



The danger of in-kind drug donations to the Global Fund

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In-kind drug donations to the Global Fund to fight AIDS, tuberculosis, and malaria (GFATM) could greatly distort market incentives for entry of generic drugs, and thus delay the development of a more competitive market for priority drugs. Donations can be detrimental to market incentives for generic competition because they reduce the size of the residual market for a particular drug, create uncertainty about future market effects of donations of other drugs, change the risk–benefit ratio with respect to patent-related issues, registration barriers, and costs of negotiating a distribution system, and reduce the market-pull advantage of an identifiable, sizeable, and sustained source of secure financing. Similarly, drug donations can distort choices about best treatment options by deterring use of effective fixed-dose combinations and other improved formulations, tying government treatment choices to particular so-called free drugs, delaying or undermining governments' motivation to select or modify treatment guidelines, affecting regulatory decisions (such as registration of generic equivalents), and complicating procurement and supply systems.

The issue of in-kind donations of drugs has been discussed within GFATM since 2002, mainly at the insistence of the private sector and certain donors.¹ Recently a joint steering committee of GFATM has commissioned a policy paper analysing in-kind donations, including potential market and sovereignty effects, for consideration at the Board's November, 2008, meeting. Civil society delegations have consistently and successfully opposed drug donations. We present key arguments against two underexplored aspects of drug donations to GFATM—namely, their distortion of market incentives and their adverse effects on therapeutic options. Drug donations to GFATM are tempting because they lower commodity costs and could increase the value of private-sector contributions. However, these apparent advantages are more than offset by the fact that drug donations might have serious adverse effects on market incentives for entry of generic drugs, and thus delay the development of a competitive and low-priced market for medicines. Similarly, drug donations can distort therapeutic options for best treatment.

Up to now, analyses of drug donations—for example, WHO guidelines,^{2,3} and studies for tropical or neglected diseases^{4–6} and for disaster relief^{7,8}—have neglected market distortion effects. An early analysis showed that costs of donations were four times higher than other alternatives such as discount prices or cash donations, after taking taxes into account.⁹ WHO prefers cash donations in the aftermath of emergencies,¹⁰ and both AIDS-related and malaria-related donations have proven problematic because of transparency, market segmentation, and conditionality issues⁴ or cost-inefficient,¹¹ but not on the basis of any thorough market analysis.

In the absence of market studies, analysis of related evidence for entry of generic drugs is useful in general,^{12–27} and of antiretroviral medicines in particular.^{4,28–31} The main findings of these studies are that the number of generic entrants: (1) affects the extent of price competition,^{12,13} and the presence of eight or more competitors is related to the greatest price reductions;^{13,29} (2) positively correlates with market size (volume of sales) and expected profits,^{13,14,16,18,22,24} and with time since generic entry,^{23,24} and (3) negatively correlates with the number of incumbent generic firms,^{13,18,22} the number of competing drugs in a therapeutic class,^{14,22} the duration of the exclusivity of a product's brand name (which builds brand loyalty),²⁵ the presence of an early-entry branded generic,^{19,20} and, paradoxically, of reference pricing in one study²² but not another.¹⁵

The fact that market size and expected profits are the main drivers of entry of generic drugs is not surprising. Similarly, if the brand-name company captures post-patent market share via a branded generic or low price drug, negative effects on entry of generic drugs and ultimately price, not surprisingly, take place. Both findings show the probable effect of drug donations on the aggregated markets of GFATM recipients, because donations also capture market share, and thus demotivate generic entrants.

The basic economic argument rests on the fact that generic companies assess market prospects, uncertainty, and risk on the basis of anticipated costs, expected returns, and a prediction about how many competitors will enter or remain in the market. In making economic forecasts about whether investment of scarce resources will be profitable, generic companies must address four key issues discussed below.

How much aggregate market demand will there be and will it be possible to sell in different markets or will the product be restricted to a few markets or market segments only?

