March 7, 2014

BY ELECTRONIC DELIVERY

Ms. Susan F. Wilson
Director for Intellectual Property and Innovation
Office of the U.S. Trade Representative
600 17th Street, N.W.
Washington, D.C. 20508

Dear Ms. Wilson:

The Biotechnology Industry Organization (BIO) appreciates the opportunity to provide additional comments to supplement its testimony provided before the Special 301 Committee on February 24, 2014. BIO represents more than 1,100 biotechnology companies, academic institutions, state biotechnology centers, and related organizations across the United States and in more than 30 other nations.

BIO membership includes both current and future developers and manufacturers of healthcare, agricultural, and industrial and environmental products and technologies. Because of the lengthy research and development timeframe in our sector, our members rely heavily on the strength and predictability of their patent portfolios to generate the necessary investment for translating innovative research into life-saving products and technologies.

In our hearing statement we underscored the important role IP plays in attracting not only financial investment, but also global partners. Intellectual property protection is important even more so today because of global economic concerns and thus, India's IP policies over the course of the past year, particularly in the healthcare space, are of great concern to our members. We asked this committee to designate India to Priority Foreign Country.

BIO greatly appreciates the opportunity to provide these supplementary comments and would be happy to discuss any of the issues raised in our comments in more detail. Thank you for your attention to this very important matter.

With Sincerest Regards,

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Supplemental Statement of the Biotechnology Industry Organization

Presented to the Special 301 Committee

BIO represents more than 1,100 biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations. Our members are involved in the research and development of products and technologies in the area of healthcare, agriculture and the environment. On February 24, 2014, BIO provided testimony to the Special 301 Committee regarding outlining its concerns with India's IP policies. We appreciate the opportunity to provide additional comments to supplement our testimony. In our hearing statement we made the case that India's policies on IP, while stated to address India's significant public health burden, have had minimal impact on these concerns, and in fact have been a boon for their local industry. We also indicated that there are effective ways that India can begin to address public health concerns working in collaboration with potential partners which will also lead to the growth of their innovative biotech sector. Finally, we pointed out that the innovative industry has indeed been working to help address India's public health concerns but it is increasingly difficult to carry out this task given the lack of an appropriate policy environment and support from the Indian government. We wish to expand on some of these arguments and also address a specific issue that was raised by another submission relating to section 3 (d) of the Indian Patent Act.

As we alluded to in our hearing statement, over the last few years, India has compulsory licensed or revoked patents on at least 10 major drugs in India and has indicated an interest to compulsory license more. All of the patents that have been revoked meet patentability standards around the world except in India. We presented at a list of least a few of this drugs in our hearing statement.

The government of India had justified these decisions on public health grounds. The public narrative reads that in a nation where more than two-thirds of the population lives on less than two dollars a day, few can afford expensive brand name drugs.[1] Indian generics, they assert, are the answer for providing access to medicines for the poor. Since patents impede generic entry, patents should be set aside in India to choose 'patients over profits.'

However, even a cursory inspection of the evidence indicates otherwise. Ninety-five percent (95%) of the World Health Organization's Essential Medicines List are not

[1] *See* http://data.worldbank.org/indicator/SI.POV.2DAY

patented anywhere in the world.[2] Yet, the World Health Organization states that the drugs on the EDL are affordable to only 20% of India's population.[3] Finally, less than 1% of all drugs available in India are patented.[4] Clearly, other factors have a much greater affect in hindering access to medicines for India's poor. At the same time, India views itself as an 'emerging market and superpower'. India has the 10th largest economy in the world by nominal GDP and 3rd largest by purchasing power parity.[5] Even though two-thirds of the population lives on less than $2 a day, around 100 million people in India have "wealth equivalent to or greater than the average European or American."[6]

In this submission we will explore the drivers behind India's healthcare access problems, and make the case that the causes of hindering access to healthcare are not primarily caused by intellectual property and are in large part a result of the relatively little investment has India has made in recent decades to its healthcare infrastructure.

Moreover, we will show that India's pharmaceutical policies since the 1970s has led to sustained growth in the domestic generics industry, such that it is now considers itself the "world's medicine cabinet". Even after India acceded to the WTO in 2005 and modified its patent law, the Indian pharmaceutical industry has continued to grow at a robust rate of approximately 18% per year. The Indian pharmaceutical industry sales (split approximately evenly between domestic sales and exports) stood at USD 15.6 billion during 2011. Forecasts predict that to double in 2016 to USD 35.9 billion.[7]

Underfunding Health

Measuring any country's attention to ensuring access to healthcare is a difficult endeavor. However, certain measurements are telling of how a country prioritizes public health over other government objectives.

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[2] See http://www.wto.org/english/tratop_e/trips_e/techsymp_feb11_e/laing_18.2.11_e.pdf and http://cameroninstitute.com/attachments/043_Pharmaceutical%20Access%20in%20Least%20Developed%20Countries.Fall2010.Draft-1.pdf

[3] "Health workforce, infrastructure, essential medicines", World Health Statistics 2009, The World Health Organization.

[4] *See* http://www.pharmaboardroom.com/article/interview-with-tapan-ray-organisation-of-pharmaceutical-producers-of-india-oppi20318

[5] World Bank Rankings. See http://data.worldbank.org/indicator/NY.GDP.MKTP.CD

[6] http://www.reuters.com/article/2012/03/18/us-india-drugs-cancer-idUSBRE82H01A20120318. For estimates of the size of India's middle class, see also: http://india.blogs.nytimes.com/2013/05/13/indias-middle-class-growth-engine-or-loose-wheel/?_php=true&_type=blogs&_r=0.

[7] BMI, Aranca Research and India Brand Equity Foundation. Found at http://www.ibef.org/download/pharmaceuticals-august-2013.pdf. See slide #8.

The first metric to review is the amount of investment made by the Indian government in healthcare. In 2011-2012, India allocated USD 5.4 billion for healthcare representing 2.13 percent of total government spending, or USD 4.50 per capita.[8] However, looking at India's government spending on health in isolation provides no context. India's healthcare investment should be compared to other major emerging economies such as Brazil, Russia, China, South Africa, Mexico, and Turkey.

Measuring a country like India also presents other challenges including its relatively vast geographic size and population. As a result, measurements that look at investment per person carry little meaning for a large emerging economy like India. That is why measuring public expenditure as a percentage of gross domestic product (GDP) becomes the appropriate measurement to analyze a country's relative commitment towards investing in health. GDP is a measurement of all goods and services a country produces and, as a result, pegging expenditure by the government to GDP measures how well a government both collects and allocates its resources. Conversely, using other variables such as budgets creates problems as countries' budgets will fluctuate on tax schemes, tax rates, and the ability to collect taxes creating additional uncertainty about how much a country is investing in healthcare in relation to other similarly situated countries.

India's Rank

Analyzing India in relation to other emerging markets requires looking at total health expenditure as a percentage of GDP, public expenditure as a percentage of total health expenditure, and then public expenditure as a percentage of GDP. India trails its peers in all three measurements.

[8] http://www.reuters.com/article/2012/03/18/us-india-drugs-cancer-idUSBRE82H01A20120318

Figure 1 below provides a snapshot of total health expenditure (public and private) compared to GDP in several major emerging economies including India from 1995 to 2011. India's total expenditure has lagged far behind its emerging economy peers.

