

Drug Reformulation Regulatory Gaming in Pharmaceuticals: Enforcement & Innovation Implications

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ABSTRACT

This article examines drug reformulation regulatory gaming as a vehicle for analyzing the way in which European courts and the Commission are currently approaching innovation issues in the pharmaceutical sector. First, the economics literature regarding pharmaceutical innovation is briefly summarized. Next, the phenomenon of regulatory gaming is introduced, followed by an analysis of the two primary theories of harm being used to address drug reformulations as a competition concern. In comparing the recent General Court decision in *AstraZeneca* to earlier U.S. court cases addressing similar conduct, it is asserted that these approaches differ in significant ways with regards to preservation of innovation incentives as well as on the basis of institutional and evidentiary concerns. Finally, this discussion is then placed into the broader context of the ongoing debate regarding pharmaceutical innovation that first surfaced in the *Syfait* cases—in particular, the desirability of sector-specific competition law analysis of pharmaceutical innovation.

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I. INTRODUCTION

The pharmaceutical industry is a useful place to begin a study of the role of competition law in innovation for a number of reasons. Patricia Danzon has highlighted two particular characteristics of pharmaceutical markets which make them interesting from a law and economics standpoint. First, standard market analysis of pharmaceuticals “must take into account its unusually high rate of R&D, which implies a high rate of technical change, critical importance of patent protection, potential for market power and novel price and product competitive strategies.”¹ Second, the industry is heavily regulated.² Furthermore, unlike other industries that have been at the center of much of the innovation debate up to this point, certain factors that can greatly complicate the analysis are not present in pharmaceuticals. For example, there are not the same network effects as is the case with computer software. Not only may this clarify and simplify the analysis, but it also may provide a useful example to compare to *Microsoft* to assess the flexibility of the enforcement agencies in adapting their innovation policy to the particulars of the industry. Perhaps the most important reason, however, is that in recent years the rate of radical innovation, in the form of novel drug introduction, has been in decline in both Europe and the US.³ Because this trend has garnered significant attention from enforcement agencies, we are presented with a situation where the agencies are explicitly attempting to use competition law levers to promote innovation.

Although these factors make pharmaceuticals a very interesting case study for questions related to innovation and the law, they also make that case a difficult one. In recognition of this, the sector has garnered increasing levels of attention in recent years—including major enforcement decisions⁴ and a sector inquiry, which was completed in July 2009.⁵ Each of these efforts demonstrates the Commission’s commitment to developing a clearer understanding of the industry, and therefore also of the nature of the innovation that drives much of the competition in the industry. This article will focus on two of these endeavors to explore the debates that arose from them and to glean from them indications of the perceptions of the Commission and the courts with regards to pharmaceutical innovation.

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¹ Patricia M. Danzon, *The Pharmaceutical Industry*, in 5880 THE ENCYCLOPEDIA OF LAW & ECONOMICS 1055 (Boudewijn Bouckaert and Gerrit De Geest eds., 1999).

² *Id.*

³ Pharmaceutical Sector Inquiry Final Report, European Commission, Competition DG at ¶80 (8 July 2009) (hereinafter “Sector Inquiry Report”) (noting that for the years 2000–2007, the average number of novel molecular entities launched was 27, whereas for the years 1995–1999, the average was 40).

⁴ IV/36.957/F3 *Glaxo Wellcome* (notification), IV/36.997/F3 *Aseprofar and Fedifar* (complaint), IV/37.121/F3 *Spain Pharma* (complaint), IV/37.138/F3 *BAI* (complaint), IV/37.380/F3 *EAEPC* (complaint), 8 May 2001, OJ [2001] L 302/1 (holding that Glaxo Wellcome’s dual pricing scheme with distributors violated Art. 81 (now Art. 101)) (“Glaxo Spain case”); *Synetairismos Farmakopoion Aitolias & Akarnanias (Syfait) v. Glaxosmithkline* (C53/03), [2005] 5 C.M.L.R. 1, [2008] 5 C.M.L.R. 20 (“Syfait I”) (involving allegations related to GSK’s supply quota system aimed at providing only sufficient supplies to meet the demand of the national market, thereby reducing the supply available for arbitrage); *Sot Lelos kai Sia EE v. GlaxoSmithKline AEVE*, Case C-468/06 (“Syfait II”).