Aggregating demand from different developing countries, including middle-income and low-income countries, and public, non-governmental and faith-based organisations, and private sectors makes the market attractive for generic entrants. If donations split the market or target specific sectors, generic entrants would be left with a small and difficult market niche and a disadvantageous cost–benefit ratio.⁴ Alternatively, if the market is large, generic companies can produce at more-efficient economies of scale; if the market is large enough, several companies will enter, promoting price competition.

How will demand grow (or shrink) over time in relation to competition from other medicines and other generic producers?

Uncertainty always exists in pharmaceutical markets because innovators might produce improved products or new therapeutic alternatives. Moreover, what makes the market attractive for one generic entrant makes it simultaneously attractive for many entrants, affecting profitability. Because generic producers must recoup their investment costs over time, the inability to be certain about size, growth, duration, and competitiveness of the eventual market increases the risk of unrecoverable sunk costs or leads to higher prices at product launch.

What is the risk–benefit ratio of costs of research and development, patent and registration barriers, and product distribution systems for markets affected by donations?

Generic companies face entry costs and other barriers that are proportionately higher in markets affected by donations than in those that are not. For example, generic companies ordinarily spend at least US\$1–1.5 million—sometimes much more—to reverse engineer and formulate a product,³² after which they must invest in production processes and capacity. Before producing commercially, generic companies must be concerned about patents in countries of production and use.^{33,34} Even the establishment of patent status is often difficult,³³ and when patents exist, generic producers must pursue compulsory licences,³⁵ which is costly, time-consuming, and uncertain.³³

Thereafter, to gain marketing approval and satisfy GFATM quality standards, generic companies have to prove bioequivalence at an estimated cost of US\$1.5 million³² or more, and face many regulatory barriers,^{36–38} including: overcoming data exclusivity;³⁹ navigating complicated and expensive registration procedures; selecting a local registration agent;²⁷ facing regulatory incapacity, delay, and corruption;^{36–38} and labelling pursuant to different regulatory and language needs.^{27,40} Because generic companies need to register in every country of sale, registration-related costs are multiplied.⁴¹ Even after registration, generic producers must secure a viable local distribution system for their product in every country of sale, because many generic companies do not have in-country distribution channels in many countries, and to develop them is expensive and time-consuming.²⁷

Will the Global Fund maintain its promise as a predictable, large-scale purchaser of medicines?

Uncertainty over future payments and their timing can deter generic entry and price.²⁷ Acceptance of donations of just one drug might create uncertainty about whether donations of other drugs will be forthcoming, possibly deterring entry of generic drugs for AIDS, tuberculosis, and malaria in general. One of the great advantages of GFATM, from a generic company's perspective, is that it offers substantial buying power, and long-term and predictable guarantees of payment. If GFATM market clout is undermined because of large-scale donations, the market will look insecure for

generic forecasters. Accordingly, effects of donations can have ripple consequences that will be amplified at the scale of programming supported by the GFATM. The effect on the generic market for medicines goes beyond the market in a particular country, beyond the particular donated drug, and even beyond the GFATM share of the market. The aggregation of large-scale purchasing power from GFATM and other large initiatives, such as President's Emergency Plan for AIDS Relief, has been responsible for pushing strong competition between different generic producers. Moreover, the security of sustained funding has motivated rapid entry by generic companies for the production of medicines for priority diseases.

All these forecasting uncertainties become worse if innovators are donating products. The donated products inevitably undercut the generic price. Similarly, they necessarily shrink the residual market, at least in the short term. Although in-kind drug donations do not directly affect sunk costs and regulatory barriers, these costs and barriers might seem disproportionate in donation-affected markets.³² Anxiety about the duration or expanded product line of drug donations is the coup de grace to entry of generic drugs.

In addition to restricting donations so as to incentivise generic entry, countries should be moving towards durable, efficacious, and safe treatment protocols such as those being recommended by WHO.^{42,43} However, being captured by the lure of donations is a risk because most people and most governments find it hard to turn down free goods. Moreover, in countries where many people with AIDS are still waiting for treatment, governments might face strong political pressure, even from treatment activists, to accept free products that could increase numbers of people treated.

