This primer outlines how COGS analyses can inform product introduction planning.

**KEY TAKEAWAYS**

- **When a drug is produced in India by a generic manufacturer, costs are generally lower than originator manufacturing in Europe or the US.**
- **Cost of Goods Sold (COGS) is defined as the direct cost to manufacture a product.** COGS do not include research and development (R&D), product development expenses, or fixed costs to set up the manufacturing processes, because these are not part of the ongoing manufacturing costs.

- Injections are a widely used administration form and many generic manufacturers have extensive experience producing them at low cost. For injectables, per person per year (PPPY) production costs can be lower than for oral tablets because long-acting products usually require lower amounts of active pharmaceutical ingredient (API) over the course of a year.

What is the difference between originator and generic drugs and why are their costs different?

**Originators and Generics:** Pharmaceutical companies are called “originators” or “innovators” when they hold the patents for a drug, either as a result of discovering it during research and development (R&D) or buying the compound from a university or another company. The patent holder has the exclusive right to manufacture and sell the product in the territory covered by the patents. These products are often referred to as “patented” drugs. Patented drugs sometimes sell at very high prices based on their clinical benefits and the fact that only one company makes the product.

When drugs are licensed to be manufactured by other companies or are manufactured by other companies after coming off patent, they are referred to as “generic products.” Generic products often compete primarily on price because many companies are in the market with the same formulation.

Drugs currently used for HIV include both patented and generic products. Many HIV drugs have been voluntarily licensed to generic firms. These licenses, often issued through the Medicines Patent Pool, grant permission for a company to manufacture the product and sell it only in the licensed territory (which typically excludes all high-income and some upper middle-income countries where the originator sells their product). Generics could also be available in countries outside the voluntary license territory where there are no patents or patent barriers have been removed.

**Cost Differences:** Drug production costs (such as raw materials, labor, manufacturing facilities, packaging, and overheads) for both patented and generic drugs are much greater when production facilities are located in high-income countries as compared to production costs in India or other low-cost settings, where many generic manufacturers are based. Since most patented HIV drugs are produced in high-income countries, whereas most generic HIV drugs are produced in lower cost manufacturing environments, such as India, patented HIV drug costs are generally higher.

Patented drugs may also have higher production costs because there is less competition and less need for cost optimization. For many high-volume HIV drugs, generic companies have built up highly efficient manufacturing capacity. Thus, generic HIV products, such as tenofovir disoproxil fumarate, lamivudine, and dolutegravir (TLD), benefit from manufacturing and supply chain cost optimization, as well as economies of scale compared to similar drugs manufactured in high-income countries.

In addition to licensing their products, some originators will sell their branded products in low- and middle-income countries (LMICs) at a “not-for-profit” or “access” price. While the “access” price includes minimal or no margin, this price does still include full recovery of direct costs and overheads. This includes cost categories that donors will, on occasion, cover or share with generic developers to keep generic prices low. Since the cost of producing a drug in a facility located in a high-income country, like the US or Europe, is much higher than in India, even the ‘not-for-profit price’ is often 3-5 times greater than the price offered for the same product by a generic firm with production in India.
Do COGS include capital expenditure and product development costs?

Capital expenditures (often referred to as “CapEx”) for equipment and facilities needed in the production process contribute to the cost of production via a depreciation charge that is usually included in a facility’s overhead cost allocation. Since equipment and facilities last for many years, only a portion of their purchase cost is expensed each year, and this is called the “depreciation charge.” CHAI includes these costs as part of API and formulation costing via the depreciation charge.

CHAI also does not include the costs of potential new upfront expenses (e.g., purchasing a nano mill), product development or R&D (which may vary among generic manufacturers) in our COGS analyses. These costs are expensed as incurred, regardless of whether a product is ever fully developed or commercialized. CHAI and partners may also consider financial support for these costs via product development risk-sharing agreements with firms willing to invest in making new HIV drugs and selling them at affordable prices.
What is the difference between COGS and price?