⁵ *Id.*

Firstly, I briefly recount the standard narrative regarding the nature of the pharmaceutical industry and the economics of drug innovation (Part II). Then I will briefly summarize the Commission's approach to enforcement in the pharmaceutical sector (Part III). I will present the *AstraZeneca*⁶ case and the two primary approaches to regulatory gaming, and offer a critique on the basis of their probable impact on innovation (Part IV). I will then introduce the ongoing debate over the proper role for industry-specific characteristics in competition law enforcement, as well as discuss the ways in which the common story regarding the nature of pharmaceutical innovation has come into question (Part V).

II. THE ECONOMICS OF PHARMACEUTICAL INNOVATION

The nature of innovation in the pharmaceutical industry has been the subject of extensive research. As one economist summarized, “[t]he pharmaceutical industry is a textbook example of a science-based sector characterized by high R&D cost, uncertainty and spillovers, for which patent protection assures appropriability, thus providing incentives for innovation.”⁷ “To the extent that market power exists, it results largely from legal restrictions and other institutional factors” such as patents and the separation of decision makers from payers.⁸ While there are two categories of supplier firms in the market, originators and generics, innovation almost exclusively comes from originator firms. Originator firms are “research-based” and “compete[] through innovation,” whereas generic firms “compete through the traditional means of price and quality.”⁹

The structure of pharmaceutical R&D is in a process of transition and change. The level of basic research carried out by firms in-house has been declining,¹⁰ and originators increasingly enter the process at the development and testing phases.¹¹ One possible reason why large originator firms have this advantage in the later stages of drug development is risk. Although the risk associated with any particular development effort is very high, the ability of large pharmaceutical firms to diversify across their portfolio of development projects brings the overall risk faced by originators down to average levels.¹² Another contributing factor is that small research firms and biotechnology firms do not usually have the resources required to carry out the testing trials required for regulatory approval. Current estimates suggest that 25-40% of current sales by large originator firms are from products that originated in the biotech sector.¹³

Pharmaceutical innovation is generally categorized as either radical or incremental.¹⁴ Radical innovations are generally taken to be a new molecular entity (NME).¹⁵ Incremental innovations, on the other hand, fall into one of two categories: (1) me-too drugs, and (2) reformulations. Follow-on drugs have been defined as “a new entrant to a therapeutic class that had already been defined by a separate drug entity that was the first in the class to obtain regulatory approval for marketing.”¹⁶ Thus, usually this involves a rival originator introducing a competing substitute product to the drug that was first in class. Furthermore, the characterization of follow-on's as incremental may be misleading since there is evidence to suggest that it is not intended to be incremental, but ends up incremental if that particular research effort doesn't reach the market first.¹⁷ Product reformulations, however, almost always involve an originator altering or improving its own product and introducing it as a new version of the original. It is commonly used as a strategy towards the end of a drug's patent life as a means of confronting generic competition.

In terms of innovation as a policy matter, the focus has predominantly been on radical innovation because the originator market is believed to operate according to a blockbuster drug structure. In this model, originator pharmaceutical firms organize their R&D expenditures and efforts around the search for drugs with

⁶ Case T-321/05, *AstraZeneca AB and AstraZeneca plc v. European Commission* Celex No. 605A0321(1 July 2010).

⁷ Magazzini et al., *Patent Disclosure and R&D Competition in Pharmaceuticals*, 18 *ECON. INNOVATION & NEW TECH.* 467, 467 (2009).

⁸ Danzon, *supra* note 1 at 1069.

⁹ Jürgen Backhaus, *Competition, Innovation and Regulation in the Pharmaceutical Industry*, 4 *MANAGERIAL AND DECISION ECONOMICS* 107, 109 (1983).

¹⁰ Robert J.W. Tijssen, *Is the Commercialisation of Scientific Research Affecting the Production of Public Knowledge? Global Trends in the Output of Corporate Research Articles*, 33 *RESEARCH POLICY* 709–733, 727 (2004) (“The observed trends in the output of corporate research articles published in recent years suggest that...corporate basic research is being downsized...”).

¹¹ William S. Comanor, *The Economics of Research and Development in the Pharmaceutical Industry*, in *PHARMACEUTICAL INNOVATION: INCENTIVES, COMPETITION, AND COST-BENEFIT ANALYSIS IN INTERNATIONAL PERSPECTIVE* 67 (eds. Frank A. Sloan & Chee-Ruey Hsieh 2007).

¹² Danzon, *supra* note 8 at 1066.

¹³ Comanor, *supra* note 11 at 54.

