The Economic Implications of the United States' dependence on imports of Active Pharmaceutical Ingredients and Generic medicine from China and India

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INTRODUCTION

On Wednesday October 2019 Janet Woodcock, M.D. Director - Center for Drug Evaluation and Research provided testimony before the House Committee on Energy and Commerce, Subcommittee on Health. The goal of the hearing was to raise awareness on the United States' growing dependence on manufacturers of active pharmaceutical ingredients (APIs) that are based in India and China, determine the risk that this dependence poses on national security, and to determine what the United States can do to reclaim domestic control of the pharmaceutical manufacturing supply chain [1].

PHARMACEUTICAL MANUFACTURING PROCESS AND THE MARKET FOR APIS

There are two general steps to manufacturing pharmaceutical products [2]. The first step is for firms to convert raw materials into Active Pharmaceutical Ingredients. This part of the process is complex and requires the labor of medicinal chemists. The second step is to mix the APIs with other non-active ingredients and press the mixture into pills, pour it into a capsule, or mix it into a solution for injection or application to the skin. The second step is called the final formulation and is a manufacturing process rather than a chemistry process. Economies of scale matter for both steps of the manufacturing process but less in the final formulation of drugs since manufacturers can mass produce final formulations within a single plant and this is not the case in the complex and technically demanding science of converting raw materials into APIs.

In 2010 the World Bank estimated that the size of the market for APIs was 76 billion [2]. Firms either sell APIs on the open market or use the APIs to produce pharmaceutical products through their own final formulations manufacturing operations. Firms that produce and sell APIs may also have to buy APIs from outside firms, it would be inefficient for a large firm that manufactures a broad portfolio of drugs to produce all of their APIs in-house.

INDIA'S LENIENT PRODUCT PATENT POLICY AND THE IMPLICATIONS ON THE GLOBAL SUPPLY CHAIN FOR API AND FINISHED PHARMACEUTICAL PRODUCTS.

Due to the size and complexity of API production and final formulation manufacturing operations firms have chosen to specialize based on their skills and market opportunities. One opportunity for global manufacturers of pharmaceutical products is to time the patent expirations of drugs that were produced in developed countries, one example of this practice can be seen in the case of Glivec, a drug produced by Novartis to treat Leukemia. When Glivec went off patent Novartis attempted to patent a similar compound with increased bioavailability, this compound did not prove increased efficacy in leukemia treatment endpoints and therefore was denied patent approval. This opened the door for Indian manufacturers to produce a generic version of the drug which dramatically reduced costs. The Indian government has historically not allowed product patents for pharmaceuticals which has allowed generic drug manufacturers to freely produce any medicine and offer it to the Indian consumer at a lower cost than they would pay if patent protections were in place **[3]**.

The case of Indian generic manufacturing and patent protection policy should be discussed further. The average Indian citizen lives on less than $2 dollars per day which decreases the demand for drugs at the prices that are set by global pharmaceutical firms. This also has implications on the market for generic medicines in the United States. The United States is a large open economy and has access to the world's market for goods and services **[F1]** and therefore adheres to the *law of one price* which states that if the prices of identical goods diverge arbitrage opportunities exists (I.e., there is an opportunity to buy a good at a lower price in outside markets and sell it within your own market for a profit) **[4]**. The law of one price and the theory of purchasing power parity does seem to be realistic for the global market for pharmaceutical products. It can be argued that these theories can be unrealistic because many goods are not easily traded, E.g., an American purchasing a haircut in a foreign market, and that tradable goods are not always perfect substitutes. The market for generic drugs satisfies these conditions because the active pharmaceutical ingredient is the same regardless of where it is manufactured, assuming that the manufacturers adhere to ethical business practices, and

these goods are easily traded. The main limitation to the free trade of pharmaceutical products is domestic patent protection rules and trader barriers such as tariffs. Once a pharmaceutical product is off patent, it is the US consumers right to purchase generic versions of the drug regardless of where they are made. Figure 1 shows that there is a strong upward trend in US imports of Indian pharmaceutical products from 2002-2019. The sharp increase in pharmaceutical imports (denoted by the solid red line representing HS Code 3004--MEDICAMENTS NESOI; MIXED OR NOT; IN DOSAGE ETC FM) from India may be due to a phenomenon known as the patent cliff [F2] in the pharmaceutical industry [5]. We can see, when comparing the Rate of Duty of both the Trump and Obama administrations that the total tax levied on these imported goods has not changed which may indicate that the dip in the price of finished goods in class HS 3004 is a result of strained trade relationships between the US and India [12], rather than an outcome of expenditure switching policies.

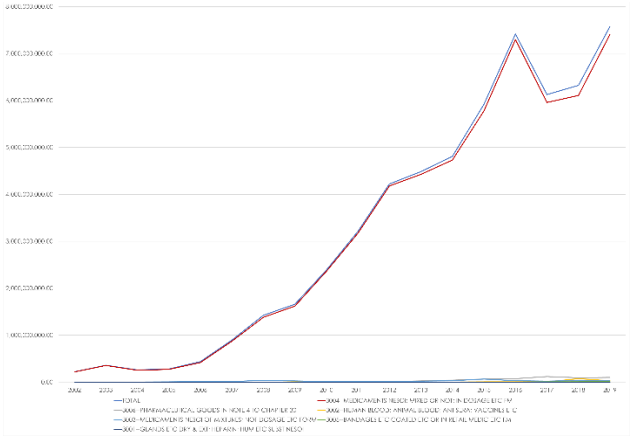

Figure 1: International Trade Administration data on HS 30 – Pharmaceutical Goods

F1 Several trade restrictions in the form of import taxes have been implemented to reduce the trade deficit with China, some of which are as high as 25%
F2 In 2010 the pharmaceutical industry experienced one of the largest waves of expirations of pharmaceutical patents in recent history. This phenomenon referred to as the "patent cliff." Once a patent expires the world's manufacturers, one being India, enter that market and siphon off a large share of sales revenue by selling essentially the same goods at a much lower price.