COGS analyses estimate the costs of manufacturing a product. While COGS can inform pricing, COGS do not estimate the price at which a product will or could be available. The price of a product will almost always be higher than the COGS because companies add a margin (see Figure 1). The margin is generally higher for originators than generics as a result of several factors, including higher R&D costs that must be recovered. All companies aim to recover their investment costs through pricing.

Pricing also depends on volumes — if low volumes are expected, a company will usually set a higher price to ensure they recover costs over the first few years after launch. If a company expects competitors to reach the market, they may try to recover costs over a shorter period of time, leading to further increases in pricing. For example, assuming production costs for a drug are $34 PPPY and a company has spent $10 million on start-up expenses, if the company anticipates 350,000 annual users and wishes to recover initial expenses in the first year, they will set a margin of almost $30 PPPY, resulting in a price over $60 PPPY:

Illustrative calculation of margin for companies to recover start-up expenses:

<table>
<thead>
<tr>
<th>350,000 annual users</th>
<th>6 vials per user per year</th>
<th>2.1 M vials</th>
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<tr>
<td></td>
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<td>$10 M start-up expenses</td>
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<tr>
<td></td>
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<td>2.1 M vials</td>
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<td></td>
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<td>$4.76 per vial or $28.57 PPPY margin needed to recover start-up expenses</td>
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Conducting a COGS analysis can help increase transparency because it enables a comparison between a product’s ultimate price to the purchaser versus the company’s production costs to manufacture it. COGS can, therefore, help consumers or buyers understand whether companies are including a large margin or whether they are offering the product at a price close to the COGS, or production costs.

Application of COGS Analyses to Long-Acting Injectable Cabotegravir (CAB-LA)

Can an injectable be inexpensive to manufacture?

Injections are a common and widely used drug delivery form. They are used to administer contraceptives, vaccines, and many other therapies. As a result, many pharmaceutical companies have significant experience manufacturing quality-assured injectable products and can make them cheaply and efficiently. For example, generic depot medroxyprogesterone acetate (DMPA), a three-month injectable contraceptive which was first introduced for contraception in the 1990s, costs $0.77 per injection, translating to just $3.07 per year (4 injections per year).

Injectable contraceptives make up a significant (and increasing) share of the contraceptive market, with shipment volumes totaling 84 M across 69 FP2020 countries in 2020.

How could an injectable HIV product be cheaper than a daily oral pill?

Long-acting products require fewer doses per year than daily oral pills because the active pharmaceutical ingredient (API) in long-acting products is more potent and is maintained at a therapeutic level in the body for a much longer period of time. Since APIs often make up a large proportion of a product’s total COGS this can translate to a cheaper product over the course of a year. As shown right (Figure 2), the amount of pharmaceutical ingredients needed for a year of TDF/FTC (365 pills) is much more than the amount needed for a year of CAB-LA (6-7 injections).
What did CHAI’s COGS analysis for generic CAB-LA find?

The production costs to manufacture CAB-LA in India at one of the larger firms supplying ARVs is estimated to be $34 per PPPY during early generic introduction, or “launch,” when there may be a small number of users. As volumes increase, COGS for API and formulation will decrease. Based on estimates for supplying CAB-LA to 800,000 annual users (lower than current oral PrEP annual initiation rates in LMICs), CHAI estimates generic CAB-LA COGS at $16 PPPY. CHAI also estimates that upfront investments would be needed for generic companies to begin manufacturing CAB-LA, including purchase of a nano mill, as well as drug development and bioequivalence study costs, both of which are expected to be more expensive than what is needed for daily oral ARVs. These upfront costs are not factored into the COGS analysis — if they are not covered by donor support, product pricing would likely be higher in order to recover these costs. This analysis was conducted by a team of technical experts, led by PhD scientists and industry experts with decades of experience in drug development and process chemistry. For more information, please see CHAI’s full analysis.

References
1. The innovator “not-for-profit” price of generic dolutegravir (DTG) (30 tablets) is $20.11 (USAID GHSC-PSM e-Catalog 2021) while the generic benchmark price is $2.35 (USAID GHSC-PSM e-Catalog 2022)
3. For example, see one patent for the pharmaceutical composition of cabotegravir here: https://patents.google.com/patent/WO2021116872A1/en