Differential Pricing for Pharmaceuticals

Review of current knowledge, new findings and ideas for action

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Preface

Pharmaceutical companies, global health donors and other stakeholders have increasingly recognized the need for a careful analysis of factors that restrict the use of differential pricing as a mechanism to improve access to medicines in the developing world without significantly compromising pharmaceutical company profits. The U.K. Department for International Development (DFID) commissioned this report to identify interventions by pharmaceutical companies and global health donors that could lead to increased use of differential pricing and therefore better access to medicines. This report analyzes the existing literature on differential pricing, examines successful and unsuccessful examples of differential pricing and recommends actions for improvement.

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Executive Summary

Adapting drug prices to the purchasing power of consumers in different geographical or socio-economic segments could potentially be a very effective way to improve access to medicines for people living in low and middle-income countries. A well-implemented differential pricing system could also lead to increase in sales for pharmaceutical manufacturers.

The pharmaceutical industry has been cautious about significantly changing its pricing models, despite the theoretical appeal of differential pricing and its success in improving access to medicines in low- and middle-income countries. This reluctance is caused mainly by concerns that differential pricing could erode profit margins in lucrative high and middle-income markets and high distribution channel markups in low income countries could dilute much of the benefits of differential pricing to poor end-patients.

Recent trends, however, are prompting the pharmaceutical industry to pay more attention to differential pricing, such as economic and demographic growth in some low and middle-income markets, which has increased the potential market size of many low and middle income countries; greater recognition by the pharmaceutical manufacturers and their investors of the social responsibilities; stronger global advocacy for access to medicines, and growing competition from generic manufacturers in emerging markets. Differential pricing allows pharmaceutical companies to signal that their pricing policies are socially responsible and consistent with their obligations to society and not just geared towards maximizing profits. In addition, differential pricing on select drugs opens opportunities to serve low and middle-income markets and creates economies of scope for pharmaceutical companies.

A review of the existing literature on differential pricing and analysis of successful and unsuccessful examples of such pricing reveal that it may lead to overall welfare benefits only when the overall sales increase as a result. The analysis also suggests that social welfare is enhanced when differential pricing opens new markets for pharmaceutical companies in countries where the affordability for the drug is significantly lower than the prevailing price in existing markets. Whether the benefits of differential pricing accrue more to the pharmaceutical company or to the patient/payer depends on the elasticity of demand and the market structure.

It is important to note that differential pricing is not a panacea to ensuring access. For patients with affordability levels lower than the marginal cost of manufacturing, donor subsidies and government support will continue to be required.

Despite some evidence that differential pricing of pharmaceuticals can benefit manufacturers and poor countries without adversely affecting higher income countries, the widespread and systematic use of such pricing has been limited to vaccines, contraceptives, and antiretrovirals (ARVs) mostly in low income countries.

Differential pricing of ARVs between high, middle and low-income markets, however, has raised complicated economic, legal, and supply chain challenges. The lure of getting prices paid by low income countries has raised substantial legal and political tensions between pharmaceutical companies, middle income country governments and non-governmental organizations. The three-tiered pricing structure used for ARVs has been the subject of intense debate in middle-income countries. Some of these countries have vast income inequalities and the average
income level does not reflect the true issues that impede access. The people in these income segments, the civil society groups that represent them, and the political support system together push for obtaining low-income prices for these population segments in lower-middle or middle-income countries.

In the case of vaccines, most now have a three-tiered pricing structure with fully loaded market prices charged in rich countries, low prices in countries belonging to the Global Alliance for Vaccines and Immunization (GAVI), and intermediate prices in middle-income countries. However, the practice of charging higher prices in middle-income countries than in the poorest countries has been contentious. Firms argue that middle-income countries, especially upper-middle-income countries such as Brazil, have substantially greater capacity to pay for vaccines than do GAVI countries. Middle-income countries argue that their populations include many poor people and the prices they pay should be not too far from what the least-developed countries are paying.

More research is required on how differential pricing can be expanded to include all essential medicines for low and middle-income countries and how fair, affordable prices should be determined. Further research is also required to understand the impact of buy-side market structure on the social welfare impact and the operational feasibility of differential pricing.

Despite its theoretical appeal and some notable successes, the use of differential pricing as a tool to improve access to medicines is not widespread. The primary causes include risks of physical arbitrage (lower priced product flowing back to the high income markets); risks of eroding margins in high income market segments due to external referencing (where countries compare the prices for new products against those prices paid by other countries within the geographical region or income class); poor knowledge of demand and supply structures; and a buying market structure that works against the poorest segments of the population.

Based on the analysis conducted for this report as well as an assessment of the existing literature, several strategies are recommended for mitigating the risks associated with differential pricing.

To help pharmaceutical firms avoid political pressure from middle income countries to lower drug prices and to increase sales in those markets, firms could use intra-country differential pricing. In lower middle and middle income countries different socio-economic segments of the population seek treatment and obtain medicines from different channels, with wealthier patients seeking treatment in channels different from their poorer counterparts. This provides a natural wedge that can be leveraged for charging different prices in the different channels and reaching specific segments of the population at price points that they can truly afford. Another natural wedge that can be leveraged for intra-country differential pricing is the urban-rural income divide in developing countries.

To prevent physical arbitrage from one channel to another within a country, firms could work closely with global agencies that have a strong reputational risk from cross channel arbitrage in the drugs they finance. This would allow them to share the risks of arbitrage and collectively create strategies such as enhancing top to bottom visibility in the supply chain to counter diversion across channels. In addition, firms could develop contractual agreements with public or private distribution channels who primarily serve the poor population segments. The contractual
agreements would agree to provide lower priced products in return for ensuring that the product is only used in the market for which it is intended.

To avoid the problem of formal or informal external referencing, firms could nudge countries to use pharmaco-economic assessments instead of reference pricing and increase local context-specific health outcomes research.

Implementation of differential pricing will require better information about markets, political will, and commitment from pharmaceutical companies and developing country governments.
1. Introduction

Charging different prices to different consumers is a common business practice in many industries including airlines, retail, electric utilities, textbooks, university tuition and pharmaceuticals. In most markets, price differentiation is a tool that allows manufacturers to incorporate the differences in the willingness to pay or the ability to pay for their product or service by different customer segments into their pricing strategy. Notable examples of differential pricing of products with significant intellectual property and high fixed costs of creating the product are found in the textbook and software sector (Fisher 2007).

In the context of pharmaceutical and other health products, differential pricing (also called tiered pricing) is the adaptation of product prices to the purchasing power of consumers in different geographical or socio-economic segments. Differential pricing could potentially be a very effective strategy to improve access to essential medicines in low and middle-income countries where most patients pay for medicines out-of-pocket and therefore cannot afford prices comparable to high income markets. In addition, a well implemented differential pricing system can lead to incremental sales for the pharmaceutical manufacturers. There is a large body of scholarly literature that attempts to demonstrate the impact of differential pricing on societal welfare. This paper provides an extensive review of such literature; demonstrates the key differences and nuances in existing literature; and recommends strategies for implementing differential pricing in a sustainable manner.

However, despite extensive discussion on the appeal of differential pricing in theoretical models, the instances of sustained differential pricing for pharmaceutical products are not widespread across therapeutic categories. Historically, the pharmaceutical industry had been cautious of extending low prices for a large number of drugs in low income markets due to the fear of eroding profit margins in high and middle-income markets. The demographic growth in some low and middle-income markets, stronger global advocacy on the issue of access to medicines and growing competition from generic manufacturers located in emerging markets has led to renewed interest and attention towards the issue of differential pricing.

If differential pricing can indeed create the win-win for manufacturers and patients, the question arises: what kind of operational models should be used for differential pricing? Many experts agree that differential pricing is the best way to price drugs around the globe, but their proposed means for implementation can vary greatly. Pharmaceutical companies and health policy planners have so far done little exploratory work to understand different operational models for achieving sustainable differential pricing.
Before delving into operational models it becomes important to do a comprehensive analysis of the currently known models of differential pricing and a retrospective analysis of factors that have either led to or prevented its widespread use in specific product categories. This report is a modest attempt to carry out such an analysis.

Clearly, differential pricing is no panacea for resolving the issue of access to medicines in the developing world, neither is it the only option for changing the pricing architecture of pharmaceuticals. In fact, a wide mix of options is required to improve access to medicines, to many of which differential pricing may be complementary in nature.

We start by a review of existing literature on the theory of differential pricing.

2. Review of the Theory of Differential Pricing

The development of pharmaceuticals and vaccines requires significant investments in research and development. R&D expense is a global joint cost that serves all consumers, in all income and geographic segments and thus cannot be recovered from any single group alone.

The need for pharmaceutical companies to be able to recoup their large R&D expenses and to create incentives for innovation results in the pharmaceutical market not being a perfectly competitive market. For a patent-protected product, the manufacturer could engage in monopoly pricing and set prices that maximize the manufacturer’s profit. Unfortunately, at a single price charged by a single manufacturer, a large number of consumers will be priced out of the market creating a welfare loss for society known as deadweight loss. Social welfare is defined (more specifically for the purposes of this paper) as the aggregate of the benefits of the manufacturer and the consumers (producer surplus and consumer surplus). Social welfare maximization is not identical with maximizing access as the former also includes the manufacturer’s profit.

The idea of differential pricing is based on the economic concept of price discrimination, which involves a profit-maximizing manufacturer selling its products to different consumers at different prices such that the price differences reflect the differences in the willingness (and ability) of each consumer to pay for the product. The alternative to price discrimination is a uniform single price for all consumers and markets that the manufacturer determines to maximize its profits based on the aggregate demand elasticity. The manufacturer chooses the price such that the cost of producing and selling an additional unit of the product is lower than the revenue from a sale. This single price would imply that some markets and consumers would not be served by the manufacturer’s price.

A considerable amount of research starting with the work of Ramsey (1927) has focused on determining the optimal method of product pricing to maximize social welfare. Ramsey’s work looked at the regulated utility industry; a natural monopoly within each local market with
government regulated rates of return, and attempted to find the optimal tax structure. He determined that the utilities should charge a different price from each customer class such that the markup over marginal cost is inversely proportional to the price elasticity of that customer class. This would maximize social welfare while still achieving the necessary rate of return for the (regulated) monopolist (Ramsey 1927). His work formed the basis of what is now commonly called Ramsey pricing theory. The Ramsey pricing model, which prescribes that customers whose demand is price inelastic pay higher prices than customers whose demand is price elastic is commonly applied to utilities, airlines, and other industries that have a reservation profit constraint to recover the high fixed costs. Ramsey pricing, however rests on the overall profit constraint to ensure that prices will be increased only enough to ensure recovery of the fixed costs. Price discrimination by an unconstrained profit maximize (often called unconstrained Ramsey pricing) may not always be social welfare maximizing.

More generally, under perfect price discrimination, consumers who were priced out of the market under the single price set by a monopolistic manufacturer re-enter the market and are charged the price they are willing to pay. Perfect price discrimination (or first degree price discrimination) where each customer is charged exactly their willingness to pay for the product is more of a theoretical benchmark than a pragmatic strategy as it requires knowing each consumer's exact willingness to pay, information which is seldom obtainable. However, it continues to serve as a good reference benchmark to measure aggregated and distributed efficiency gains from any differential pricing scheme. It is also important to remember that even under perfect price discrimination there may still be some consumers that remain priced out of the market due to their inability to pay even the marginal cost of the product.

The more commonly observed form of price discrimination is second-degree price where the manufacturer does not know how much each consumer is willing to pay, but induces them to reveal their preferences through techniques such as volume discounts. If some consumers gain higher utility from the product than others, and if the firm offers a pricing scheme where the marginal price declines with volume, it will typically make higher profit than if it offers the same price to all consumers. Such price discrimination is routinely practiced in many industries where downstream market structure facilitates volume-based pricing. Competition authorities in many countries question the social efficiency considerations from quantity discounts or volume-based pricing as it may favor the incumbent and may create barriers to entry.

More generally, two-part tariffs (where price has a fixed and a variable component) may offer a better method for pricing, which leads to increases in total welfare (Tirole 1988). Under linear pricing, the firm always sets prices above its marginal costs resulting in deadweight losses because of those who do not buy the product at this price. With a two-part tariff consisting of a fixed and a variable price component, however, a firm can extract profit using the fixed charge,
while leaving marginal prices close to marginal costs, thereby maximizing the size of the “pie” to be shared between consumer and firm. The aggregate gains in welfare come more strongly from profit increases for the manufacturers while consumers are typically worse off (Armstrong and Vickers 2001). In countries where there is a price regulator, it can opt for a two-part tariff by paying the R&D costs through a lump-sum payment to the manufacturer and then setting the variable price to be charged to each consumer (Felder 2004).

