining success in public health terms:** In a field in which public health and industrial considerations are deeply intertwined, debate among key stakeholders is urgently needed to clarify goals, define “successful” initiatives, and set broadly shared targets that include public health goals.
- **Further research:** Further research is required, particularly in two areas: (1) measuring private-sector technology transfer flows and (2) understanding the conditions under which local production leads to improved access to medicines and the pathways through which such improvements occur.

“Local production of pharmaceuticals and related technology transfer: A series of country case studies”

As part of Phase 1 of this project, a number of case studies examined in depth some examples of pharmaceutical and vaccine manufacturing currently taking place in developing countries (United Nations, 2011a). The case studies were designed to explore the extent to which local production capacities are promoted by related technology transfer and how that contributes to access to medicines. Manufacturers were chosen to reflect the diverse range of local production initiatives in developing countries, including one example of a subsidiary of a multinational corporation.

The following pharmaceutical manufacturers were the subject of the case studies: Laboratorio Elea in Argentina; Beximco and Square (two firms) in Bangladesh; Tecnoquímicas in Colombia; Sino-Ethiop Associates in Ethiopia; PT Eisai Indonesia in Indonesia; Jordan Pharmaceutical Manufacturing Company in Jordan; Government Pharmaceutical Organization (GPO) in Thailand; and Quality Chemicals in Uganda. Modes of production examined include indigenous firms that licensed in technologies from developed countries (Argentina, Bangladesh, Colombia, Jordan); developing country subsidiaries of research-based pharmaceutical transnational corporations (Indonesia); joint ventures between local firms and large generic manufacturers in developing countries (Ethiopia, Uganda); and state-owned enterprises (Thailand). A number of the firms are located in LDCs (Bangladesh, Ethiopia, Uganda).

The case studies used a uniform research methodology that was structured in two stages. In the first stage, secondary data (published reports and literature), policy documents and consultations with other agencies active in the field were used to narrow down firms and countries for investigation. The second stage comprised field investigations and visits to the firms in question to gather information through open-ended face-to-face interviews of a wide range of stakeholders in the target country. In addition, a semi-structured questionnaire designed to capture the dynamics of firm-level activities related to production and technology transfer was administered to the firms, the results of which are included in the case studies where relevant. The field investigations were designed to provide an understanding of the wide variety of models of pharmaceutical production (wholly owned subsidiaries, joint ventures, locally owned pharmaceutical firms, state-owned enterprises) and to provide an understanding of the range of pharmaceutical products (e.g. over-the-counter medicines, ARVs, antimalarials, vaccines) being produced in key developing countries (other than China and India, for which a good deal of data and literature already exist).

Although the eight case studies would not be sufficient to fully capture the reality of pharmaceutical production in all developing and least developed countries today, the studies provide an important snapshot of how firms in some important countries produce medicines and vaccines, how they source their technology for production, the difficulties they face, and how their products are linked with access to medicines. The findings from this work are

included in section 3, which presents a discussion of common themes on local production, technology transfer and access to medical products.

The findings of the work focused specifically on vaccines and diagnostics are summarized together with the findings, as they highlight some of the specific issues related to the local production of these medical products.

“Increasing access to vaccines through technology transfer and local production”

The purpose of this study was to develop a landscape of technology transfer for vaccines (WHO, 2011c). This research was conducted through a series of methods, including a combination of literature and Internet research, interviews with suppliers and recipients of technologies, and an Internet-based survey of manufacturers.

Additionally, a global workshop was organized in 2010 that brought together the main players in vaccine technology transfer, including industrialized country vaccine manufacturers, developing country vaccine manufacturers, public-sector vaccine developers, NGOs, and public health agencies and funding agencies. Findings from the landscape analysis background paper were presented and validated during the meeting, along with case studies of technology transfer from manufacturers (from developed and developing countries). The main conclusions of this work are summarized below:

- Technology transfer to developing countries has contributed significantly to increasing vaccine supply, and increased access to many vaccines has been documented. In several cases this technology transfer has also resulted in lower prices of vaccines, but this is not always so. For several vaccines within EPI there is a risk that supply may soon outstrip demand, and establishment of new manufacturers for these vaccines could be counterproductive, potentially leading to some established manufacturers leaving the market.
- Establishing local vaccine manufacturing is not necessarily cost-effective; however, vaccines should not be seen purely as commodities, and factors such as national health security need to be considered. The establishment of a vaccine policy by countries may assist countries in identifying how and when to consider local production.
- There is a changing dynamic in vaccine technology transfer, with joint ventures, acquisitions and establishment by multinational manufacturers of subsidiaries in developing countries becoming more frequent. Developing-country stakeholders recognize that the establishment of research-based entities developing and providing new vaccines may also squeeze existing generic manufacturers out of the market. The latter will need to invest in R&D to remain competitive.
- The biggest barrier to vaccine technology transfer, perceived by both technology recipients and donors, is lack of R&D capacity in developing countries. Failure by manufacturers to invest in R&D, and failure by governments to create an enabling local environment of research infrastructure, makes technology transfer less likely to succeed.

- For technology transfer to be attractive and successful, a win–win condition is required, which is facilitated by a commitment from the government to support the technology transfer or a large local or regional market. As the public sector seeks to promote technology transfer for vaccines, the above points need to be considered.

“Increasing access to diagnostics through technology transfer and local production”

The purpose of this study was to develop a landscape of technology transfer for diagnostics (WHO, 2011d). The data for this report were gathered and collated through a combination of desk research and interviews with stakeholders in the sector. The views of a wide range of stakeholders involved in the manufacture and development of diagnostics were also taken on board during a global workshop in October 2010.

The main findings were as follows:

- Developing countries have variable capacity for diagnostic R&D and local production of diagnostics. Manufacture in the non-industrialized world is most often undertaken in countries with large domestic markets and emerging economies such as China, India and Brazil.
- There are several models by which technology transfer for local production can be accomplished. These range from the transfer of R&D know-how to enable local product development, to partnering with a company in the developing world to manufacture a product without increasing local capacity for R&D.
- Successful partnerships have involved small and medium-sized companies, multinational companies, non-profit-making organizations and the public sector. The most successful example to date includes the transfer of a novel technology from an in vitro diagnostic (IVD) company registered in the United States of America to a non-profit-making public institution (Fiocruz) in Brazil. The agreement not only permits local production of tests based on this technology but also allows further R&D using the novel technology to produce tests for diseases prevalent in that country.
- Although the long-term solution is to build capacity for diagnostic innovation in developing countries, technology transfer to support local production can be an effective and sustainable strategy by which to increase access to diagnostic tests.

3.1.5 Discussion of common themes on local production, technology transfer and access to medical products

From an examination of the findings reported in the Phase 1 outputs listed above and by reviewing the existing literature, a number of common themes emerge. These are summarized below.

At the high end of the spectrum, pharmaceutical firms in China and India have moved rapidly up the value chain, seeking profits both in their large domestic

markets and in export markets. Both countries, along with the Republic of Korea, are also significant global suppliers of APIs.

Companies in these countries are investing in R&D related mainly to production processes, medicine-delivery systems, formulations, dosage forms (e.g. for children) and (fixed-dose) combinations of existing medicines, although some of them have started to invest in R&D of new chemical entities and biological products.

The Brazilian Government is encouraging local production and putting in place financing and support programmes to upgrade facilities, consolidate manufacturing and reinvigorate API production.

In many other developing countries there is significant local manufacturing, but operations are dependent on import of raw materials (APIs and excipients).¹⁷ The focus of manufacturing is largely on medicine formulation, packaging and labelling. In sub-Saharan Africa, most local production (pharmaceuticals) is at the tertiary level – that is, the repackaging of already formulated ingredients.

Evidence from Phase 1 suggests that some activity has taken place to transfer technology to enable local production of medicines within the context of private business transactions. Much of this has been geared towards the production of medicines that make sense from a business perspective. Major public technology transfer initiatives to date have, however, concentrated on medicines used to treat a limited number of diseases, namely HIV/AIDS, TB, malaria and pandemic flu. As such, the access debate is skewed towards improving access in these major infectious diseases, for which there is a major global burden and for which there have been a number of public–private partnerships that have responded at the global level.

Therefore, there is a need to explore technology transfer for local production of medicines in other therapeutic areas, such as chronic and neglected diseases, and to develop the capacity of local medicine manufacturers to reverse-engineer medicines.¹⁸ Vaccine production is even more concentrated in a few countries, although the mechanisms for technology transfer for vaccines appear to be better established and more used than those for other medical products.

In the area of diagnostics there is a familiar set of barriers to establishing local production with regard to the establishment of local capacity and infrastructure. These obstacles are compounded further by a market that has very little regulation and a consequent proliferation of poor-quality diagnostics tests.

17 For example, the UNCTAD country case studies offer overviews of the industry in the respective countries, showing the extent to which second-tier countries are dependent on imported APIs (United Nations, 2011a).

18 Noncommunicable are diseases of long duration and generally slow progression. These diseases, such as heart disease, stroke, cancer, chronic respiratory diseases and diabetes, are by far the leading cause of mortality in the world, representing 63% of all deaths. Of the 36 million people who died from chronic diseases in 2008, 29% were aged under 60 years and half were women (WHO, 2011n).

Evidence from countries with a successful local manufacturing industry shows that coherence across national policies plays a very important role in the development of local production. A mutually supportive combination of policies working together is required to ensure long-term sustainability and development of local production, especially in regulation; industrial and investment policies; science, technology and innovation policies; intellectual property policies; insurance policies; procurement policies; and technology transfer policies.

It is also well documented that the growth of the pharmaceutical sectors in India and China took place before TRIPS compliance. Therefore, manufacturers in LDCs are interested in exploring the feasibility of establishing local production, particularly in the pharmaceutical sector, before the extended 2016 deadline for the granting and enforcement of pharmaceutical patents in LDC WTO Members, which would otherwise be required under the TRIPS Agreement. A possible further extension of the more general transition period beyond 2013, that would allow the local manufacture of generic medicines in LDCs that are patented elsewhere, will be discussed in the WTO TRIPS Council in 2012 on request of the LDC Group of Countries. Such an extension would provide an additional incentive to build local production as a means to improve access to medicines. This will not address the barriers faced by diagnostics manufacturers, however, which may need to access a number of patented technologies within a single test platform.