¹⁴ It is worth noting that more detailed categorization schemes have been used. See Christian Sternitzke, *Knowledge Sources, Patent Protection, and Commercialization of Pharmaceutical Innovations*, 39 *RESEARCH POL'Y* 810, 813 (2010) (used a four category scheme to differentiate types of innovations: (1) Incremental Innovation – minor changes in the technology base, low extra benefits to consumers; (2) Market Breakthrough – minor changes in technology, high level of consumer benefits; (3) Technology Breakthroughs – novel technology base, low consumer benefit; (4) Radical Innovation – novel technology base, substantial consumer benefit).

¹⁵ *Id.*

¹⁶ Joseph A. DiMasi & Cherie Paquette, *The Economics of Follow-On Drug Research and Development: Trends in Entry Rates and the Timing of Development*, 22 *Supp. 2 PHARMACOECONOMICS* 1-14 (2004).

¹⁷ *Id.*

the greatest revenue potential (based on potential patient population size and that population's ability to pay). This is borne out in econometric studies, which have observed that the distribution of sales revenue in the industry is highly skewed.¹⁸ In 2000, Grabowski & Vernon found that the top decile (in terms of profitability) of drugs accounted for 56% of overall sales revenue.¹⁹

This skew can be explained as a result of the fact that the originator industry is characterized by fixed costs that are high relative to variable costs. "A consequence of such a cost structure is that, in the short run, it will be profitable for the firm to sell output at prices that cover the lower incremental costs and yield some margin above those costs, but fall far short of total average unit costs."²⁰ This results in many drugs being marketed "despite very small peak revenues and quasi-profits that are a small fraction of mean R&D costs because if the uncertainties surrounding a compound's prospects are not resolved until clinical development is largely complete, most R&D costs are sunk."²¹ While it is universally understood that pharmaceutical R&D entails a high rate of failure,²² late stage failure is especially troublesome because drug testing trials (which is what happens during these later stages of development) are very expensive.²³

Recently, however, some have argued that this almost exclusive focus on radical innovation has overlooked and disregarded legitimate and meaningful incremental innovations. The incremental innovation associated with drug reformulations, although to a lesser extent than NMEs, requires the dedication of significant R&D resources. One study estimates that post-approval R&D expenditures constitute approximately 25.8% of total R&D expenditures.²⁴ Furthermore, there is evidence that these incremental innovations may provide significant benefits to consumers. Berndt, Cockburn, & Grepin (2006), in their study of drug utilization and supplemental indications, found that in two of the three drug classes they studied "utilization in patients with diagnoses outside each drug's initially approved indication accounts for 70-80% of total use."²⁵ They concluded that these results support the notion that incremental innovation seems to constitute an important metric of overall productivity.²⁶

Aside from their value as stand-alone innovation directly providing benefits to consumers, drug reformulations may also play a role in radical innovation. One possibility arises from the fact that the pharmaceutical industry is one in which knowledge spillovers between firms and from other research sources (government and universities) play an important role. The heavy reliance on patents aids this system by encouraging new knowledge disclosure in patent applications. Both failures and successes can be valuable spillovers.²⁷ These spillovers can encourage innovation on two levels: (1) increase the likelihood of success of current research efforts by offering insights from other efforts and facilitating in-licensing of developments from other sources; and (2) incentivizing R&D expenditure by firms to enhance their ability to incorporate these spillovers, known as "absorptive capacity".²⁸ Absorptive capacity is thought to be essential to pharmaceutical R&D efforts because "[a]lthough a public good, science is not a 'free' good. Internal scientific capacities are critical for taking advantage of the public good."²⁹ One recent study concluded that absorptive capacity is more important for generating radical innovations, than for other types of innovation.³⁰ Thus, the R&D related with product reformulations may spillover into efforts to develop new novel drugs.

The other avenue by which product reformulations may drive radical innovation is that the expectation of potential opportunity for further innovation to improve a product may provide incentives to engage in novel drug development. In other words, it is possible that anticipation of the possibility of improving a product, such as a drug, is an important source of incentives to develop new branded drugs in the first place.³¹ Others, however, criticize this suggestion, arguing that full recognition of incremental innovation weakens incentives to

¹⁸ Henry Grabowski & John Vernon, *The Determinants of Pharmaceutical Research and Development Expenditures*, 10 J. EVOL. ECON. 201 (2000).