Third-degree price discrimination, which is most relevant to this paper, occurs when the manufacturer does not know consumers’ willingness to pay, but is able to place them into groups that correspond roughly to their wealth. These groups are typically referred to as markets.

Multiple studies starting from Schmalensee (1981) have shown that differential pricing by a single profit-maximizing manufacturer leads to improvements in overall social welfare, if as a result of the differential pricing the total sales increase. However, it is important to note that an increase in sales due to differential pricing is only a necessary but not a sufficient condition for enhancements in welfare. Similar findings are reported in Varian (1985) and Schwartz (1990). However, it is less clear as to how much of an increase in sales would be sufficient to increase social welfare.

Layson (1994) shows that if a monopolistic firm serves two markets; one with higher willingness or ability to pay and another with lower willingness/ability to pay with a large market size and larger profit margin in the higher value market, then price discrimination will enhance social welfare. For a more general case of many different markets, Maluog and Schwartz (1994) show that price discrimination would increase social welfare when there are large differences in demand.

There is very little research that examines the impact of price discrimination in the case of an oligopoly (products with a few but more than one manufacturer). Using a simplified model, Fudenberg and Tirole (2000) predict that that when firms in an oligopoly practice price discrimination, prices charged are initially high and then decline, and consumers are better off in aggregate.

Research is also not strong on the impact of price discrimination on a firm that serves two independent markets, one of which is monopolized by the firm but there is a rival firm in the other market. This analysis is important for understanding the impact of differential pricing where generic competition exists in some markets but other markets have patent exclusivity. Armstrong and Vickers (1993) show that in such an environment the firm sets monopoly price in the first market and prices in the other market are determined by the competitive interaction between the two firms. If the firm cannot successfully set different prices in the two markets due to price regulation or other factors, the firm may end up choosing a reduced price in the captive market and raised prices in the competitive market.
In summary, research concludes that the impact of price discrimination by a monopolist producer on societal welfare depends on its effect on sales. If price discrimination does not lead the firm to expand sales, it will cause societal welfare to decrease. However, it is not easy to find conditions that characterize when societal welfare would increase with price discrimination, and detailed knowledge of consumer demand is needed to answer this question. The literature also agrees that for differential pricing to succeed in increasing societal welfare, the more inelastic market should also be the large market, the manufacturer should have high degree of influence over the price paid by the end consumer and there should be a high degree of separability in the market segments defined according to price elasticity. The impact of differential pricing on different stakeholders depends upon the detailed market structure for a given product category. The extent to which the profits of pharmaceutical firms are constrained by price competition among themselves determines this impact. It is impossible to ascertain to what extent each market structure leads to a strong or a hard constraint on profits.

In addition to work on the welfare effects of price discrimination in economics literature there is also a large stream of research that focuses on the societal benefits of differential pricing specifically for pharmaceuticals. Pricing for pharmaceuticals involves a trade-off between consumer benefits today (through greater access at lower price) and consumer benefits in the future (through greater innovation).

Hausman and MacKie-Mason (1988) note that in addition to increasing social welfare in a static sense, price discrimination is more likely to increase dynamic welfare, given the positive effects on research and development.

Danzon (1997) compares the welfare effects of differential pricing for pharmaceuticals in the United States and the European Union (EU). Danzon and Chao (2000) compared the prices of a limited sample of drugs across countries. Several other studies by Danzon and co-authors have explored the issue of differential pricing between the United States and other countries primarily to inform policy about pharmaceutical pricing in the United States.

Dumoulin (2001) examines the pricing of essential innovative medicines by comparing a single global price with differential prices based on country income. Using a simulation model, the author calculated the pharmaceutical manufacturer’s profit and the affordability of drugs to the population. The analysis shows that differential pricing maximizes both indicators and increases access by a factor of roughly 4–7 times. The simulation model also shows that for countries with the same average GDP per capita, the country in which wealth is most concentrated will face a higher price under price discrimination because in such markets companies would rationally price for the rich market rather than the numerically larger (in terms of people) lower income market.

Scherer (2004) compared the welfare effects of a scenario under which medicines were protected by product patents in all countries to a scenario under which poor countries were allowed access
to generic versions of medicines protected by patents in rich countries. His findings suggest that globally welfare is increased by allowing poor countries access to low-cost medicines because the marginal utility of income (the benefit derived from one extra unit of currency) is greater in poor nations than in rich ones. However, this may lead to negative welfare effect in the rich countries.

Danzon and Towse (2003) show that differential pricing can enhance access while preserving incentives for innovation. Thus, it would benefit patients in both developing and developed countries in the long run. They conclude that one possible way of implementing sustainable differential pricing is to bilaterally negotiate discounted prices between individual companies and governments through a system of confidential rebates. This is based on the assumption that pharmaceutical companies operating under a profit constraint are best able to judge how to select the best price for a given country while still covering their joint costs on a global basis.

It is difficult to obtain prices that reflect the willingness or ability to pay of patients in different countries or market segments. Lopert et al. (2002) recommend a mechanism of setting prices in each country based on the incremental cost per life-year gained for each country based on its per capita GDP as a proxy for a patient’s ability to pay. The World Bank has suggested that health care interventions may be considered cost-effective if they buy a year of healthy life for less than the national average per capita gross national income (GNI). This leads to a method for pricing for each country based on its GNI per capita and efficacy measures (Lopert et al. 2002). An illustrative figure for antiretrovirals (ARVs) using this methodology is included. In Figure 1.

**Figure 1. Indicative Prices for ARVs Using Cost Effectiveness and Income Methodology in Lopert 2002**

![Indicative Prices for ARVs](image)

*Source: Kaplan W., R. Laing and others, Priority medicines for Europe and the world, A report prepared by WHO for the Netherlands Government*
There have also been concerns that when differential pricing is used and some of the countries use price ceilings, this would result in higher prices in countries that do not have price ceilings. Mujumdar and Pal (2005) show that under differential pricing when one country regulates the prices of pharmaceuticals, it has no impact on the prices charged in the other country. This is because as long as there is no price referencing, pricing decisions are made independently for each market.

Differential pricing for pharmaceuticals could also be implemented by using voluntary licensing (Grace 2003). Locally produced drugs could be more easily differentiated from more drugs produced for more expensive markets and the production costs of high quality drugs manufactured in developing countries could be somewhat lower even if not drastically.

Reich and Bery (2005) discuss differential pricing among various options of improving access to AIDS medicines. They list three possible mechanisms for a differential pricing system: internal company policy based differential pricing, international agency facilitated differential pricing and wider distribution of price information to different actors.

Flynn et al (2009) argue that the highly uneven income distributions in developing countries lead to a large portion of the market being underserved when the manufacturer chooses its optimal price.

Based on an extensive literature search, Lang and Hill (2004) conclude that differential pricing can lead to improved access for low-income countries, increased market share for companies and no price increases for high-income countries.

The welfare gains from differential pricing arise from the argument that it leads to improved access for patients in developing countries without necessarily harming either the profits of the pharmaceutical companies or access for patients in developed countries. Differential pricing permits the pharmaceutical firm to open new markets in countries where the affordability for the drug is significantly lower than the prevailing price in existing markets. Thus, when differential pricing opens new markets for a firm, it increases both the consumer surplus and producer surplus.

However, in reality multiple factors determine who would gain and lose from differential pricing. The above models do not capture supply chain structure issues such as purchasing power of each buyer, competition, elasticity of demand, price controls, and distribution channels. In the absence of understanding these factors, the conditions under which differential pricing benefits the patients in the lower income and more price-sensitive market; the patients in the higher income and less price-sensitive market; and the manufacturer, remain unclear. Without knowledge of the incentives of each stakeholder it becomes difficult for pharmaceutical companies or global policy makers to institute a global strategy for differential pricing.
An issue that is unexplored in the research literature is the impact of a pharmaceutical manufacturer charging differential wholesale prices to downstream buyers who then supply the product to final consumers. The contract structures offered to large organized buyers are often much more complex than those typically offered to final consumers.

**Box 1. Key Findings From Differential Pricing Theory**

- Differential pricing may lead to overall welfare benefits only when the overall sales increase as a result of differential pricing.
- Social welfare is enhanced when differential pricing permits the pharmaceutical companies to open new markets in countries where the affordability for the drug is significantly lower than the prevailing price in existing markets.
- Under a market-driven differential pricing scheme, countries with a high degree of wealth concentration will face a higher price because in such countries companies would choose to price for the rich market rather than the numerically larger (in terms of people) lower income market.
- Whether the benefits of differential pricing accrue more to the pharmaceutical company or to the patient/payer depends on the elasticity of demand and the market structure.
- Differential pricing is not a panacea to ensuring access. For patients with affordability levels lower than the marginal cost of manufacturing, donor subsidies and government support will continue to be required.
- Theoretical models of differential pricing do not explicitly differentiate between manufacturer’s price and end-patient price.
- Existing literature inadequately captures the impact of differential pricing when the markets have heterogeneity in the purchasing market structure (e.g. out of pocket vs. organized group purchasing).

Most of the theoretical models discussed in this section assume that the only difference between high and low income countries is that low income countries have lower patient paying power. However, methods of financing for pharmaceuticals vary considerably between rich and poor countries and also within the low-income countries. In states with a large public sector role in paying for medicines, the government negotiates, solicits bids or engages in other strategies to obtain favorable prices on products. Some low and middle-income countries also use price ceilings on pharmaceuticals e.g. South Africa. The nature of price controls among low and middle-income countries varies significantly in methodologies and extent of enforcement. Similarly, the exact nature of intellectual property rules varies from country to country. The trade-related aspects of intellectual property rights (TRIPS) provide a basic minimum standard but the
exact rules on the scope and term of patents vary considerably from country to country. As a consequence, products may be marketed as a monopoly in one developing country, and face competition in another, a nuance that most current models do not incorporate. Incorporating many of these operational assumptions into the existing theoretical models may impact the social welfare implications of differential pricing. It may also help explain the use of differential pricing being limited to certain product categories.
3. Pharmaceutical Industry’s Drivers for Differential Pricing

Research has looked at the effects of differential pricing on access, societal welfare and the profits of the pharmaceutical companies. At a more pragmatic level, there are several other reasons that prompt the pharmaceutical industry to engage in differential pricing. Although many of these are strong drivers, the innovative pharmaceutical industry has historically been cautious of experimenting with pricing models because of the potential of eroding margins in the developed markets. Typically, differential pricing is less central to the business models of generic manufacturers, who serve multi-source product markets and compete on cost and other product attributes. Admittedly, there are instances of multi-sourced products where generic manufacturers charge differential prices in different markets.

3.1 Socially Responsible Pricing

Pharmaceutical companies face tremendous pressure of meeting societal expectations about affordable drugs to all segments of the population in return for being able to pursue profits in developed countries. Failure to respond to issues pertaining to access to medicines can quickly lead to reputational harm (Vachani and Smith 2004). Differential pricing allows pharmaceutical companies to signal that their pricing policies are socially responsible and consistent with their obligations to society and not merely geared towards maximizing their profit. New initiatives such as the Access to Medicine Index monitor highlight the efforts of pharmaceutical companies to increase access to medicines in developing countries. The ATM Index defines equitable pricing as a mechanism that is intended to lower financial barriers to pharmaceutical access. Equitable pricing and affordability are key aspects of how pharmaceutical companies are rated on this index. Differential pricing would lead to better ranking on indicators such as this which measure a pharmaceutical company’s fulfillment of its societal obligations.

3.2 Opening New Markets

Many low and middle-income markets could not be served earlier due to lack of overall affordability and demand across an overall drug portfolio. Differential pricing on select drugs opens opportunities to serve these markets and creates economies of scope for pharmaceutical companies. Sales of high volume low priced drugs help pharmaceutical companies learn about the distribution and regulatory infrastructure in these countries. This also helps build better influence and leverage over the stakeholders in this segment. Economic and demographic growth in low and middle-income markets and a change in the disease burden from communicable to non-communicable diseases have increased the potential market size of many low and middle-income countries. Differential pricing can provide opportunities to tap these new consumers and help build relationships that will continue to last when these consumers reach higher levels of income/ability to pay.
3.3  **Threat of Compulsory Licensing**
Compulsory licensing is authorization permitting a third party to make, use, or sell a patented invention without the patent owner's consent. The TRIPS agreement allows compulsory licensing wherein the patent holder is forced to allow a local entity to produce the patented product in a number of circumstances. In the event of national emergencies and public health crises such as HIV/AIDS, tuberculosis and malaria, prior negotiation with the patent holder is not required for voluntary licensing. There are no restrictions on the therapeutic classes for which compulsory licensing could be invoked. Countries can determine themselves what they consider a national public health emergency and no multilateral agency needs to be involved for this purpose.