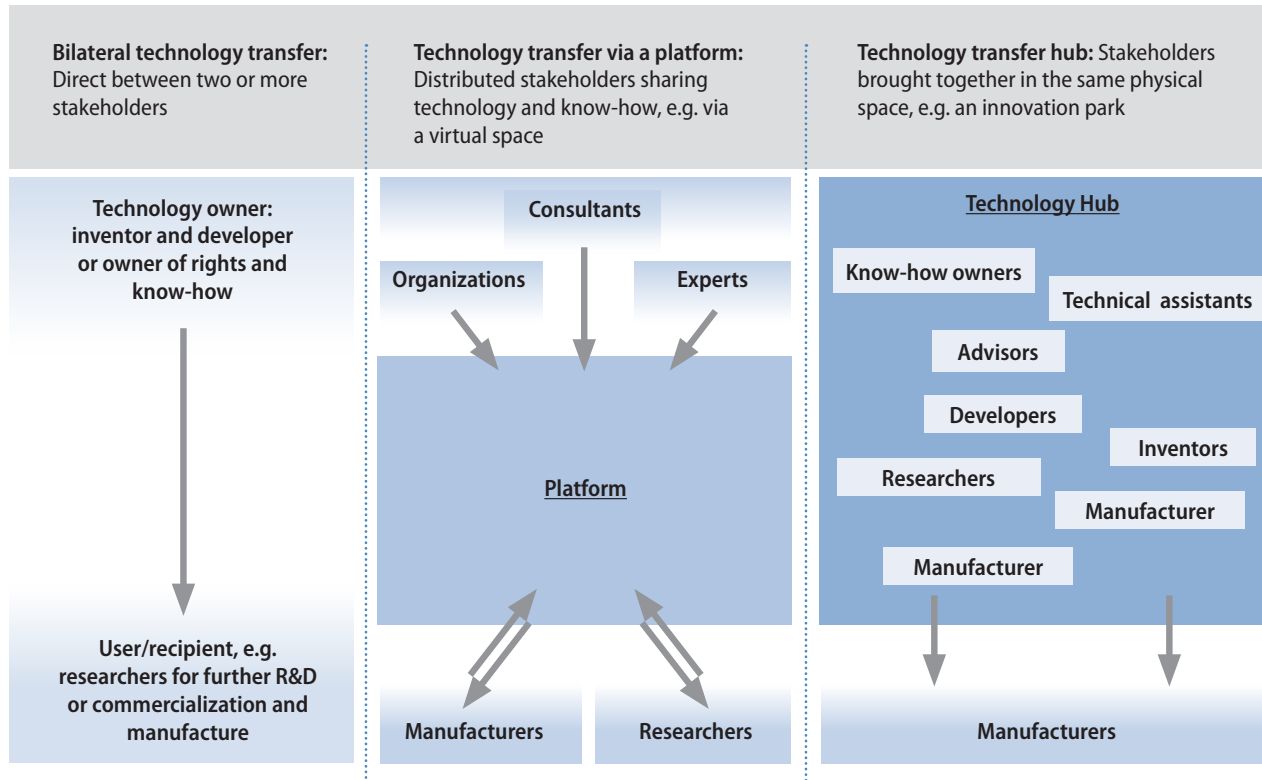
For example, the use of multiple patents to protect a piece of technology, commonly known as “patent thickets”, has been seen as an action to delay the entry into the market of generic manufacturers and was the subject of a European Commission inquiry into the impact of intellectual property on innovation within the European market (European Commission, 2009). The impact of intellectual property varies according to the type of medical product. For the essential medicines list, the majority of medicines are no longer patent protected, as is the case for vaccines in the WHO EPI. For newer medicines and vaccines, particularly where the product is a compound formulation, a range of patents may exist across the component technologies. In the diagnostics area, the component technology required to make a device can include chemical, mechanical and electrical technology, each with separate patents.

The number of vaccines manufacturers around the world is significantly much smaller (fewer than 40 manufacturers globally, with over 95% of vaccines produced by 15 of these companies; the number of producers has also declined over a period of time) compared with pharmaceutical producers. UNICEF, one of the big purchasers of vaccines, adopted a strategy in the 1990s to address a supply crisis by promoting new suppliers from developing countries through intensive programmes for technology transfer. As a result of this technology transfer, currently 64% of all EPI vaccines purchased by UN agencies are made by developing country manufacturers.

The vaccines study was able to capture and analyse almost all technology transfer initiatives that occurred in the vaccines industry in the past two decades before 2010. A total of 101 technology transfer initiatives were identified, with 92 verified. The study therefore provides a fairly comprehensive landscape.

Technology transfer, very broadly speaking, happened along three paths (see Figure 1). In one pathway, a private entity, usually an originator company from an industrialized country, entered into a direct arrangement as a technology donor with a recipient firm in a developing country; the arrangement could be an outright acquisition, a joint venture or a new subsidiary in the recipient country. The other pathways for transfer involved shared platforms or hubs of technology; this tended to be the preferred mode of technology transfer for public-sector/non-profit-making donors and involved multiple recipients. Examples of these include the WHO/PATH shared technology platform for the development of a meningitis vaccine for sub-Saharan Africa (Meningitis Vaccine Project); the PATH enabling platform for rotavirus vaccine (a toolbox of technologies, training, methodologies and material designed to meet common needs among emerging vaccine manufacturers and maximize global availability of rotavirus vaccines); and the influenza technology transfer hub at the Netherlands Vaccine Institute, where a central hub has been established by the public sector to provide technology to numerous recipients.

Figure 1 *Three pathways for the transfer of technology to support the local production of vaccines*



In the case of the technology transfer at the Netherlands Vaccine Institute for the influenza vaccine, the public-sector players, including WHO, were instrumental in actualizing the transfer. The report summarizes instances where transfer of technology to developing country producers significantly contributed to access. Know-how issues, more than registered intellectual property rights issues, currently challenge the local production of vaccines in developing countries. This situation is changing, however. On the one hand, some of the developing country vaccine manufacturers that have been making increasingly sophisticated vaccines for the past decade now have an experienced workforce, so know-how is less of a challenge; but on the other hand, over the past decade there has been intense activity in the patenting of novel vaccine concepts (with over 10 000 Patent Cooperation Treaty applications with many patents coming for example from China), so many of the new vaccines coming on to the market may be subject to intellectual property constraints. An example of this is the human papilloma virus vaccine, for which patents in several developing countries are one of the impediments to local production.

A number of factors can be used to characterize the local production of medical products in developing countries. When these factors are compared across diagnostics, pharmaceuticals and vaccines it is important to note that the impact of these factors varies considerably (see Table 2). For example, the production of diagnostics and pharmaceuticals is predominantly a private-sector activity driven by market dynamics. For pharmaceuticals, this is often mediated by collective or centralized procurement, with an established regulatory process. For diagnostics, there is rarely any centralized purchasing and virtually no regulation or quality assurance. Vaccine production occurs in the private sector, but purchasing and distribution are heavily mediated by the public sector and global purchasing initiatives, for which WHO prequalification is mandatory.

Table 2 Comparison of factors that characterize local production of medical products in low- and middle-income countries

Factor	Type of medical product		
	Pharmaceuticals	Vaccines	Diagnostics
Manufacturers	Multinationals and small and medium-sized enterprises	Small number of large producers	Some multinationals; large number of small and medium-sized enterprises
Role of public-private partnerships in establishing local production	A number of public-private partnerships at work for developing medicines for neglected tropical diseases, ARVs, TB and malaria; some successes (e.g. Drugs for Neglected Diseases Initiative (DNDi) and Sanofi Aventis)	Numerous successes in transferring new technology to existing vaccine manufacturers (e.g. India, Brazil, Indonesia)	Successful in Brazil

Factor	Type of medical product		
	Pharmaceuticals	Vaccines	Diagnostics
Role of regulatory agencies	Mandatory; often weak enforcement of regulation at country level	Mandatory	Largely absent; some regulation in public sector in some countries, but control over private providers is rare
WHO prequalification	Mandatory for purchase by global initiatives (TB, HIV, malaria); not required in other disease areas	Mandatory (for purchase by UN agencies)	Mandatory for global purchase, but only 2 products listed (malaria test)
Importance of product pricing in relation to access at point of care	Critical (if not covered by insurance, aid programme or government interventions)	Often not applicable, as either free of charge to consumer or subsidized through national immunization programmes	High to patient for test (if not covered by insurance or aid programme)
Importance of product pricing at source in relation to access	Moderate; most end-user prices are related to taxes and mark-ups rather than manufacturer's costs	High; often mediated through national purchasing or global initiatives (e.g. GAVI) to ensure affordable dose	High; plus additional costs of purchase and maintenance of test equipment and service
Post-sales technical support	Not required, but distribution strongly supported through private-sector marketing	Not required	Important, but dependent on level of technology
Intellectual property	Integral to new products; generic production possible; with widespread patent expiry, more generic products likely to be produced	Integral to new products (biologicals); most existing vaccines for use in EPI are no longer-patent protected; true generics do not exist since no concept of bioequivalence	New technology and constituent components often patent-protected

Factor	Type of medical product		
	Pharmaceuticals	Vaccines	Diagnostics
Market competition	Limited therapeutic competition during patent life; generics play major role in reducing price if there is no patent protection or off patent; varies greatly by country	Limited during patent life; most new vaccines produced by large producers, limiting competition; most EPI vaccines have numerous competing producers	High for some products (e.g. HIV, malaria); lower for some neglected diseases
Route of access to market	Mixed centralized, local and over-the-counter purchasing	Centralized purchasing, including some global and multilateral agencies	High product-based segmentation; limited centralized purchasing

As mentioned previously, no single source of evidence is sufficient to draw a conclusive link between local production of medical products and access. Consideration of the common themes, however, does highlight a set of findings that should be factored in to the planning of local production and improved access to medical products.

3.2 Common findings from Phase 1 actions on local production, technology transfer and access to medical products

3.2.1 Local production is growing in developing countries

A second tier of countries beyond India and China are actively engaged in local production. Many firms in these countries produce medicines competitively, not only due to economies of scale but also because of other factors such as effective product differentiate strategies, and are likely to expand over the next decade. Firms in these countries are well poised to be important suppliers of medicines and can have a potentially great impact on access in poor countries. For example, from this project, the Argentina case study shows that local firms have attained a level of sophistication and technical capacity that contributes to greater access to medicines through development of generic medicines and vaccines locally, such that they now supply over 60% of the total market by value. In Bangladesh (an LDC), two local companies are among the largest pharmaceutical companies in terms of capital and market share; both companies produce and supply more than 30% of the total Bangladesh market by value and are fast expanding into export markets.