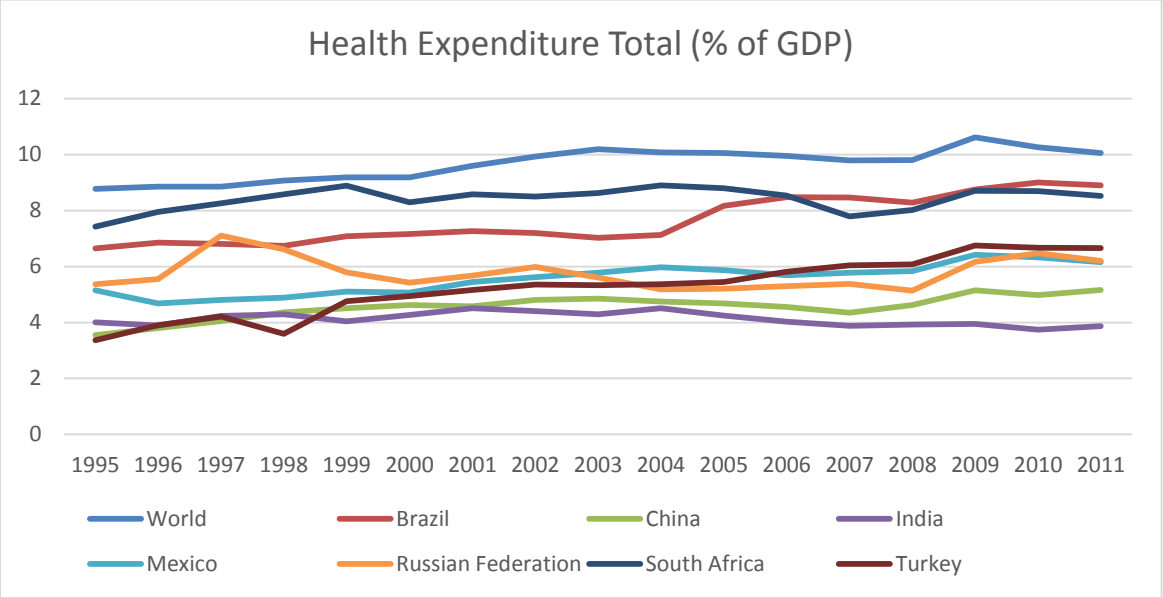
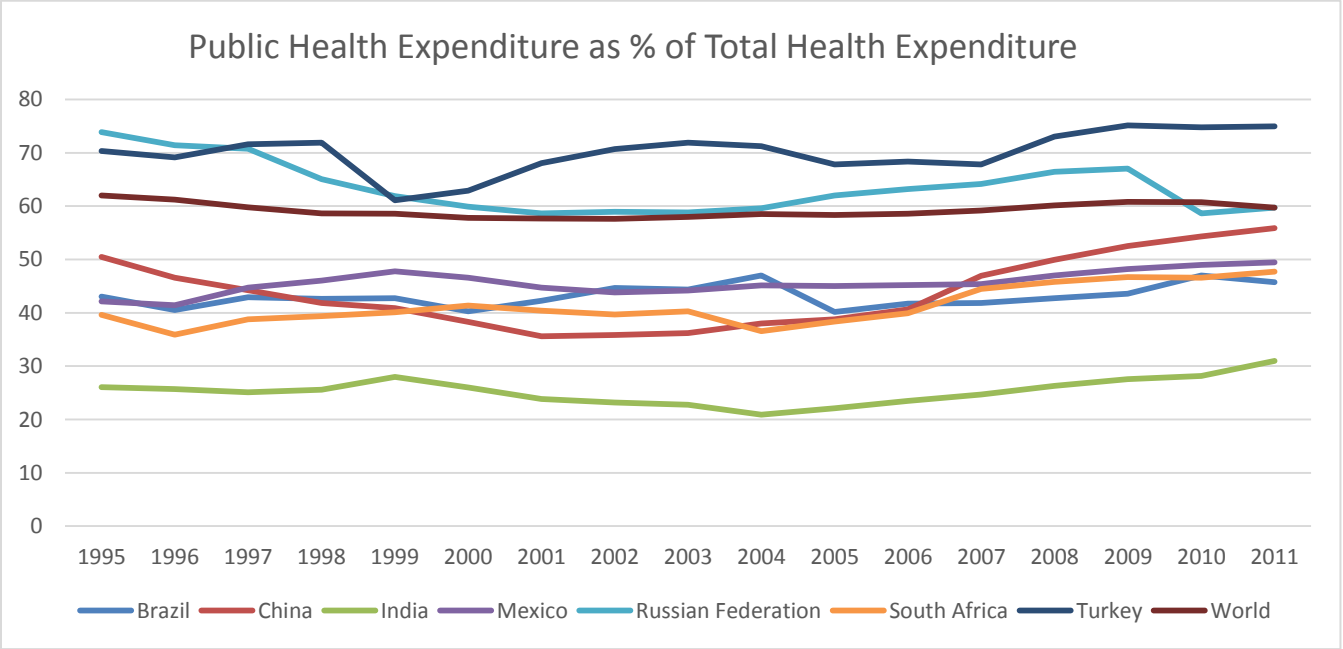


Figure 1

Source: World Bank Statistics
http://data.worldbank.org/indicator/SH.XPD.TOTL.ZS

Public health expenditure in relation to total health expenditure reveals how much of the healthcare spending is provided by the government. Once again, the Indian government trials other emerging economies spending 10 percent less than the next lowest spender (Brazil).

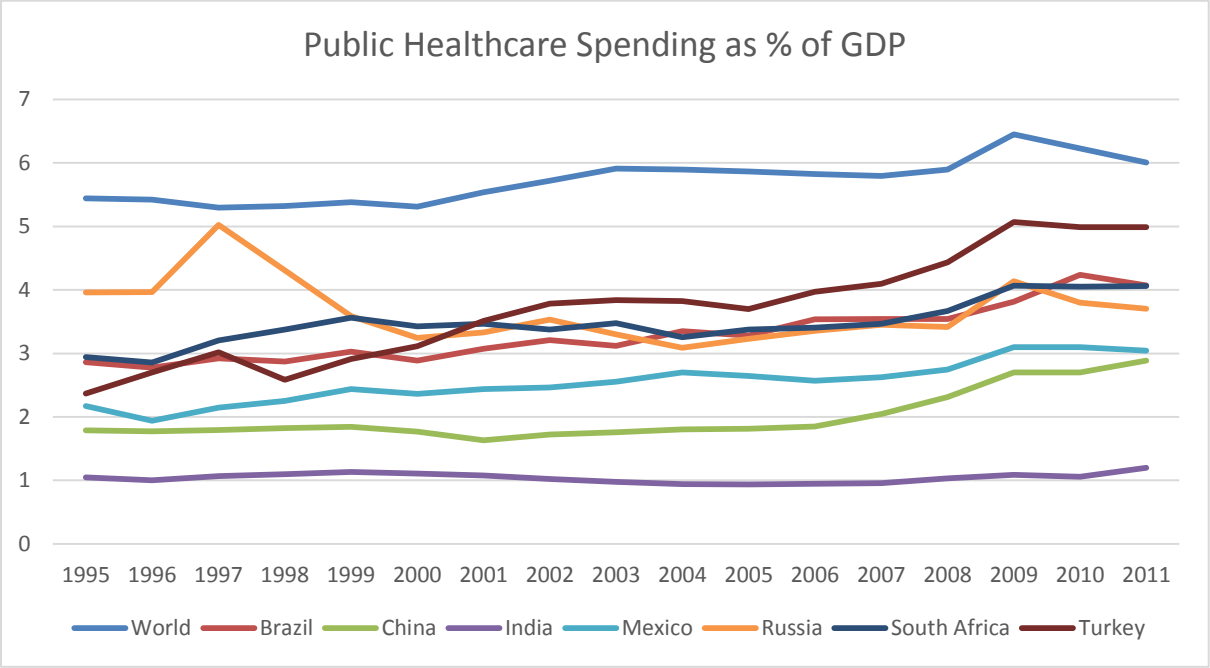
Figure 2



Source: World Bank Statistics

Finally, calculating country's public expenditure as a percentage of GDP reveals how much of each country's available resources the government applies to healthcare. India is the lowest line in the graph below and is nearly three times lower than the next closest country China.