At a World Trade Organization (WTO) meeting in 2003, members agreed that developing countries without manufacturing capacity could import generic variants of drugs under patent to address such public health threats as malaria, AIDS, or tuberculosis (TB). The agreement enables low-income countries to import generics from medium-income countries rather than being forced to set up domestic production to have access (Hellenstein 2004). For research-based pharmaceutical companies, competition resulting from such compulsory licensed products would lead to price pressure not only in the market that invokes the compulsory license but in other low and middle income markets as well. Differential pricing with lower prices in low and middle-income countries is a good strategy to thwart such a threat and risk having strong price pressures on an important product.

3.4  **Competition From Generic Producers**
A number of large generic producers have evolved in India, China and Brazil with extensive pharmaceutical manufacturing capacity. They are eligible to produce drugs in a large number of therapeutic classes. As these generic manufacturers capture higher market shares in their domestic markets, they achieve better economies of scale to compete in international markets. Many of the large Indian generic manufacturers have already established their international footprint through operations in Africa, Latin America and North America.

Generic competition acts as a catalyst for price reductions and the start of differential pricing programs. The fall in the price of first-line combinations of stavudine (d4T), lamivudine (3TC), and nevirapine (NVP) from over $20,000 in 2000 to $90 in 2010 and the start of multiple tiered pricing programs by large ARV manufacturers is attributed largely to generic competition by some authors. (Wilson P 2010).

Generic entry significantly erodes profit margins in the markets where generic substitutes become available, and higher scale economies for generic competitors could further amplify this effect. Differential pricing would allow maintaining a fairly significant market share in key therapeutic segments in the domestic markets of generic manufacturers, and could act as a mechanism for entry deterrence in high income markets. Although there is limited knowledge of cost structures,
differential pricing could also enable research-based pharmaceutical companies to maintain their competitiveness in production and distribution costs with generic manufacturers by maintaining a balance of market share in low income markets. Little evidence exists to understand the impact of differential pricing on the price of first entry generic producers (Waning et al. 2009).

4. Segmenting Products and Drivers for Differential Pricing

From the preceding sections it is clear that the drivers for differential pricing and the extent of its societal impact could be different depending on the market structure i.e. whether a drug is single-sourced or multi-sourced. The biggest benefit potential from differential pricing holds for single-sourced drugs where the pharmaceutical company has a clear incentive to maximize its profits and enter new markets through lowered pricing.

Prices for pharmaceuticals are typically measured at three points in the distribution chain: the ex-manufacturer price, the ex-wholesale price, and the retail price. In low and middle income markets, the wholesale and distribution markups constitute a larger portion of the end patient cost for both multi-sourced generic and single sourced patented products. The manufacturers exercise less control over the distribution chain markups and the price paid by the end-patient. For such products the societal benefits of differential pricing at the manufacturer price level are only of a limited measure.

A large number of essential drugs are not under patent protection and are multi-sourced i.e. manufactured by multiple manufacturers. Lowered prices for such drugs can be achieved through efficiencies in the manufacturing and distribution costs through better planning and coordinated buying mechanisms. Many mechanisms have been proposed to incentivize generic competition in off-patent product categories. Many new initiatives such as pooled procurement, bulk buying, etc., have been suggested to reduce cost to the patients.

A key prerequisite for inter-country differential pricing is the existence of two distinct markets: one with higher income and affordability and another with lower income and affordability. Throughout this report we use the term “products with dual markets” for products that have a higher income as well as a lower income market. However, there are single and multi-sourced drugs e.g. antimalarials that are used exclusively in low income countries. For drugs that treat almost exclusively diseases of the developing world, the prices that the average patient in a low income country can afford to pay are sometimes insufficient to cover even the marginal costs of production, leave alone the R&D expenses. Thus, a combination of external subsidies on the supply side such as grants to Product Development Partnerships (PDPs) to reduce amortization of R&D costs in drug pricing, and new uptake increasing mechanisms or affordability gap filling mechanisms such as the Affordable Medicines Facility for malaria (AMFm) have been created. The drugs in this PDP-developed category would be unique and would not exactly fit the single-
source patented or generic drugs as described before. However, there are significant opportunities for differential pricing under many of these new and innovative mechanisms.

Table 1. Drivers for Inter-Country Differential Pricing for Different Categories of Drugs

<table>
<thead>
<tr>
<th>Category</th>
<th>Drivers for Differential Pricing</th>
<th>Theoretical Welfare Gains from Differential Pricing</th>
</tr>
</thead>
</table>
| Single Source Dual Market       | • Profit Improvement  
      • Corporate social responsibility  
      • Opening new markets  
      • Threat of compulsory licensing  
      • Competition from generic producers | High                                                |
| Single Source Low Income Market Only | • Corporate social responsibility  
      • Threat of compulsory licensing  
      • Learning about low income markets for other more profitable drugs | Moderate                                            |
| Multi source Dual Markets      | • Corporate social responsibility  
      • Opening new markets  
      • Profit improvement | Marginal                                            |

5. The Current State of Differential Pricing

This section explores whether differential pricing is prevalent in some form in the global pharmaceutical market today. If pharmaceutical companies were engaging in differential pricing based on income elasticity and if per capita income (GDP) is a good index of demand elasticity, we should find a high positive correlation when comparing pharmaceutical prices across countries with differences in per capita income. However, multiple studies have found this fit to be poor and in fact in many instances concluded that observed prices may be inversely correlated with the per capita income, implying poor countries pay higher prices (Scherer and Watal 2002, Maskus and Ganslandt 2002, Hellerstein 2004, Lai and Yadav 2007, Waning et al 2009).

Interviews with manufacturers conducted during this study revealed that they choose different prices based on a combination of factors, most importantly:

- affordability of the market
- buy side market structure
• volume of purchase
• security of financing (in the case of public sector or institutional buyers)
• transaction cost associated with selling to that buyer

It is noteworthy that income/affordability is only one of the variables used in the pricing model. In instances where there are strong natural relationships between the other variables and the income/affordability of the market segment, this may lead to welfare maximizing differential pricing. In instances where the other variables are negatively correlated with the income and affordability of the market, the pricing model could lead to potentially adverse outcomes from the standpoint of social welfare maximization.

Despite (limited) evidence that differential pricing of pharmaceuticals can be beneficial to manufacturers and poor countries without adversely affecting higher income countries, the use of differential pricing to date has been limited to vaccines, contraceptives and antiretrovirals, mainly in low income countries. Further research is required on how differential pricing can be expanded to include all essential medicines for low and middle-income countries and how fair, affordable prices should be determined.

Several surveys have been conducted on the ex-manufacturer prices and retail prices of essential drugs across countries with varying incomes. For example, Scherer and Watal (2002) concluded that prices of many life-saving medicines for HIV/AIDS were not significantly lower in developing countries of Africa and Latin America than in the rich OECD countries in the late 1990s. Other empirical studies (Scherer and Watal 2002, Maskus and Ganslandt 2002, Hellerstein 2004, Lai and Yadav 2007, Waning et al 2009) when comparing prices of specific class of pharmaceuticals (mostly generic but some also singe sourced) across countries do not find any significant correlation between price and per capita GNP or any other proxies for income.

The comparison of prices between different markets, different countries, or different time periods poses methodological challenges that many of these studies suffer from (Danzon, P. M and J. Kim 1998).

Figure 2 shows the average prices for a basket of generic and branded medicines (reported as ratio of the median price of medicine in surveyed outlets with the Management Sciences for Health generic bulk procurement price) in low, lower-middle and upper middle-income countries. It is evident that there is little correlation between the price paid and the income class of the country.
The observed lack of differences in prices in low income countries vs. those paid by higher income counterparts could be due to price-gouging at the wholesale or retail level due to lack of retail or wholesale competition. Non-linearity in the markup structure would imply that the price paid by the patient is not entirely correlated with the manufacturer’s price. The findings from the empirical studies on differential pricing should be interpreted in light of the above. As mentioned earlier in this report, the contract structures between the pharmaceutical companies and the downstream entities that distribute the product to the end patients are complex and not simple single tariff contracts. This does not always allow careful analysis of both the extent of differential pricing observed and the net welfare gains resulting from it.

Next we present a few observational studies to complement the empirical studies mentioned above.

### 5.1 Differential Pricing for ARVs (Single Source Dual Market Drugs)

One of the main examples of differential pricing has been in ARVs for HIV/AIDS where pharmaceutical companies have used different prices in low, middle and high income countries.

Until 2000 there was little variation in the prices of ARVs between the high and low-income countries (Hellerstein 2004). In 2000, under a new public-private partnership called the Accelerated Access Initiative (AAI) several originator pharmaceutical companies with ARVs announced a voluntary price reduction program for patients in poor countries. The originator companies also made price offers through bilateral negotiations with individual governments, mostly of least developed countries (LDCs). Merck and Roche also offered discounted price

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**Figure 2. Retail Price of Essential Medicines Across Income Groups**

![Figure 2](image.png)

*Note: MPR = Median Price of Drug as a ratio of the MSH generic bulk procurement cost.*

*Source: WHO/HAI. Analysis conducted by Denis Ross-Degnan, Harvard Medical School*
programs for select medium-income countries. A two-tiered pricing structure was typically used with manufacturers specifying how countries could be eligible to purchase in the discounted tier. Manufacturers restricted the discounted tier to LDCs or a composite criterion based on the country’s income level, geographic location (Sub-Saharan Africa) and the prevalence of HIV infection. Some manufacturers offered discounted prices for LDCs or countries in Sub-Saharan Africa but for other low-middle and middle-income countries prices were negotiated bilaterally on a case-by-case basis. In mid 2001, Merck started publicly disclosing its ARV price structure to each country. For the most part, this ended the era of bilateral price negotiations for ARVs and brought more transparency on the price and eligibility criterion as others followed. A three-tiered pricing structure emerged, which included discounted prices for lower-middle and middle-income countries as well. Most ARV prices declined from 2000 to 2003 as a result of these tiered pricing arrangements and increased generic competition from mostly Indian and in some cases Brazilian manufacturers (Hellerstein 2004). Between 2002 and 2004 many middle-income countries in Latin America bargained for lower prices using the collective buying power resulting from pooling their purchases of ARVs through the Pan American Health Association (PAHO) (Hellerstein 2004).

Today, Abbot, Bristol Myers Squibbs, Roche, Boehringer Ingelheim, Gilead and Merck offer two different discounted prices for developing countries (category 1 and category 2 countries). The exact eligibility for each of the categories varies slightly for each manufacturer. In the case of Merck it also varies by the product type. GlaxoSmithKline offers a discounted pricing structure for its ARVs to all LDCs, all countries in Sub-Saharan Africa and all ARV programs financed by the Global Fund to Fight AIDS, TB, and malaria, and the President's Emergency Plan for AIDS Relief (PEPFAR). For other low and middle-income countries, public sector prices are negotiated by GlaxoSmithKline on a case-by-case basis, either bilaterally or through the Accelerating Access Initiative. Each manufacturer determining its own eligibility criterion and bilaterally negotiated prices has led to confusion and a feeling of unfairness. The case of Kaletra® (from Abbott laboratories) and challenges to its pricing structure as media uproar and use of compulsory licensing has highlighted the importance of transparent, objectively determined and industry norm based eligibility criterion for three tiered differential pricing to be sustainable (Alcorn 2007). Abbott now uses preferential pricing structure where Africa and least developed countries obtain the lowest price of $500 per patient per year, followed by low income and lower middle income countries at $1000 per patient per year and the remaining countries get the regular price.

Differential pricing between high and low-income markets, however, has raised complicated economic, legal and supply chain challenges. The three-tiered pricing structure has been the subject of intense debate in middle-income countries. The lure of getting prices paid by low income countries has raised substantial legal and political tensions between pharmaceutical companies, country governments and NGOs. Some of these middle-income countries have vast
income inequalities and the average income level does not reflect the true issues impeding access/affordability. Figure 3 shows that the two lowest income quintiles in Brazil, (an upper middle-income country that does not have access to the deeply discounted pricing for the low income tier) have an income level lower than the average income in Thailand, a lower middle-income country. Similarly, the poorest income segments in India have an income level much lower than the average income of Uganda, which is a low income country and gets preferential prices. The people in these income segments, the civil society groups that represent them, and the political support system together push for obtaining low-income prices for these population segments in lower-middle or middle-income countries. The discontent of the population channeled through its civil society creates pressure on the government to negotiate better prices for the poorest segments of their population.