The project, supported by other literature, shows that there are other countries on the horizon where firms are growing and expanding their production activities. In these countries, with domestic support and external partnerships, firms tend to focus on niche products and niche markets, such as in Ethiopia (an LDC), where the firm is producing hard gelatin capsules, and in Uganda

(an LDC), where the firm focuses exclusively on medicines for HIV/AIDS and malaria.

3.2.2 Technology transfer is an important factor in coping with barriers to enable local production

In the area of pharmaceuticals, the countries that demonstrated the most advanced levels of production were consistently strengthened by technology transfer in addition to having greater coherence in their domestic policies that increased their absorptive capacity (human skills and scientific infrastructure) throughout their growth and expansion. Many of the companies studied in this project have had some form of collaboration with multinational companies with headquarters in developed countries through technical collaboration and licensing arrangements, which has built their capacity in many different ways. In other countries where multinationals do not necessarily have the incentive to transfer technology, such as Uganda and Ethiopia, technology transfer from other sources has been critical. It is worthwhile to note that in these two cases, the axis for technology transfer was south–south – that is, from firms in India and China to firms in Uganda and Ethiopia, respectively.

Technology transfer continues to support firms as they expand into new product categories for both local consumption and exports. Technology transfer helps companies to expand their export markets and product portfolios. Collaborations for technology transfer help countries to increase their quality standards. In the case of Uganda, Cipla supplied the technological know-how to Quality Chemicals, which enabled it to pass a WHO GMP inspection of its manufacturing plant in Kampala and manufacture – based on processes developed by Cipla – for two prequalified products.¹⁹

Technology transfer for API production, which could be on a north–south or south–south axis, helps to increase the competitiveness of local production initiatives for medicines. The case studies of Bangladesh, Uganda, Argentina and Jordan point to examples where efforts are under way to attempt to produce APIs locally.

3.2.3 Intellectual property rights are important for decisions on local production and technology transfer

The international intellectual property regime plays an important role in shaping the pharmaceutical industry in developing countries, especially LDCs. Important generic manufacturers in developing countries that previously did not offer patent protection over pharmaceutical products must now cope with an environment where such protection is required. This affects, for example, India, which began offering such patents in 2005, and it will no doubt shape the future of the generic industry in that country and beyond. Although India has made use of many of the TRIPS flexibilities to ensure the survival of its

¹⁹ At the time of publication, the products manufactured at Quality Chemicals are WHO prequalified, but this prequalification remains assigned to Cipla as the applicant manufacturer with responsibility for ensuring that the product continues to meet WHO prequalification requirements.

generic industry, it may no longer reverse-engineer, manufacture and sell generic equivalents of molecules that have been granted patent protection in India. LDCs, however, are not affected yet, since they have been granted a grace period for pharmaceuticals until 2016 to comply fully with the provisions of the TRIPS Agreement. A possible further extension of time to comply for LDCs is currently under discussion in the TRIPS Council. The waiver for LDCs to comply with TRIPS provisions on pharmaceutical patents until 2016, or potentially longer if the waiver is extended, provides an important window of opportunity for generic pharmaceutical manufacturers to locate production in LDCs.

The case studies for Bangladesh and Uganda show that the environment for local production of pharmaceuticals in these two LDCs is shaped to a large extent by the ability to serve as a base for the generic manufacture of the ingredients (chemicals, molecules) that have been patented elsewhere, offering a potential alternative to importing patented medicines. The firms examined in these studies manufacture, for example, generic versions of ARVs that are patented in other markets by importing the APIs.

TRIPS-plus provisions in preferential trade, investment agreements and in negotiations surrounding accession agreements for new WTO Members can extend exclusivity periods and thus limit the space for local production (Abbott et al., 2007).

3.2.4 Local production has the potential to improve access to medical products


The firm-level surveys, stakeholder interviews and case studies in this project, when taken as a whole, demonstrate that local production has the potential to enhance access to medical products in countries with a well-established local presence. This improvement can be both for the local population and for people in countries to where the medicines are exported. There are a number of ways in which local production has been found to impact on access positively, but realizing this potential depends upon many conditions and the context of the specific countries, with assurance of quality being a major consideration. Nevertheless, the following synthesis of the possible impact of local production on improving access to medical products in developing countries is, in the longer term, promising:

- **Local production can offer price-based competition in the market and improve affordability:** Firms in Bangladesh, Argentina and Indonesia demonstrate this well, by catering to between 60% (Argentina) and over 87% (Bangladesh) of the total local market. Clearly, market participation of local firms is not a direct indicator of improved access, and the key question is whether the local firms make a difference in terms of availability and affordability of medical products. This is important for all poor countries, where the majority of the population is unable to afford medicaments imported from developed countries. The Bangladesh study found in this case that local firms make a significant difference in promoting access to medicines for the local populations in both urban and rural areas. In

Argentina and Indonesia, there is market segmentation between locally produced generics and branded medicines from multinational companies, offering wide availability of a variety of drugs. To support access, these governments source their public medicine procurement from local companies due to comparative cost advantages. Price comparisons in the diagnostics market are more difficult to interpret, as the quality of goods varies widely, with some products being ineffectual and misleading (e.g. see WHO & Special Programme for Research and Training in Tropical Diseases, 2011).

- **Local production has catered to local health needs:** Firms in all the case studies catered to specific health needs by producing medicines for which there was local demand. These included antibiotics, anti-infectives, vaccines, antimalarials and ARVs. Firms in Bangladesh, Argentina, Indonesia and Uganda produce ARVs and antimalarials. Firms in Bangladesh are beginning to venture into vaccines for rabies, typhoid, tetanus and polio. Indonesian firms are specifically engaged in producing vaccines and heat-resistant ARVs. The firms in Jordan and Argentina are expanding into product categories (including diagnostics), which resulted in incremental adaptations and improvements to existing products.
- Local firms can produce products for local needs that either are not produced at all by the multinational companies or are in short supply: In these cases, such products address diseases that disproportionately affect developing countries. Examples include production of paediatric ARVs by Indian companies, and production of the meningitis A vaccine by the Serum Institute of India. The Bangladesh firm Beximco is engaged in production of chlorofluorocarbon inhalers, which it also supplies to global procurement agencies. In Brazil, Bio-Manguinhos (Immunobiological Technology Institute), a unit of the Oswaldo Cruz Foundation (Fiocruz), supplies the public sector with diagnostic reagents and kits for HIV, leptospirosis, leishmaniasis, Chagas disease, dengue fever, hepatitis and rubella.
- **Local firms can be more adept at creating distribution networks that cater to the needs of poor people in remote areas:** The existence of distribution networks and pharmaceutical supply chains is a starting point for the development of formulation capabilities in countries and expansion into other niche areas. Quality Chemicals, a Ugandan firm producing ARVs, was a distributor for Cipla's medicinal products and has extensive distribution networks in rural Uganda. Similarly, most local companies are adept at using context-relevant strengths for distributing their products and in creating newer modes of distribution for their medicinal products. Historical narratives of the pharmaceutical sector show that many pharmaceutical firms in developing countries, including Bangladesh, Kenya and India, are offshoots of distribution companies.

It is important to remember that to the extent that the world relies on the private sector for the delivery of many health products, the profit motive remains central to the decision by a firm to manufacture medicines, diagnostics and vaccines. Firms can and have been encouraged to respond to local demand in terms of pricing and availability.



The outputs of Phase 1 show that such positive impact of local production on access to medicines can be strengthened further through coordinated policy incentives. At the same time, a number of potential issues need to be borne in mind so that the impact of local production on access is not diminished. For instance, evidence gathered in the case studies shows that promoting the local industry remains an important goal, but one that needs to be balanced with the imperative of access. In the long term, even when medical products are produced by local firms, competition in the market is highly relevant to ensure reasonably priced medical products.²⁰ Similarly, tariffs on imported goods and equipment often tend to raise the price of inputs, leading to higher cost of manufacture in developing countries. The evidence garnered shows the need to address such factors in a holistic way.

²⁰ The Bangladesh case study demonstrates this trade-off between nurturing a protected local industry and ensuring that drugs produced by the local industry meet internationally accepted drug quality standards and are available at reasonable costs to local people.

4. The need for a policy framework for local production and access to medical products in developing countries

The growing and changing trends in local production of medical products in developing countries are likely to continue. There is now more international awareness and support for local production in developing countries. The Pharmaceutical Manufacturing Plan for Africa was developed following the African Union Assembly Decision adopted in Abuja in January 2005 (African Union Assembly, 2005). The GSPA-PHI emphasizes transfer of technology and local production to improve innovation and access in developing countries;²¹ the European Parliament passed a resolution in favour of local production in developing countries; and bilateral and multilateral donor initiatives exist to support local production in developing countries.²² In the wake of pandemic influenza, vaccine production capacity has been significantly enhanced in 11 developing countries through international cooperation and technical support of WHO, and this work is continuing.

Private-sector investments are motivated by business opportunities in terms of return on investment; in the case of pharmaceuticals, this is as true for generic manufacturers as it is for multinational companies. Keeping in view the unmet and underserved public health needs in developing countries, and the huge gaps in access to needed medicines and other medical products, there are expectations that local producers in these countries will do more to explicitly align their production to address these needs. Profitability of the enterprise (the ability of the investment, whether private sector or government-driven, to recoup costs and generate sufficient revenue to operate) and viability, however, remain the main determinants of investment decisions by the private sector; but left to market forces alone, market failure, combined with institutional shortcomings, leads to unmet needs and insufficient access to medical products. Moreover, a purely short-term economic analysis also ignores the long-term vision and potential spill-over effects of local production for the domestic economy.

At a global level, significant efforts have been made to create strong incentives and assured markets with initiatives such as the Global Fund to Fight AIDS, TB and Malaria, the United States President's Emergency Plan for AIDS Relief (PEPFAR) and GAVI. The entry level to supply products to these initiatives, however, will exclude local producers that cannot supply at global volumes

²¹ GSPA-PHI Element 4.1(b) promotes transfer of technology and production of health products in developing countries through investment and capacity-building. Element 4.1(c) promotes transfer of technology and production of health products in developing countries through identification of best practices, and investment and capacity-building provided by developed and developing countries where appropriate.

²² The Government of Germany, through the Federal Ministry for Economic Cooperation and Development (BMZ) and Gesellschaft für Internationale Zusammenarbeit (GIZ), supports a number of firms in developing countries in developing capacity to produce medicaments. Germany has also provided financing to UNIDO and UNCTAD for advisory and capacity-building support under projects that aim to strengthen the local production of essential generic medicines in developing countries.

or cannot meet the mandatory quality standards of WHO prequalification. In addition, these efforts are dependent on donor support for their long-term sustainability and are focused on certain major diseases. As such, they do not provide a sustainable model for universal access to all affordable medicines, and to date there is no such global initiative in the area of noncommunicable disease.