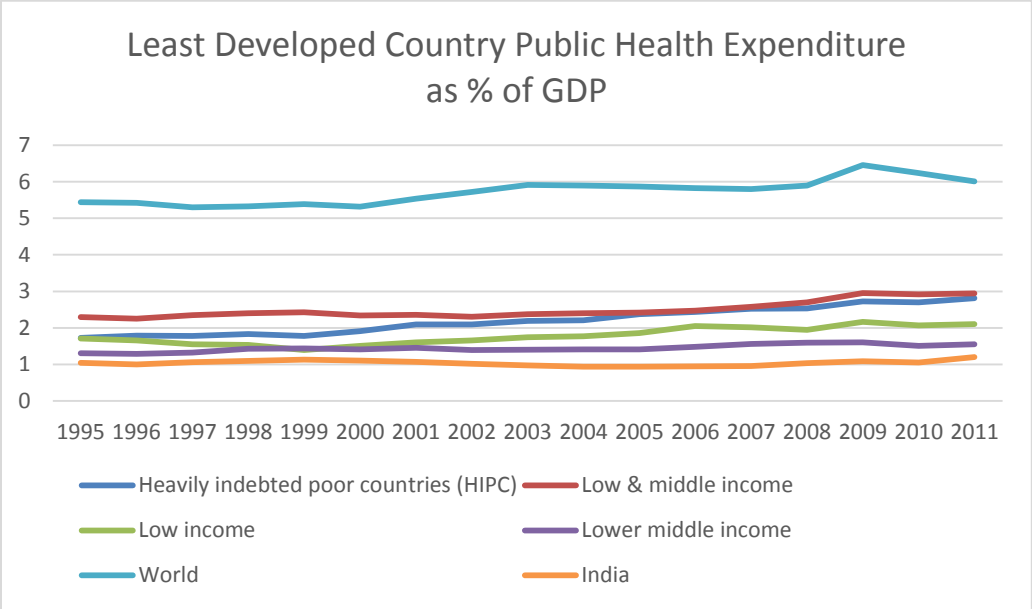
Figure 3



Source: World Bank Statistics

Unfortunately, India's commitment to healthcare is not just low for emerging economies but low for least developed countries as well. The World Bank data also categorizes the data for countries that are 'heavily indebted poor countries', 'low income', 'low & middle income', 'lower middle income', and 'world'. India's public health expenditure ranks below all of these categories.

Figure 4



Source: World Bank Statistics

This extremely low level of investment in healthcare by the Indian government relative to other governments seems to contradict the government's message that they prioritize healthcare access for their people. A refusal to invest in healthcare can only lead to negative health outcomes for the Indian people, even if the government eliminates all patents for medicines.

The Role of Health Insurance

Around the world, the major mechanism by which countries and their citizens afford healthcare is through the provision of some form of health insurance, e.g. National Health Insurance or Universal Health Care. Health insurance is critically important since it provides families with an ability to pay for unexpected medical expenses without going into debt. According to the World Bank, 86% of health expenditures are paid for out-of-pocket in India; in the United States, only 21% of health expenditures are out-of-pocket.[9]

[9] http://data.worldbank.org/indicator/SH.XPD.OOPC.ZS

In India, only 15% of the country's 1.2 billion people (or 180 million people) are covered by any type of health insurance.[10] Most available health insurance schemes (public and private) have numerous exclusions and provide no reimbursement for outpatient costs, including pharmaceuticals, making even patients in India with health insurance extremely price sensitive.

When patients do not have access to comprehensive insurance plans or healthcare facilities, healthcare policies that target the prices of a few patented drugs will not have any meaningful effect, particularly when those drugs are used in the context of highly specialized medical care involving trained specialists and expensive medical equipment and diagnostics. Another complicating factor is that 65% do not have access to modern healthcare facilities.[11] When Indian patients cannot get to a hospital in the first place and cannot afford generic drugs, focusing efforts on limiting prices of patented medicines would have *de minimis* impact.

Struggling Health Infrastructure

"India may be the world's largest producer of generic medicine, but its health care system is an unregulated mess. The poor have to rely on low-quality — and sometimes exploitative — private medical care, because there isn't enough decent public care. While China devotes 2.7 percent of its gross domestic product to government spending on health care, India allots 1.2 percent." *Amartya Sen, a Nobel laureate and professor of economics and philosophy at Harvard.*[12]

Healthcare infrastructure and access to that infrastructure remains a real problem for all Indians. The World Health Organization (WHO) has collected several data sets in its World Health Statistics 2013 publication. The data sets provide a unique perspective on how India has progressed on key health indicators to evaluate existing infrastructure. Measuring the number of health personnel, hospital beds, and health service coverage all provide imperative information to assess whether a country can deliver effective healthcare with or without patented drugs.

First, comparing access to medical professionals presents a unique picture to evaluate India's place among its emerging economy peers. India only slightly outpaces South Africa by having 8.5 physicians per 10,000 population. Unfortunately, this is close to half of Brazil and China. In contrast, India leads all countries in number of pharmacists which indicates that the people in need of medical care routinely turn to pharmacists with minimal training in medicine in the absence of available physicians. These

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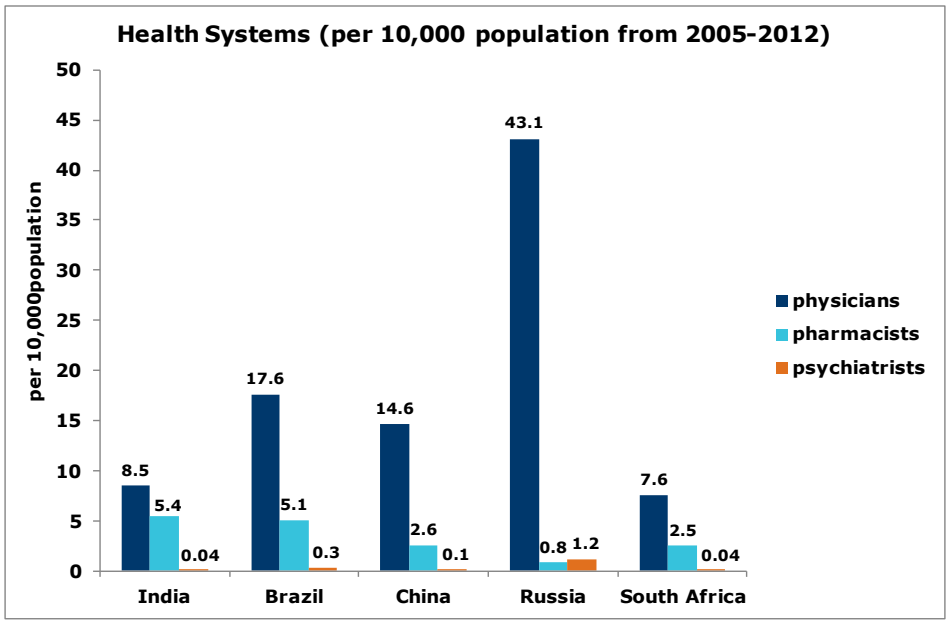
[10] See http://www.reuters.com/article/2012/03/18/us-india-drugs-cancer-idUSBRE82H01A20120318

[11] *See* http://pharma.financialexpress.com/20120415/management01.shtml

[12] http://www.nytimes.com/2013/06/20/opinion/why-india-trails-china.html?_r=0

pharmacists in turn naturally will recommend whatever medicines they deem appropriate.