In countries such as Brazil, Thailand and Russia, there are some people with high incomes who can afford the prices paid in high income countries, although a vast majority of the population cannot. The average income in these countries is not a good measure for basing the affordability and differential pricing structure as there is relatively high concentration of wealth. The poor in middle or lower-middle income countries such as Brazil, Thailand and Russia often purchase their medicines by out-of-pocket payments thereby exposing them to the high prices that are charged based on the average income. Civil society organizations build pressure on the government to seek price reductions for the poor. Even in cases where the government is the main provider of medicines, there is considerable political pressure on the government to seek price reductions.

**Figure 3. Income Distribution In Select Group of Low-Income, Lower-Middle and Upper-Middle-Income Countries (Source: Author's analysis from World Bank data)**
Differential-pricing schemes for ARVs did not generally lead to prices of branded ARVs close to those of generic ARVs. In a recent study, Waning et al (2009) found that 79 percent of all solid ARV dosage forms that were commonly purchased were available to some countries through differential pricing schemes provided by the brand name manufacturer. For over 83 percent of ARV dosage forms, purchases made under differential-pricing schemes were significantly more expensive than generic purchases with price differences ranging from 23 percent to 498 percent. Only two ARV dosage forms had prices under its differential pricing scheme lower by an average of 68 percent as compared to the generic counterpart. The few notable exceptions include lopinavir, 133.3 mg, plus ritonavir, 33.3 mg, a branded combination purchased under a differential pricing scheme which was 73 percent less expensive than its generic equivalent. These instances are attributed by some authors to lack of competition among generic manufacturers for these products (Waning et al 2009).

In addition to political turmoil about prices and feeling of unfairness among many countries, there has also been some evidence of physical arbitrage where lower priced ARVs were flowing back into Germany and Netherlands (Geoff Dyer, FT 2002). Physical arbitrage is, however, not a significant flow and is at best a minor fraction of total global trade or national purchases.

### 5.2 Differential Pricing for Other Dual Market Drugs

In the last few years differential pricing has been used for some non-ARV dual market drugs. These differential pricing decisions reflect increasing recognition by pharmaceutical companies that economic and demographic growth and a change in the disease burden from communicable to non-communicable diseases have vastly increased the potential market size for many of their patented drugs in some low- and middle-income countries. Differential pricing can provide opportunities to increase revenues and also helps build relationships beyond these products that will last when these providers and consumers reach higher levels of income/ability to pay.

Many large pharmaceutical companies are changing their prices in developing countries so that they better reflect each market’s ability to pay. The increased focus on revenue growth from some of these markets has lead to a more decentralized pricing strategy where providers, patients and payers are consulted before choosing the price for each market. The stakeholders in each market are empowered to make pricing decisions that are optimal for growing the business in that market. This is an example of decentralized differential pricing.

For instance, Merck launched Januvia®, a type-2 diabetes drug, in India at a price of less than US$ 1 a pill, roughly a fifth of its price in the US. Merck consulted 350 Indian doctors and patients to decide on an India-specific price and has so far been successful in its differential pricing strategy for this drug.
GSK has reduced the prices of their patented medicines in LDCs to less than 25 per cent of their price in the United Kingdom. In addition, it has also reduced the prices of some off patent GSK products in LDCs where they were considered to be of public health advantage. Prices in other middle-income and low-income markets are set based on a more flexible strategy which includes factors such as each market’s ability to pay, structure of health system and market shares of competitors.

Pfizer is also pursuing a pricing strategy that is based on each market’s ability to pay and the competitive dynamics. It prices its anti-convulsant drug Lyrica® in developing countries at a price that is on an average 55 percent lower than the U.S. market price. Similarly, its product Mycobutin® is sold in developing countries at a price 60 percent lower than the developed country price.

Novo Nordisk has a differential pricing program that provides insulin to the public health systems in LDCs at prices less than 20 percent of the average price in Europe, Japan and North America. In 2009, Novo Nordisk offered this pricing scheme to all 49 LDCs and 36 purchased insulin at this price from Novo Nordisk.

5.3 Differential Pricing for Single Source Low Income Market Only Drugs
For single sourced patented drugs with markets primarily in low income countries, there are some examples of intra-country differential pricing. A notable example is the differential pricing of Coartem® for public and private sector used by Novartis. The public sector and NGO distribution channels receive a much lower price as compared to the for profit private sector.

Figure 4. Channel-Based Pricing for Coartem® From Novartis

Coartem® and channel based market segmentation and pricing

<table>
<thead>
<tr>
<th>Public Sector</th>
<th>Non-Premium Private Sector</th>
<th>Private Sector</th>
</tr>
</thead>
<tbody>
<tr>
<td>100-160 million patients</td>
<td>100-200 million patients</td>
<td>20-25 million patients</td>
</tr>
<tr>
<td>Coartem® $0.36 – 1.30</td>
<td>Currently, Coartem® $8-12</td>
<td>Coartem® $8-12</td>
</tr>
<tr>
<td>Risk of leakage into private channel also presents itself as reputational risk to the financing agency (GF, WB, USPMI)</td>
<td>Various initiatives underway to provide preferential price to this sector</td>
<td>Riamet® (Europe) $50-60</td>
</tr>
<tr>
<td>Small controlled pilots show little leakage into the premium private sector</td>
<td>Source Data: Novartis 2009</td>
<td></td>
</tr>
</tbody>
</table>
In addition there is also a small market in the developed world for travelers who visit malaria endemic countries where it is sold as RIAMET® at a price of around $50.

Although there are reports of leakage of public sector Coartem for sale in the private for profit sector, differences in packaging have allowed better tracking and monitoring of such leakages.

Since the provision of Coartem in most of the public sector programs is financed by agencies such as the Global Fund, USAID/PMI or the World Bank, any physical arbitrage from the public sector to the private sector not only erodes the private sector profit margins of Novartis, it also creates significant reputational risks for the donor agencies. These donor agencies work with the country governments to ensure that leakage is minimized. The risk of physical arbitrage is shared with those actors who can best manage that risk and can exert effort to minimize it.

5.4 **Drug Donation Programs**

Many pharmaceutical companies run large drug donation programs, which in theory amount to differential pricing where the low-income country price is set at zero. Tax benefits resulting from such donations allow companies to offset at least some portion of the marginal cost of the drugs. However, economic theory and some authors (Scherer & Watal 2001) suggest that by donating the drugs for free, manufacturers do not risk revealing the marginal cost to buyers in high-income markets. The risk of political pressure to reduce prices that come from the buyer knowing the marginal cost does not exist as there is no price involved as long as it is a philanthropic donation. However, these programs have their own set of pitfalls. In the absence of market signals, demand for donated drugs is more difficult to estimate and this may lead to wastages and poor utilization of the donated drugs. Such donation programs have worked well for neglected disease such as river blindness and elephantiasis but are not sustainable for large-scale provision of pharmaceuticals.

In summary, although there is some evidence and a few success stories for differential pricing in single sourced HIV, malaria, and TB drugs; it has not been widely used for other essential drugs (Steinbrook 2007). Significant differentials are observed in the price of essential medicines within and across countries both in the ex manufacturer prices and the retail prices. There is, however, no systematic evidence of the use of differential pricing with the objective of improving access to medicines. In fact, some studies that compare retail prices of medicines find that the prices of essential medicines are higher in low income countries as compared to high income countries due to markups. Multiple other studies that consider retail prices of medicines including pricing surveys carried out by the World Health Organization and Health Action International (Cameron et al 2009) also reflect similar differences in prices for drugs across countries that are not correlated to income differences. A large number of new larger scale differential pricing programs
have been started by pharmaceutical companies and are in their early stages. Their impact on prices will start reflecting in large scale empirical studies on differential pricing in a few years.

Although this report focuses mostly on drugs, differential pricing has already been achieved with reasonable success for vaccines and contraceptives. We therefore also study current state of differential pricing in these categories to distill key learnings.

5.5 Differential Pricing for Vaccines

For vaccines with both high-income and developing-country markets, tiered pricing has been widely accepted as a way to facilitate access in low- and middle-income countries. For vaccines for diseases of the developing world and with little prospect of rich-world sales, a combination of push and pull research funding has been used in order to de-link the price of the vaccine from the cost of R&D. Vaccines are mostly purchased by the government for administering in government run vaccination clinics which makes it easier to sustain differential prices across countries.

Traditionally, vaccines have had market driven differential pricing, but lower prices for developing countries would only start several years after the launch of the vaccine when R&D costs have been recovered to a large extent. At this stage the vaccine was sold at a different price for high income countries as compared to the price for middle- and low-income countries. In addition, there is also a further differential between the public sector price and the private-market price which is significantly higher. Vaccine manufacturing has significant economies of scale and manufacturers had large underutilized capacity which accentuated the benefits of using differential pricing. The use of multi antigen vaccines and more complex manufacturing technologies has reduced the scale effects but the marginal cost of production still diminishes more with scale in the case of vaccine manufacturing than in drugs.

Most vaccines now have a three-tiered pricing structure with fully loaded market prices charged in rich countries, low prices in countries belonging to the Global Alliance for Vaccines and Immunization (GAVI), and intermediate prices in middle-income countries. However, the practice of charging higher prices in middle-income countries than in the poorest countries has been contentious. Firms argue that middle-income countries, especially upper-middle-income countries such as Brazil, have substantially greater capacity to pay for vaccines than do GAVI countries. Middle-income countries argue that their populations include many poor people and therefore the prices they pay should be not too far from what the least-developed countries are paying.

The buy-side market structure for vaccines is dominated by the United Nations Children’s Fund (UNICEF) and PAHO. UNICEF procures a majority of the vaccines for the low income and least developed countries at the lowest possible price for the low income countries and LDCs. For any middle-income country that buys vaccines through UNICEF, it negotiates the prices with the manufacturers on a case-by-case basis. The vast majority of vaccines for most of the countries in
the Latin America and Caribbean region are procured by PAHO. PAHO obtains a single low price for all of its member countries, rather than a differential price despite the fact that its member countries have highly varied income levels.

Table 2 illustrates the three tiered pricing structure for vaccines and in order to remove dosage and packaging effects it also compares the cost of vaccination in each case.

**Table 2. Differential Pricing for Different Vaccine Types**

*Note: All prices are weighted average prices per dose*

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>UNICEF/ GAVI1</th>
<th>PAHO1</th>
<th>U.S. public sector</th>
<th>No. of doses as per WHO recommendations</th>
<th>Cost of vaccination UNICEF/GAVI1/ per child</th>
<th>Cost of vaccination PAHO/ per child</th>
<th>Cost of vaccination U.S./ per child</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCG (PAHO 20 dose vial)</td>
<td>0.11</td>
<td>0.10</td>
<td>--</td>
<td>1</td>
<td>0.11</td>
<td>0.10</td>
<td>--</td>
</tr>
<tr>
<td>DTPw</td>
<td>0.18</td>
<td>0.15</td>
<td>--</td>
<td>3+1</td>
<td>0.72</td>
<td>0.60</td>
<td>--</td>
</tr>
<tr>
<td>MMR (Zagreb strain for UNICEF &amp; PAHO)</td>
<td>0.93</td>
<td>0.92</td>
<td>18.64</td>
<td>2</td>
<td>1.86</td>
<td>1.84</td>
<td>37.28</td>
</tr>
<tr>
<td>Yellow Fever</td>
<td>0.90</td>
<td>0.65 Brazil Origin 1.15 France Origin</td>
<td>--</td>
<td>1</td>
<td>0.90</td>
<td>0.65-1.15</td>
<td>--</td>
</tr>
<tr>
<td>HepB (1 dose vial)</td>
<td>0.27***</td>
<td>0.28</td>
<td>10.25</td>
<td>3+1</td>
<td>1.08</td>
<td>1.12</td>
<td>41.00</td>
</tr>
<tr>
<td>Hib (lyophilized)</td>
<td>3.40 (1 dose vial)</td>
<td>2.25 (1 dose vial)</td>
<td>8.66 (10 doses vial)</td>
<td>3+1</td>
<td>13.60</td>
<td>9.00</td>
<td>34.64</td>
</tr>
<tr>
<td>DTP-HepB-Hib (pentavalent; 1 dose vial, liquid)</td>
<td>2.94</td>
<td>3.20</td>
<td>--</td>
<td>3+1</td>
<td>11.76</td>
<td>12.80</td>
<td>--</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>5.15 Rotateq 7.50 Rotarix</td>
<td>59.18 Rotateq 83.75 Rotarix</td>
<td>3 Rotateq 2 Rotarix</td>
<td>15.45 Rotateq 15.00 Rotarix</td>
<td>177.54 Rotateq 167.50 Rotarix</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumococcal (7-valent for PAHO and U.S., 10- or 13-valent for GAVI)</td>
<td>7.00 (AMC price)</td>
<td>20.00</td>
<td>91.75</td>
<td>3</td>
<td>21</td>
<td>60.00</td>
<td>275.25</td>
</tr>
</tbody>
</table>

*Source: Adapted from Wilson 2010*

In addition to the market based differential pricing, efforts are also underway to establish a global architecture for the differential pricing of certain vaccines.
Vaccines also present good examples of intra-country differential pricing. For example the Hepatitis B vaccine was offered by GSK at two different price points within India. It was sold to the private sector market around US$2/dose, and to the government and NGOs around $1.00/dose. Similarly, in Brazil the price of Hepatitis B vaccine varied from $5/dose to the private sector to $0.58/dose in the public sector with multiple other prices in between (Source GAVI documents).