Finally, the public's right of access to essential medicines and medical products must also be considered in such discourse, because accepting this tenet helps to justify government support and incentives for public health-oriented local production.

4.1 Why a policy framework for local production and access to medical products in developing countries is needed

Governments in developing countries have often supported pharmaceutical production from an industrial development perspective. In this context, there is a tendency to see the feasibility of local production in pure market terms, without recognizing its special importance as a source of commodities that directly affects the health of the people. This is to be expected, as the world in general relies to a large extent on private firms to deliver their supply of medicines.

Ethiopia, for instance, couched its aspiration to further develop its local pharmaceutical industry by indicating it as a priority sector in its August 2010 Growth and Transformation Plan, rather than as part of a public health initiative. Although this enables local firms to avail of certain duty privileges and investment incentives, these advantages are not tied to any health priorities as such.

The impressive development of the Indian pharmaceutical industry is a good example of this approach. During the 1970s, the Indian Government consistently provided a conducive policy environment in which the pharmaceutical industry could continue to grow. India introduced product patents only after fully using the transitional period available to developing countries in 2005. The result of these policies is a multibillion-dollar pharmaceutical industry that had become the third largest pharmaceutical industry in the world by volume in 2010. Now it is actively investing in R&D and expanding its exports in the markets of high-income markets, especially through contract research and manufacturing activities (Gehl Sampath, 2010: Chapter 3).

Although India's generic manufacturers as an industry have made a major contribution in lowering drug prices in India and in many other developing countries, a large number of people in India still have only limited access to health services. In the diagnostics sector, issues relating to quality are still to be resolved, with substandard diagnostics freely marketed to the private sector, which is a substantial provider of health care to the Indian population (WHO, 2011d).

The results of Phase 1 show that a focus on developing a medical products sector that focuses strictly on industrial development tools and measures may support the creation of a profitable domestic industry, but there is certainly no guarantee of improved access outcomes.

Industrial and health policies most often remain separate, disconnected policy spheres. Investment promotion agencies, such as the one in Bangladesh, promote investment in local production of pharmaceuticals from a purely business perspective (e.g. see Bangladesh Board of Investment, 2011). The case study of the efforts by two major Bangladeshi firms currently centres on meeting European quality standards for export rather than on the domestic market. Similarly, in India, it is arguably not the responsibility of the local firms to ensure nationwide access to health services; this onus vests with the Government of India.

At the other end of the spectrum, the government-use licences on ARVs, cancer drugs and other drugs promulgated in Thailand from 2006 to 2008 in favour of the Government Pharmaceutical Organization were issued under the authority of the Thai Minister for Health.²³

To avoid discontinuity between these disciplines, there is a need to consciously bring the health and industrial policy spheres closer together to harness the potential of local pharmaceutical industry to address the local health needs, and at the same time to contribute to national economic development. Brazil is a good example of a country that has succeeded in bridging these two spheres.

Brazil has taken the constitutional responsibility of providing free health care (including free ARVs to people with HIV) to 190 million people in the country since 1990.²⁴ Free distribution of HIV medicines became a reality in 1996 by law. As a consequence, from 1997 to 2003, AIDS mortality dropped by 40–70%, morbidity decreased by 60%, there were 360 000 fewer hospitalizations, and 58 000 new AIDS cases were avoided (Ford et al., 2007).

Three factors have been suggested as critical to this success: (1) Legislation for free access to treatment, (2) public-sector capacity to manufacture medicines, and (3) strong civil society action to support the Brazilian Government initiatives to improve access. Brazil has adopted an approach that means the national health service can act as an engine for national industrial development (Gadelha et al., 2010). The creation of the Health Economic-Industrial Complex has guided and amplified biotechnological research and pharmaceutical, vaccine and diagnostics production, and has helped to create jobs and national economic growth. The recently announced industrial policy

²³ These government-use licences were issued with a view to first importing generic versions of the drugs, and then to commencing local production by the Government Pharmaceutical Organization (Ministry of Public Health and the National Health Security Office of Thailand, 2008).

²⁴ Through Sistema Universal da Saude, the Brazilian public health sector covers 190 million people and is one of the largest public systems in the world.

of Brazil provides further tax cuts to companies and promotes the policy of “Buy Brazil” (*The Economist*, 2011b).

Brazil believes that the right to health is as important as economic gain and that, with the right approach, both can be pursued without one being detrimental to the other (Bliss, 2010).

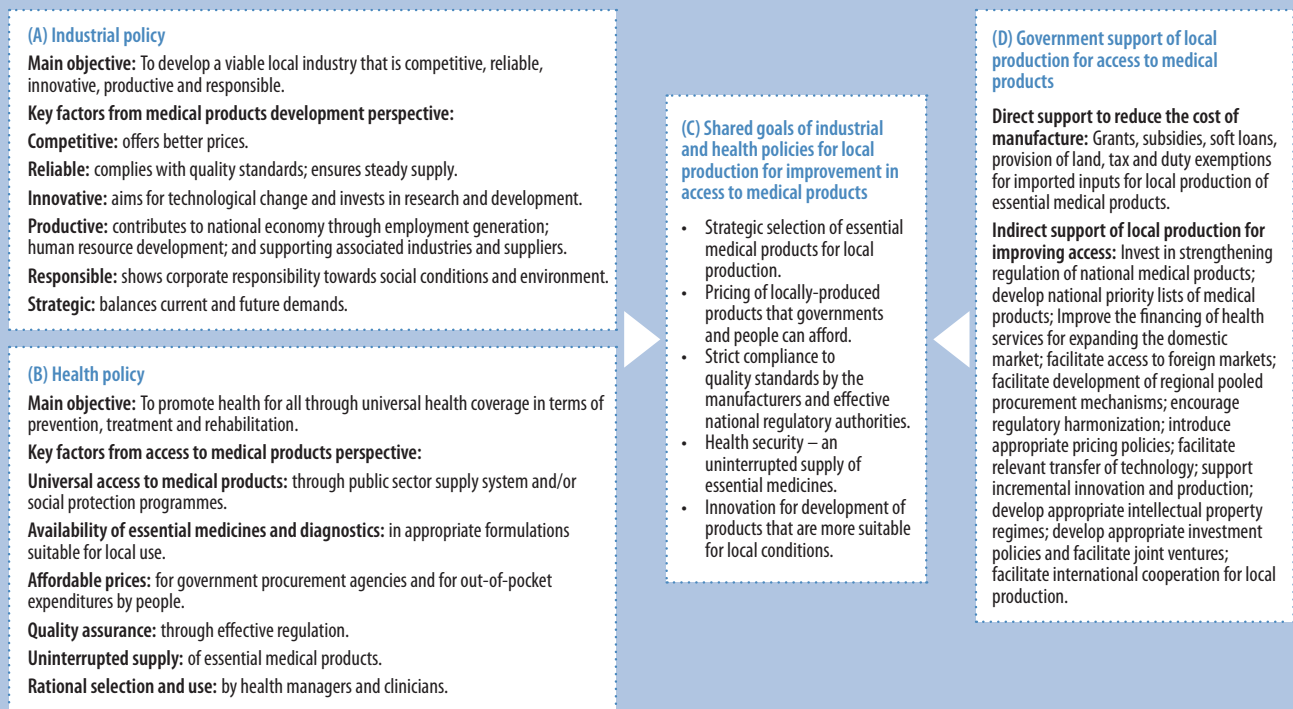
The need for public health concerns to take centre-stage in a policy framework for local production of medical products is thus essential for the following reasons:

- the presence of local production alone is insufficient to reap the benefits of greater access to medicines in developing countries;
- to develop a common understanding for policy coherence for both industrial development and health development;
- to guarantee that public investments in institutional development of national regulatory bodies are made to ensure locally produced medical products are quality-assured;
- to assist governments identify and justify the various fiscal and non-fiscal incentives to local producers;
- as one means to address a future scenario where the supply of affordable generic medicines at a global level is uncertain;
- to coordinate international support for industrial development and health development.

The following sections outline the factors that are relevant from an industrial policy perspective (see Figure 2, Box A) and the factors that are relevant from a public health perspective (see Figure 2, Box B). We suggest there are common or shared goals between these two perspectives, such that the objectives of industrial policy can meet those of public health (see Figure 2, Box C).

Although the catalyst for production comes mainly from the private sector, this is regulated within a national jurisdiction, so the key player in creating a conducive environment is government. The government role ranges from direct and indirect financial incentives and creating coherence across the regulatory and policy arena (see Figure 2, Box D).

Figure 2 Local production and access to essential medical products: A framework for improving public health



4.2 The industrial policy perspective: Factors of relevance for local production

Local producers and manufacturers are responsible for the creation of their own business plan when deciding on future products for their domestic or potential export market. Assistance is available from a wide range of sources, including numerous professional associations, government schemes and international programmes in, for example, building capacity, managing intellectual property, managing technology transfer, establishing infrastructure and achieving international standards of manufacturing quality. Although this project, in its second phase, will develop Web-based platforms to facilitate access to these resources and explore potential gaps in this support, such as mentoring for business management, this document does not expand on that planning process. The focus here is the identification at a high level of the areas that national policy-makers need to address to ensure there is an environment conducive to local manufacturing being established, growing and at the same time contributing to priority public health needs (see Figure 2, Box A).