¹⁹ *Id.*

²⁰ Uwe Reinhardt, *The Pharmaceutical Sector in Health Care*, in PHARMACEUTICAL INNOVATION: INCENTIVES, COMPETITION, AND COST-BENEFIT ANALYSIS IN INTERNATIONAL PERSPECTIVE 34-35 (eds. Frank A. Sloan & Chee-Ruey Hsieh 2007).

²¹ *Id.*

²² A study by the Pharmaceutical Research and Manufacturers of America found that for every 10,000 potential compounds investigated by American drug originator firms, only one ultimately successfully is approved for patient use by the FDA. *Id.* at 31.

²³ William S. Comanor, *The Economics of Research and Development in the Pharmaceutical Industry*, in PHARMACEUTICAL INNOVATION: INCENTIVES, COMPETITION, AND COST-BENEFIT ANALYSIS IN INTERNATIONAL PERSPECTIVE 59 (eds. Frank A. Sloan & Chee-Ruey Hsieh 2007).

²⁴ DiMasi, et al., *The Price of Innovation: New Estimates of Drug Development Costs*, 22 J. HEALTH ECON. 185 (2003).

²⁵ Ernst R. Berndt, Iain M. Cockburn, and Karen A. Grepin, *The Impact of Incremental Innovation in Biopharmaceuticals: Drug Utilisation in Original and Supplemental Indications*, 24 Supp.2 PHARMACOECONOMICS 69, 81 (2006).

²⁶ *Id.*

²⁷ Magazzini et al., *supra* note 7 at 469.

²⁸ See e.g., Wesley M. Cohen and Daniel A. Levinthal, *Innovation and Learning: The Two Faces of R&D*, 99 ECON. J. 569 (1989); Sternitzke, *supra* note 14.

²⁹ Comanor, *supra* note 23 quoting Alfonso Gambardella, *SCIENCE AND INNOVATION: THE U.S. PHARMACEUTICAL INDUSTRY DURING THE 1980S* 103 (Cambridge University Press 1995).

³⁰ Sternitzke, *supra* note 14 at 816.

³¹ Berndt et al., *supra* note 25 at 71 ("The available evidence suggests that the prospect of additional sales beyond the initial indication provides commercial justification for extensive R&D expenditure.")

generate radical innovations. “Although generic competition drives out economic profits on brand-name products post patent expiration, rather than rest on their laurels, such competition forces brand-name pharmaceutical manufacturers to invest in new products and maintain a healthy pipeline of products under development.”³² Although there are no definitive answers as to which of these ideas is more accurate, this debate exposes two very different perspectives on the consumer benefits associated with drug reformulations.

At first blush, generic-branded competition appears to be different than many of the other innovation cases we’ve seen because generics and branded drugs are substitutes for one another, whereas the other cases predominantly involved complementary goods. But part of what makes this theory of harm so complex though is that the drug substitution laws functionally transform the relationship between generics and branded drugs into one with complementary goods characteristics. “The generic manufacturer needs prescriptions for the branded product to take advantage of automatic substitution by the pharmacist...[t]he generic requires the brand to make automatic substitution sales.”³³

The drug reformulation regulatory gaming cases discussed in Part III are the product of this disagreement over the value to consumers from these reformulations, combined with the fact that market power in pharmaceuticals arises largely from legal and institutional factors. Depending on the specific form of the reformulated drug, introduction of such drugs may harm generic competition in two ways: (1) delay entry of generics, and/or (2) impeding generic substitution for branded prescriptions. In the US, for example, the introduction of a product line extension “delays generic substitution for the new branded product because the firm must file a second ANDA, which faces the same lengthy FDA review as the first one.”³⁴ Strategies to delay generic entry can be particularly important because of the significant role timing plays in the success of the product switch.³⁵ Product switches are much more difficult, and therefore less likely to succeed, where “generic versions of the old product have already entered the market before or simultaneously with the reformulated product.”³⁶ One possible cause for this are the differences in the nature of the pricing environment in these situations—if generics enter first, the price will have already dropped and therefore switching to a follow-on or reformulation would involve a price “penalty” on the consumer.³⁷

III. THE COMMISSION’S APPROACH TO PHARMACEUTICALS

The past decade has seen a major shift in the approach taken by the Commission towards enforcement efforts in the pharmaceutical sector. The general trend has been away from predominantly intra-brand concerns and towards an emphasis on inter-brand issues. “Traditionally, the Commission’s anti-trust enforcement activity in the pharmaceutical sector has focused on removing private obstacles to parallel trade in pharmaceuticals within the Single Market.”³⁸ These intra-brand cases have been pursued under both Article 101 (concerted conduct), as we saw in the *Glaxo Wellcome*³⁹ case involving the Spanish market, as well as Article 102, as was the case in *Syfait*, which involved GlaxoSmithKline in the Greek market.⁴⁰

