Conference Report

„Local Production and Access to Medicines“

21 February 2013, Gustav-Stresemann Institute, Bonn

Insufficient access to essential medicines is a common health burden in developing countries. The reasons behind are numerous and include at national level poverty, high medicine prices, insufficient health budgets and poor pharmaceutical logistics and lack of human resources. Globally, trade restrictions and intellectual property rights worsen the situation for developing countries. However, local pharmaceutical manufacturing in Africa is often debated. Unfavorable economies of scale, lack of human capacity, unsatisfactory infrastructure and weak regulatory bodies limit its contribution to improved access to high-quality low-cost essential medicines in low income countries.

This one day international conference aimed to discuss challenges and chances of local production and its impact on access to health by bringing together different stakeholders, particularly from Africa.

Conference Opening

Hans-Christoph Boppel, Head of Department for Development Policy, State Government North-Rhine Westphalia, Germany, opened the conference highlighting that access to essential medicines still remains a major problem in developing countries leading to millions of needless deaths caused by treatable diseases. He stressed that high-quality pharmaceutical production in the developing world is an important step to gain independence from drug donations and imports.

Peter Nagel, State Director, Gesellschaft für Internationale Zusammenarbeit (GIZ) North-Rhine Westphalia, Germany, welcomed speakers and participants on behalf of GIZ, one of the co-organizers of the conference. He pointed out that this conference is timely and important as local pharmaceutical production has the potential to contribute to sustainable access to medicines in developing countries. Difficulties and challenges such as human resources constraints, poor infrastructure, lack of collaboration between key actors, high costs, lack of economies of scale and low production quality standards need to be addressed and overcome.

Bernd Pastors, Speaker of the Board at action medeor e.V., referred to the long experience of action medeor in the field of improving access to medicines. He explained that access to medicines included several dimensions, namely availability, affordability, acceptability, accessibility and quality of medical products. He emphasized the importance of collaboration between different stakeholders in the field to improve local production in developing countries and underlined his statement by referring to the East-African saying “Umoja Ni Nguvu – Unity is Strength”.

Keynote Speeches

Dr. Lembit Rägo, Coordinator Quality Assurance and Safety: Medicines, World Health Organization (WHO), analyzed chances and challenges of local pharmaceutical production in Africa particularly in the light of improving access to essential medicines. He introduced the concept of local production and presented related WHO activities.

Referring to WHO’s experience, he stressed the importance of a favorable national environment for local pharmaceutical production as well as collaboration between countries and access to markets. He clarified that some pharmaceuticals such as blood products and antivenoms are more feasible to be produced locally than others. Local manufacturing may facilitate access to essential medicines, but that it is not a goal in its own right. There have been problems in quality of locally produced essential medicines; furthermore prices can be higher than those of imported medicines. He stressed that locally produced medicines must meet international standards for quality, safety and efficacy. A risk-based step-by-step approach for producing medicines locally might be possible, but there should be no compromise on the final goal: good quality medicines for all people. At the end, health care providers and patients do not care where the medicines are produced as long as they are safe, affordable and of good quality.

Frank Schmiedchen, Governmental Director, German Federal Ministry for Economic Cooperation and Development, analyzed local production from the perspective of a donor country, particularly taking into account its contribution to economic development. He introduced a programme to foster local pharmaceutical production in developing countries that was initiated by the German government. So far, more than 100 million Euros have been invested and additionally private investments of more than 250 million Euros have been activated in Sub-Saharan Africa, South and South East Asia, the Middle East and Latin America. It is the explicit goal of the programme to support developing countries to achieve the Millennium Development Goals (MDGs) by supporting their local pharmaceutical industry, improving access to medicines as well as fostering private sector development and trade capacities. The activities of the programme include assisting local enterprises to produce high quality essential medicines, technology and know-how transfer to the local pharmaceutical industry, capacity development of national and regional entities responsible for quality assurance as well as of quality infrastructure and of human resources working in the pharmaceutical sector. It also aims at strengthening public institutions and local and regional pharmaceutical business organizations.

In the following discussion, the audience raised questions concerning the role of market structures and market access as well as quality standards in the light of fostering or hampering local production. Frank Schmiedchen stated that local pharmaceutical producers in Africa at present can hardly compete with other manufacturers. Rägo said that market access is essential; if there is no market for quality products these products will simply not be available. Both speakers reiterated the importance of harmonized quality standards of medicines no matter where they are produced.