The main objective, therefore, from the industrial policy perspective is to support the development of a viable local industry that is competitive, reliable, innovative, productive, responsible and strategic:

- **Competitive:** Any medical product produced locally has to be able to compete with what is already available from either other domestic suppliers or via imports. The challenges to achieve this without government support, particularly in the early stages of development, are considerable. A number of incentives, from seed-funding to tax credits, can be considered, provided they are structured in a manner to be compliant with the country's international obligations. Linking access to this funding to a national health strategy would be one approach in aligning industrial policy with public health.
- **Reliable:** For stakeholders, including prescribers, dispensers and patients, to gain confidence in a local producer, the product supplied has to be of assured quality for marketing but also continuously quality controlled to maintain the same high quality with regard to efficacy and safety of the product. The production flow also must be assured to meet demand at all levels of the health system at all times.
- **Innovative:** To build manufacturing capacity into the future, incentives should focus on companies with the capacity to innovate – for example, not only to develop novel materials but also to adapt existing medical technologies to the local context through new formulations or medical equipment that can be operated and maintained locally. The industrial policy should seek to facilitate those companies to invest in innovation and R&D, either within its own structures or through collaboration with other companies or academia.
- **Productive:** The industrial policy needs to take into account a broad view of the potential benefits that contribute to the national economy through employment generation, human resource development, the collection of revenues and spill-over into associated industries and suppliers. Government incentives may be critical in building up a critical mass of management expertise and a skilled workforce to support a medical products manufacturing base.
- **Responsible:** The industrial policy needs to take into account a broad view of the corporate and social responsibilities of the industry with regard to employment practice, sound financial governance, and protection of the health and environment.
- **Strategic:** Most essentially, the industrial policy needs to combine these considerations to form a strategic view with regard to future scenarios. Imports today may indeed provide a better strategic choice with regard to price and quality. With the shift in intellectual property regimes and the potential for global suppliers of inexpensive medicines to change their priorities in the future, an assessment of the long-term health security issues may provide a strong incentive to invest in local or regional production. There may also be a strategic advantage to support generic manufacture and its attendant governmental policies as a mechanism to leverage better prices on imported products. Finally, for LDCs, compliance with TRIPS does not apply until 2016 and this may be further extended, thereby creating a window of competitive advantage to build a generic medical products manufacturing base.

4.3 The health policy perspective: Key factors to ensure access to medical products

Access to medical products in poor countries is hindered by multiple obstacles. Inadequate access is rarely the result of a single failure but rather is generally a combination of market failures, government failure and development assistance failure. Addressing these multiple failures requires many steps directed at the global, national and local level. Medical products may be developed and even centrally procured and yet still not delivered to the people who need them the most. Research into these delivery issues (implementation research) has a major role in identifying bottlenecks in the supply system and acceptability by prescribers and users (Frost & Reich, 2009).

Measurement of access to medical products is also a challenge. In 2004, WHO estimated, on the basis of a 1999 survey conducted using a questionnaire, that about 30% of the world's population, or some 1.3–2.1 billion people, did not have access to the essential medicines they need.²⁵ In India, WHO estimated that 499–649 million people (50–65% of the country's population) did not have regular access to essential medicines. Throughout Africa, a further 267 million people (almost half the population, or 15% of the world total) lacked access. Since then, the measurement of access has become relatively more empirical. WHO now presents access measured through key indicators of availability and prices on medicines in both the public and private sector. Summary figures from national medicine price surveys between 2001 and 2009 have shown poor medicine availability, particularly in the public sector, which is a key barrier to access to medicines. Public-sector availability of generic medicines is on average less than 60% globally. Private-sector availability of generic medicines has been found to be higher than availability in the public sector in all regions. For example, surveys in the WHO Eastern Mediterranean and Western Pacific regions found that in the public sector where patients have to pay for medicines, prices of generic medicines were 1.9–3.5 times more expensive than international reference prices. Generic medicines paid through out-of-pocket expenses by people in the private sector were 2.5–9.5 times more expensive than international reference prices (WHO, 2011f).

Significantly, there is little comprehensive analysis about the availability and prices of identical products that are locally produced compared with those that are imported or foreign-made.

The drive for developing at least a degree of self-sufficiency in supply of medical products in view of health security concerns inter alia national industrial development has led governments to encourage local production of medicines and other medical products, and they have continued to pursue technology transfer discussions at different levels. In 2007, for example, the Pharmaceutical Manufacturing Plan for Africa was adopted by the Summit of the African Union, which saw local production as a means to “improve/enhance self-sufficiency in medicine supply” in view of “unreliable medicine

25 This study is being updated and expanded upon; see WHO (2011f).

supply systems [that] continue to hamper access” (African Union Conference of Ministers of Health, 2007).

The African Union Commission conducted a drug production capacity-mapping exercise in line with the Assembly decision on local drug production in the continent in collaboration with WHO. At the WHO African Region Office 56th Regional Committee Meeting held in Maputo (AFR/RC55/10), discussions on strengthening local production of essential medicines emphasized that policy decisions about whether to import essential medicines from reputable sources or to promote local manufacturing should be based on careful situation analysis and realistic appraisal of the technical feasibility and financial viability underpinned by sound regulatory systems. A market size that would ensure sustainability as well as technical and financial viability was considered imperative. The WHO Regional Committee for Africa adopted resolutions that emphasize essential medicines, local production of essential medicines and African traditional medicines.²⁶

Availability of medicines is only part of the picture. For many conditions, access is dependent on diagnosis. Whereas medicines for TB are freely available in the WHO African Region, access is low because less than half of incident cases are diagnosed each year.

Key factors must be considered if a medical product is to be accessible, including policies to guarantee universal access to the needed medical products; availability of required medicines in forms that are suitable for local conditions; affordable prices; assured quality; an unhindered supply line; and policies to ensure rational selection and use (see Figure 2, Box B).

4.3.1 Universal access to medical products

Universal coverage for health care is now a globally recognized goal for national health systems. Health inequities are a major concern at all levels, and renewal of primary health care is considered as an approach to address exclusions by introducing universal coverage reforms (WHO, 2008). Along the same lines, there are a growing number of initiatives for setting up social protection schemes and health insurance systems in developing countries. Improvement in access to essential medicines, vaccines, diagnostics and other health technologies is an inherent part of the expansion of health services. Local production of medical products can potentially help in achieving universal coverage and must be seen as a contributory supply-side factor for expansion in health services. Many developing countries are far from a situation where all citizens are covered by national health services; nevertheless, this is the direction in which health systems are moving. Local production of medical products must be cognisant of this vision, which can bring economies of scale from a business point of view, if not immediately in the national context then maybe in other countries in the vicinity.

26 WHO-AFRO Resolutions AFR/RC/49/R5 and AFR/RC38/R19.

4.3.2 Availability of essential medical products

Essential medical products must be available at all times at the appropriate level within the health-care system. This means that required medicines and medical products have to be continuously developed and existing ones modified in forms that are suitable for local conditions in developing countries. Ensuring the availability of essential medical products requires many different efforts, ranging from R&D and innovation to rational selection of medicines in accordance with the needs and level of the health-care facilities and establishing reliable supply systems.

WHO promotes an essential medicines concept and defines essential medicines as those that satisfy the priority health-care needs of the population (WHO, 2011m). WHO has been preparing, and revising every 2 years, a Model List of essential medicines since 1977. The current list is the seventeenth revised edition. From 2002, however, affordability changed from a condition to a consequence of selection. Before 2002, expensive medicines were often not included on the Model List because their inclusion was seen as unrealistic. Under the new definition, a cost-effective medicine can be selected even if the price is high, and the fact that it is considered essential then implies that it has to become available at an affordable price. The first examples of this new approach were the first-line ARVs, which were added to the Model List in 2002 (Mirza, 2008). A total of 156 countries are reported to have a national essential medicines list (WHO, 2002a).

Promotion of local production in developing countries must be in the context of an essential medicines concept. From a needs-based local production perspective, the analysis of the national essential medicines list is important. Such an analysis, along with analysis of the burden of disease, can potentially inform about the potential consumption of the medicines (market size). We can also determine how many of the medicines on the national essential medicines list are already being locally produced or imported, and at what price. From the point of view of local production, it is important to know that more than 95% of medicines on the WHO Model List are not patent-protected, and so their production does not require any licensing arrangements with the patent holders – although this situation is not static and it is worth noting that not all generic firms in developing countries would be able to immediately take advantage of available information concerning off-patent molecules and produce medicines from that information. Local API production would enable the potential for local firms in the region to undertake medicine formulation. With the exception of some large developing countries, the innovation capacity (R&D) for discovering and developing new medical products is weak in developing countries. The capacity to adapt existing molecules to local conditions does exist in some developing countries, however. A similar process should be undertaken for diagnostics and vaccines.

Various approaches can be used to build innovation capacity in a stepwise manner. Adaptation of various essential health technologies to make them more suitable for local conditions is one such approach – for example, development and production of heat- and humidity-stable medicines and

diagnostic tests. Many medicines are available only for adult use, and their paediatric formulations have never been developed; R&D and production of such formulations is an area for possible innovation in developing countries. A list of high-priority essential medicines required for children under the age of 5 years for the main causes of mortality and morbidity in developing countries (pneumonia, diarrhoea, malaria, neonatal infections, HIV, TB) has been developed (UNICEF & WHO, 2010).

Such analysis could produce a list of essential medicine prioritized for local adaptation, which could be divided into two groups: (1) Products already available but not necessarily in optimal pack sizes and strengths and (2) products for which further development is needed. To improve compliance, especially for long-term treatment of people with HIV, TB, and noncommunicable diseases such as hypertension, other cardiovascular diseases and diabetes, new fixed-dose combinations are needed. Many neglected tropical diseases are also waiting for treatments to be developed or improved, and little investment has been made by R&D-based pharmaceutical companies due to a lack of attractive markets in developing countries. Encouraging local production and innovation in these neglected areas has a strong justification from the public health perspective. Diagnostic tests are needed for key causes of morbidity and mortality that cannot be managed symptomatically. Infectious diseases should be prioritized where early diagnosis (and treatment) prevents transmission.

Without appropriate government support and incentives, however, local producers will face the same challenges in making such production viable. Some essential medicines are still missing from the market, even though their formulation and production is relatively simple. Examples include ferrous sulphate for the treatment of anaemia and phenobarbital for the long-term treatment of epilepsy. Often these medicines are not produced because of low profit margins and lack of policy attention; instead, much more expensive therapeutic equivalents are imported. Attention to such issues can improve the availability and access to such essential medicines through local production.

4.3.3 Affordable prices

Governments and people must be able to afford medicines, whether imported or locally produced. If medicines are produced locally, then there is a higher expectation that their prices would be more in line with the purchasing parity of the local population; this may, however, not always be the case. Locally produced generic medicines may not be cheaper than their imported equivalents, or at least not in the initial stages of local production, unless a combination of efficiencies in production and economies of scale can be achieved. Unaffordable prices of medicines can be a function of the high cost of local production or of weaknesses in the pricing policy regimes; more often, it is a combination of the two. In addition, the distribution network can significantly increase the final cost of the product to the patient (Health Action International, 2011).