HTS Number	Description	Unit of Quantity	Rate of Duty Trump Administration (2021 HTS)	Rate of Duty Obama Administration (2016 HTS)
3004.10.10	Containing penicillin G salts	["kg"]	15.4¢/kg + 49%	15.4¢/kg + 49%
3004.31.00.00	Containing insulin	["kg"]	25%	25.00%
3004.32.00.00	Containing corticosteroid hormones, their derivatives or structural analogues	["kg"]	25%	25.00%
3004.41.00.00	Containing ephedrine or its salts	["kg"]	25%	25.00%
3004.42.00.00	Containing pseudoephedrine (INN) or its salts	["kg"]	25%	25.00%
3004.43.00.00	Containing norephedrine or its salts	["kg"]	25%	25.00%

PROTECTIONIST TRADE POLICIES AND THEIR IMPACT ON THE GLOBAL PHARMACEUTICAL MARKET

The price may be impacted by tariffs such as the ones President Trump imposed as a part of his plan to *Declaring American Independence* in which he sought to implement a protectionist policy to cut the US trade deficit [7]. This protectionist policy directly undermined President Trump's promise to lower prescription drug prices. In fact, the tariffs that were placed on Chinese goods included active ingredients in pharmaceuticals, surgical equipment, and materials that are used to manufacture medical devices [8].

STIMULATING TECHNOLOGICAL GROWTH IN THE MANUFACTURING INDUSTRY

India does in fact allow firms to patent manufacturing techniques which could increase the incentive for firms to compete and patent the best technology for production. If an outside firm wishes to enter the market they would have to abide by the process patent laws in India. This provides firms a strong incentive to develop novel and original technology that they can patent and profit from. According to the Solow Growth model the way to increase output while keeping the exogenous variables of labor and capital fixed is increase technological progress, which augments labor and increases per worker output. The Indian and Chinese market for pharmaceutical manufacturing is attractive for many reasons. One of these reasons is the competitive advantages that they enjoy in the cost of labor. As we can see in Figure 2, labor costs in US dollars will never be a a competitive advantage for the US. According to the Solow Growth Model production is a function of labor and capital. We can see by reviewing Figure 2 that we the US is not competitive on labor. The US worker may be more produtive due to the increased financial incentize to produce, it is estimated that the US worker is about 3 times more productive that the average worker in India [6]. It is estimated that the wage will grow at a CAGR of 10-15% year over year for China and India due to some workers reaching senior management levels and some workers completing post-doc studies in the US and returning home to higher salaries. The Solow Growth model accounts for this in the theory of the Marginal Product of Capital (MPK) which measures the amount of output that is obtained from the allocation of an additional unit of capital. As we can see in Figure 4, the MPK curve shows that the allocation of capital reaches a point of dimishing returns. This is mostly irrelevant for Indian and

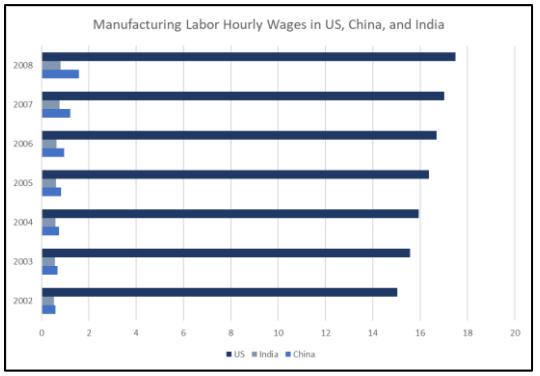

Figure 2: Wage data from the US Bureau of Labor Statistics

Chinese manufacturers who has a much larger labor force; They will both win in the race to compete for efficiency in the manufacturing process against the US. Advances in the manufacturing process through the FDA's emerging technology program as was cited as a possible way to increase competition in Janet Woodcock's congressional testimony in October 2019. Technological progress is shown in the Solow Growth Model to be a main driver in growth by augmenting exogenous variable (labor) in the production function. This strategy relies on a favorable regulatory landscape and regulators willingness to revisit their Good Manufacturing Process regulations which were designed for batch manufacturing, not the continuous manufacturing process that the FDA is currently promoting.

COVID-19 IMPACTS TO THE GLOBAL PHARMACEUTICAL SUPPLY CHAIN

It is apparent that the pharmaceutical supply chain relies heavily on trade with India and China. The supply chain is usually planned on a monthly or quarterly basis in the pharmaceutical industry. This can give firms that import API from overseas lead time to react to pending tariffs and prudent firms may even choose to stockpile these ingredients (most of which have an exceptionally long shelf life [9]) in order to avoid the consequences of future protectionist policies. When the coronavirus outbreak hit there was widespread concern there would be a supply shock for two essential medicines that are used in the treatment of the coronavirus, penicillin and heparin, which prompted industry stakeholders to promote the stockpiling of essential medicines [10]. One economic implication of this is the impact that the adverse supply shock and increase in aggregate demand would have on the prices for these essential medicines. There have been 1,324,488 total cases of COVID-19 in the US [11], if each one of these patients received one does of the essential medicines than that alone represents a shock to aggregate demand that is substantial enough to raise prices without considering the possibility of a supply shock in the market for penicillin and heparin due to the COVID-

19 pandemic and the protectionist policies implemented by President Trump. The pharmaceutical supply chain has proven to be very resilient and these firms are able to pivot quickly to second- and third-line vendors in order to procure essential medicines and API.

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