The global impact of Indian generics on access to health

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Introduction

"Everyone has the right to a standard of living adequate for the health and well-being of himself and of his family, including food, clothing, housing and medical care" (Universal Declaration of Human Rights, 1948).

Over the last decades, most countries have indeed acceded to at least one global or regional covenant confirming the right to health (1). The right to health should be achieved, among others, by making essential medicines of assured quality at an affordable price (2). But in this respect, a significant gap exists today between the majority of high-income countries, where the state has sufficient resources to ensure access to quality medicines to people in its territory; and many low- and middle-income countries, where the state lacks the capacity to do so. Despite the availability of centres of excellence for several major diseases, and adequate treatment options, the lack of global equity in health and in access to healthcare and good quality medicines can be regarded as one of the chief human rights dilemmas in the 21st century (3).

Therefore, a global equity effort is needed to make quality medicines accessible to all, irrespective of the income of the countries and of the individuals, and as a part of the global effort to ensure the human right of access to health for everybody. The Indian pharmaceutical sector currently plays a pivotal and unique role in this effort: not only locally for Indians, but on a larger scale, thanks to its increasingly important role in supplying affordable generic medicines to the humanitarian and not-for-profit sector in the developing world (4). In fact, it has been estimated that 80% of donor-funded antiretroviral medicines (ARV) in Africa come from Indian generic manufacturers (5). The title "pharmacy of the developing world" (6), widely adopted to refer to India since 2007, when Novartis first challenged some key provisions of the Indian Patent Act (7), clearly indicates that Indian manufacturers are key suppliers of affordable medicines to Africa and potentially to other low-income regions.

However, a report from the Indian Parliamentary Standing Committee on Health and Family Welfare has revealed, in 2012, some important shortcomings of the Indian Central Drugs Standard Control Organisation (CDSCO), highlighting the vulnerability of quality standards of medicines (8, 9). The fact that the findings from this report were brought to the attention of the international scientific community through an editorial opinion of *The Lancet* (10), further underscores the global importance of Indian medicines.

The Indian pharmaceutical industry and the global market

Pharmaceutical companies are profit-driven enterprises, whose primary objective is not global health. Indian pharmaceutical companies are no exception to this rule. However, while the western-based pharmaceutical companies have largely neglected populations and public health needs in low-income countries, Indian manufacturers have made major investments in the African market, as well as in the "humanitarian" market (major donors, United Nations agencies and big non-governmental organisations). And not without success: indeed, a significant proportion of the wealth of Indian millionaires originates from the pharmaceutical industry (11). These investments were clearly encouraged by the unique Indian national intellectual property (IP) legislation, which incorporates essential provisions to protect public health for all in India, making the production of affordable generic drugs possible. The ethical controversy arising here, of IP protection versus assured access to essential medicines for the poorest quintiles of the population, was clearly addressed in favour of the right to health for all Indians. Indirectly, this resulted in substantial benefits for global health as well, especially in the field of HIV/AIDS, for which the availability of quality-assured Indian generics allowed an unprecedented scaling-up of access to the ARV treatment worldwide (5).

Recently, the Indian Patent Office issued India's first-ever compulsory licence, which ended Bayer's monopoly in India on the anti-cancer drug sorafenib: an Indian generic producer was authorised to manufacture and sell the drug for 3% of Bayer's price in the country, while paying the company a royalty (12). This decision was taken in the interest of public health and it shows once more that affordable quality Indian generics have the potential to make treatment available to a larger proportion of patients, and in therapeutic fields other than HIV/AIDS. This could apply outside India as well, as indicated by the 2012 dispute between an Indian generic manufacturer and Sanofi-Aventis in South Africa, concerning the anti-cancer drug docetaxel. The Treatment Action Campaign, an independent South African organisation that advocates for access to treatment for people living with HIV, intervened in the dispute to argue that the court's decision should be based on the public interest and the right of access to healthcare. Eventually, the Supreme Court ruled in favour of Sanofi-Aventis; however, after the Indian competitor's entry into the market, Sanofi-Aventis introduced its own cheap generic version of the drug (13).

Indeed, the Indian judiciary's position in recent judgments may be seen as favourable to public health on a global scale (not limited to HIV/AIDS) and it could act as a model for other countries.

But important caveats remain. In particular, the recent reports concerning poor regulatory enforcement of medicine quality requirements seem to indicate an unexpected gap between the valuable effort to build on universal *access* to essential medicines and a parallel effort to guarantee universal *quality* of all essential medicines. Nevertheless, *access* and *quality* need to be achieved simultaneously, to fulfill the basic ethical requirement of equity and to provide adequate and safe treatment to all.

The threats of a "variable" regulatory standard

A number of Indian drug manufacturers have demonstrated their ability to offer affordable essential medicines that comply with stringent quality standards. The WHO has prequalified several of their products and they have become major suppliers for the Global Fund, various UN organisations and several public and not-for-profit treatment programmes in low- and middle-income countries. WHO's prequalified medicinal products search reveals 304 drugs which list India as their manufacturing site and have been prequalified by WHO (14). Meanwhile, many Indian manufacturers also tap into the richest global private markets, and partnerships between the largest Indian generics manufacturers and multinational pharmaceutical companies are becoming more and more frequent.