Panel 1 – Quality Matters! – The Controversial Issue of Quality Standards of Locally Produced and Imported Medicines

Dr. Lembit Rägo, Coordinator Quality Assurance and Safety: Medicines, WHO, explored the issue of capacity building within the context of the WHO Prequalification Programme (PQP) – a global medicines quality assurance programme. Within the PQP, not only medicinal products but also active pharmaceutical ingredients (API) and quality control laboratories (QCL) are prequalified. In 2012, PQP prequalified 48 medicines for priority diseases, bringing the total number of prequalified medicines to 317. PQP also contains a strong capacity building component aiming at regulators and local manufacturers. In 2012, the programme (alone or in collaboration with partner organizations) organized 27 capacity building exercises that involved a total of 1561 staff from manufacturers, regulators and QCLs from 78 countries. In addition, PQP welcomed three fellows from national regulatory authorities to a three month rotational post at WHO headquarters.

He concluded that the WHO PQP is a powerful engine to promote the quality medicines agenda globally and to ensure the quality during the whole life cycle of products (including variations made to specifications or manufacturing processes, and dealing with quality complaints).

Hiiti Sillo, Director General, Tanzania Food and Drugs Authority, went into regulatory enforcement and the risk of counterfeits and substandard medicines using Tanzania as an example. The Tanzania Food and Drugs Authority (TFDA) is an Executive Agency that was established in 2003 and is a regulatory body mandated to regulate safety, quality and effectiveness of food, medicines, cosmetics and medical devices. He pointed out that counterfeits and substandard medicines pose a serious public health problem for both developed and developing countries. Counterfeit medicines are dangerous when they are used to treat life threatening conditions, e.g. malaria. Inadequate access to essential medicines, including high medicine prices in many countries, is the breeding ground for counterfeits. Furthermore, inadequate legal frameworks, weak penal sanctions on national levels, un-harmonized regulatory systems in neighboring countries and a limited number of drug inspectors seriously hamper the fight against counterfeits. He presented various cases of counterfeit medicines in Tanzania that have been documented since 1999 to illustrate the challenges faced in the fight against them. He stressed the fact that combating counterfeit medicines requires collaboration at national, regional and international level with political will as prerequisite for success. A legal framework clearly defining counterfeit medicines and recognizing its serious criminal nature is as much needed as a strong regulatory framework backed by legislation. Tanzania did take an important step in the fight of counterfeit medicines by establishing a joint police and customs taskforce.

Dr. Eliangiringa Kaale, Senior Lecturer and R&D Lab Manager at Muhimbili University of Health and Allied Sciences in Dar es Salaam, gave an overview on quality impact in the light of shortage of human resources. He highlighted the high potential of the Eastern African region for domestic pharmaceutical production, but investment in human resources is necessary. There are still various challenges for local manufacturers to produce quality-assured medicines such as the technical standards for production, compliance with WHO Good Manufacturing Practices, lack of R&D laboratories specifically for generic producers and lack of skilled personnel. East African manufacturers either “import” skilled personnel from other countries (e.g. India) or take the risk to manufacture medicines without paying adequate attention to quality demands. Based on his own experience at Pharm R&D Lab at MUHAS and its product development projects he concluded that availability of skilled personnel still remains a major challenge. Therefore, various stakeholders such as the industry, universities, governments, and NGO have to collaborate to address quantity, quality and types of required skills.

Daisy Isa, Head of Marketing & Strategy, CHANMedi-Pharm, Nigeria, introduced a wholesaler’s perspective on local pharmaceutical production. Her starting point was the poor availability of quality assured medicines globally while the situation in Africa is especially severe. Many African countries still rely heavily on pharmaceutical imports despite having local manufacturing companies. There is evidence for a high demand for locally manufactured products from reputable manufacturers in Africa, however various challenges still prevent the manufacturers from using the opportunities the region offers. Moreover, the chaotic and unregulated pharmaceutical supply chain system in many developing countries leads to poor and unreliable accessibility of products, thus contributing to the growth of the informal sector. She pointed out that CHAN Medi-Pharm’s experience regarding contract manufacturing with local manufacturers has not been very satisfactory, especially concerning final cost of products, level of customer services and range of products options. Based on

that experience, CHAN Medi-Pharm would at present still prefer to work with international instead of with local manufacturers. From a wholesaler's perspective, she concluded that there is a future for local manufacturing in Africa. Problems mentioned before have to be understood as initial problems in the process of charting a new course. As the market develops and regulatory bodies become stronger, more players will invest in this sector and the service level will improve substantially, eventually leading to increased access to medicines.