In 2005 however, the *AstraZeneca* case (discussed more fully in Part III), signaled a major shift in the enforcement priorities of the Commission with respect to pharmaceuticals. This shift was explicitly driven, at least in part, by innovation concerns. According to then Commissioner Kroes, cases like *AstraZeneca* were aimed at the promotion of inter-brand competition “in innovation for patented medicines between the pharmaceutical producers,..., and to encourage inter-brand competition from generic substitutes after patent expiry” thereby increasing price competition.⁴¹ Indeed, in its Pharmaceutical Sector Inquiry Final Report, the Commission asserted that its initiatives include “creating a business environment that stimulates research, boosts valuable innovation and supports the competitiveness of the industry.”⁴² Alongside this goal, however, the Commission acknowledged that drug prices and public budgets are also a major concern and “are under significant constraints” so “[c]ompetition, in particular competition provided by generic medicines, is essential...”⁴³

³² Frank A. Sloan and Chee-Ruey Hsieh, *Conclusions and Policy Implications, in PHARMACEUTICAL INNOVATION: INCENTIVES, COMPETITION, AND COST-BENEFIT ANALYSIS IN INTERNATIONAL PERSPECTIVE* 270 (2007).

³³ Richard Gilbert, *Holding Innovation to an Antitrust Standard*, 3 *COMPETITION POL’Y INT’L* 47, 74 (2007).

³⁴ Stacey L. Dogan & Mark A. Lemley, *Antitrust Law and Regulatory Gaming*, 87 *TEX. L. REV.* 685, 687 (2009).

³⁵ Sector Inquiry Report, *supra* note 3 at ¶1010.

³⁶ *Id.* at ¶1024.

³⁷ *Id.* at ¶1026.

³⁸ Nadia De Souza, *Competition in Pharmaceuticals: the challenges ahead post AstraZeneca*, *Competition Policy Newsletter* No.1 39–43, 39 (Spring 2007).

³⁹ *Glaxo Spain*, *supra* note 4.

⁴⁰ *Syfait I*, *supra* note 4.

⁴¹ *De Souza*, *supra* note 38 at 41 quoting Commissioner Neelie Kroes’ reply to Oral Question put by the honourable Member of the European Parliament Mr. von Boguslaw Sonik (H-0459/06).

⁴² Sector Inquiry Report, *supra* note 3 at ¶5.

⁴³ *Id.* at ¶11.

Although not expressly framed in this way, it seems implicit in this approach that the Commission views vigorous post-patent lapse competition from generics as also contributing to innovation incentives for originator producers. The rationale behind such a perspective would presumably be that generic competition drives down the rents reaped by originators on existing drugs, which motivates them to seek the monopoly rents possible with the development and introduction of novel drugs. This more nuanced and focused approach indicates that the Commission is intent on taking a more active approach in using competition law enforcement as a tool to stimulate innovation in pharmaceuticals. That being said, however, many questions remain as to the Commission's perspective on many specific innovation policy questions related to competition law enforcement. This paper hopes to highlight two in particular: (1) how to balance and/or prioritize the importance of incremental vs. radical innovation in a particular industry; and (2) the extent to which industry-specific characteristics should influence competition law rules and their application.

IV. DRUG REFORMULATION REGULATORY GAMING

As noted above, a distinctive characteristic of the pharmaceutical industry is that it is subject to extensive regulation. In addition to those aimed at protecting public health and safety, some regulations are intended to address market competition concerns—particularly the idiosyncrasies of demand for pharmaceutical drugs. For example, information asymmetries exist between patients and physicians, and between physicians and pharmaceutical firms, as to overall efficacy and the price-quality tradeoff of various drugs.⁴⁴ This, combined with problems of agency and moral hazard arising from the fact that those responsible for selecting drugs are not the same entity paying for them, results in price being less responsive to quality.⁴⁵ A problematic side-effect of imposing broad and wide-ranging regulation covering things like firm entry, product introduction and withdrawal, and using regulations to promote the use of generic drugs where possible, is that it creates opportunities for players to use those regulations to achieve ends unintended by regulators. This type of conduct has come to be known as “regulatory gaming” and has been defined as “private behavior that harnesses pro-competitive or neutral regulations and uses them for exclusionary purposes.”⁴⁶