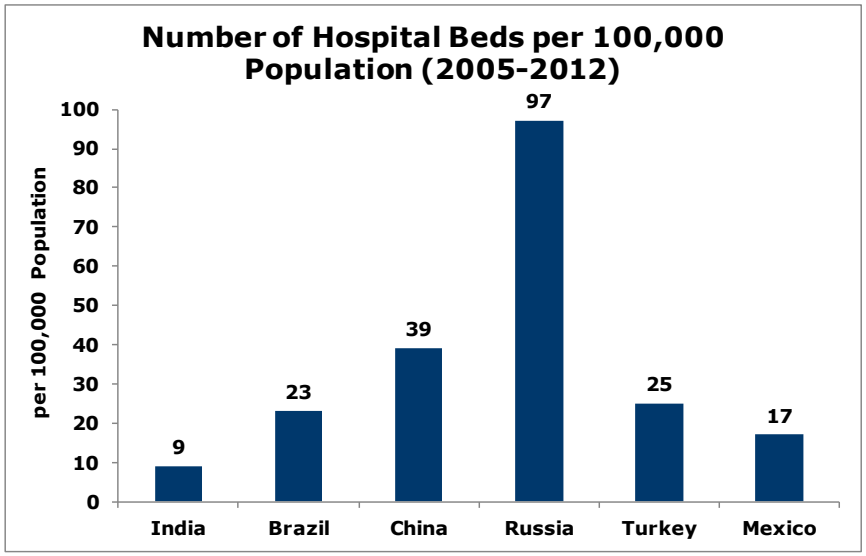
Figure 5



Source: WHO World Health Statistics 2013
http://apps.who.int/iris/bitstream/10665/81965/1/9789241564588_eng.pdf

However, evaluating infrastructure also requires the availability of physical facilities for the population. Hospital beds per 100,000 provides a proxy for availability of clinics and hospitals for the population. India trails its peers once again registering almost half of the second lowest country (India 9, Mexico 17).

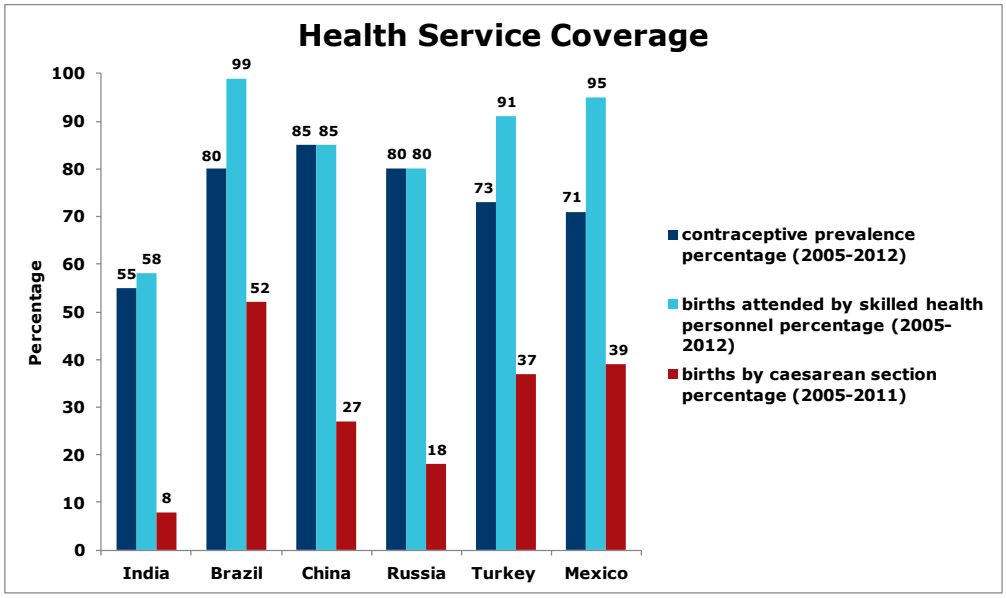
Figure 6



Source: WHO World Health Statistics 2013

Finally, India falls short of its peers when evaluating specific health service coverage. Contraceptive prevalence in India trails 15% behind the country's next closest peer. Births attended by skilled health personnel also seems alarmingly lower than its peers. Finally births by Caesarean section remains much lower which, coupled with hospital and personnel availability numbers, seem to reflect a lack of access to such procedures when needed.

Figure 7



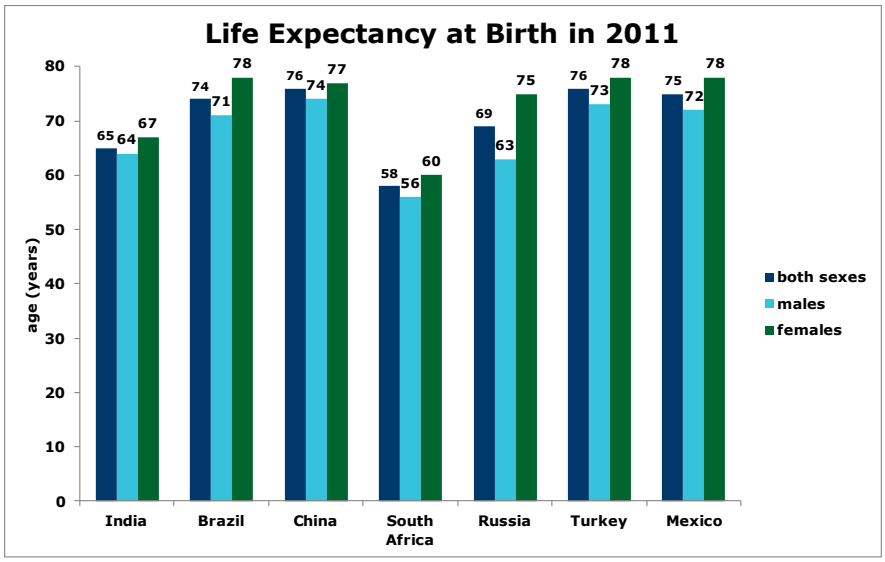
Source: WHO World Health Statistics 2013

Health Outcomes

The final measurement for access to healthcare involves the health outcomes for Indian citizens in relation to other emerging economy peers. World Health Organization statistics once again provide an accurate picture of the health outcomes in India.

Figure 8 below provides initial insight into India's life expectancy at birth rate in 2011. India trails several emerging markets with the exception of South Africa.

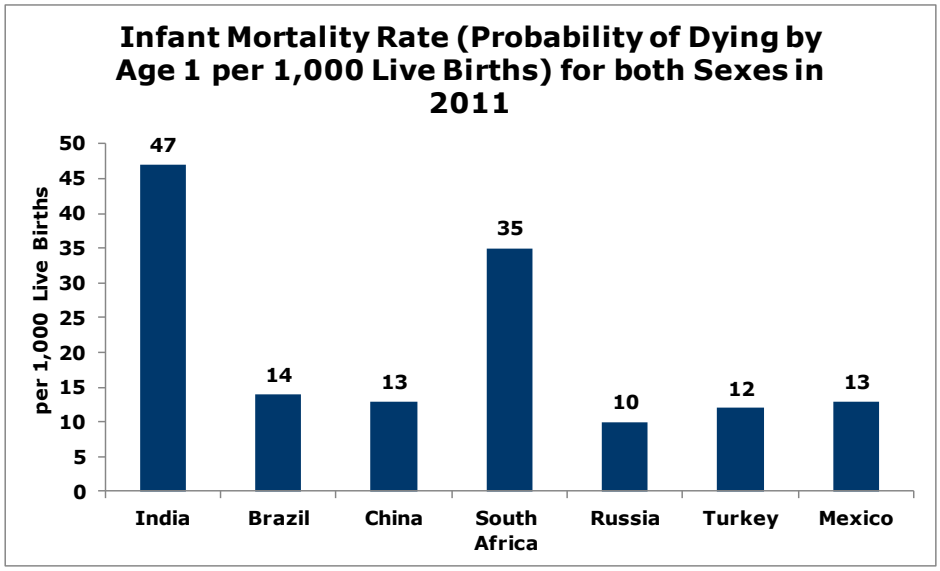
Figure 8



Source: WHO World Health Statistics 2013

The WHO's review of the Infant Mortality Rate (death rate during first year of life) also reveals India trailing behind other emerging markets. The probability of dying by age 1 per 1,000 live births stood at 47 which is 12 more than then next closest emerging market (South Africa at 35) and more than three times higher than the next emerging market (Brazil at 14).