In the discussions that followed, the question whether profit orientation of pharmaceutical producers can be balanced with public health interests was raised. Dr. Rägo stated that this depends on product groups and various circumstances, e.g. if governments see long-term benefits of local production, or if local manufacturers come up with good products at a reasonable price. Other panelists agreed that differing interests can be balanced, although the commitment of all stakeholders to strengthen local pharmaceutical production and improve access to essential medicines is of key importance.

Reflecting the developments in local production in the last decade, all panelists recognized substantial improvements be it in the packaging, the evolvement of regulatory systems or product quality itself. It was emphasized that local manufacturing is not a competition-free zone and investments have to be made so that the best companies will survive in the long-run.

World Café – Why to Produce Medicines Locally?

During the World Café, conference participants had the opportunity to discuss different questions and themes in small groups; each group was supported by a resource person who gave a short input before the discussions started.

Station 1: Do India and China provide a transferable blueprint for African countries wishing to repeat their success in the field of local production? Resource person: Prof. Sudip Chaudhuri (Indian Institute of Management, India)

Prof. Chaudhuri pointed out that the political will and commitment had been an influential factor for the flourishing of pharmaceutical industries in India, while China experienced multinational investment. Both countries share the characteristic of having huge national markets. Participants also mentioned that India might have been filling the need for generics. Several obstacles that hinder African countries from succeeding in local production were identified. Educational systems in Africa do not prepare students for an industrial carrier and linkages between academic institutions and the industry are lacking. Governments do not actively support and nurture local pharmaceutical industries, in addition to local regulations such as taxes not being as favorable as in India and China. Most national markets are also limited in size.

Some enabling factors to overcome the shortcomings were also discussed: Regional markets (e.g East African Community) could be utilized to increase market capacities. TRIPS flexibilities (not applicable to both India and China) might offer further incentives for local production in African countries. Good governance was identified as one of the most important enabling factor for a successful local production.

Station 2: How can local production capacities be built until 2016 so that LDCs can make use of TRIPS flexibilities? Resource person: Dr. Paul Lartey (President and CEO of LaGray Chemical Company, Ghana)

The group identified that the advantage of local production in Least Developed Countries (LDCs) clearly lies in the production of drugs that are already under patent in the rest of the world, for example 2nd and 3rd line ARVsand drugs against multi-resistant TB. The group pointed out certain ways for (immediate) action to enable LDCs to establish local production and make use of the TRIPS flexibilities: The organization of neighboring countries as “LDC-regions” was suggested thus overcoming the focus on single countries. Moreover, countries should not start the production from scratch but make use of already existing experience in pharmaceutical production and start in countries with favorable conditions in regard to infrastructure (water, roads, electricity, security, human capacities etc.). Furthermore, it was pointed out that local production has to be done on large scale and the national context has to be taken into account. It has to be assured that support from the government(s) and necessary laws are in place. The starting point for local production should be the regional harmonization relating to rules and standards; governments should remove unnecessary barriers. An improved environment for investment in the countries would also enhance their potential for local production.

Furthermore, in the context of advocacy, the focus should be on long-term benefits of local pharmaceutical production. All too often national governments (and local investors) focus too much on short-term-benefits and consequently shy away from initiating local production.

Station 3: Which role can technology transfer play to push local production and what are the obstacles? Resource Person: Dr. Wilhelm Volk (Head International Business, 1A Pharma)

The role of technology transfer and possible obstacles were discussed. A main problem was identified, namely how to maintain low prices and high quality at the same time, especially when taking into account that assuring the quality in producing medicines locally requires continuous funding. In addition, technology transfer takes time and its impact is not immediately visible. Hence, the incentives to invest in high quality production seem low also with respect to the fact that the poor local infrastructure leads to high transportation costs, at times higher than the profit margin. Among the outlined challenges, the insecure funding and the lack of benefits and incentives are the major obstacles for local manufacturers to invest in the improvement of their quality standards. This is exacerbated by the availability of markets for low-quality medicines, that can be sold without having to fear economic consequences.