Some commentators have gone so far as to suggest that “[t]he pharmaceutical industry presents a perfect storm for regulatory gaming.”⁴⁷ Indeed, regulatory gaming in the pharmaceutical context has taken many forms. One form in particular though has been receiving increasing attention in recent years in both the US and Europe—drug reformulations. These drugs are second-generation versions of successful branded drugs, and for this reason have also been called “product line extenders” by the industry. Follow-on drugs commonly take the form of drug reformulations, different dosing protocols, and new delivery methods, sometimes resulting in new indications in which the drug can be used.⁴⁸ Critics argue that this practice generally involves little, if any, true innovation and is primarily aimed at delaying generic entry or otherwise hampering the competitiveness of generic drug firms by closing off important means of distribution, which results in higher drug costs.⁴⁹ Others, however, defend follow-on drugs as a legitimate form of incremental innovation because they increase the range of products available to consumers and can often offer significant benefits to some or all patients taking the drug.⁵⁰

A major reason why regulatory gaming has attracted so much attention of late is that some have drawn a link between the aforementioned decline in radical drug innovation rates and an uptick in the number of follow-on drugs. Although innovation is usually viewed as the very essence of pro-competitive activity, there has been a judgment by some that these trends are bad for consumers. These concerns are two-fold. First, some have argued that follow-on drugs do not genuinely reflect true innovation and are merely used to disrupt effective generic competition. Others assert a more fundamental objection—arguing that even if these drugs are in some sense innovative, they do not contribute to consumer welfare enough to make up for the welfare lost as a result of foregone cost savings arising from reduced use of generic drugs. The notion that enforcement will ultimately benefit consumers, however, relies on the assumption that competition enforcers and courts are able to accurately distinguish between follow-on drugs that are pro-competitive and those that are merely used merely

⁴⁴ Henry Grabowski, *Competition Between Generic and Branded Drugs*, in PHARMACEUTICAL INNOVATION: INCENTIVES, COMPETITION, AND COST-BENEFIT ANALYSIS IN INTERNATIONAL PERSPECTIVE 164 (eds. Frank A. Sloan & Chee-Ruey Hsieh 2007).

⁴⁵ Douglas Lundin, *Moral Hazard in Physician Prescription Behavior*, 19 J. HEALTH ECON. 639, 641 (2000); see also Danzon, *supra* note 8 at 1069.

⁴⁶ Dogan & Lemley, *supra* note 34 at 687.

⁴⁷ *Id.* at 709.

⁴⁸ Berndt, *supra* note 25 at 71.

⁴⁹ See e.g., Sector Inquiry Report, *supra* note 3 at ¶1018 (quoting a European consumer association condemning these practices as “evergreening” and resulting in “higher health care expenditures and/or higher prices for consumers”); Michael A. Carrier, *A Real-World Analysis of Pharmaceutical Settlements: The Missing Dimension of Product Hopping*, 62 FLA. L. REV. 1009 (arguing that the combination of settlements and product hopping results in anticompetitive harm).

⁵⁰ See Berndt et al., *supra* note 25 at 12.

as a mechanism by which to inhibit generic competition; or alternatively, to discern the extent to which the market functions properly, and where it does not, the direction and extent of the market error. The central importance of innovation to competition in pharmaceuticals, the nature of drug R&D, and the two-tiered competition structure involving originators and generics, however, makes assessment of the overall impact of these products very difficult.

In an industry as heavily regulated and at the same time reliant upon innovation as pharmaceuticals, the question arises as to what impact, if any, enforcement actions against regulatory conduct, necessarily affects the incentives to invest the associated innovative efforts. Evaluating the impact of these enforcement efforts on innovation requires analyzing the nature and process of pharmaceutical innovation, as well as administrative and institutional concerns regarding the practical ability of agencies and courts to formulate rules that accurately distinguish between pro- and anti-competitive regulatory gaming and to consistently apply those rules. Up until now, this form of pharmaceutical regulatory gaming has largely been discussed as a homogeneous category of conduct.⁵¹ In this heading, we suggest that there are important differences amongst the cases alleging anticompetitive conduct involving follow-on drugs—differences which alter the error-cost mix associated with enforcement and, in turn, incentives for innovation.