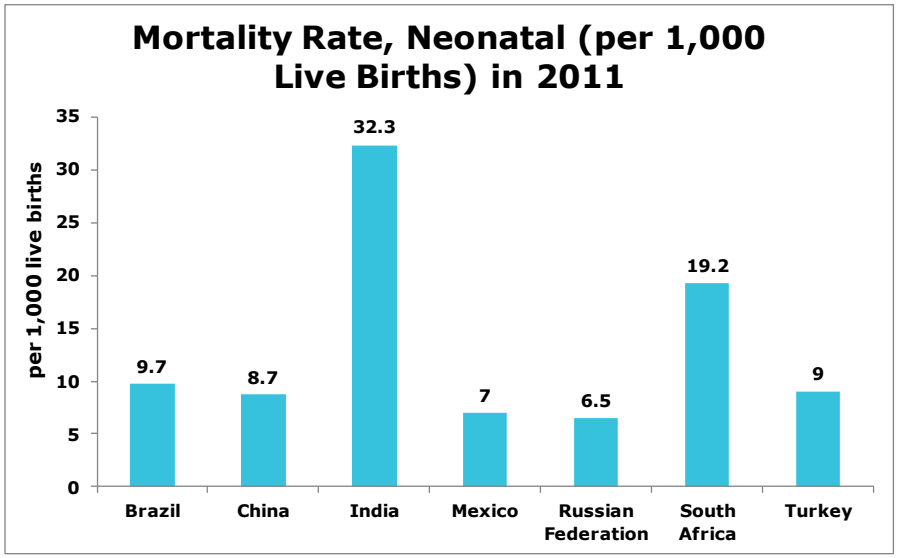
Figure 9



Source: WHO World Health Statistics 2013

A review of neonatal mortality rate (death rate during the first 28 days of life) also reveals India falls far behind its peers (Figure 3). At 32.3 deaths per 1,000 live births, India stands apart from other countries with South Africa registering 19.2 deaths per 1,000 and other countries registering between 6.5 and 10 deaths per 1,000.

Figure 10

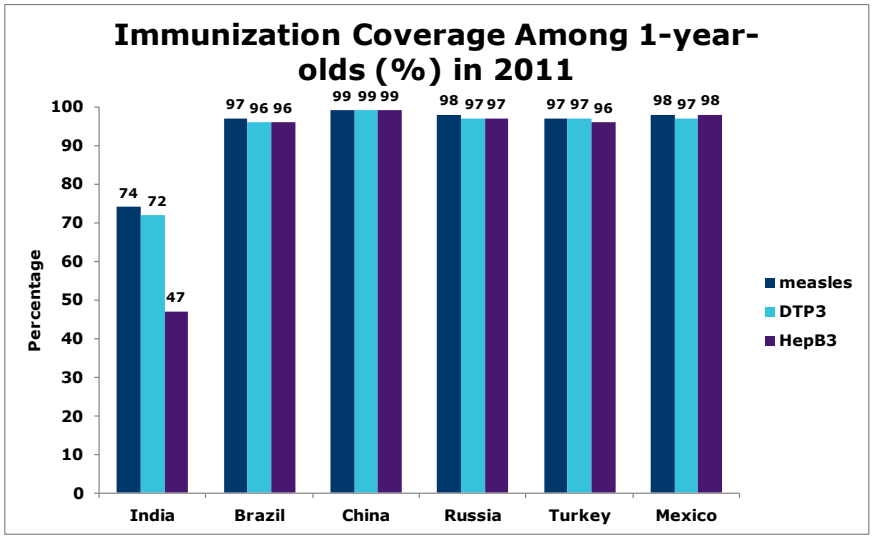


Source: World Bank Statistics at http://data.worldbank.org/indicator/SH.DYN.NMRT

Another important indicator of health outcomes involves the immunization rates among children. This particular indicator is illustrative of the state of India's health care system because India is the largest producer of vaccines, often supplying low-cost vaccines to WHO and UNICEF programs.

Despite government programs to provide vaccines at **no cost** to children, India trails other emerging markets in immunization coverage among one-year olds in 2011. While other emerging markets achieve near 100% immunization rates for measles, DTP3, and HepB3, India only achieves 74% for measles, 72% for DTP3, and 47% for HepB3. The lack of immunization coverage is clearly attributable to problems that go well beyond affordability.

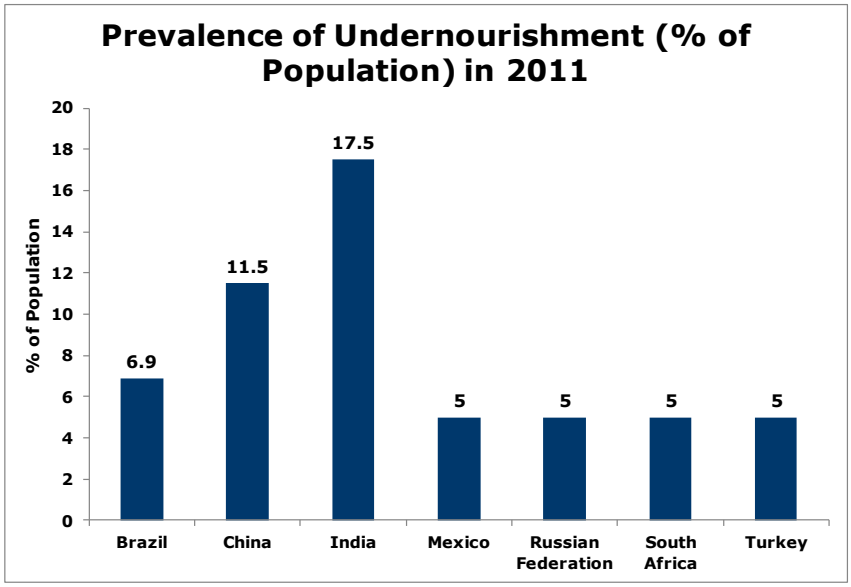
Figure 11



Source: WHO World Health Statistics 2013

Discussion of health outcomes also include other systemic variables outside the healthcare system but remain within the hands of government. One such measure that has a profound influence on health is undernourishment in a population. Once again, India registered the highest level of undernourishment among emerging economies (see Figure 12).