Many manufacturers offer a deeply discounted pricing structure for vaccines in their portfolio. For instance, GSK uses a significantly reduced price for its HPV vaccine Cervarix® in the Philippines, Vietnam, Indonesia, South Africa and many other middle-income countries resulting in significant volume increases (see Figure 6 in Section 6).

The convergence of multiple factors leads to market-driven differential pricing emerging in vaccines but not in drugs. First, the threat of physical arbitrage in the case of vaccines is low because vaccine supply systems are largely publicly owned and since vaccines are typically administered through injection they cannot be sold freely like drugs. The fact that vaccines require a cold chain from the start till the end of the distribution cycle implies there is better monitoring capability that acts to prevent arbitrage.

The production cost economics in vaccine manufacturing are such that the absence of differential pricing may lead to extremely high degrees of market concentration even though there may be no patent on the vaccine. Fixed costs of manufacturing vaccines are very high and after multiple firms incur the high fixed costs and setup production capacity, firms would be willing to supply at marginal cost to recover as much of their sunk fixed costs as possible. In equilibrium, all firms will exit the market except one or two dominant players who will enjoy the benefits of scale economies. To prevent such an outcome in the long run for generic vaccines, UNICEF uses a contracting model which distributes the overall volume across 2-3 suppliers rather than using the winner-take-all approach. A well-developed differential pricing solution for vaccines would lead to a better equilibrium state where multiple firms could supply by recovering their fixed costs differentially from different markets.

5.6 **Differential Pricing for Drugs With Service Bundling**

It is well acknowledged that it is more difficult to engage in arbitrage in markets for services as compared to products. An excellent example of combining some service component while providing differentially priced drugs is the case of treatments for leprosy. The standard therapy consists of clofazimine and dapsone, which must be taken daily along with rifampicin taken once a month. Given the lack of any viable commercial market for clofazimine and dapsone in high income markets, there is little risk of physical or informational arbitrage. Rifampicin is however used for treating many infections including those in the developed world and has a commercially viable market in the higher income segments of the developing world. Under Novartis' scheme,
patients are given a month’s supply of clofazimine and dapsone but rifampicin is administered in the clinic, when the patients return every month to receive their next packet of drugs. This minimizes the risks of diversion of the rifampicin to higher priced markets and also ensures better clinical compliance.

5.7 Differential Pricing for Reproductive Health Commodities
Reproductive health commodities are distributed in low and middle-income countries through a range of distribution channels. These consist of government-run programs, non-governmental organization (NGO)-run social marketing programs and a small for-profit private market in most countries. The range of channel options have been chosen to reflect the needs of access, use, and privacy of the different market segments with prices also varying across distribution channels. The global purchasing for reproductive health commodities is carried out through the United Nations Population Fund (UNFPA), the U.S. Agency for International Development (USAID) and the International Planned Parenthood Federation (IPPF), and the prices obtained are much lower than the prevailing prices in high-income markets. Table 3 shows the vast difference in prices for different reproductive health commodities procured by UNFPA and the market price in the United States.

| Table 3. Comparison of UNFPA and U.S. Market price for Reproductive Health Commodities |
|-----------------------------------------|-------------|-------------|
| Condom (piece)                         | 0.025       | 0.50        |
| IUD (Unit)                             | 0.430       | 350.00      |
| Injectable (dose)                      | 0.675       | 65.00       |
| OCs (cycle)                            | 0.175       | 30.00       |
| Spermicides (tablet)                   | 0.060       | 1.20        |
| Implants (set)                         | 23.000      | 393.00      |

*Source: UNFPA data 2005*

Reproductive health products typically have relatively low volume and weight compared to value, can tolerate long distance transport, and have long shelf lives, which makes them particularly conducive for arbitrage. However, very little arbitrage is reported for such products as the manufacturers pursue differential branding, packaging, and product versioning in the two markets. Another key reason for the sustainability of large price differentials in this case is the organized purchasing that occurs for developing country markets as compared to the individual purchasing in the case of the United States.
Table 4 summarizes salient features of the differential pricing approach used for different categories of health products.

**Table 4. Summary of Current State of Differential Pricing for Different Categories**

<table>
<thead>
<tr>
<th>Category</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential medicines</td>
<td>- Few clear examples of positive differential pricing on a large scale</td>
</tr>
<tr>
<td></td>
<td>- No significant volume or income effects on prices found in empirical studies</td>
</tr>
<tr>
<td></td>
<td>- Many manufacturers have started large scale differential pricing programs only recently</td>
</tr>
<tr>
<td></td>
<td>- Drug donation programs with $p = 0$ commonly used</td>
</tr>
<tr>
<td>HIV/AIDS Drugs</td>
<td>- Multiple examples of tiered-pricing</td>
</tr>
<tr>
<td></td>
<td>- Political pressures from low and middle income countries to reduce prices</td>
</tr>
<tr>
<td></td>
<td>- High risk of informational arbitrage to erode margins in high income markets</td>
</tr>
<tr>
<td></td>
<td>- With new entrants, supply market dynamics working in favor of using price differentials</td>
</tr>
<tr>
<td>Contraceptives</td>
<td>- Price of contraceptives in low income countries is lower by a factor of 10-100</td>
</tr>
<tr>
<td></td>
<td>- Careful product versioning and differential branding</td>
</tr>
<tr>
<td></td>
<td>- Social marketing and social franchising often used as the sales channel</td>
</tr>
<tr>
<td>Vaccines</td>
<td>- Price of vaccines is much lower in developing countries</td>
</tr>
<tr>
<td></td>
<td>- Vaccines are purchased by UNICEF, PAHO and vaccination programs are run by state and NGO actors</td>
</tr>
<tr>
<td></td>
<td>- Higher opportunities for differentiation due to multi-valency</td>
</tr>
<tr>
<td></td>
<td>- Little risk of leakage and good supply chain traceability</td>
</tr>
<tr>
<td></td>
<td>- Buy side market structure creates challenges for differential pricing</td>
</tr>
<tr>
<td>Malaria Drugs</td>
<td>- Intra country price differential between public and private sector</td>
</tr>
<tr>
<td></td>
<td>- Plans to further differentiate the prices within the private sector channel to better reflect ability-to-pay of each segment</td>
</tr>
</tbody>
</table>
6. Factors That Impede Use of Differential Pricing

Differential pricing is a complex economic, political and logistical problem and it is important to understand what factors limit its success. Theoretically conjectured prerequisites for differential pricing and their practical ramifications need to be considered in tandem. Understanding these factors helps map out a set of issues that need to be resolved if differential pricing is to be viable and sustainable, either through better collaboration or through innovative models.

6.1 Discontent With Prices In the Middle-Income Tier

The highly skewed income distribution in some lower-middle and upper-middle-income markets is one of the most prominent challenges that hinder the ability of a sustainable international architecture for inter-country differential pricing. In countries such as Brazil, India, and Thailand, the richest 10 percent of the population owns more than 30 percent of the wealth (Table 5) and their per capita income is comparable to those living in high-income countries. The poorest 10-20 percent of the people in these countries have a per capita income much lower than the average per capita income in least developed countries (See Figure 3).

Table 5. Wealth Concentration in Select Developing Countries

<table>
<thead>
<tr>
<th></th>
<th>Brazil</th>
<th>Thailand</th>
<th>India</th>
<th>Uganda</th>
</tr>
</thead>
<tbody>
<tr>
<td>Income share held by highest 10 percent</td>
<td>43.03</td>
<td>33.72</td>
<td>31.13</td>
<td>34.07</td>
</tr>
<tr>
<td>Income share held by highest 20 percent</td>
<td>58.73</td>
<td>48.99</td>
<td>45.34</td>
<td>49.33</td>
</tr>
</tbody>
</table>

Pharmaceutical companies argue that middle-income countries, especially the upper-middle-income countries have substantially greater capacity to pay for pharmaceuticals and their governments should institutionalize systems to manage more equitable distribution or covering the out-of-pocket expenditures. Middle-income countries argue that their populations include many poor people and that the prices they are asked to pay are very high compared to what least-developed countries pay. Unless differential pricing can guarantee affordable prices to the poorest population segments in lower-middle and middle-income countries, a long term sustainable differential pricing structure is unlikely to emerge. Consumer groups and civil society organizations in lower-middle and middle-income countries exert political pressure on the bureaucracy to obtain prices comparable to populations with similar income levels in least-developed countries. Interestingly, such consumer groups and civil society organizations are particularly strong in the lower-middle and middle-income countries of Latin America and South East Asia. Donors, civil society, and public health officials are concerned about access to medicines for the poor and their interest in finding prices favorable to the poorest segments of the society results in pressures for price reduction. All of these stakeholders are also involved in designing better health financing systems to reduce out-of-pocket health expenditures and
implementing other more sustainable but long-term policy measures to improve access to medicines.

The root cause of this strong effect of income inequality on affordability is the lack of a risk pooling system for pharmaceutical provision. The pooling of risks through either a state-run health provision system or a social insurance scheme is crucial to ensuring that the poor in the middle-income countries are not adversely impacted by differential pricing based on average per capita income, and to ensure the economic sustainability of their health sector. Currently, a large portion of the expenditure on drugs in these low- and middle-income countries is out-of-pocket expenditure due to a lack of health insurance and risk protection. According to the WHO Health Systems report 2000, up to 87 percent of health expenditure in India is out of pocket). Countries that have chosen a state-run health system have government health care institutions, including those in rural areas that lack pharmaceuticals. Some countries, such as Brazil, have made significant progress in this field through its public healthcare system Sistema Unitário de Saúde (SUS) that provides essential drugs to patients. However, the pooling of risk and pharmaceutical buying power through social insurance leads to another set of drivers that work against sustainable differential pricing. In trying to achieve the goals of minimizing their pharmaceutical expenditure, administrators of social insurance programs engage in price reduction measures, many of which counteract with the objectives of differential pricing.

Setting up and organizing social health insurance schemes and embedding them into national policy will continue to be a lengthy and difficult process. As they are focused solely on the pharmaceutical needs of their population, the incentives of nascent and even mature social insurance programs will be to reduce their pharmaceutical expenditures to the maximum extent possible. Their success is often measured by financial sustainability and increased coverage, which translates into their ability to obtain the lowest possible price for pharmaceuticals. It is unlikely that they would consider the impact of their decisions (such as mandating low income country prices) on pharmaceutical prices in other parts of the world, the pharmaceutical industry’s profitability, investments in R&D, and improved global access to medicines. They would argue that improved access in other parts of the world should be achieved through donor funding to the poorest countries rather than differential prices, which would overburden the lower-middle and upper-middle-income countries.

This remains to be a key politico-economic hurdle to the creation of an expanded and more sustainable global system of inter-country differential pricing.
6.2 Poor Knowledge of Demand Elasticity and Inappropriate Buy-Side Market Structure

To be win-win, differential pricing requires that the manufacturer can set a higher price in those markets where consumer demand is inelastic, and charge a lower price in those markets where demand is elastic (relatively more responsive to changes in price). The ability to separate economic markets based on demand elasticity is a prerequisite for differential pricing that can lead to welfare gains. Determining the prices depends on knowledge of product price sensitivity for a specific market segment (see Figure 5). Often, however, there are no external means of determining the nature of a consumer's demand and price sensitivity. Pharmaceutical companies have very limited data on demand elasticity and income is often used as a proxy for price elasticity in selecting prices.