Station 4: Should donors and other international entities put effort into promoting local production and “self-sufficiency” in developing countries? Resource person: Jürgen Reinhardt (Project manager, UNIDO)

The group reflected on a number of justifications typically put forward in support of the local production of pharmaceuticals (LPP) in Africa, pointing at strategic considerations for the industry’s development. In this context, LPP is seen to have a potential to (i) mitigate supply shortages, prevent stock-outs and ad-hoc procurement, (ii) ensure the continuity of supplies beyond the current ‘era of drug donations’, (iii) facilitate regulatory oversight, (iv) more effectively combat the spread of substandard and counterfeit medicines, and to (v) secure the spillovers of a knowledge-intensive industry. Some discussants expressed skepticism regarding the feasibility of a viable manufacture of quality medicines in challenging environments. While a consensus emerged that a growing LPP on its own does not necessarily lead to access improvements, there was also agreement that any assistance provided by donors and development partners for LPP would need to be guided by a thrust on quality drugs and commercial viability considerations. This objective would best be achieved by advocating a holistic approach that seeks to improve the operating environment for pharma manufacturers at various fronts simultaneously. An extended list of constraints impeding the build-up and growth of a viable industry thus requires synchronized action at policy, institutional and sector/company levels alike. Some discussants were in favour of starting investments ‘in a less complicated industry’, thereby allowing for quicker wins. There was, however, agreement that any successful LPP intervention would hinge on the long-term commitment of national actors (policy-makers, business actors) as well as an ensuing donor engagement for the sector’s development. In this context, the increasing emphasis placed on the need for LPP at highest levels, as for example reflected in the African Union’s 2012 ‘Pharmaceutical Manufacturing Plan for Africa – Business Plan’ was also referred to as an important expression of ownership for this agenda on the part of African decision-makers.

Station 5: How can African manufacturers become competitive with Asian producers regarding price and quality of medicines? Resource person: Harvinder Singh Alag (CEO, Zenufa Laboratories)

The group first discussed the challenges of local production in Africa and why Asian manufacturers are often more competitive: China and India profit from the sheer size of their national markets (economies of scale) and also enjoy export benefits. On the other hand, African producers face challenges concerning quality, production of too many products in small quantities (of each manufacturer), lack of support services (repair etc.) and dependence on imports (mainly of APIs) that come along with high customs, transport costs and delays.

These challenges should be addressed by only focusing on a limited number of products and investing in those (markets could even be shared among the local manufacturers), producing at scale, e.g. for the whole region, keeping “minimum” quality standards (national authorities should set priorities), improving the infrastructure and building up supporting industries (for packaging materials etc.) as well as providing low-cost finance possibilities. Taxation policies and public procurement processes should be improved to favor local manufacturers. Through these measures,

the production base can be enlarged leading to lower prices even in the private market. Local manufacturers should target the local market as much as the donor market; cooperation with international partners involving technology transfer need to be considered.

The idea of banning specific basic products from import in order to boost local production was controversially discussed because it might not have the desired effect but on the contrary lead to reduced availability and dependence on few manufacturers.

Station 6: Does local production of essential medicines improve public health? Resource person: Dr. Zafar Ullah Mirza (Coordinator Department of Public Health, Innovation and Intellectual Property, Health Systems & Innovation Cluster, WHO)

The group agreed that the question is very complex as it would be necessary to take into account the particular conditions in each country to find an adequate answer. Nevertheless, the discussion was controversial: some group members saw local production as the long-term solution to ensure country ownership and to build country capacity. According to this scenario, countries with no local production of essential medicines might suffer from a worse public health situation than the others. Others doubted that existing challenges can be overcome by more local production. It was stressed that accessibility, affordability and good quality of essential medicines is of primary importance, not their origin.