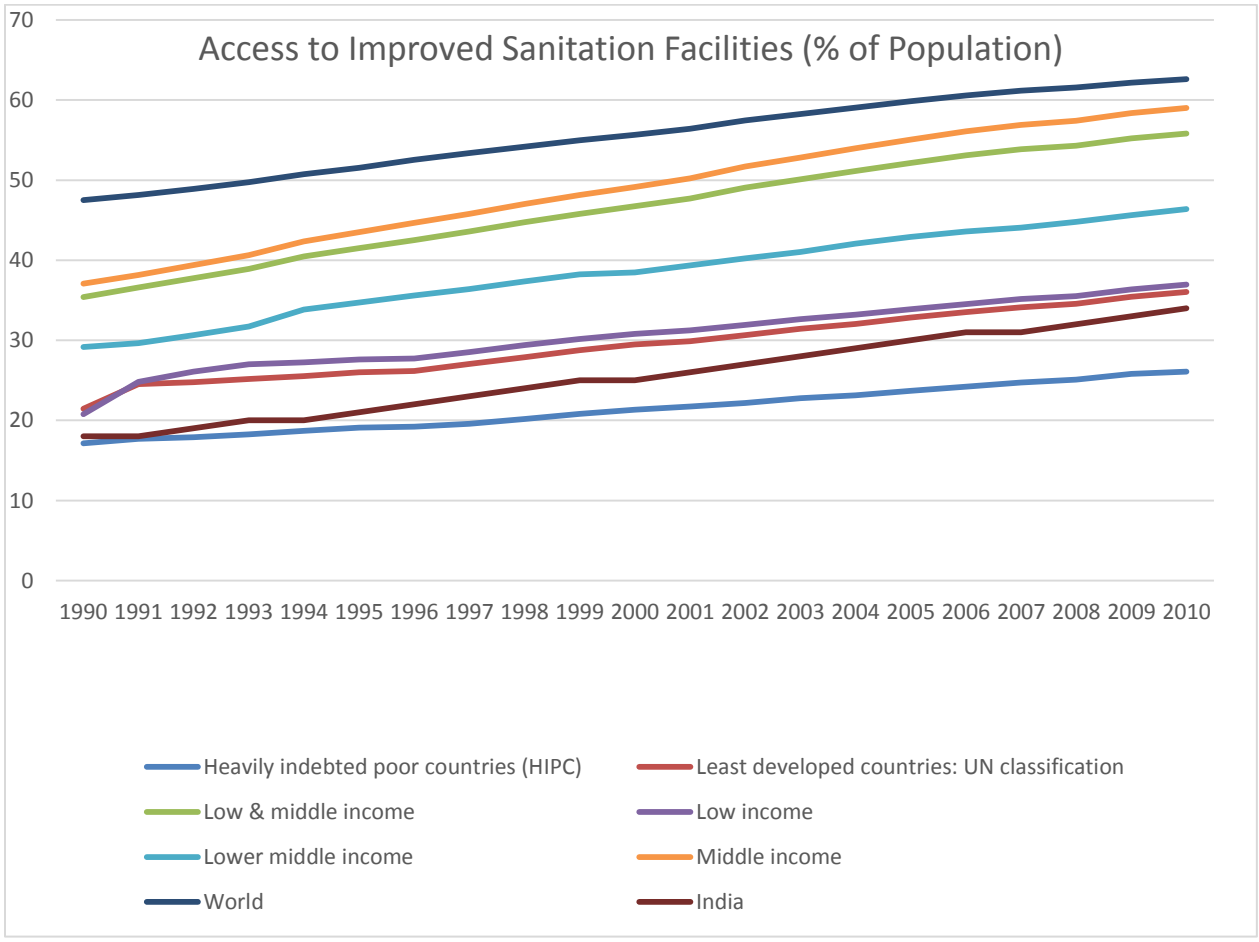
Figure 12



Source: World Bank Statistics at http://data.worldbank.org/indicator/SN.ITK.DEFC.ZS

Finally, evaluating access to improved sanitation facilities (a predicate for eliminating several health risks) reveals that India only registers above 'heavily indebted poor countries' but remains below 'least developed countries', 'low income', and all other categories.

Figure 13



Source: World Bank Statistics at http://data.worldbank.org/indicator/SH.STA.ACSN

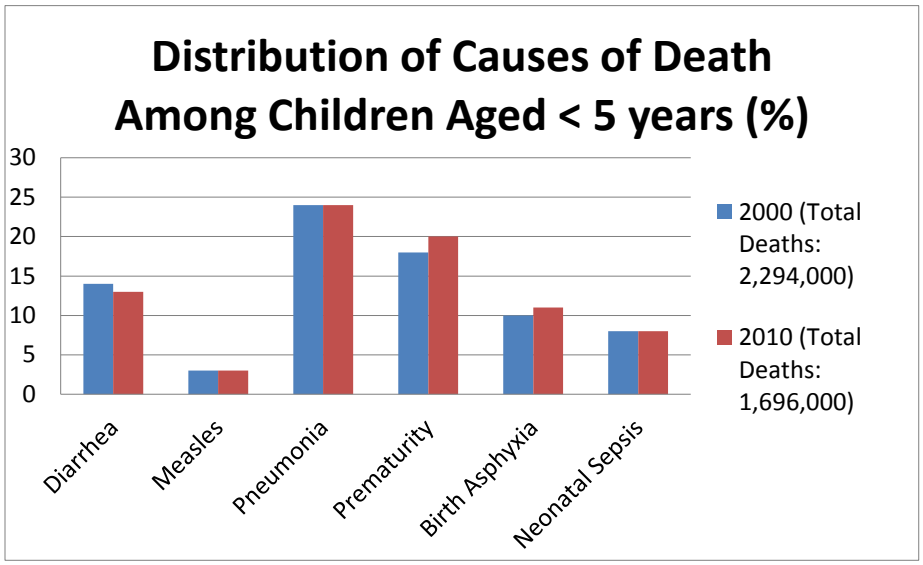
Country Specific Challenges

After reviewing the health outcomes for India in relation to other emerging markets, any systematic approach to understanding how India can move forward in providing health care for its people requires a review of the disease indications specific to India.

First, reviewing the distribution of causes of death among children under 5 years in 2000 and 2010 reveals little improvement in the situation. Fourteen percent (14%) of children died of diarrhea in 2000 and in 2010. Twenty-four percent (24%) died of

pneumonia both in 2000 and 2010. Prematurity and birth asphyxia became slightly worse from 2000 to 2010.

Figure 14



Source: WHO World Health Statistics 2013

The World Health Organization tracks several selected infectious diseases and the number of reported cases in several countries. As Figure 15 indicates, India struggles with Tuberculosis and Malaria with over a million cases each in one year. CDC-recommended treatments for Tuberculosis include isoniazid, rifampin, rifapentine, ethambutol, and pyrazinamide none of which are protected by patents.[13] India lists various drugs to treat of malaria of which are patented.[14]

[13] http://www.medguideindia.com/drugs_new.php
[14] http://www.medguideindia.com/drugs_new.php and http://mrcindia.org/TreatmentGuidelineswithAddendum.pdf

Figure 15

Source: WHO World Health Statistics 2013

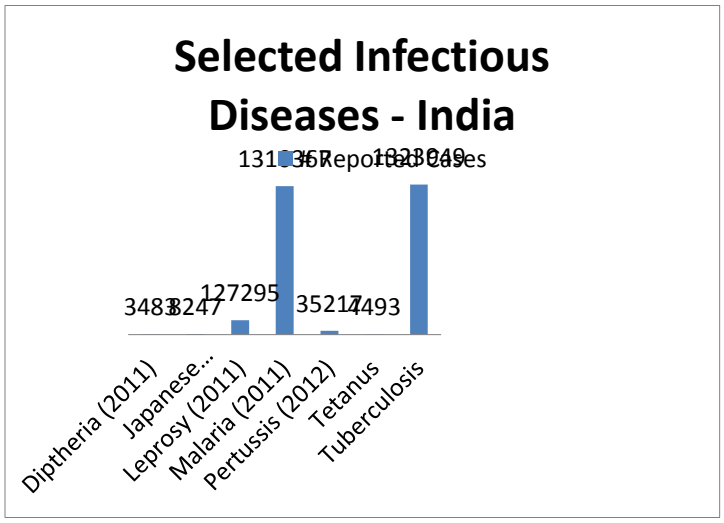
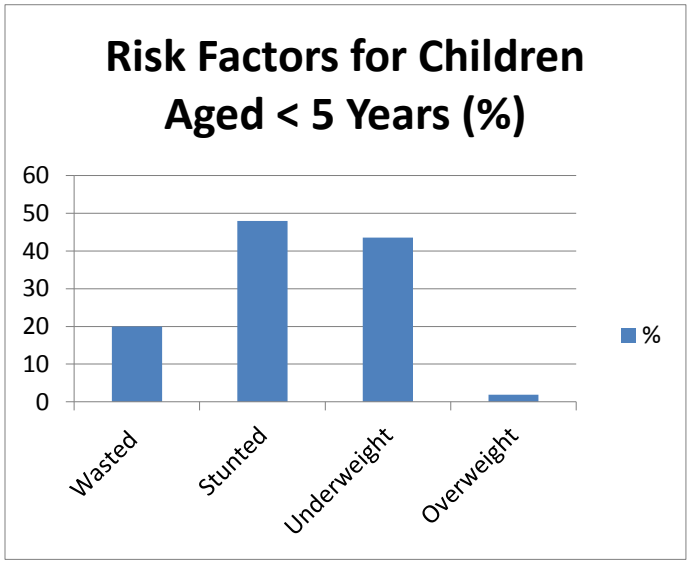