Figure 5. Examples of Demand Elasticity Curves Required for Welfare Improving Differential Pricing (Source: Author's analysis)

However, demand elasticity does not always coincide with income levels. Most drugs in high-income markets are paid through private or public insurance, whereas most drugs in low- and lower-middle-income markets are purchased out-of-pocket. The existence of insurance (private health plans, social insurance or nationalized health service) creates a wedge between the true demand curve and co-payment demand curve. Thus, richer countries with insurance have lower demand elasticity and the manufacturer maximizes its profit by selling to these inelastic segments at higher prices to achieve its margin. In addition, the presence of social insurance implies there
is a single or a few large payers for drugs in the country, creating an oligopsony power of large buyers in the market who negotiate good prices with the manufacturers. On the other hand, since most of the purchasing in low-income markets is out-of-pocket, there is little buying power and the manufacturer ends up choosing a higher price in the low income markets and a lower price in the high income markets. Because marginal costs of producing most pharmaceuticals are very low relative to the cost of research and development, pharmaceutical companies have a lot of degrees of freedom to make volume-price trade-offs with the large buyer in an oligopsony.

Pricing and its impact on volume is a complex issue that involves multiple uncertainties apart from a poor understanding of demand elasticity. *Volume increase comes only when actors in the distribution chain pass the manufacturer’s price reductions to end patients. It thus remains unclear to the manufacturer if reduction in prices will be accompanied by increases in volume as is theoretically predicted.*

A notable example here is of GSK, which has significantly reduced the price for its HPV vaccine *Cervarix®* in the Philippines, Vietnam, Indonesia, and South Africa. In the Philippines, after reducing the price of *Cervarix®* by 60 per cent, sales of the vaccine increased significantly, with equilibrium sales of six times the volume of vaccines sold before the price reduction was introduced. Interviews with company representatives revealed that similar increases were observed in many other products whose prices were significantly reduced.

**Figure 6. Increase in Sales as a Result of Price Reduction:**
**Case of GSK’s Cervarix**

![Image of Figure 6](source: GSK website)

### 6.3 Inefficient and ‘Black-Box’ Distribution Systems

As described earlier, differences in prices paid by patients in developing countries often are the result of factors other than differences in the price charged by the manufacturer. Channel margins (wholesale, retail) are much higher in low and middle-income countries and constitute a very
significant part of the retail price; the ex-manufacturer price is not reflective of the price paid by the end-patients. The wholesale and retail margins can be as high as 500 per cent in some developing countries, due to lack of competition and other inefficiencies (Cameron et al 2009). Thus, even when pharmaceutical companies try to set differential prices, the end-patient prices for poor patients in low income countries could be high due to price-gouging at the wholesale or retail levels due to lack of retail or wholesale competition. Tariffs and taxes also add to the cost of pharmaceuticals in many countries such as India where pharmaceutical manufacturing is a key economic activity. Data on distribution margins and other drug cost components is not systematically collected and/or published for most developing countries. More recently, the WHO/Health Action International medicine price survey (Cameron et al 2009) has become a standard tool for the collection and analysis of retail price data from medicine outlets. Prices paid by patients for a set of 30 specific essential medicines and a few other medicines of local interest in different types of outlets are collected. Many of these surveys show that the retail price of pharmaceuticals is higher by an order of magnitude as compared to the manufacturer’s price. In addition, the retail price includes the cost of transportation, storage, import tariffs and taxes, and wholesale and retail markups, in addition to the manufacturer’s price. These “hidden costs” can more than double the manufacturer’s price (Levison and Laing 2003, Figure 7). Cameron et al (2009) report that in a study of 36 developing and middle-income countries, the private sector wholesale markups ranged from 2 percent to 380 percent, whereas retail markups ranged from 10 percent to 552 percent.

Such high wholesale and retail markups often dilute the manufacturer’s incentives to engage in differential pricing as the sales gains would only result if the end patients obtain the drugs at the reduced prices.

Table 6. Components of Non-Manufacturer Costs in Retail Price of Medicines in Developing Countries

<table>
<thead>
<tr>
<th></th>
<th>Sri Lanka</th>
<th>Kenya</th>
<th>Tanzania</th>
<th>South Africa</th>
<th>Brazil</th>
<th>Armenia</th>
<th>Kosovo</th>
<th>Nepal</th>
<th>Mauritius</th>
</tr>
</thead>
<tbody>
<tr>
<td>Import tariff</td>
<td>0%</td>
<td>0%</td>
<td>10%</td>
<td>12%</td>
<td>0%</td>
<td>1%</td>
<td>4%</td>
<td>4%</td>
<td>5%</td>
</tr>
<tr>
<td>Port charges</td>
<td>4%</td>
<td>8%</td>
<td>1%</td>
<td>4%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clearance and freight</td>
<td>1%</td>
<td>2%</td>
<td>2%</td>
<td>2%</td>
<td></td>
<td>5%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-shipment inspection</td>
<td>3%</td>
<td>1%</td>
<td>1%</td>
<td>2%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pharmacy board fee</td>
<td>25%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>15%</td>
<td>10%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Importer’s margins</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>12%</td>
<td>20%</td>
<td></td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>VAT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central govt tax</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>State govt tax</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wholesaler</td>
<td>9%</td>
<td>15%</td>
<td>0%</td>
<td>21%</td>
<td>7%</td>
<td>25%</td>
<td>15%</td>
<td>10%</td>
<td>14%</td>
</tr>
<tr>
<td>Retail</td>
<td>16%</td>
<td>20%</td>
<td>50%</td>
<td>50%</td>
<td>22%</td>
<td>25%</td>
<td>25%</td>
<td>16%</td>
<td>27%</td>
</tr>
<tr>
<td>Total markup</td>
<td>64%</td>
<td>54%</td>
<td>74%</td>
<td>74%</td>
<td>82%</td>
<td>88%</td>
<td>74%</td>
<td>48%</td>
<td>59%</td>
</tr>
</tbody>
</table>

*Source: adapted from Levison and Laing 2003*
In drugs with predominantly public markets, the poor functioning of the public sector drug provision system could lead to extremely poor availability of the drug to the end patients despite the pharmaceutical manufacturer providing lower prices to the government. The pharmaceutical manufacturer’s incentives for differential pricing that tie back to the availability of drugs to the patient are thus diluted in such cases and the inefficiencies in distribution systems defeat the very purpose of differential pricing. The lack of knowledge about distribution systems and their physical and socio-economic reach leads to inertia within pharmaceutical companies about starting a differential pricing scheme. Such knowledge can be developed through the systematic collection and wider dissemination of data on product flow through in-country supply chains. The Medicines Transparency Alliance (MeTA) and the ACT Watch project (www.actwatch.info) have
conducted one-off studies to understand product flow through the supply chains. An ongoing flow mapping and tracking project with manufacturers will lead to enhanced knowledge about how the product flows through the supply chain and result in higher comfort levels and reduced inertia about differential pricing.

6.4 Lack of Market Segmentation (Physical Arbitrage and External Reference Pricing)

For differential pricing to function, it is imperative that there is a robust means to prevent the diversion of the lower-priced product into the higher priced markets, but also an insulation of prices in the higher-priced market from any materially significant psychological or political effects that might flow from the existence of lower prices in the other markets.

6.5 Physical Arbitrage

The threat of physical arbitrage i.e. lower priced product flowing back to the high income markets, is often presented as a key barrier limiting the widespread use of differential pricing. In theory, pharmaceutical companies can contractually prohibit arbitrage of their products. In drugs that are sold to largely private fragmented pharmaceutical markets, multiple layers of pharmaceutical distributors and retailers exist and there is no ability to track the source of arbitrage to invoke contractual provisions. Pharmaceutical companies selling their products at significantly lowered prices in developing countries need strong assurances that there is very limited risk of low-priced product flowing back into their profitable high-income markets. Often times manufacturers have a low degree of control over the publicly run distribution system in many low-income countries to consider investing in robust mechanisms to prevent arbitrage.

The ability to engage in arbitrage varies greatly with the characteristics of the product, the nature of the market, and the system of distribution and the transaction cost of purchasing and selling the drug relative to its cost. Drugs sold in discrete units face the greatest threat of physical arbitrage as low-priced buyers can resell the product in the high-price market. The profits from arbitrage accrue mostly to the benefit of the third-party companies that buy and resell these medicines, with the end-patients, payers, or the pharmaceutical companies gain nothing from such arbitrage. Such arbitrage has been the focus on intense discussion and debate within the EU and to some extent in North America. The argument that increased price competition due to parallel trade reduces overall pharmaceutical prices, benefiting payers and patients have been refuted in recent studies (Kanavos and Costa-Font 2005, Kanavos and Vandoros, 2010). In fact, unexpected shortages were often observed in countries that were net exporters in the arbitrage e.g. Greece or Spain as manufacturers tried to limit the quantities they would sell to wholesalers in countries with lower prices in order to avoid arbitrage to the United Kingdom and Germany. Government regulated price cuts and currency fluctuations make the flows in the parallel trade in pharmaceuticals to be dynamic. For instance, in the United Kingdom, a government-imposed
price cut and the weakening of the sterling against the euro during 2009 meant that it was no longer a profitable market for arbitragers from other EU states for most drugs and in fact made the United Kingdom a net parallel exporter. However, the parallel trade in the EU stems primarily from the integrated EU with no borders.

Outterson (2005) argues that the potential for product diversion from developing countries is not a significant constraint for firms to engage in differential pricing. He argues that despite existing large price differences for some drugs there is no evidence of large scale international smuggling. Pharmaceutical companies also manipulate design, dosage and packaging of the drug to prevent product diversion. For example, GlaxoSmithKline uses specially designed access packs and red rather than white tablets for Epivir® and Combivir® to facilitate easy tracking of any diverted product.

6.6 External Reference Pricing and Informational Arbitrage

The promise of differential pricing stems from the dynamic interaction of supply, demand and the differences in the willingness and ability to pay for a product. However, given that pharmaceutical companies have not always followed the benevolent policy of differential pricing, national buyers and price regulatory authorities in developed countries often adopt some form of price control, to determine the price of a product in their country. A commonly used method involves comparing the prices for new products against those prices paid by other countries within the geographical region or income class, a practice commonly known as external price referencing. Various methods are used to build the basket of prices for referencing and either the mean, median or in some cases the lowest price is selected as the price for reimbursement. For example, Canada considers a referencing basket consisting of the United States, France, Germany, Italy, Sweden, Switzerland and the United Kingdom. The price of any new product cannot exceed the median of the prices. Countries such as Spain and Greece simply demand the lowest price in Europe. Many countries such as Saudi Arabia also select countries from outside their income class for price referencing (Kanavos and Reinhardt. 2003). In addition, some countries such as Jordan also include price in the country of product origin for external referencing.

Multiple studies (Kanavos et al 2008, Pavcnik, 2002, Kanavos and Reinhardt. 2003) suggest that reference pricing can be very effective in bringing down prices. However, the literature looks mostly at only price and competition effects of reference pricing without explicitly considering its welfare impact. It is also crucial to understand the way reference pricing is actually implemented. Although the literature may recommend the use of value-based or current-substitute-based reference pricing, low and middle-income countries implement an external reference pricing methodology.
In addition to a formally published formula for reimbursement prices based on prices in a basket of countries, reference pricing is also commonly used informally to obtain price concessions in negotiations between public purchasers and the pharmaceutical industry. Many countries and large supranational buyers employ an extreme form of reference pricing, asking pharmaceutical companies to give them the lowest price that they offer to any buyer in the world. Although the intention is to lower price for low income countries, such lowest price reference pricing acts as a barrier to differential pricing. Pharmaceutical companies are wary of aggressive differential pricing in low income markets as the price provided would be used a negotiating tool by large powerful purchasers in middle-income countries or becomes the price they are required to provide to large buyers with lowest price reference pricing.

Physical arbitrage is not the most serious threat pharmaceutical companies face in safeguarding their margins in high income markers. Reference pricing leads to a form of informational arbitrage that is far more important to pharmaceutical companies than physical arbitrage from one market to another. Setting lower prices in developing countries implicitly reveals information about the cost structure and leads to price reduction pressure.

The welfare implications of price control and reference pricing cannot be established unconditionally for all markets as they depend upon the market structure and balance of power between suppliers and buyers in each market. However, it is evident that whenever there are price controls, manufacturers invest resources in lobbying and other influence activities to maintain the regulated price. These are wasted resources and lead to welfare loss.

