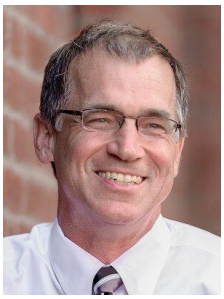
A Look At The Economic Impact Of Drug Patent Differentiation

By **Jonathan Putnam, Ngoc Ngo and Ratib Ali** (September 23, 2024)



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Recently, the Federal Trade Commission has pushed to compel the delisting of certain patents held by branded drug manufacturers from the U.S. Food and Drug Administration's "Orange Book" database, on the grounds that they do not claim the underlying drug.

Such patents may instead claim a method of treatment or some other aspect of formulating or delivering the drug. While some manufacturers have complied with the FTC's demands, others, like Boehringer Ingelheim Pharmaceuticals Inc. and Teva Branded Pharmaceutical Products R&D Inc., have challenged them.[1]

Behind the FTC's effort to delist Orange Book patents lies its belief that so-called junk listings delay generic competition and inflate drug prices.[2] Under FTC Chair Lina Khan's expansive view of the FTC's enforcement authority, improper patent listing may "constitute unfair methods of competition in violation of Section 5 of the Federal Trade Commission Act."[3]

The Orange Book policy statement refers pointedly to the possibility of criminal liability and the prospect of referral to the U.S. Department of Justice, and even to scrutiny of "a firm's history of improperly listing patents during merger review."[4]

Leaving aside the nature of liability, the economic question is: What would competition have looked like if it had not been — allegedly — delayed?

In addition to occurring sooner, that competition would not have occurred between two or more identical products, but between products that are said to be differentiated.

Differentiated Product Competition

When multiple patents protect different aspects of the same product, the product is differentiated.

For example, a simple drug — whose active ingredient may have gone off-patent — may be differentiated by different formulation, delivery or method-of-treatment patents.

Differentiation — a time-honored way to improve an initial innovation like an active ingredient — expands the dimensions in which buyers compare and match themselves to other product features, and trade off price for features. When protected by patents, such differentiation also extends an innovator's partial exclusivity over the product and softens competition with products, like an off-patent generic, that lack the patented features.

In litigation, product differentiation complicates the creation of a "but-for" world, which is usually instrumental in determining both antitrust liability and infringement damages. To construct such worlds, economists often must take into account more complex substitution

patterns, induced by nonoverlapping product features, which are not reflected in simple market shares.

For example, suppose products A, B and C have market shares of 20%, 30% and 50%, respectively. Under the Mor-Flo rule, or proportional diversion, removing product C entirely from the marketplace, at a 0% share, implies but-for market shares for A and B of 40% and 60%, respectively.

Similarly, if — through the loss of some but not all differentiation, such as allegedly would be accomplished by patent delisting — C's but-for market share falls to 40% instead of 0%, then A's would be 24% and B's would be 36%.

But when products are differentiated, the diversion of C's share to B may be more than proportional, if B is a closer substitute for C than is A.[5] For example, if A is a "taking a train to the city," B is "taking a blue bus," and C is "taking a red bus," then it is much more likely that consumers who can no longer choose C will choose B than A.

In differentiated pharmaceutical markets, product C may be available, but the scope of its true patent protection may, allegedly, be different from that listed in the Orange Book, allegedly requiring a partial redistribution of its market share between better and worse substitutes that practice different patents.

Moreover, such substitution patterns depend in general on patient characteristics, not just product or patent attributes, so the potential redistribution patterns may be even more complex to infer from actual market shares.

Case Studies

Two recent cases illustrate the need for better economic analysis of such substitution patterns in differentiated pharmaceutical markets.

In Amgen Inc. v. Hospira Inc. in the U.S. District Court for the District of Delaware in 2018, Amgen sued Hospira and Pfizer Inc. for infringement of a process patent allegedly used in the manufacture of Pfizer's biosimilar for the treatment of neutropenia in cancer patients; Amgen did not itself use the patent.

Because biosimilars are only "similar" to the reference biologic, they need not produce the same patient response and thus need not substitute perfectly for the reference product.

Amgen alleged that, in the market segment for short-acting neutropenia treatments, or filgrastim, competition from Pfizer's biosimilar Nivestym had a disproportionately large downward effect on the sales and price of Amgen's short-acting biologic Neupogen, with consequently large damages.

An econometric model, based on the widely employed BLP differentiated products method,[6] was used to estimate the model on data collected and published by Intercontinental Medical Statistics. The analysis established two critical facts.

First, Nivestym's actual substitution for Neupogen was substantially less than that predicted by Nivestym's share alone. Second, much of the market substitution for Neupogen actually came from Amgen's own long-acting neutropenia treatment Neulasta, or pegfilgrastim, even though Neulasta is generally classified in a different market segment.

In other words, the econometric results showed both the lesser substitutability of the defendant's product, and the greater substitutability of the plaintiff's differentiated — albeit competing — product. Both results diminished the impact of Nivestym on Neupogen's sales and price erosion, sharply reducing damages.

A different economic puzzle presented itself in Exeltis USA Inc. v. Lupin Ltd. in the District of Delaware in September, which concerned an oral contraceptive.

There, a defendant challenged a patentee's commercial success evidence by arguing that "a 2% market share does not establish commercial success," and that because the patentee charged a much higher price than its generic competitors, the patentee's "revenue share analysis is 'unhelpful' because oral contraceptives are largely generic products that cost less, so a revenue share analysis 'will be driven more by price differential and less by volume.'"[7]

Ultimately, the court redefined the market — apparently without formal economic analysis — and believed that the patented product's "acquisition of a substantial market share exceeded expectations and is evidence of commercial success."[8] The court also found a nexus of success to the patent, based on technical testimony.