Figure 16 reflects the wide prevalence of undernourishment. In India, 20% of children under 5 years of age are "wasted" and 47.9% are "stunted" accounting for 2/3's of the Indian population. As the WHO explains "stunting reflects the cumulative effects of under-nutrition and infections since birth – and even before birth."

Figure 16



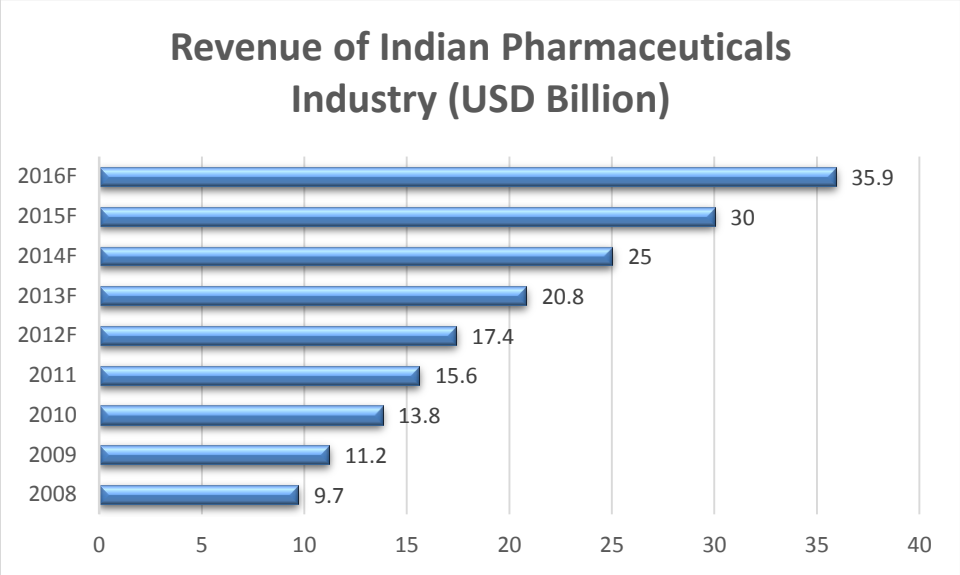
Source: WHO World Health Statistics 2013

Successful Industrial Policy

While India has struggled to keep up with other emerging markets in providing healthcare, India's pharmaceutical policies has led to explosion in the domestic generics industry since the 1970s when India first modified its patent laws to disallow product patents. Even after the patent law was again modified in 2005, the Indian pharmaceutical industry has continued to grow at a robust rate of approximately 18% per year. The Indian pharmaceutical industry sales stood at USD 15.6 billion during 2011. Forecasts predict that to double in 2016 to USD 35.9 billion.[15]

[15] BMI, Aranca Research and India Brand Equity Foundation. Found at http://www.ibef.org/download/pharmaceuticals-august-2013.pdf. See slide #8.

Figure 17

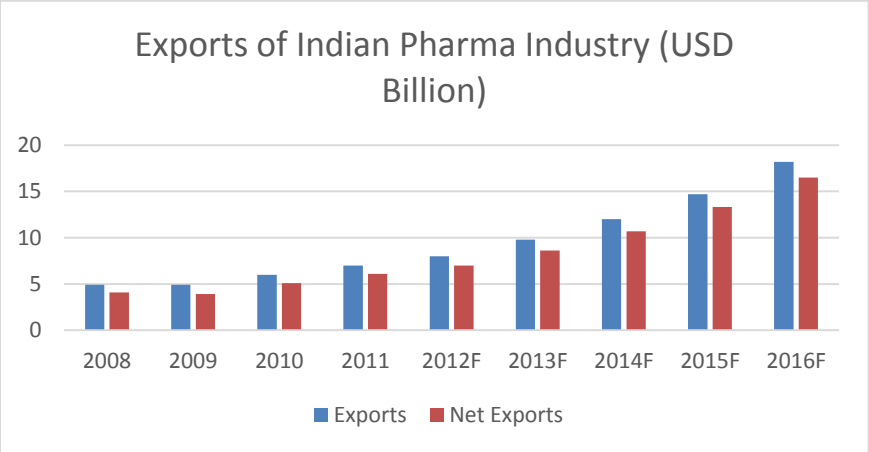


Source: IBEF and Aranca Research

India pharma exports from India are projected to double over the next five years resulting in a trade surplus of USD $16 billion by 2016. In terms of value, pharmaceutical products exports have increased at a rate of 26.1 per cent to USD 10.1 billion during FY06–13.[16] At the same time, pharmaceutical imports are under USD $ 2 billion.

[16] *Id.*

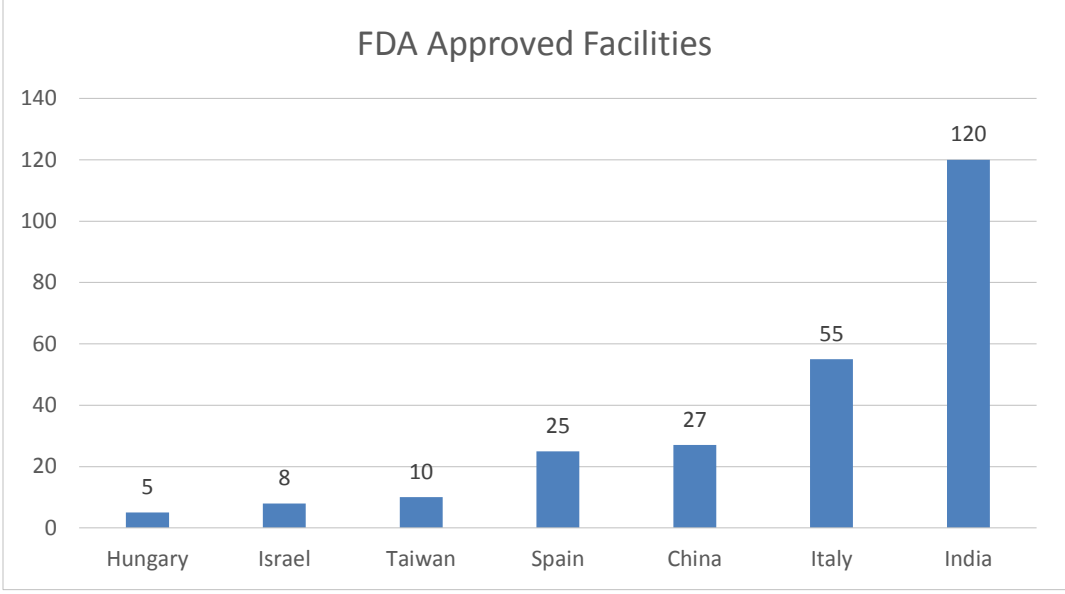
Figure 18



Source: IBEF and Aranca Research

India also seems well positioned to continue its generic dominance with over 120 FDA approved and 84 UK MHRA-approved manufacturing facilities. [17]