6.7 Drug Resistance and Exhaustibility of Drugs
Parasites, bacteria and viruses mutate over time, making existing treatment ineffective. For example, antibiotics lose effectiveness over time as bacteria develop resistance, ARV treatments require switching to second line treatments as the AIDS virus mutates, multidrug resistant strains of tuberculosis have emerged and the artemisinin-based treatments for malaria are under the threat of resistance. The theoretical models of differential pricing do not incorporate the exhaustibility aspect of drugs for infectious diseases. Evidence shows that resistance develops more quickly with higher use of the drug and when patient's compliance with the dosing regime is high (Laxminarayanan and Brown 2001). Differential pricing would lead to higher usage of the drug, particularly in environments with poor compliance, increasing the potential for the drug to be ineffective way before the patent expires. The pharmaceutical manufacturer's interest would be to provide the exhaustible drugs to those market segments that can afford the drug at the highest price. Differential pricing for low income countries for such drugs becomes challenging and may require a non-market allocation mechanism.
7. The Case for Intra-Country Differential Pricing

Theoretical evidence and examples from different categories of health products demonstrate that differential pricing is feasible and price differentials between market segments can be preserved without significant pressure from high priced segments to reduce prices. These examples also suggest that the key to managing expectations of different stakeholders on fairness perception is the selection of right market segments. The discussion on differential pricing has focused on prices charged across countries being different to reflect the differences in their income level or affordability of patients. A wider discussion of intra-country differential pricing i.e. charging different prices to different income segments within a country has been missing primarily due to the perceived risks of leakage from one channel to the other.

As discussed earlier, the highly skewed income distributions within lower-middle and middle-income countries seriously hinder the ability to do differential pricing. Inter-country differential pricing cannot guarantee affordable prices to the poorest population segments in lower-middle and middle-income countries, as that would imply pharmaceutical companies forego the profits from the higher income segments in these countries. At the same time, the poorest segments and their advocacy groups feel "entitled" to the prices provided to low income and least developed countries.

Economic analysis similar to that for inter-country differential pricing can be used to show that intra-country market segmentation and price discrimination in countries with highly skewed income distribution could significantly increase affordability for low income populations and in fact lead to higher profits for the pharmaceutical companies. Figure 8 shows that choosing a single price in a country with a wide income distribution leads to less than 30 percent of its population having access to the drug. The choice of a high single price that only covers high income segments of the population results from the highly convex demand curves in countries with large inequities in income distribution. However, choosing two prices with sufficient barriers between the two markets can lead to up to 90 percent of the population having access to the drug and increases the manufacturer's overall revenue from the market.
The results presented in Figure 8 only hold true when the high income and low income markets in the country obtain the drugs from different channels and the channels are assumed to be perfectly sealed i.e. no product can flow from one channel to another and customers in one market are not able to purchase the drug in the other channel.

**Figure 9. Leveraging Differences in Channel Socio-economic Reach for Intra-country Differential Pricing**
Most developing countries have two health provisioning channels: publicly financed government delivery systems and privately (largely out of pocket) financed market systems. The relative proportions of patients seeking treatment in each system vary significantly by country and by disease. For instance, a large fraction of malaria treatment is obtained in the private sector in many high malaria endemic countries despite the availability of free anti-malarials in the public sector. Also, different socio-economic segments of the population seek treatment and obtain medicines from different channels owing to a variety of factors such as the cost of treatment, cost of transportation costs, amount of time spent, and location of the household. Ability to pay is also an important factor in the choice of where to obtain drugs, with wealthier patients seeking treatment in channels different from poorer counterparts. This provides a natural wedge that can be leveraged for charging different prices in the different channels and reaching specific segments of the population at price points that they can truly afford.

Another natural wedge that can be leveraged for intra-country differential pricing is the urban-rural income divide in developing countries. Although there is generally a large divide between income levels in urban and rural parts of India, China, and Brazil, inner-urban income inequality is much higher in India and Brazil than in China because there are a large number of urban poor. China thus provides an excellent example of a country where utilizing the urban-rural divide in income levels can be used to create a price differential scheme for pharmaceuticals.

A key prerequisite here is the separability of the different channels and whether adequate safeguards can be put in place to prevent the diversion of the product or patients from one channel to another. Admittedly, such separability is hard to ensure in the absence of robust tracking and tracing ability. Examples from the Hep B vaccine and malaria drugs has shown that this is feasible with careful design of the differential pricing scheme and selection of partners that can better manage the risk of diversion.

It has also been argued that differential pricing across channels within a country could lead to high income customers switching to the channel where low income segments currently purchase their drugs. However, our modeling work shows that even if there is some limited switch over of patients in where they seek treatment to exploit the price differential, the overall revenue of the pharmaceutical manufacturer would still be higher under differential pricing. Differential pricing should be considered even in the face of some leakages of customers from high income to low income. In reality, such leakage is low due to high transaction costs associated with obtaining treatment in the channel where the manufacturer chooses a low price. Examples include the longer waiting times and longer administrative issues associated with obtaining drugs at public health clinics. Interestingly, the transaction cost is usually income dependent and higher income customers face a higher transaction cost due to the cost of their time being higher. This limits the
fraction of high income customers who will travel long distances or wait in long lines to obtain better priced product. Clearly, the extent of the price differential also matters as patients with chronic illnesses and significant out of pocket drug costs will be willing to incur a high transaction cost. However, this argument works well for malaria drugs, where patients are able to obtain higher priced treatment in the private sector instead of incurring the higher transaction cost of visiting a public clinic to obtain free drugs.  

In many developed markets pharmaceutical companies use multiple channels to reach the end patients. Pricing to these channels has been based on volume or purchasing, transaction cost, and the ability to drive drug utilizations. Thus, intra-country differential pricing exists and is feasible although the prices charges are not reflective of the affordability of patients seeking care in each channel.

Table 7 shows the prices for 12 different branded and generic pharmaceutical products in different type of medicine outlets in India, including a government run clinic, a pharmacy run by a cooperative society, private for profit pharmacy and a dispensary in a private hospital. The extent of price variation between these different outlets generates some evidence that intra country differential pricing can potentially be carried out if each of these outlets types serve a different type income segment and have a centralized supervisory function.

**Table 7. Selling Prices (Rs./tablet) of 12 Commonly Used Drugs Under Five Settings**

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand</th>
<th>Society</th>
<th>Government</th>
<th>Private pharmacy</th>
<th>Spatial monopoly</th>
<th>Private hospital medicine store</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paracetamol</td>
<td>-</td>
<td>0.40</td>
<td>0.57</td>
<td>0.60</td>
<td>0.50</td>
<td>0.88</td>
</tr>
<tr>
<td>Ampicilin</td>
<td>-</td>
<td>3.00</td>
<td>6.40</td>
<td>5.40</td>
<td>6.50</td>
<td>6.60</td>
</tr>
<tr>
<td>Amoxycilin</td>
<td>Mox</td>
<td>5.75</td>
<td>7.03</td>
<td>7.40</td>
<td>7.00</td>
<td>7.30</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>Rantac</td>
<td>0.50</td>
<td>0.50</td>
<td>0.53</td>
<td>0.55</td>
<td>0.50</td>
</tr>
<tr>
<td>Cetirizine</td>
<td>Zetazine</td>
<td>2.98</td>
<td>3.29</td>
<td>3.30</td>
<td>2.50</td>
<td>3.15</td>
</tr>
<tr>
<td>Alprazolan</td>
<td>Alprax</td>
<td>0.90</td>
<td>0.96</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Penicillin G</td>
<td>Voveran</td>
<td>1.45</td>
<td>1.55</td>
<td>1.70</td>
<td>1.50</td>
<td>1.60</td>
</tr>
<tr>
<td>Atenolol</td>
<td>Aten</td>
<td>1.85</td>
<td>1.92</td>
<td>2.00</td>
<td>2.10</td>
<td>2.00</td>
</tr>
<tr>
<td>Glyben Glamade</td>
<td>Daonil</td>
<td>0.60</td>
<td>0.63</td>
<td>0.70</td>
<td>0.70</td>
<td>0.66</td>
</tr>
<tr>
<td>Enaprel</td>
<td>Envas</td>
<td>2.25</td>
<td>2.23</td>
<td>2.40</td>
<td>2.45</td>
<td>2.30</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>Ciplox</td>
<td>7.70</td>
<td>8.90</td>
<td>9.00</td>
<td>8.75</td>
<td>8.40</td>
</tr>
</tbody>
</table>

*Source: Godwin S K and D. Varatharajan*

Examples of such differences in the retail price charged to the end patient in different channels are abundant but do not always imply that the differences in the retail prices are the result of
manufacturer-run differential pricing schemes. They could be examples of second degree price discrimination based on volume of purchase carried out by the distribution channel or merely differences in the cost of distributing for each of the channels.

An interesting example of such intra-country differential pricing for single sourced and also multiple sourced drugs is the United States where there are large price differentials between different market segments. Differential pricing is not based on differences in the prices offered on contract but on a complex system of rebates and discounts. The price of drugs paid by the consumer is determined by a system of negotiated volume-rate contracts between manufacturers, pharmacy benefit managers (PBMs), wholesale distributors, pharmacies, and health insurance companies. The price charged by each entity in the chain is largely driven by the ability of contracting entities to sell specific volumes of certain drugs or achieve a certain share of a specified market. It is also affected partially by the value each entity brings to the subsequent actors in the supply chain. Also, four federal agencies, the Veterans Administration, the Department of Defense, the Public Health Service, and the Coast Guard set an upper limit on the price they pay, which should be less than a certain percentage of the weighted average nonfederal selling price for the product.

The system of "differential pricing" within the United States is not based on income or affordability of the buyer but works on the principle of offering lowest prices to those purchasers who have an ability to influence market share by systematically favoring one drug over another within their enrolled patient base. Admittedly, this is not the welfare enhancing differential pricing this report argues for. Nevertheless, the U.S. example demonstrates that prices can be charged differentially to different market segments in a country without large leakages due to the separation between the selling channel, the ordering channel, the physical distribution channel, and the payment channel for each of the segments. True intra-country differential pricing that depends on income and affordability of market segments can successfully learn from this flow separation, especially in therapeutic areas where the market structure support this. The U.S. model of intra-country differential pricing also demonstrates is that if differential pricing occurs purely based on market mechanisms, its form and outcome are highly dependent on the structure of the supply chain, and the distribution of buying power between different market segments.

*Market structure, costs to serve the market, and buying power all work against the poor in most low and lower-middle-income markets.* Flynn et al (2009) analyze the effect of inequitable income distribution on the pricing and output decision of a monopolist in a given country. They say that although price discrimination is possible within a country, in practice the consumers that benefit from such discrimination are not the poor but rather the well organized (e.g. insurance providers, the government or other large purchasers). They also state that price discrimination focused on preferential pricing to government agencies, with the assumption that such agencies will service
the poor, is unlikely to reach large segments of the population. Poor segments of the population who do not access government operated clinics and earn too little to afford private insurance can only obtain drugs at the high prices being targeted towards the highest income quintiles.

Nevertheless, the degree of separation between the distribution channel through which the poorest income quintiles seek treatment and the distributional channel through which the richer segments seek treatment in developing countries provide opportunities for intra-country differential pricing that may not be available in OECD contexts.

8. Recommendations for Action

Despite its theoretical appeal and some notable successes, the use of differential pricing as a tool for pharmaceutical companies to improve access to medicines remains very limited. The primary causes include risks of physical arbitrage; risks of eroding margins in high income market segments due to external referencing; poor knowledge of demand and supply structures; wholesale and retail markups that corrupt any well intended differences in ex-manufacturer prices; and a buying market structure that works against the poorest segments of the population. Implementation of differential pricing will require better information about markets, political will, and commitment from pharmaceutical companies and developing country governments.

Based on the analysis conducted for this report as well as an assessment of the existing literature, the following strategies are recommended for mitigating the risks and obstacles associated with differential pricing.