In conclusion, the group agreed that local production can improve public health under certain conditions like secured access to private markets and private procurement as well as favorable rules and regulations that are in place and taken seriously. Moreover, it was highlighted that government action is needed to enable local manufacturers accessing markets, making their companies profitable and finally ensuring access to essential medicines for the local population. It was recommended to build the required infrastructure in Africa and to subsidize locally manufactured medicines to get local production started.

Panel 2 – Improved Access to Medicines through Local Production?

Martha Gyansa-Lutterodt, Director of Pharmaceutical Services, Ministry of Health, Ghana, elaborated on access to essential medicines and the role of local production taking Ghana as an example. Access to medicines remains a global challenge and affects Least and Middle Income Countries (LMICs) to varying degrees, including Ghana. Based on her experience, local manufacturing of medicines contributes significantly to the improvement of access to medicines through supply chains that meet local demands.

She mentioned an assessment for child specific medicines in Ghana that was conducted in 2011. In the assessment it was noted that local manufacturers either produce or have the capacity to produce medicines in most of the therapeutic categories for even some special therapeutic groups, e.g. child-specific medicines. They also produce or have the capacity to produce medicines containing 20 out of the 26 active pharmaceutical ingredients (APIs) with regard to these child-specific medicines. The assessment further revealed that only 27% of these medicines are produced locally in the

required dosage form and strength, while there is local capacity to produce a further 38%. Overall, local manufacturers have the potential to produce 65% of the targeted child-specific medicines. She explained that Sub-Saharan African pharmaceutical manufacturing contributes 25 to 30 percent to the continent's need – which is concentrated in South Africa, Nigeria, Ghana and Kenya.

The argument for access to medicines using local production is as relevant today as it was ten years ago. Interventions are needed to build capacity of local manufacturers to tackle the production of innovative products, to encourage investment into new and existing product lines, to promote market access across the sub-region and to promote public private partnerships (PPPs) geared towards sustainable access to medicines and taking into account public health interests as much as private sector interests.

Simonia Mashangoane, Treatment Action Campaign South Africa, explored from an activist's point of view the question of possible benefits of patients from locally produced medicines. She compared present figures on ARV treatment and HIV infection rates with those from ten years ago. There is a significant decline in vertical HIV transmission and treatment costs and a vast increase in people on ARV treatment. She highlighted that high medicine prices in South Africa are driving up the costs of healthcare delivery: Medicine costs increased by 25.2% between 2008 and 2010, while medicine usage only increased by 5.8%. The top 5 countries from which South Africa imports medicines are: Germany, the US, France, India and UK. At the same time, South Africa has a relatively large and competitive generic pharmaceutical industry and most medicines used in current ARV treatment regimen are manufactured by local pharmaceutical companies. However, all APIs for ARVs are imported and not produced locally. In addition, many newer and better ARVs are not available in the public health sector due to high costs. In fact, no third line ARV treatment is currently provided by the public health sector.

She further explained that for many medicines in South Africa it is not the lack of APIs but rather patent restrictions that drive up medicine prices. She introduced the planned joint venture between the government and Lonza Ltd to set up a local API manufacturer called Ketlaphela. Generic manufacturing companies will then be able to purchase APIs from this joint venture. The initial focus of Ketlaphela is on HIV, moving into Malaria and TB and later expanding into medicines for other diseases.
Mashangoane concluded that without legislative reform of South Africa's Patents Act, it is likely that Ketlaphela's cost-saving potential will be undermined by strict patent barriers. If the joint venture is restricted to producing off-patent APIs or finished medicines, Ketlaphela will be roped into a part of the market that has already seen massive price reductions due to generic competition.

Astrid Berner-Rodoreda, Bread for the World, talked about TRIPS flexibilities and related chances and challenges for least developed countries. She introduced the TRIPS agreement and explained the key role of India for the provision of ARVs to developing countries. She pointed out that the comparative advantage of LDCs lies in making use of TRIPs flexibilities and the transition period for LDCs until 2016 and actually tackling the production of newer ARVs that are still under patent protection. If instead LDCs start to produce first line ARVs, there might be little benefit, as first line medicine is usually produced at much lower prices in India. It is not realistic that the transition phase

until 2016 allows enough time for LDCs to build local production capacities for those newer medicines. Therefore, the period for WTO compliance for LDCs needs to be extended beyond 2016. Ideally, the transition period should be extended for LDCs for as long as the country is actually classified as LDC. She concluded by stressing that TRIPS plus provisions in Free Trade Agreements (FTAs) and other trade agreements need to be prevented. In any case, it needs to be weighed up, if local production or imports from India provide better access to medicines.

