

Generics competition in the EU, US and Canada

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The availability of generic medicines can lead to significant price reductions and savings in both developing countries (Medecins sans Frontieres: campaign for access to essential medicines, 2008) and developed countries (“Generics – providing extraordinary savings for Americans,” 2009). One of the key factors in producing these price reductions is the level of competition in the generic market (Danzon & Furukawa, 2004). In the United States (US) there is only a 6% reduction in the brand name price if there is a single generic competitor but with 2 competitors there’s a 48% reduction and with 9 competitors an 80% drop. “Without robust competition, generic manufacture does not lead to the lowest prices” in either developed or developing countries (Steinbrook, 2007).

Depending on the actions of brand name companies and the pharmaceutical policies that have been adopted, generic competition can be either delayed and/or limited thereby reducing its effectiveness. This chapter will explore both of these topics using information primarily from Canada, the European Union (EU) and the US.

In many countries there are barriers to achieving generic competition. Both Canada and the US have provisions in their patent laws that block the marketing of generic medicines if the brand name company alleges that one or more of the patents on the originator product is still valid. Such an action in these countries means that the regulatory authorities (Health Canada and the Food and Drug Administration (FDA)) cannot license the generic and the involvement of the court system is automatically triggered unless the companies involved can reach a voluntary settlement. In Canada such a manoeuvre on the part of the brand name company can delay the appearance of generics for 24 months and in the US the delay is for 30 months, or until a decision is reached in litigation.

January 2008 saw the launch by the European Commission of an inquiry into the pharmaceutical sector. The final report of the inquiry, which was released in July 2009, documents a number of tactics used by the brand name industry to delay the introduction of generic products (European Commission, 2009). Among other things, the Commission found that originator companies created “patent

clusters” to make it more difficult for generic competitors to determine if they could develop a generic version of the original medicine without infringing one of the many patents of originator company; increased the number of patent litigation cases against generic companies by a factor of four between 2000 and 2007; and appeared before national regulatory agencies claiming that generic medicines were less safe, less effective and of inferior quality compared to theirs. Some medications such as the blockbuster cholesterol medication atorvastatin are protected by 50 or more patents.

Originator companies also are increasingly marketing generic versions of their own medicines either directly through subsidiaries or through licenses with other companies. Such “authorised generics” or “pseudogenerics” have now captured about 25% of total prescription sales in Canada (Hollis, 2003). On the surface it may appear that authorised generics would increase competition and further lower prices but in reality that is not what occurs. These products are typically marketed before the appearance of independent generics thereby capturing a significant market share. Moreover, their early entry can reduce the incentive for independent generics to accelerate entry into the generic market since the “prize” for being the second or third generic is small. Of even greater concern is that the presence of authorised generics can completely block generic entry into smaller markets where the volume of sales, and hence potential profits, is not large enough to support more than a single generic (Hollis, 2003).

The first generic applicant to file for approval in the US is awarded 180 days of marketing exclusivity, during which the FDA may not approve a subsequent generic application for the same drug product. This 180-day period was intended to increase the economic incentives for a generic company to be the first to file an application and get to market. The 180-day delay for subsequent entry of new generics does not apply to authorised generics. A second FTC report revealed that if an authorised generic entered the market during the 180-day exclusivity period the independent generic would see a revenue drop of between 47% to 51%. To prevent this loss of revenue, a generic company may be willing to delay its entry in return for a brand’s agreement not to launch an authorised generic during the 180 days of marketing exclusivity. Between 2004 and 2008 the FTC reviewed 76 final patent settlement agreements between brand and generic companies and about one-quarter of these involved an explicit agreement by the brand not to launch an authorised generic combined with an agreement by the generic to

defer its entry by an average of almost 3 years. Five of the settlements covered products with annual sales of \$1 billion, \$1.1 billion, \$2.1 billion, \$2.5 billion, and \$5.3 billion (Federal Trade Commission, 2009) The FTC has sued Cephalon the maker of modafinil (Provigil®) for entering into a 2008 agreement with 4 generic makers the result of which will be that generic competition will be delayed until 2012 (George, 2008).

A relatively new approach to delaying generic entry is the focus on data protection. To gain marketing approval, generic companies typically demonstrate that their product is bioequivalent to a patented product (that is, that the generic is chemically similar and works the same in the human body) and then rely on the patented product's efficacy and safety data to earn regulatory approval. The North American Free Trade Agreement (NAFTA) establishes a minimum of 5 years of data protection. In-other-words, during this 5 year period generic companies are not allowed to use the efficacy and safety data generated by the originator company to get their own products approved. Similarly, Article 39(3) of the Trade Related Aspects of Intellectual Property Rights (TRIPs) treaty requires World Trade Organisation member countries to adopt measures to protect undisclosed test data submitted by pharmaceutical companies against "unfair commercial use", but the length of time for that protection is not specified. Although generic companies cannot use this data, neither TRIPs nor NAFTA prohibit regulatory authorities from relying on the data in their possession for the approval of competing products, a practice that falls outside the definition of unfair commercial use (Reichman, 2006).