Although little direct evidence exists of donations' effect on government therapeutic choices, free drugs at the scale of GFATM-funded programmes might detract from the development of coherent national drug policies⁶ or, even worse, result in overcommitment by governments to therapeutically worse treatments or to selection of branded versus generic supplies of medicines.

Free products can deter or delay modification of national treatment guidelines to specify therapeutically better products, and can subtly undermine government motivation to weigh best therapeutic options independently. Donations of individually formulated products could deter government use of therapeutically improved fixed-dose combinations, many of which are only available in generic form, and of improved formulations of drugs (eg, drugs with improved stability or tolerability). They could also cause premature start of second-line regimens or reduce options for preferred, simplified second-line regimens. Finally, donations of tied products could deter use of therapeutic alternatives. For example, a therapeutic preference or true cost advantage of atazanavir and ritonavir might exist over

lopinavir and ritonavir, or of tenofovir and lamivudine over tenofovir and emtricitabine, that could be thwarted by donations.

Moreover, free products can result in product familiarity, brand loyalty, and previous-use preferences by physicians and patients, and can negatively affect prescriber practices with respect to generic equivalents.⁷ Donations often bypass drug regulatory processes, creating advantages over generic drugs. They can also cause governments to question the propriety of registering generic equivalents,⁴ and can distort drug procurement and supply systems where they result in separate arrangements for anti-retroviral drugs.⁴

Even when major pharmaceutical companies have a genuine desire for charitable donations and to act with corporate responsibility, other reasons for donations that mainly serve self-interests might exist. Tactical donations can be used to: (1) shrink market size and the certainty of sizeable GFATM financed purchases, and essentially under-cut generic drugs; (2) enhance or regain corporate goodwill through favourable publicity; (3) build product loyalty with both patients and clinicians (thereafter, when donations end, prescription habits and patient preferences continue); (4) develop or reinforce drug distribution systems for the benefit of their other drugs; (5) obtain tax advantages; (6) retain monopoly access to the private sector;⁴ and (7) discourage use of trade-related aspects of intellectual property rights (TRIPS) safeguards by both generic producers and developing countries.³³

Even more sinister motivations could result in predatory donations timed after generic companies have made substantial investments, crossed regulatory barriers, and secured distribution chains, thus punishing early entrants and warning all other prospective entrants.

Our main concern with drug donations is that emerging and more competitive pharmaceutical markets will be distorted by donations that reduce aggregate market size for competing generic products and thus deter entry of generic drugs.²⁶ Donations that produce smaller markets and fewer generic entrants will retard the development of competitive markets in which multiple generic entrants produce at efficient economies of scale, and thereafter compete for sales at or near marginal costs of production. These shrunken-market effects will negatively affect both domestic and worldwide generic producers.^{7,30} Although entry decisions of major generic producers, such as those in India, will be affected by the aggregate worldwide market,²⁷ negative effects of donations on small local producers, such as those emerging in Africa,^{44–48} will probably be even greater. Moreover, even one donation can create uncertainty about the size of the future generic market for other medicines where donations might happen, and thus donations of a subset of medicines can create uncertainty about worldwide market for an entire priority disease market, especially for antiretroviral drugs.

Treatment activists, multilateral institutions, such as WHO, developing countries, and board members should work together to resist drug donations to GFATM. Failure to defeat this revived donation initiative could pose substantial risks to GFATM's reputation. Additionally, accepting donations could have important negative effects on future costs of life-saving medicines and on future therapeutic choices.

Conflict of interest statement

BKB is a member of the Contact Group of the Northern non-governmental organisation Delegation to the Board of the GFATM, and is Chairman of Health Global Access Project, an HIV/AIDS activist organisation. EO is the Coordinator of the Ecumenical Pharmaceutical Network and an adviser of World Council of Churches. We declare that we have no conflict of interest.

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