Prof. Maureen Mackintosh, Open University UK, highlighted research gaps concerning local production and their impact on accessibility of medicines. She presented research findings from Tanzania that reveal an urban bias in medicine distribution. The availability of medicines in general is lower in rural areas, but the medicines that are available in rural areas is locally produced to a large extent. In other words, Tanzanian produced medicines are more likely to reach rural areas than imported ones. Her research findings furthermore indicate that local producers can compete with imports across a wide range of products, since mean prices did not differ significantly by country of origin. She concluded that users find local products acceptable and cautioned that imports from India into East Africa may not be sustainable, while local and regional suppliers do have the potential for further development.

Open research questions include the issue of urban / rural bias in medicine supply and especially the local producers' advantages in supplying the rural areas of other countries than Tanzania. Moreover, more research is needed to find out how the health sector itself can increase its support to good quality local manufacturing, for example by targeted local production geared to a particular disadvantaged field of health care.

Within the discussion, it was highlighted that steps have to be taken to make the pharmaceutical industry more attractive to young graduates in order to ensure that companies have qualified personnel. It was reiterated that local production cannot improve public health, if it is not feasible. It cannot be ignored that local companies face serious competition with Indian and Chinese producers that also benefit from governmental support. Dr. Zafar Ullah Mirza from WHO took the opportunity to introduce a project on local production and access to medicines which is funded by the European Union. Within its first phase the landscape of local producers in developing countries was assessed and country case studies were conducted in order to develop an approach to help local producers to improve access to medicines. Dr. Mirza emphasized that industrial policies have to be combined with public health policies within the countries. He also stated that the linkage of local production and access to medicines is not very clear. He gave the example that 80% of all ARVs in Africa come from India, but at the same time not all persons in need have access to these ARVs in India either. He pointed out that the often repeated arguments that local producers have no market and are not competitive enough are invalid if you look at industrialized countries where market protection has enabled industry to grow. Whereas, it has to be acknowledged that most LDCs would start under worse conditions than the industrialized countries.

Another conference participant, who fully supports local production, said that governments have to take the necessary steps to develop local production by securing markets for the products. This was agreed by a another participant from the audience who said that public procurement enables companies to step into private markets and find customers in different sectors. Moreover, it was said that to further support local production the quality of products has to be put at the centre of the initiative. Furthermore, it was added that many companies have indeed benefited from local production, since they have reduced their profit margins. To fully use TRIPS flexibilities and produce cheaper drugs, countries have to change their patent law. The added value of local production lies in producing drugs that are under patent elsewhere and by using TRIPS flexibilities. LDCs could play a great role in this context, but at the moment they do not fulfill this role yet. Apart from LDCs, it is also necessary to look at middle income countries and to ensure access to essential medicines there, especially since the majority of HIV patients will live in middle income countries by 2020.

Closing

Christoph Bonsmann, Speaker of The Board of action medeor, briefly summarized the conference and expressed his gratitude to the Ministry for Federal Affairs, Europe and Media in North-Rhine Westphalia and GIZ for financing and co-organizing this important and timely conference. He emphasized that there is enough evidence that good pharmaceutical quality can be produced at any place in the world, including in developing countries. Local production is easier to achieve, if local manufacturers work in alliance. Bonsmann also pointed out that good-quality products have their price that is probably higher in Africa than in Asia because of the lack of supportive infrastructure. A key role is that of the national drug regulatory authority. Existing laws must be enforced, human capacity strengthened and misbehavior of the market players (be it the manufacturer or the local wholesaler) sanctioned. It is not acceptable that poor manufacturers are being kept at the market for political reasons. In other words, the national drug regulatory authorities need the commitment and financial support from their national government to act independently. Local production will play an essential role if it can contribute increased access to quality products at affordable prices. In this regard ethical behavior of the manufacturers is mandatory in order to produce quality products. If the shareholder value or the short term return on investment is the paramount motivation quality will be only second.

Presentations and a video documentation are available on our website: www.medeor.de