The Canadian courts relied on this interpretation of NAFTA and TRIPs to rule that "When a generic manufacturer files an Abbreviated New Drug Submission (ANDS), [a marketing application] the safety and effectiveness of the generic product may be demonstrated by showing that the product is the pharmaceutical and bioequivalent of the innovator's product. If the generic manufacturer is able to do so solely by comparing its product with the innovator's product which is being publicly marketed, the Minister will not have to examine or rely upon confidential information filed as part of the innovator's New Drug Submission (NDS). In such case, the minimum five year market protection referred to in the regulation will not apply" (Correa, 2002).

This interpretation was an anathema to the brand name industry as witnessed by the following quote from Pharmaceutical Research and Manufacturers of

America “Canadian authorities allow parties other than the right holder to effectively gain marketing approval in direct reliance of protected confidential data. This violates TRIPS Article 39.3 as it eliminates the TRIPS requirement to prevent “unfair commercial use” of protected data. We urge the United States to move data protection to the top of the bilateral commercial agenda with Canada” (Pharmaceutical Research and Manufacturers of America, 2003). As a result of lobbying by the pharmaceutical industry, Canada amended its regulations on data protection to allow for 8 years of data exclusivity (i.e., during this time Health Canada cannot use the safety and efficacy data from the originator product) such that, in the government’s words, “Eligible innovative drugs ... will thus receive an internationally competitive, guaranteed minimum period of market exclusivity” (Government of Canada, 2006).

Extending data protection domestically and internationally is on the agenda of both the US and the EU. Since the TRIPs agreement came into effect, the US has negotiated a series of bilateral free trade agreements (FTAs) that significantly extend the obligations with respect to data protection. “They oblige the [other partners in the FTAs] to grant exclusive rights for at least five years counted from the date of approval of the product, irrespective of whether it is patented or not and, in most cases, of whether the data are undisclosed or not. Such exclusivity will apply irrespective of whether the national health authority requires the submission of the data or not (i.e. even in cases where it relies on the approval made in a foreign country)” (Correa, 2006). Within the US legislation is before Congress that would guarantee manufacturers 12 years of market exclusivity for a new biologic agent irrespective of whether or not the original product had a valid patent. “Manufacturers could also obtain an additional 12-year exclusivity period by making minor changes to the structure of an approved product, such as those that could lead to changes in administration schedules (e.g., from weekly to monthly)” (Engelberg, Kesselheim, & Avorn, 2009).

Although as recently as 2004, EU countries were strongly opposed to FTAs with increased protection for intellectual property rights, that position has changed. The EU is now pursuing FTAs with developing countries such as Colombia, Peru, India, the Central American trading bloc, and the ASEAN countries. As part of the negotiations the EU is seeking up to 11 years of data protection (Correa, 2006). Domestically, the EU went from a situation where the Member Countries had data protection ranging from 6 to 10 years to a position where all members are required to grant 8 years of data exclusivity. There are also 2 additional years of

market exclusivity during which time generic companies can start the necessary bioequivalence studies in anticipation of patent expiry (however the product cannot be licensed until this 2 year period has passed) plus one additional year of protection for new indications of original products (Adamini, Maarse, Versluis, & Light, 2009).

Finally, brand name companies engage in a practice termed “evergreening”. Evergreening is a term that encompasses a wide variety of tactics all of which are aimed at extending the effective monopoly period enjoyed by brand name products. In some cases, companies develop new formulations of products such as extended release versions that can be taken once a day instead of 2 to 3 times per day required with the original product. Abbott Laboratories has agreed to pay \$22.5 million to settle allegations brought by 23 US state attorneys general that it tried to block generic competition to a cholesterol medicine. The lawsuit alleged that Abbott had made minor changes to the formulation of [SEP]the medicine to prevent the launch of less expensive generics (Perrone, 2010).

Other times companies may combine the existing product with a second active ingredient. Typically these “new” drugs are marketed just before the time when the patent on the original medicine is due to expire in a bid to switch prescribing before generic versions of the original medicine appear (Steinbrook, 2007). A slightly variation of evergreening involves taking a medicine that is a racemic mixture (i.e., one that has two mirror image molecules, only one of which is the active ingredient) and marketing the active molecule as a new drug. Examples of this practice are omeprazole (Losec®) and esomeprazole (Nexium®) and citalopram (Celexa® in the US and Canada) and escitalopram (Lexapro® in the US and Canada) (Svensson & Mansfield, 2004).

Although a few of the practices described in this section have been found to be illegal mostly they are legal efforts by the brand name companies to extend their monopoly period and increase the profits that they derive from their products. In order to ensure that generic competition produces the maximum benefits it will be necessary to reorient laws around intellectual property rights to accelerate the introduction of generics. For example, companies could be limited in the number of patents that they are allowed to file for any individual drug or extensions to data protection could be rolled back. As expenditures on prescription medicines continue to increase generic competition will become increasingly important as one method of restraining spending in this area.

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