A. AstraZeneca v. Commission

In a highly anticipated decision, in July 2010 the General Court of the European Union upheld a decision by the European Commission finding that AstraZeneca (AZ) had abused its dominant position in the market for its popular proton pump inhibitor (PPI), Losec, by withdrawing marketing authorizations in three member states.⁵²

In extremely brief summary, the facts giving rise to this claim of abuse are as follows. In anticipation of the expiration of patent protection for the active ingredient in Losec, omeprazole, AZ developed a multi-prong strategy to address the impending impact of generic competition. As part of that strategy, AZ developed a new version known as omeprazole that would serve as the basis for a reformulated version of Losec—Losec MUPS. Losec MUPS was intended to be an intermediate product until AZ could introduce a new patented product—Nexium. Once Losec MUPS was completed and ready to be introduced to the market, AZ requested withdrawal of the market authorization for the original capsule form of Losec in Denmark, Norway, and Sweden in 1998.⁵³ In May 1999, two generics producers filed a complaint alleging that AZ’s conduct, namely removal of the market authorizations, prevented them from introducing generic versions of Losec in the European Economic Area markets.⁵⁴

The substance of the claim of abuse alleged that AZ manipulated pharmaceutical regulatory schemes through steps taken in the course of introducing a new tablet version of Losec, to replace the original capsule form. The regulation at issue in the case was Directive 65/65, which provided for an abbreviated procedure for granting marketing authorizations for generic drug products.⁵⁵ At the time, in order for a generic company to use the abridged procedure, two requirements had to be satisfied: (1) the reference drug had been authorized in the Community for 6-10 years, and (2) the reference product must still have a valid market authorization in place at the time the generic manufacturer files an application for the abridged procedure.⁵⁶ The Commission framed the abuse as follows: the request for deregistration of the marketing authorizations, in combination with AZ’s withdrawal of the original form of Losec from the market and the launch of a reformulated version, Losec MUPS, blocked or delayed entry by generic producers and parallel importers, thereby harming competition.⁵⁷

In reviewing the Commission’s decision, the General Court was careful to point out, however, that “although [the Commission] defined the abuse of a dominate position as the combination of those elements, the central feature of the abuse consists in the deregistration of the Losec capsule marketing authorizations,” the other elements of the abuse merely constituting the context in which the de-registrations were executed.⁵⁸ Thus, introduction of the new product form and removal of the old form, alone, would not have constituted an abuse. It was the de-registrations that exceeded the scope of competition on the merits, since this is the “sole element which could be capable of producing the anticompetitive effects alleged by the Commission,” namely erecting barriers to entry blocking generics and parallel importers.⁵⁹

AZ made several arguments in its challenge of the Commission’s decision. First, AZ asserted that as the holder of the market authorization, it was legal for AZ to “withdraw it as it pleases, or to let it expire,

⁵¹ See e.g., Jessie Chang, *An Antitrust Analysis of Product Hopping in the Pharmaceutical Industry*, 108 COLUM. L. REV. 1471 (2008); Dogan & Lemley, *supra* note 34.

⁵² AstraZeneca, *supra* note 6.

⁵³ *Id.* at ¶691.

⁵⁴ *Id.* at ¶3.

⁵⁵ Council Directive 65/65/EEC of 26 January 1965 (Official Journal 022, 09/02/1965, p.0369/0373).

⁵⁶ AstraZeneca, *supra* note 6, at ¶617 and ¶666.

⁵⁷ *Id.* at ¶804.

⁵⁸ *Id.* at ¶807.

⁵⁹ *Id.* at ¶811.

without being obliged to provide a reason in this respect and without concerning itself with the effect of that decision.”⁶⁰ Second, AZ argued that even dominant firms are under no obligation to assist competitors and potential competitors by maintaining the market authorization for a drug product the firm is no longer interested in offering, particularly where such maintenance involves ongoing pharmacovigilance obligations.⁶¹ Third, AZ emphasized that generics were not entirely blocked from entering the market because of the availability of the published literature exemption as an alternative means of qualifying for the abridged procedure.⁶² Fourth, AZ argued that Losec MUPS was an objectively improved product over the capsule form of Losec, and therefore its introduction was pro-competitive and not exclusionary.⁶³ Indeed, AZ acknowledged that the purpose of introducing Losec MUPS was to minimize the downward pressure on the price of Losec that would result from the entry of generic versions of omeprazole, but insisted that this does not constitute an abuse.⁶⁴