A large number of medicine pricing surveys conducted jointly by Health Action International and WHO have shown high prices of medicines in developing countries when compared with international reference prices, especially in the private sector. Although these surveys do not make a distinction between locally produced and imported medicines, they do help in understanding the disparities between international and local prices for the same medicines and indicate policy approaches that could be used to reduce the prices. In the context of high out-of-pocket expenses, which in many cases lead to catastrophic expenditure, further pushing people into poverty, affordability of medicines is a critical issue in the local production of medicines. One real benefit to the understanding of local production and its contribution to access through affordable prices would be to collect price data that disaggregate between domestic and imported medicine prices.

Governments can develop pricing policies that act as incentives for local manufacturers. Such policies need to be balanced, however, with affordability aspects. A careful selection of reference prices, analysis of price components, including import duties and wholesale and retail margins, and rationalizing these can be the basis for a good pricing policy. Simple-to-produce essential medicines are often missing from the market because their prices are controlled and never revised, and local manufacturers do not see any profit in manufacturing such medicines. Appropriate policies in this area can act as a stimulus for local production.

4.3.4 Quality assurance and regulatory support

The discussion and efforts to promote local production of medical products in developing countries are incomplete without simultaneous emphasis on and investment in quality-assurance systems in those countries. This is critical from a public health point of view. It is much better not to have local production of medical products than to have substandard production, because substandard medical products can potentially harm rather than benefit users, for example through misdiagnosis or treatment with ineffective formulations. It is important to ensure that manufacturers follow internationally acceptable standards of production and that there is a regulatory infrastructure to inspect and ensure the quality standards of locally produced medicines and diagnostics.²⁷ Policy-makers interested in promoting local production in their countries must therefore simultaneously strengthen their national regulatory authorities.²⁸ Quality and safety aspects of locally produced medicines cannot be emphasized enough.

Developing countries vary in their capacity to regulate medicine and vaccine production. WHO has an ongoing programme for strengthening regulatory

²⁷ For example, the standards and guidelines established under the auspices of WHO (2011j).

²⁸ National medicine regulatory authorities or equivalent responsible departments of ministries of health for regulation of medicines and health technologies.

systems in developing countries (WHO, 2011o).²⁹ It also develops technical standards and guidance in this area, such as GMP, registration of medicines, pharmacovigilance, inspection of manufactures, and quality control and quality testing of medicines and vaccines. WHO has developed numerous technical standards and offers technical assistance to developing countries in these areas.

Strengthening the national regulatory system can have multiple positive effects. Apart from ensuring the quality of medicines for better health outcomes, it also builds confidence among prescribers and consumers of locally produced medical products, which enhances the local market. Stringent regulation builds confidence in the export markets, which also bring more business from foreign market. For diagnostics, regulatory mechanisms are weak, and few developing countries have the capacity to monitor the quality of diagnostic products.

Harmonization of regulatory standards and procedures between developing countries at a regional or subregional level is sensible from a local production point of view. Precedents exist such as the Common Technical Document between Europe, Japan and the United States of America (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use). Although harmonization is ideal, more realistically mutual recognition of regulatory technical standards and requirements by national medicine regulatory authorities across countries can avoid a lot of effort on the part of manufacturers in terms of market authorization. Governments have an important role to play to support such harmonization efforts with other countries. One such initiative is at work in Africa at the level of regional economic communities under the auspices of the African Union and the New Partnership for Africa's Development (NEPAD) (WHO, 2010c).

Delays and barriers in market authorization due to inefficient procedures in regulatory authorities are common and affect manufacturers.³⁰ Since most of the medicines produced locally in developing countries are generics, and their safety and efficacy data are already available, theoretically there should be no long delays in providing market authorization. National medicine regulatory authorities can devise a system of fast-track registration for locally produced medicines of public health importance. This also means investing more in national medicine regulatory authorities in terms of human resource development and development of technical guidelines and appropriate procedures. Financing such investment will be a major challenge.

²⁹ Established in March 2004, the European Commission–African, Caribbean and Pacific Island (ACP)–WHO Partnership on Pharmaceutical Policies dedicates €25 million to the strategic and technical support of ACP countries in the development and implementation of essential medicines strategies (WHO, 2011p).

³⁰ This potentially includes the practice of linkage, whereby drug regulatory authorities are required to examine whether there is a patent over a product that is submitted for marketing approval.

4.3.5 Uninterrupted supply of medicines

Local production of medical products has to contribute to ensuring steady supplies to overcome the problems posed by foreign suppliers in terms of long lead times, interruptions in supplies and stock-outs. Local companies are well placed to sustain uninterrupted supplies and establish good supply networks in the country.

Some countries have a condition for providing market authorization, among other conditions, that suppliers and manufacturers have to maintain a steady supply of their product through the public and private sectors so that there is no shortage of the registered product.

4.3.6 Rational selection and rational use of medical products

To ensure access, quality-assured affordable locally produced medical products would need to be included on a national essential medicines or priority device lists. Their rational use for procurement in diagnosis and prescribing should be reinforced through, for example, use of a number of interventions recommended by WHO. These include, among others, the establishment of a multidisciplinary national body to coordinate policies on medicine use; the development and use of a national essential medicines list; the establishment of drug and therapeutics committees in districts and hospitals; the use of independent information on medicines; the avoidance of perverse financial incentives; and the sufficient government expenditure to ensure availability of medicines and staff (WHO, 2011h).

5. Building a framework for government support for local production and access to medical products

Medical products are produced to a large extent by private-sector actors, although some production, typically for certain vaccines, can occur in government-funded facilities. The private sector is therefore responsive to the policies, laws and regulations established by government. The range of policies that may be deployed to better ensure that local manufacturers of medical products in developing countries are encouraged to meet access needs in their own and other developing countries is diverse and constitutes what this paper terms the “framework”. These policies are discussed in turn below and form the basis of the range of policies that phase 2 interventions will examine in the context of providing capacity-building and related technical advice.

It should be noted that the project partners uniformly believe that no single set of policies will necessarily lead to a positive outcome in terms of access, and that the set of policies that needs to be put in place for one country may not be appropriate for another country. A major factor is the level of development and the unique features of the pharmaceutical market in the country in question. It is for this reason that the set of recommendations to be provided to improve the policy framework governing the manufacture of medical products will necessarily have to be grounded on field-based fact-finding missions that investigate the current state of the respective policies enumerated below.

5.1 The shared goals of industrial and health policies for local production and improvement in access to medical technology

Industrial and health policies need not be mutually exclusive – there are points where the two can, and should, meet. These are the areas on which we propose to focus in phase 2 of this project – policy analysis, technical assistance and capacity-building at the national level – in order to better orient existing local production activities to serve access needs. Each of these policy areas is discussed in turn below.

5.1.1 Policies to ensure strategic selection of essential medical products for local production

Strategic selection of essential medical products for local production means focusing on the medical products that are important from a local public health needs point of view, that are in short supply, and that can be produced locally with some support. Left to the market alone, there is a risk of not meeting domestic health needs, especially for segments of the people who have no ability to pay.

For identification of such medicines, a good starting point is the national essential medicines list, providing the list has been reviewed regularly and systematically. For countries with basic formulation capabilities, ideal

candidates could be simple-to-produce essential medicines that are in short supply and for which expensive alternatives are being imported; medical products such as ferrous sulphate, zinc sulphate, magnesium sulphate and oral rehydration solution are examples. In some cases south–south and north–south collaborations can be developed, whereby even more sophisticated medicines can be produced. An example is Uganda, where a joint venture between Cipla from India and Quality Pharmaceuticals from Uganda joined hands to produce ARVs and antimalarials. The Government of Uganda has played an important role by supporting this venture in several ways. Such ventures can be sought for other medicines in other developing countries, including LDCs. Public-sector support is a key factor in such collaborative local production.

The economic feasibility for the production of such medicines needs to be developed; here, the role of national and, where appropriate, regional policy-makers is important in terms of facilitating public-sector uptake of locally produced medicines. This will better ensure a predetermined market that will instil investment confidence among manufacturers. This simple approach has to be adopted for varying contexts in different developing countries.

The establishment of facilities to manufacture these compounds enables a stepwise entry point into the marketplace to build human resource and manufacturing capabilities. It should allow for sustainable growth and build up investment to achieve the necessary expertise in GMP.

5.1.2 Policies to enable pricing of locally produced medical products that governments and people can afford

Striking the correct balance between affordability and economic feasibility is a challenge. Government support to help local producers of selected essential medicines in terms of fiscal and non-fiscal incentives can be very important. In addition, rational pricing policies with appropriately selected external reference prices can also be helpful.

The prices of medicines from local producers may be relatively high in the short term, but with a good incentives package – for example, including an assured market – these prices can become more affordable to the consumer and overall in the medium to long term. A price-controlled market was one of the successful strategies used by the Brazilian Government. At the same time, price controls can often result in distorting production incentives for local firms. For instance, in India, local firms tended to avoid producing drugs that were in the price control categories simply because it was not lucrative to do so, especially when compared with other drugs that were not under price control (Gehl Sampath, 2005).

5.1.3 Policies to ensure strict compliance to quality standards by manufacturers and effective national medicine regulatory authorities

No local production of medical products is desirable without quality assurance, and any government incentives have to ensure strict compliance with required quality control systems in accordance with acceptable international and national quality standards of pharmaceutical production. Therefore, it is important that there is investment in institutional development and strengthening of capacity in national regulatory authorities to ensure effective regulation.

5.1.4 Policies that ensure health security – an uninterrupted supply of essential medical products

To ensure health security there must be a continuous availability of required essential medicines at different levels of health care. In the public sector, medicine supply systems stock-out is a common phenomenon; in the private sector, market forces rather than health needs dictate the supply of medicines. For various reasons, short supply of essential medicines in private-sector pharmacies is common in developing countries. Regulatory authorities can introduce a condition of market authorization requiring companies to provide assurances that supply of their product will be maintained through the public and private sectors. Such criteria for market authorization can assert better control over local companies than importers.

Long lead times for offshore import of medical products cause difficulties in medical supplies and are partly responsible for stock-out situations. Local production of these products can add value in terms of diversifying sources and ensuring smooth and steady supplies.

Local producers sometimes have an advantage that they have their own supply networks and can deliver their products directly to the facilities and private pharmacies in remote areas more efficiently than other channels. Sometimes local manufacturers are known to have evolved from local suppliers. Their edge in having established supply channels in the country can have a positive effect in improving geographical access to medicines.

Taking a longer-term strategic perspective local production is one area that could contribute to greater health security and access, particularly to mitigate the potential risk that supplies of affordable quality medical products may not be available to import from the current global suppliers. Where production is reliant on imported ingredients (e.g. APIs or components), the security of these supply chains will also need to be protected and ensured.