But simultaneously, various studies have reported cases of medicines manufactured in India not complying with adequate quality standards, and the quality of some medicines from India has been questioned in larger studies (15, 16). A survey published in 2009 reported that 7% of all drugs tested from pharmacies in two major Indian cities were of poor quality, with a striking 12% in India's capital city Delhi; figures could be higher in poorer and rural areas, where no equivalent survey was conducted (17). These reports are obviously not homogeneous. Some are from the specialised medical press and some from the lay press. Some are suggestive of counterfeiting, which, according to the WHO, implies deliberate misrepresentation of the identity of a pharmaceutical product and is always illegal; and some are suggestive of substandard pharmaceutical products, which do not comply with appropriate standards despite being approved by the competent authorities, and may be due to incidents on the production line or to systematic negligence regarding good manufacturing practices. However, irrespective of the nature of specific cases, these findings echo other reports at the national and international levels, and they are fuelling a more general perception of the Indian pharmaceutical industry as a source of bad medicines (18).

The lack of strict regulatory supervision over the licensing, manufacturing and sale of medicines, acknowledged by the Parliamentary Report (8), seems to represent the most important factor that makes the Indian pharmaceutical sector permeable to poor-quality medicines. This situation is common to all those countries that cannot rely on a solid and rigourous regulatory system (according to the World Health Organization, this includes almost 80% of all its member states (19)).

Thus, the contradictions of the Indian pharmaceutical scenario somehow mirror the contradictions of the international pharmaceutical market, which is characterised by a situation of multiple quality standards (20), where quality is *de facto* demand-driven. But is this situation ethically acceptable? If health is a human right, can we accept the fact that quality of medicines will depend on market mechanisms rather than on regulation? If health is a human right, the creation of the conditions needed to achieve access to health belongs to the sphere of relationships between the State and the individual (1). Thus, the State and not the market has a primary responsibility toward citizens (persons) to create such conditions, including *both* the control of prices *and* assurance of the quality of essential medicines. If the State does not take this responsibility, we will keep on tolerating a *status quo* where people may or may not have access to quality healthcare depending on the strength or weakness of the market. In fact, we advocate that States should not delegate this health-related matter to the market. In the same way, States should not delegate the agenda of pharmaceutical research and development to the traditional business-oriented private sector that, being based on market incentives, has failed to address the needs of neglected populations.

In India, a lot is being done to ensure affordable prices of essential medicines, but more should be done to ensure their quality. This may be achieved, in practice, by strengthening and enforcing regulation, instead of letting prices and quality be determined by market-mechanisms.

Poor regulation is generally associated with nonavailability of resources and industrial backwardness, as is the case in low-income sub-Saharan African countries (21) and in some countries of Latin America and the former Soviet Union. In the case of India, conversely, there seems to be an unexpected and disproportionate gap between the outstanding technological advancement in the national pharmaceutical sector, and the State's capacity to regulate pharmaceutical quality. This gap inevitably leads to a variable level of protection of patients (22), and embeds a dramatic contradiction: while the Indian generic sector has the potential to fulfil the promise of affordable essential medicines to patients, in its own country as well as in others, a poor regulatory environment with unequal multiple standards might cause direct harm to public health, especially to the poor and needy, in India and elsewhere.

In addition to directly threatening the well-being of patients, the poor regulation is endangering confidence in the generic industry as a whole; and the de-legitimisation of the generic industry brings an indirect yet major harm to global health. In fact, quality-assured Indian generic medicines are essential to promote the scaling-up of essential treatments in low-income countries, and they put positive pressure on the global pharmaceutical market towards fair pricing of pharmaceuticals (23). The current situation of "variable standards" (due to "variable regulation") of the Indian pharmaceutical sector decreases confidence in the generic manufacturing sector as a whole. The resulting, generalised lack of confidence concerns not only "bad products", but also – and unjustly – all those

generic products that are indeed of good quality, affordable and essential to fulfil the ethical imperative of universal access to quality medicine.

The way forward: fair regulation for global health

In this brief reflection we are not able to address all the intricacies of pharmaceutical production and its impact on global health. Nonetheless, it appears that the variable regulation of medicine quality in India has both direct and indirect negative consequences for public health. On the one hand, it may allow poor quality medicines to reach patients, causing unnecessary morbidity and mortality, mainly among the most vulnerable populations in India and elsewhere; on the other, it delegitimises its own quality products, which are fundamental to expand health coverage at both national and global levels. It is vital to solve the current paradoxical situation, where the Indian pharmaceutical sector concurrently appears as a threat and an essential contributor to public health.

The positive signals are there in that the State is willing to fulfil its ethical obligations toward individuals and community: notably, the minister of state for health announced in 2012 that the central government will work at strengthening regulatory policies for food and drug sectors, and that the task will be integrated in the 12th Five Year Plan. On the same lines, India's drug regulators recently announced a plan that would put tight restrictions on the sale of antibiotics, in a renewed effort to fight the emergence of antibiotic resistance (24).

It is urgent that these important announcements are followed by implementation, accompanied by the necessary investments in financial and human resources, to overcome the current gap between the outstanding effort to make essential medicines available and affordable on one side, and the insufficient effort to adequately ensure their quality on the other. As Indian civil society and health policymakers debate the possible steps for India to progress towards universal health coverage, the time is ripe for effective drug regulation. Further, we would like to suggest that the Indian regulators make an effort to acknowledge the role that the Indian pharmaceutical industry is playing *de facto* on the global stage and adopt a collaborative approach *vis-à-vis* the regulators of the developing countries to which Indian products are exported. A proactive exchange of "quality information" (e.g., results of inspections, results of product assessments, etc.) would concretely help the regulatory agencies of low-income countries to prevent the import of poor quality medicines.

A well-regulated and transparent pharmaceutical sector in India is essential to further building and maintaining universal access to quality healthcare and true global equity in the right to health for all.

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