Figure 19

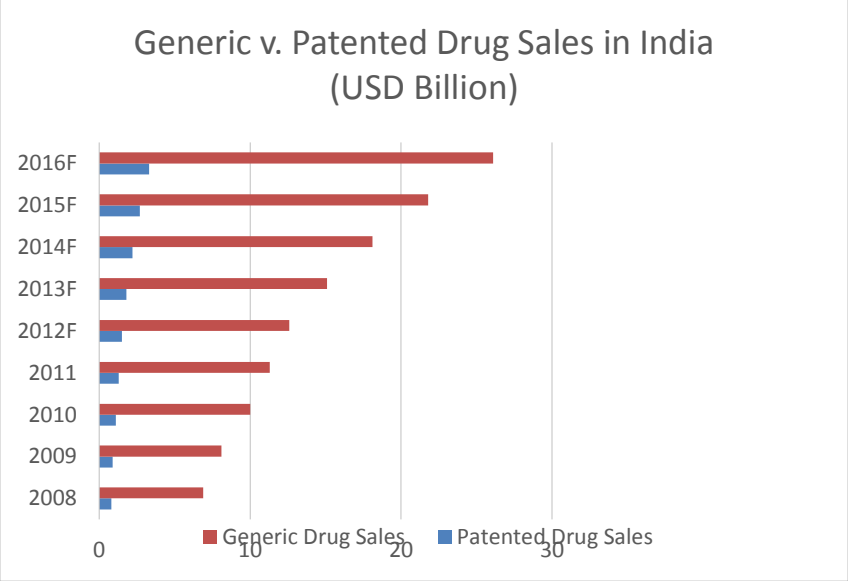


[17] *Id.*

Source: BMI, Aranca Research and India Brand Equity Foundation

Finally, generic versus patented pharmaceutical sales reflects both the dominance and health of generic companies in India. Projections indicate that generics will represent 90% of the prescription drug market by 2016.[18] The small share of patented drug sales also indicates generic dominance and contradicts assertions that patents in India are causing an explosion of sales for patented medicines. In fact, the only explosion of sales that has occurred has been on the generic side.

Figure 20



Source: BMI and Aranca Research

The above graphs, facts and figures demonstrate that India's current pharmaceutical policies have minimal effect on public health, but appear to have bolstered the Indian generic sector. We take the government at its word when it states its desire to address public health needs. Many of BIO's members have facilities and operations within India and they stand ready to work with the government to help address its public health needs. But this requires an open and frank dialogue about the underlying challenges in

[18] *Id.*

the Indian healthcare system and effective ways to address them. Moreover, we believe that there are many companies not yet operating in India that would be open to collaboration given the appropriate policy environment. Many of these companies are open to working with Indian partners to develop innovative research into cutting edge products. However, over the past few years we have noticed a reluctance on the part of many companies to fully engage in India despite promising research in India's institutions. While we cannot attribute this solely to the environment in India, we cannot ignore the timing of this cautious approach.

Section 3 (d)

We now wish to respond to the below excerpt from a testimony recently presented by Professors Srividhya Ragavan, Brook Baker and Sean Flynn. In the section below they maintain that a Federal Circuit (CAFC) decision in the case of *Pfizer v. Apotex*[19] involving the patented besylate form of amlodipine is analogous to the rationale behind section 3 (d) of India's patent act. They contend that the CAFC ruled that patent claims to amilodopine besylate did not exhibit unexpected superior results from the patented maleate amilodopine compound and were therefore found to be invalid. We disagree with this characterization.

> *In the United States such patents are easily issued although they can be invalidated by litigation. Rather than accepting the resource investment, cost, judicial time and the loss of access to the public inherent in the U.S. model for combating evergreening, India's Section 3(d), enacted in the 2005 amendment,15 prohibits patenting of new uses of known substances, including medicines. Similarly, patenting new forms of known substances is not allowed unless there is evidence of significantly enhanced efficacy. The logic of this interesting provision is along the exact lines of the opinion of the Court of Appeals for the Federal Circuit (CAFC) in the case of Pfizer v. Apotex involving the Pfizer's patenting of the besylate form of amlodipine (salt form) which Apotex claimed was obvious in the light of Pfizer's own patent on the base compound amlodipine.16 The CAFC, in agreeing with Apotex that the patent on the besylate form was invalid, highlighted the besylate form lacked the unexpected superior results from the base compound in order for the salt form to be patented.17 Indeed, the Manual for Patent Examination Procedure in section 716.02 and in 2144.09 specifically memorializes unexpected results as a test to demonstrate nonobviousness of structurally similar compounds like isomers and homologues.18 Thus, India's standard is well within the lines of what has been allowed in the United States.*

Prof. Ragavan et al. frame their comments in the context of non-obviousness/inventive step which contradicts Indian legal interpretation. India's highest court has drawn a

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[19] Pfizer v. Apotex, 488 F. 3d 1377 (Fed. Cir. 2007)

clear line between inventive step and the new and distinct requirements of section 3(d). In the Novartis Gleevic case (2013), the Supreme Court of India clarified that section 3(d) provides a "second tier of qualifying standards for chemical substance/pharmaceutical products" that is above and beyond inventive step. Therefore, from the start the use of a CAFC decision on non-obviousness to justify and interpret section 3(d) is not tenable.

Section 3(d) of the Indian patent act prohibits the patenting of new forms of known substances which does not result in "the enhancement of **the known efficacy** [emphasis added] of that substance or the mere discovery of any new property or new use for a known substance or of the mere use of a known process, machine or apparatus unless such known process results in a new product or employs at least one new reactant."

The CAFC never considered efficacy as a criteria in its ruling and in fact, efficacy was never an issue in the case as the patentee claimed that the besylate form showed all of the medicinal properties of the maleate form. The issue in the case related to the solubility and stability of the new besylate compound in comparison to the maleate compound. The CAFC followed the reasoning as set forth in *Graham v. John Deere Co.,* 383 U.S. 1, 17, 86 S.Ct. 684, 15 L.Ed.2d 545 (1966) used to determine obviousness criteria of (1) the scope and content of the prior art, (2) the level of ordinary skill in the art, (3) the differences between the claimed invention and the prior art, and (4) objective indicia of non-obviousness. Following this rationale the court held that the prior art as a whole provided the motivation to achieve the claimed invention, and that a clear and convincing case was made to show a reasonable expectation of success in obtaining the claimed compound.

The issue of "superior results" was addressed by the court as a secondary consideration where evidence of unexpected results can be used to rebut a prima facie case of obviousness. Here the court held that any superior property must be "unexpected" to be considered as evidence of non-obviousness. *In re Chupp,* 816 F.2d 643, 646 (Fed.Cir.1987). In their examination of the case they determined that the patentee had not shown "unexpected" results and that the prior art as a whole showed that the resulting besylate compound would have been expected to be more stable and soluble than the maleate compound. They held that the superior properties of amlodipine besylate were due to nothing more than routine optimization that would have been obvious to one of ordinary skill in the art and would have been within the capabilities of one skilled in the art.

Section 3 (d) requirements differ from this ruling in three ways—first, section 3(d) requirements are simply separate and distinct from non-obviousness as India's Supreme Court has said; second, therapeutic efficacy was never a factor that was discussed in the cited case; and third, section 3 (d) requires evidence of enhanced efficacy regardless of whether a prima facie case of obviousness can be made. In other words, the

requirement of 3 (d) is above and beyond the obviousness and novelty requirements in US patent law.