5.1.5 Innovation policies for development of formulations more suitable for local conditions

Innovation capacity is a critical prerequisite not only for R&D leading to new drug discovery but also for the development of products that are incremental

improvements, such as formulations that are more suitable for local conditions in developing countries. Fostering such innovation capacity across countries is important to promote the development of such incremental products, the greater availability of which will lead to extensive public health benefits in developing countries and LDCs. The ability to innovate incrementally is a step in the process of building capabilities for health research and product development for the creation of new drugs, vaccines and medical products. Domestic innovation capacity in several countries, including India, Brazil and Cuba, has been built using policy incentives that also focused on local production, whereby manufacturing, regulation and R&D capacity were able to grow incrementally.

As noted earlier, the gradual movement of the pharmaceutical sectors in developing countries such as India and China towards compliance with TRIPS raises the issue of how we can address the growing demand for public health-related medicines across the developing world, especially at a reasonable cost. This is as much of an opportunity as a challenge for all other developing countries and LDCs. Policy work and data being generated in this area by the international community show many examples of medical products that are currently not available in packing and dosage forms appropriate for local conditions and use. These include several drugs currently not available in heat-resistant forms or paediatric formulations despite the fact they are required for public health needs in developing countries (UNICEF & WHO, 2010). The local manufacture of such medical products can be fostered through the design of appropriate health innovation policies for developing countries.³¹

Developing countries have a range of policies that focus on aspects of science and technology, R&D, education and public health. Coherent health innovation policies in developing countries, however, calls for a rethink on the ways in which such policies can be updated or revised to ensure a more coherent framework for science, technology and innovation for medical products. Such a framework should focus on promoting linkages and networks among different actors in the health innovation systems, with the aim to promote learning and accumulation of technological capabilities to cater to local health needs. The role of local demand and how it is factored into local health innovation efforts remains a primary goal of health innovation policies.

In order to reap these benefits, the private-sector actors that produce important medical products must be incentivized with appropriate and coordinated health, economic and other policies established by the government. The section below discusses the range of policies that may be strategically

³¹ An example of international efforts to improve access to paediatric medicines is the UNITAID activities in the area of paediatric ARVs. Specifically, UNITAID is fostering the expansion of paediatric AIDS treatment and is working to decrease prices. In cooperation with the Clinton HIV/AIDS Initiative, UNITAID has provided predictable funding for large-scale purchases of paediatric ARVs. By ensuring minimum order volumes from a reliable funding source, incentives have been created for producers to enter the niche market of paediatric ARVs. The average number of suppliers per paediatric product has doubled, the coverage of treatment of children in need increased from 10% in 2005 to 38% in 2008, and the price of good-quality AIDS medicines for children has dropped by 60% since 2006 (United Nations, 2011d).

deployed, depending upon the country and context, and stresses the need to build the capacity among developing countries to be able to implement those policies effectively.

5.2 Government Support to local production for improving access to medical products

A wide range of industrial and economic policy incentives have been used to support the local manufacture of medical products. Such policies have often been grouped under the heading of industrial policy or policies that support the investment climate for pharmaceuticals.

From public health point of view it is important that such support is not just for industrial development, but it also explicitly aims to improve access of the people to what medical products are locally being produced. To achieve this it is important that government incentives are aimed at supporting the shared goals of industrial and health policies. There are a number of interdependencies between these policies. For example, seeking to access foreign markets, to ensure economic viability, will not be possible without ensuring an effective regulatory authority to provide quality assurance.

Government support must be based upon a long term vision to see the local industry eventually becoming competitive in the market place. Such support neither can be unlimited nor can it be static. There is no one fixed formula for the kind of support and combination of incentives that governments should provide to the private enterprises. It will vary in accordance to the context and should evolve over time. There are three important considerations however for governments to provide and calibrate their support by adjusting and re-adjusting between different incentives 1) that any support should encompass the shared goals of industrial and health policy that seek to improve access; 2) the provision of direct support, through grants and loans; and 3) indirect support through facilitating access to foreign markets or improving the financing of health services.

Each policy tool has a different purpose, however, and they are discussed in turn below.

5.3 Direct government support to the local manufacturers of essential medical products.

5.3.1 Policies that reduce the cost of manufacture

Firms that manufacture medical products cannot be competitive without being able to minimize production cost while maintaining appropriate quality standards. For a number of reasons, manufacture of medicines in many developing countries will be relatively more expensive than their import, at least in the short run. A number of measures initiated by the government and the local policy framework can help to alleviate the short-run effects of high initial costs of manufacture. These include the following:

- **Grants, subsidies, loans and land:** Governments sometimes provide direct fiscal support in terms of grants, subsidies and affordable loans. Governments may also provide land to set up manufacturing plants free of charge or at special concessional prices, either in the form of industrial zones with supporting infrastructure or for individual companies.
- **Tax and duty exemptions for imported inputs for local production of essential medical products:** Tax exemptions and concessions for import of APIs, excipients, packaging materials and pharmaceutical production machinery can be a good direct incentive for local manufacturers. This helps to ensure that local manufacturers that must import raw materials are on equal footing with domestic producers in the larger developing countries that also produce APIs domestically.
- Although such measures can be made available for any industry, the important point for the purposes of phase 2 would be to ensure that these incentives are tied to the manufacture of products that meet local medical needs.

5.4 Indirect government support to the local manufacturers of essential medical products

5.4.1 Invest in strengthening national medical products' regulation

Governments need to recognize and support the development of strong national regulation authorities as an essential part of improving access to good-quality products. Local production that meets the criteria of improving access should be considered for fast-track authorization.

5.4.2 Develop national priority lists of medical products list

Governments need to create priority health product lists. To improve access, local production should be encouraged to meet the health challenges that are identified within those lists as local priorities. Linkage between the industrial incentives outlined above with the public health needs those products are expected to meet will serve both policy objectives.

5.4.3 Improve the financing of health services for expanding the domestic market

No investor will be interested in starting up an enterprise to manufacture medical products unless there is a prospect that the firm will be able to sell products at a profit. In the developing country context, however, the dynamics differ from those in developed countries in so far as there may be no insurance to cover the cost of medicines and vaccinations for a large part of the population, and that the burden of providing medicines to the many people who may not be able to afford them is taken up by government. Universal access has already been mentioned as a means to encourage countries to establish health insurance coverage for the population at large. In addition, there are policies that can help to ensure a market for locally made medical products, for example preferred public-sector procurement. Procurement is the policy complement to universal access and public health insurance. Medicines

procured by governments are generally distributed through public health programmes (e.g. government pharmacies and hospitals). Governments that are not otherwise bound by treaty to provide non-discriminatory treatment in procurement can decide to give explicit preference to locally produced medicines, vaccines and other medical products in public-sector procurement for supplies to public-sector facilities. However, such a policy, in reducing competition, can result in higher prices and increasing prices to the consumer must be avoided, through appropriate pricing policies (see below) or moderated through adequate health service financing otherwise access is likely to be reduced.

5.4.4 Facilitate access to foreign markets

Governments can help to expand markets for local manufacturers through export facilitation. Incentives for exports and trade agreements for market access with other countries are approaches through which local manufacturers can penetrate markets at subregional and regional levels and later to far-off markets. It should be recalled, however, that exporting to developed country markets may not help access in developing countries, unless such exports are to, for example, bilateral or multilateral donor agencies.

5.4.5 Facilitate development of regional pooled procurement mechanisms

Regional economic markets also help to form a larger economic unit to which a local manufacturer in a developing country may sell its products. Pooled procurement at a regional level, where feasible, could also act as an incentive in terms of a relatively large market for the local producers within that region (WHO, 2007). A number of regional treaties give preferential support to such intraregional production and trade.

5.4.6 Encourage regulatory harmonization

As a complement to regional pooled procurement mechanisms mentioned above governments within a region should seek to achieve greater recognition and harmonization of their regulatory procedures between countries. This will expand the potential market areas to enable local production to meet regional needs and allow for the mutual cooperation and strengthening of national regulation authorities by undertaking joint capacity-strengthening activities.

5.4.7 Introduce appropriate pricing policies:

Medicine pricing policies and pricing policies for other medical products play a very important role in access and affordability. For a number of established market failures in this area all countries directly or indirectly regulate prices of medicines and other medical products to keep them affordable. Pricing policies combined with financing of health services including health insurance and other social protection schemes determine financial access in private and public sectors. In developing countries where a high proportion of people have to buy medicines through out-of-pocket expenditures, the medicine

policies of governments are very important. Medicine pricing policies range from direct price control to pre-marketing negotiations.

With regard to promoting local production it is important for governments to have in place supporting medicine pricing policies. Since, in the short to medium term the prices of locally produced medical products can be higher than their imported equivalents it is important to rationalize the pricing policies with two objectives: one, that local manufacturers are supported and two, that effect of high prices is not passed on to the consumers. There are many ways in which governments can rationalize their pricing policies, for example: using appropriate internal and external reference prices; exempting essential medicines from sales tax; rationalizing whole sale mark-ups and retail sale mark-ups including having a system of regressive mark-ups.

5.4.8 Facilitate relevant transfer of technology

Because many developing country firms cannot readily use information in the public domain or relevant patent information to commence production locally, Phase 1 results show that a key enabling factor is the transfer of technology. This transfer need not occur on a north–south basis but also occurs on a south–south basis, for example from a generic manufacturer in China or India to a generic manufacturer in an LDC. It can also happen in the context of bilateral donor assistance efforts to support local manufacture of medical products.

Governments can facilitate transfer of technology in close collaboration with other governments, international organizations, foreign companies and local enterprises through policy incentives that are specifically designed for the acquisition not only of codified technologies (in the form of blueprints or equipment) but also of tacit know-how. Such policies need to promote and encourage technology transfer between developed and developing countries, and also between developing countries themselves or between developing countries and LDCs (south–south technology transfer), in order to enable the creation of a sound and viable technological base for health innovation. In particular, policies could, inter alia, facilitate the negotiation of joint ventures, licences and subcontracting arrangements; and facilitate information flows by creating a forum for the exchange of views between technology providers and recipients. Such policies will also need to pay equal attention to the presence of an adequate enabling environment for technology absorption and use in the country, which depends on the availability of human capital, finance, enterprise formation and the legal framework, among other factors. This calls for coordinating technology-transfer policies with innovation and investment policies with a view to promoting their effectiveness. Efforts should also be made to ease the search process for relevant technologies, which is often a major hindrance for firms in developing countries seeking to access technologies from abroad.