Table 8. Strategies for Mitigating Risks and Obstacles for Differential Pricing

<table>
<thead>
<tr>
<th>Risk</th>
<th>Mitigation Strategy</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Arbitrage</td>
<td>Share risk with agencies that have reputational risk from arbitrage</td>
<td>Lower price for Global Fund financed drugs as compared to private sector prices in the same market. The risk of product diversion is thus also borne by the Global Fund as some form of reputational risk. Used in the case of Novartis Coartem®</td>
</tr>
<tr>
<td></td>
<td>Create top to bottom visibility in the supply chain</td>
<td>Vaccines have effectively used this. Manufacturers have been more receptive to differential pricing than for drugs</td>
</tr>
<tr>
<td>Risk</td>
<td>Mitigation Strategy</td>
<td>Examples</td>
</tr>
<tr>
<td>------</td>
<td>---------------------</td>
<td>----------</td>
</tr>
<tr>
<td><strong>Physical Arbitrage (Contd.)</strong></td>
<td>Differential branding/packaging in different markets</td>
<td>GSK’s red rather than white tablets for Epivir® and Combivir® to prevent product diversion. GSK’s drug Zantac was sold as Zinetac in India with the price of Zinetac much lower than Zantac sold in the U.S./EU.</td>
</tr>
<tr>
<td></td>
<td>Contractual agreements with the group purchaser who receives lower priced product to ensure that the product is only used in the market for which it is intended.</td>
<td>Social franchise organizations for reproductive health commodities</td>
</tr>
<tr>
<td></td>
<td>Drug provision in clinic with service bundling</td>
<td>Multi-drug treatment for leprosy where clofazimine and dapsone are provided as a month long supply in blister packs as they have no significant high income market. Rifampicin, which has a commercially viable market, is administered in the clinic when the patients come to obtain their drugs.</td>
</tr>
<tr>
<td><strong>Formal or informal external referencing</strong></td>
<td>“Nudge” countries to use pharmaco-economic assessment instead of reference pricing</td>
<td>The international unit at NICE has a program to assist developing countries in this regard. Conduct empirical research to understand the welfare impact of external reference pricing</td>
</tr>
<tr>
<td>Risk</td>
<td>Mitigation Strategy</td>
<td>Examples</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Political pressure from middle-income countries to obtain low income prices</td>
<td>Intra-country differential pricing in lower middle and middle-income countries</td>
<td>Novartis Coartem</td>
</tr>
<tr>
<td></td>
<td></td>
<td>GSK Hep B vaccine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>GSK, Pfizer and Merck’s evolving pricing models in emerging markets</td>
</tr>
<tr>
<td>Poor knowledge of demand and supply structures</td>
<td>Invest in understanding the distribution channels and their reach</td>
<td>IMS Health DDD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ACT Watch</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MeTA supply chain work</td>
</tr>
<tr>
<td></td>
<td>Invest in market research to understand price sensitivity of different market segments in low income countries</td>
<td>Price-setting decisions in OECD countries use IMS health data as key input</td>
</tr>
<tr>
<td>Buy side market structures work against the poorest segments of the population</td>
<td>Incentivize the creation of some degree of monopsony purchasing power for pro-poor distribution/retail channels</td>
<td>Patient-led buyer clubs in Thailand</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Social franchise pharmacy chains in Africa</td>
</tr>
<tr>
<td></td>
<td>Invest in scaling up health insurance in the developing world</td>
<td>Various examples in South East Asia</td>
</tr>
<tr>
<td></td>
<td>Engage with pooled procurement platforms like global fund’s Voluntary Pooled Procurement, UNICEF, PAHO, GCC to ensure there is flexibility for differential pricing</td>
<td></td>
</tr>
</tbody>
</table>

We describe below a few high impact action points for donors and pharmaceutical companies that can make differential pricing more feasible and politically sustainable. Although most of these recommendations require close collaboration between industry and international donors, we also highlight whether a particular recommendation is best led by international donors or by pharmaceutical companies. Many of these recommendations will act as enablers of differential pricing and will contribute to the implementation architecture for differential pricing.
8.1 Partner to Generate Visibility of Channel Flow Information (Donor and Industry Led)

The case of vaccines demonstrates that having some capability to understand the path of healthcare products through the supply chain as they move from the manufacturer to distributors, clinics, and patients reduces both the real and perceived risks of product diversion. Having such information reduces the risk for pharmaceutical companies of their product being diverted back into high-income market segments. Clearly, such capability is not easy to create for drugs and at present manufacturers have a product hand-off model under which very little information flows back to them about their product after it is sold to the government or to large importers in the country. In many OECD countries, data consolidators such as IMS Health provide wholesaler and outlet level flow data that captures flow information, This information is routinely used to understand channel flows, and track product diversions and parallel imports before they become significant. No such capabilities currently exist in the developing world.

Partnership models should be created where industry associations such as the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) work with the national governments to increase visibility of flows in the government distribution system to manufacturers. Global health financiers like the Global Fund also have a reputational risk in case products financed by their grants are diverted from their primary recipients to unintended users. Pilot projects should be conducted to build capabilities of inventory visibility in government-run distribution systems and evaluate the impact of such visibility on product diversion.

Such visibility will help alleviate manufacturer’s fears of widespread product diversion, and what is viewed largely as a black box distribution system by many manufacturers will become more transparent. In addition to helping differential pricing, such an exercise will also prevent the proliferation of counterfeit drugs. Initiatives such as the Medicines Transparency Alliance (MeTA) could potentially play a key role in this activity. Pharmaceutical companies should widely publicize and disseminate examples such as the one presented in Figure 6 to allay fears among multiple stakeholders that lowering manufacturer prices in developing countries does not always lead to significant increases in volume.

A combination of enhanced knowledge about the distribution channel flows on one end and treatment-seeking behavior on the other will help develop better targeting strategies for intra-country differential pricing.
8.2 Create Incentives for Strengthening Pro-Poor Distribution Channels (Donor Led); Preferential Pricing for Pro-Poor Distribution Channels (Industry Led)

Differential pricing should lead to preferential prices for health systems that target poor segments of the population in developing countries. Providing lower prices only to the public sector does not suffice as the poor also seek treatment in a private sector consisting of private pharmacies, licensed drug sellers, private clinics, and informal channels. Although many such channels are directed towards the poor they are very fragmented. Pharmaceutical companies have shown willingness to provide such systems with lower priced product if they can ensure that the product is only used in the market for which it is intended. However, the excessive fragmentation of these channels implies that no entity is able to control directly the distribution of the product to the point of final consumption. In addition, the transaction costs of contracting such pricing arrangements with multiple smaller players are high. A majority of the rural poor for whom targeted pricing strategies can be created live in areas which pose enormous distributional challenges. As a result, pharmaceutical companies have so far limited their preferential pricing programs to the public sector or the NGO sector.

The creation of some degree of monopsony channel power and the bulking of purchasing and distribution will allow pro-poor channels to obtain better prices and will provide pharmaceutical companies the opportunity to work with a few committed partners who will distribute their products in poor market segments without the risk of product diversion. International donors need to incentivize the strengthening of pro-poor distribution models through grants and technical assistance. Demand side financing and the strengthening/creation of health insurance systems would enable some degree of monopsony for the pro-poor channels and would solve some of the issues stemming from excessive fragmentation of distribution channels that serve the poor. Many global health donors are already engaged in demand side financing initiatives but their designs need to be more carefully evaluated to include differential pricing.

In the interim, pharmaceutical companies should provide preferential prices to health systems that have demonstrated their reach to the poor and have robust systems in place to guarantee flow tracking. Innovative technology solutions that reduce the transaction cost of dealing with small fragmented markets should be utilized to ensure that smaller distribution/retail players who are targeting the poor segments can have access to lower prices.
8.3 **Explore Innovative High-Volume Low-Margin (HVLM) Distribution Models in Low and Middle-Income Countries**

Differential pricing would lead to lowering the prices in many low and middle-income countries and is based on the prerequisite that price reduction is likely to bring in more sales. This creates pressure upon the entire organization to do higher volume of business to sustain profitability. Large pharmaceutical companies are not necessarily organized to operate their distribution business in developing countries with thin margins. Pharmaceutical distribution in developing countries is organized slightly differently as compared to OECD countries. On one hand government-run health programs buy large volumes of product through a tendering process. On the other hand, small private sector retail pharmacies that cannot keep a large number of medicines in stock due to capital constraints rely on an extensive network of sub wholesalers instead of buying directly from large manufacturer-appointed distributors. This leads to the existence of multiple third parties between the manufacturer and the dispensing pharmacists; increases the retail price due to multiple distribution markups’ and does not leave enough transparency to prevent product diversion in a robust manner.

As the business model moves from a high margin-low volume (HMLV) model to a high volume-low margin (HVLM) model, the importance of operational efficiency as well as the need of achieving high distribution reach becomes crucial. A successful transition will require questioning conventional wisdom and adopting new mindsets. This change in the way of doing business will come with an initial “costs of reorganization” in sales and marketing, distribution and manufacturing.

In the long run, this will require reconstructing the value chain and redefining the roles and incentives for all participants in the system, the manufacturers, the country office, the distributors, and the end patients.

As a vast majority of the volume will come from market segments that are hitherto underserved by large pharmaceutical companies, innovative approaches and new routes for reaching patients will have to be identified. New technologies and business process redesign will be required for many of these solutions. Some of these underserved market segments face the multiple challenges of physical access, fragmented demand, shortage of working capital, and high cost of capital. Distributors of large pharmaceutical companies also have to be engaged in this discussion and their involvement will require redefining the approach and metrics currently used to assess annual targets and profits.

A shift from the HMLV model to a high volume-low margin (HVLM) can also lead to significant quality risks in the storage and distribution of medicines and the dispensing advice provided.
Mechanisms to guarantee quality, such as limiting access through drug outlets with some form of quality accreditation like the Accredited Drug Dispensing Outlets (ADDO) in Tanzania, will be needed.

All of this requires deep collaboration between organizations and working closely with different governmental and non-governmental local stakeholders. We recommend the creation of a task force within the Industry Government Forum on Access to Medicines (IGFAM) to explore the issues in managing the successful transition from a low-volume, high-margin pharmaceutical business to a high-volume, low-margin pharmaceutical business in low and middle-income countries.

8.4 Create Incentives and Support for Countries to Transition From External Reference Pricing to Pharmaco-Economic Assessment (Donor Led)

The impact of external reference pricing used by a middle-income country on global access to medicines remains unclear. Empirical and analytical research needs to be conducted to understand how reference pricing affects prices outside the given and the basket countries.

It is clear that to manage the political needs of providing high quality care combined with the reality of very limited financial resources, developing countries will utilize some form of reference pricing in their state run or social insurance systems. It becomes important then to ensure that the form of reference pricing used includes better methods of price referencing as compared to the external basket method that is most commonly used. Pharmaco-economic assessment should be used in making pricing and reimbursement decisions both by developing and developed countries. This would help untangle the complex web of interrelationships in price that exist between countries and make manufactures wary of changing price in any country due to the resulting cascading effects.

Measures of income and affordability can be used as input into the pharmaco-economic assessment resulting in different prices for different countries. Such an approach is more likely to be perceived as fair by all participating stakeholders. Pharmaco-economic assessments by their very nature are technically challenging and effort-intensive, and would thus require external technical and budgetary assistance from donors if developing countries were to start using it extensively. The National Institute for Health and Clinical Excellence in the United Kingdom has an international division that has been helping low and middle-income country governments develop better methods to substitute external reference pricing with value-based pricing. Creating and putting into practice such guidance about the optimal form of price assessment can be a challenging exercise. Some countries such as South Korea who have introduced pharmaco-
economic assessment have achieved mixed results due to the lack of local studies and other methodological issues. A pilot project to develop better operational understanding and assess the techno-economic feasibility of using a more involved price assessment methodology in developing countries should be investigated.

8.5 Conclusion
Differential pricing can enhance access to medicines, improve quality of medicines and achieve higher profits for pharmaceutical manufacturers. However, differential pricing can be sustainable only if it aligns the incentives of the different stakeholders: pharmaceutical manufacturers, national governments, end patients and civil society organizations. Pharmaceutical manufacturers would want become more receptive to differential pricing if the risks of physical arbitrage could be managed collectively together with national governments, international donors and large NGOs. In addition, firms could develop contractual agreements with group purchasers who receive lower priced products to ensure that the product is only used in the market for which it is intended and administer certain drugs only in clinics to avoid the leaking of these drugs to other markets. Intra-country differential pricing in lower middle and middle income countries would help avoid political pressure from middle income tier countries in to reduce prices. To avoid the problem of formal or informal external referencing, firms could nudge countries to use pharmaco-economic assessments instead of reference pricing. Additional empirical research is needed to understand the welfare impact of external reference pricing. Implementing the recommendations in this paper would require inputs and collaboration from several parties in addition to those who are recommended to lead each of the specific recommendations. The national governments of low and middle income countries have a key role to play in providing the political will and objectively determined reimbursement policies to enable differential pricing.
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