The Exeltis court's "belief" – that market share exceeded expectations — could be and was tested directly using econometric methods in Newron Pharmaceuticals SpA v. MSN Laboratories Private Ltd. last April, in which the defendants challenged the validity of Newron's patent on Xadago, or safinamide, an MAO-B inhibitor used in the treatment of Parkinson's disease.

Like the oral contraceptive market, the MAO-B inhibitor market is differentiated, comprising multiple branded and generic products, among which only Xadago faced no generic competition and charged a high price. Here, Xadago's market share was only 3%. Thus, given Xadago's very low share, was the product "commercially successful" and, assuming success, was there a nexus to the disputed patent?

The same econometric model answered both questions, by explaining market share in terms of each product's observable characteristics, notably including its price.

In Xadago's case, its high price undoubtedly contributed to its very small share. But econometric estimates determined that Xadago sold more than three times as many units as would have been expected from its high price alone.

In other words, a surprisingly large segment of the patient population preferred Xadago, even at its high price, over its much cheaper alternatives, definitively exceeding expectations. Those excess sales revealed consumer preferences for the characteristics uniquely offered by the Xadago patent, also establishing nexus.

Liability and Damages When Pharmaceutical Products Are Differentiated by Patents

Given the FTC's recent emphasis on unfair competition based on disputed patent listings, pharmaceutical litigants are likely to require nuanced characterizations of actual and but-for market competition when the parties dispute which patents differentiate competing products.

Beyond claims for delayed competition, litigants must grapple with potentially complex

product substitution patterns among therapeutically distinct products, including substitution patterns that never occurred, but that must be inferred from existing data. Such inferences play a role in determining liability — whether based on pricing or quantities — and in damages for overcharge or delay.

Private litigants who face — or wish to bring — a claim for improper Orange Book listings would do well to bear in mind the need for, and the utility of, formal econometric methods that go beyond simple heuristics like market shares and prices.

As in Amgen, econometric evidence helps to determine market substitutes and thus to define markets, which is essential to the correct determination of market shares.

Because not all substitutes are created equal when products are differentiated, econometric evidence also helps determine the cross-price elasticity of demand and other evidence regarding the second choice of a consumer who selected a product that either should not have been available, or that was allegedly mislabeled. Such evidence also helps determine whether, if a product was mislabeled, another product would have been the consumer's first choice.

When confronting differentiated product markets, only formal econometric evidence, like that presented in Newron, can test beliefs about the relationships among unit sales, prices and revenues. Such evidence may prove central to arguments about whether any given patent — whether one erroneously listed, or an undisputed one — did or did not cause sales.

Ultimately, differentiated product market analysis requires many of the same tools as merger analysis, where market definition and substitution patterns play central roles.

While the FTC, and and the U.S. Department of Justice, obviously have vast merger experience, a private litigant can use such history to its advantage in holding the agencies to the same economic standards as they have applied in the past, even as they seek to expand their regulatory reach.

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Disclosure: The firm acted on behalf of Pfizer in the Amgen-Hospira case and on behalf of Newron in Newron v. MSN Laboratories.

[1] See e.g. Elai Katz, Lisa Rumin and Betty Zhang, "How Orange Book Antitrust Scrutiny Is Intensifying," Law360.com, July 29, 2024. Available at: https://www.law360.com/articles/1861297.

[2] "By filing bogus patent listings, pharma companies block competition and inflate the cost of prescription drugs, forcing Americans to pay sky-high prices for medicines they rely on," said FTC Chair Lina M. Khan. "By challenging junk patent filings, the FTC is fighting these

illegal tactics and making sure that Americans can get timely access to innovative and affordable versions of the medicines they need." U.S. Federal Trade Commission, FTC Expands Patent Listing Challenges, Targeting More Than 300 Junk Listings for Diabetes, Weight Loss, Asthma and COPD Drugs, April 30, 2024. Available at: https://www.ftc.gov/news-events/news/press-releases/2024/04/ftc-expands-patent-listing-challenges-targeting-more-300-junk-listings-diabetes-weight-loss-asthma.

[3] U.S. Federal Trade Commission, Federal Trade Commission Statement Concerning Brand Drug Manufacturers' Improper Listing of Patents in the Orange Book ("Orange Book Policy Statement"), September 14, 2023. Available at: https://www.ftc.gov/system/files/ftc_gov/pdf/p239900orangebookpolicystatement092023.pdf.

[4] Id.

[5] Non-proportional diversion is an extension to non-price features of the "law of demand," which the Federal Circuit has said "all markets must respect." Crystal Semicond. v. Tritech Microelec., 246 F.3d 1336, 1359 (Fed. Cir. 2001).

[6] Berry, Steven, James Levinsohn, and Ariel Pakes. "Automobile Prices in Market Equilibrium." Econometrica 63(4) (July 1995): 841–90.

[7] Trial Opinion, Exeltis USA, Inc., et al. v. Lupin Ltd. and Lupin Pharmaceuticals, Inc., C.A. No. 22-00434-RGA (D. Del. September 4, 2024), slip op. at 60.

[8] Id. at 61.

[6] Berry, Steven, James Levinsohn, and Ariel Pakes. "Automobile Prices in Market Equilibrium." Econometrica 63(4) (July 1995): 841–90.