5.4.9 Support incremental innovation and production:

Although local firms in many developing countries may not have the potential to carry out advanced R&D on, for example, new chemical entities, many

developing country firms are in a position to learn to locally produce a product and to incrementally adapt upon it, given the right set of incentives. These may include policies that support learning and technical change at the firm level in medical products, venture capital, and supportive intellectual property policies such as sui generis utility model systems to encourage incremental innovation and compensatory liability systems, among many others.

Ensuring a conducive policy environment for R&D for medical products by investing in science and technology and ensuring policy coherence: No manufacturer of health technology would consider manufacturing in a developing country without human resources that are capable of manufacturing good products that meet appropriate quality standards. A critical mass of chemists, pharmacists and engineers is essential; these human resources can be developed only if they are backed by a policy environment that supports the sciences, technology and innovation. Moreover, developing a comprehensive national innovation policy and bringing together the relevant ministries and national institutions can bring huge benefits to local production in the long run.

5.4.10 Develop appropriate intellectual property regimes

There can be no uniform approach to the use of intellectual property to promote local pharmaceutical producers. Where a country's national intellectual property system should draw the line between exclusive rights on the one hand, and the promotion of competition on the other hand, depends on the existing capacities of the domestic pharmaceutical sector and their strategic objectives.³²

Countries with no or only incremental pharmaceutical capacities may tend to provide their producers with a maximum degree of access to existing pharmaceutical technologies and know-how by limiting the scope of exclusive rights in pharmaceutical substances. The TRIPS Agreement provides a multitude of options ("flexibilities") in this respect. In particular, LDCs that are WTO Members should benefit fully from transitional periods. Developing countries, although subject to TRIPS disciplines, may legally benefit from a number of tools to maintain a broad public domain in the area of pharmaceuticals and to promote incremental technological learning. Aside from the transition period, these include the flexibility to frame appropriate patentability standards (novelty, inventive step, and industrial application) that promote high quality patents. Countries should ensure that they properly define the concept of "inventive step": A lax standard (low level) of the inventive step means a proliferation of patents over a given technology, whereas a stringent standard implies that improvements that are not significant cannot be accorded a patent right. It has been argued that setting a high level of inventive step allows firms in developing countries to engage in incremental innovations, since these will not be allowed to be patented within their domestic contexts (Gehl Sampath, 2011). Providing for public-health sensitive patent examination guidelines

³² For a detailed discussion, see United Nations (2011b).

(Correa 2007) as well as pre- or post-grant opposition procedures can help to prevent the patenting of products and processes that lack innovation.

Countries should also ensure that other relevant limitations and exceptions are included in the patent law, including the additional flexibility agreed by WTO Members that allows a country with manufacturing capacities to issue a compulsory license for export of pharmaceutical products to countries with no or limited manufacturing capacities (UNAIDS, WHO, UNDP 2011).

It is essential, therefore, that developing country policy-makers are aware of the potential provided under international intellectual property rules to use intellectual property rights as tools for creating an “adequate enabling environment for technology transfer” – that is, to build domestic technology absorption capacities through the development of appropriate legal frameworks and human capital.³³

Increased domestic technological capacities are a prerequisite for licensing agreements with advanced pharmaceutical producers from abroad, which in many cases have contributed to further domestic technological learning.³⁴

Technologically more advanced developing countries, on the other hand, may be able to benefit more from intellectual property rights by providing incentives to their domestic producers to invest in pharmaceutical R&D. Countries that want to develop a research industry might consider opting for more stringent standards in order to set incentives for research. In any case, it is important for countries to adapt the intellectual property system to their local needs in order to support the development of local healthcare industries. It is also essential to have in place a system of checks and balances to prevent the abuse of exclusive rights to the detriment of patients (in terms of medicines affordability) and technological innovation (in terms of medicines availability). Competition law and policy play an important role in this regard, as does interagency cooperation between officials dealing with intellectual property, trade and public health. A balanced approach to intellectual property protection is also an important element of a country's domestic science, technology and innovation policy.

5.4.11 Develop appropriate investment policies and facilitate joint ventures

Improving the investment climate: A well-tailored investment policy can bring more internal and external financing for local production. Elements of such a policy include simplifying the requirements for doing business in pharmaceutical and other medical products (e.g. business licensing), making it easier for expatriate experts to be dispatched to provide technology transfer

³³ See Article 231 of the EU–Central America Trade and Association Agreement. This link between intellectual property rights and technology transfer is also made expressly in other EU bilateral agreements, such as the European Partnership Agreement with the countries of the Caribbean Forum.

³⁴ See, for example, the case studies in this project on Argentina, Bangladesh and Colombia (United Nations, 2011a).

(e.g. longer visas for highly skilled technicians sent by technology providers), and establishing high-technology parks with good infrastructure that can supply reliable power and clean water. Guidance for policy-makers is now available in this area (United Nations, 2011e).

Facilitating strategic joint ventures: Governments can facilitate strategic joint ventures for local production of important essential medical products between local companies and companies from industrialized countries and large developing countries. Such joint ventures in most cases are possible only with the political and direct and indirect fiscal support of governments. Apart from production of medical products that otherwise cannot be produced locally, such ventures can help to ensure complete technology transfer and build local capacity.

5.4.12 Facilitate international cooperation for local production

Governments can negotiate support for local production by inviting international organizations such as UNCTAD, UNIDO and WHO, and bilateral donors, to support special projects for building local production capacity for medical products. Care needs to be taken to ensure that donor initiatives are not working at cross-purposes with private local production initiatives in ensuring greater access to medicine and medical products.

6. The way forward: Using the framework to advance industrial and health policy goals with regard to local production

WHO and its partners will continue to develop this framework with the support of the European Union as the project moves into phase 2. The intention is to support work in a series of pilot countries and with relevant partners to improve this framework, with a view to maximizing the potential for sustainable local production to meet the priority public health needs for low-income countries.

The policy framework that this paper seeks to generate would serve as a tool for policy-makers from the industrial policy and health policy arenas, so that they may use it in their efforts to promote greater access through local production. WHO, working with its partners and supported by the European Union, will seek to advocate for this policy approach to ensure that where local production is encouraged, it is done in a way that offers the best opportunity to improve access to medical technology.

The following sections list the recommended activities for developing or building a coherent policy environment that can meet development objectives and serve public health.

6.1 Policy analysis for policy coherence

Countries that are interested in strengthening and establishing local production that contributes to improvement in access to essential medical products first need to develop a clear policy vision. Existing policies and plans, in whatever form, in health, including national medicines and diagnostics policy, vaccines policy and industrial policy, need to be examined. Allied policies in trade, investment, science, technology and education also need to be looked at. The aim should be to bring coherence of vision in terms of supporting local production of essential medical products so that the people who need these products have better access to them. The following activities will support such policy coherence:

- mapping and analysis of relevant policies in health, industry, trade, investment, intellectual property, science and technology, and education;
- analysis of the national essential medicine list to determine which medicines are already being produced locally, which medicines are imported, the affordability of medicines and degree of health security, and, given the existing level of pharmaceutical production capability and capacity, which medicines are suitable for local production in line with this framework;
- undertaking a similar analysis for vaccines and diagnostics, and expanding the analysis into other medical products such as medical devices and other essential medicines such as blood products;
- contact with local pharmaceutical companies and foreign-invested pharmaceutical companies to understand their perceptions about the relationship between local production and public health needs and to

provide a sense of their plans for investment in future local production in the country;

- establishment of an intersectoral national committee of experts on local production and access to medicines;
- development of a national policy document with input from all the relevant policy-makers and stakeholders on local production and access to essential medical products in the context of the existing level of development of the pharmaceutical and vaccine manufacturing facilities in the country. Apart from formulating a policy vision, this exercise must also include a plan for local production of selected medical products over a period of time and required government support for such production.

6.2 Development of global resources on local production, technology transfer and access to medical products

In order to provide support to interested developing countries to pursue local production under this framework, there is a need to establish a global repository or innovation platform of technical materials. Such a repository would need to include the following technical guidelines:

- database of relevant technical literature;
- links to experts and organizations providing support in this area;
- technology-transfer support initiatives;
- country experiences shared through online networks and workshops;
- information on the patent status (where necessary) of medicines and technologies considered essential to meet the high-priority national public health needs.

It is also recognized that the evidence base on the contribution of local production to access to essential medical products is incomplete. For this reason, it will be useful to continue research in and analysis of selected topics to further the understanding of how, for example, investment or science, technology and innovation policies affect local production of medical products.

6.3 Advocacy for policy framework for local production and access to essential medical products

A policy framework for local production and access to essential medical products needs to be advocated to countries that are interested in establishing or strengthening local production so that the public health perspective in local production is promoted.

This paper needs to be distributed widely and used with policy-makers and other stakeholders. The framework for improving public health proposed in this paper should aim to become the basis for future capacity-building activities to strengthen local production.

6.4 Capacity-building and technical assistance for local production of selected essential medical products

The value of this policy framework will be in its application. Interested policy-makers in pilot developing countries will be engaged; with their support, an analytical exercise can be undertaken to identify the essential medical products that are needed, that can be produced with the existing local production capability and capacity (or by enhancing it), and that are currently not being produced. Specifically, there needs to be work to ensure:

- identification of essential medical products that can be produced in the country;
- development of feasibility for production, both technically and in market terms;
- identification of specific areas where capacity-building at the policy level, at the national regulatory authority level or at the firm level is required;
- identification of areas where government support is required for such local production and to build a case for such support by clearly showing public health dividends in terms of improved access to these products;
- monitoring and evaluation to assess the degree to which local production has an impact on access.

7. Conclusions

Ensuring access to medical products is a complex undertaking requiring governments through their relevant policies to balance the availability of quality products (supply side) with meeting priority public health needs with products that are acceptable and affordable (demand side).

It is clear that supporting local production is one means by which governments in the developing world may seek to maintain this balance. This project has reviewed many of these activities in a number of countries – some demonstrating a real potential to make a difference in the area of improving access.

In order to ensure a strong linkage between what is produced locally and what improves access, however, a comprehensive system-wide approach is needed. This approach has to bring coherence between industrial policy and health policy so they share the common objectives of a focus on essential medical products (i.e. those that meet the priority local health needs) that are quality-assured, affordable and available in the right form to serve the local context.

We hope the framework offered here, and the related reports from Phase 1 of this project, begin the process of identifying the appropriate policy areas and actions that need to be taken so that governments can ensure that local production of medical products can contribute to the development of the country, while meeting their public needs.

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