In upholding the Commission’s theory of harm on this charge of abuse, the General Court rejected each of AZ’s arguments in turn. According to the General Court, it was irrelevant that under Directive 65/65 it was legal for AZ to request withdrawal of the authorization because “compliance or non-compliance with other legal rules” did not determine the scope of application of Article 82.⁶⁵ The court also rejected AZ’s proffered objective justification based on the pharmacovigilance requirements. The court noted that AZ was still required to comply with the requirements in the six other member states where AZ continued to offer the capsule form.⁶⁶ Moreover, because AZ had held the authorizations for five years, the risk of serious adverse reactions was low.⁶⁷ Further undermining this argument was the fact that AZ had not withdrawn its market authorizations in either Germany or the Netherlands, where the company had ceased the sale of Losec capsules, and yet AZ made no argument that the pharmacovigilance requirements were in some way applied in a more burdensome way in the countries where withdrawal was requested.⁶⁸ With regards to AZ’s argument that the availability of the published literature exemption meant that generics were not entirely blocked from the market and therefore the conduct could not be exclusionary, the court found this argument to fall short. “[T]he fact that the regulatory framework offers an alternative route to obtaining a marketing authorisation does not remove the abusive nature of the conduct of an undertaking in a dominant position where that conduct, considered objectively, has the sole object of making the abridged procedure...unavailable.”⁶⁹ Finally, the court dismissed AZ’s emphasis on the fact that Losec MUPS was a better product than Losec or that the capsules were withdrawn because of consumer preferences, the court found this argument to miss the mark since the Commission was not asserting that the transition of sales from capsules to Losec MUPS itself created any barriers to entry, and therefore did not harm competition themselves.⁷⁰

In summary, according to the General Court, it is not an abuse for a firm to deploy a strategy “whose object...is to minimize erosion of its sales and to enable it to deal with competition from generic products” so long as the strategy does not involve conduct that goes beyond competition on the merits.⁷¹ However, the court went on to state that “an undertaking in a dominant position cannot use regulatory procedures solely in such a way as to prevent or make more difficult the entry of competitors on the market” absent some objective justification or otherwise related to the defense of some other legitimate consideration of a firm competing on the merits.⁷²

B. Impact on Innovation Incentives

The theory of harm advanced in *AstraZeneca* is a subtle divergence from earlier U.S. cases addressing similar conduct,⁷³ with potentially significant implications for pharmaceutical innovation. One common thread through all of these cases is that they do not allege that the introduction of a reformulated product itself inflicts the harm

⁶⁰ *Id.* at ¶622.

⁶¹ *Id.* at ¶635.

⁶² *Id.* at ¶637.

⁶³ *Id.* at ¶700 and ¶715. AZ contended that Losec MUPS was better because omeprazole, the active ingredient in Losec, “degrades rapidly and loses its efficacy if it is exposed to the acid conditions of the stomach.” *Id.* at ¶715.

⁶⁴ *Id.* at ¶739.

⁶⁵ *Id.* at ¶677.

⁶⁶ *Id.* at ¶658.

⁶⁷ *Id.* at ¶691.

⁶⁸ *Id.* at ¶659, 694.

⁶⁹ *Id.* at ¶829.

⁷⁰ *Id.* at ¶811.

⁷¹ *Id.* at ¶804.

⁷² *Id.* at ¶817.

⁷³ *Abbott Laboratories v. Teva Pharmaceuticals*, 432 F.Supp.2d 408 (D.Del.2006) (holding that charges by Teva, a generic pharmaceutical producer, alleging regulatory manipulation were sufficient to support a monopolization claim against Abbott for conduct related to its drug TriCor); *Walgreen Company v. AstraZeneca Pharmaceuticals*, 534 F.Supp.2d 146 (D.D.C. 2008) (dismissing a monopolization claim by Walgreens that AstraZeneca “deliberately switched the market” from its drug Prilosec to a reformulated version called Nexium, on the grounds that AstraZeneca did not remove the Prilosec from the market when it introduced Nexium and therefore there was no consumer coercion).

to competition. Instead, they assert that the harm results from the combining of the introduction of the new version of the drug with conduct to some degree ancillary to that introduction. The General Court in *AstraZeneca* dedicated the most effort to making this distinction clear when it stated numerous times that it was neither the introduction of the new formulation nor the removal of the old formulation that was the conduct at issue, but instead the combination of those two actions, coupled with the request for withdrawal of market registration.⁷⁴ In the U.S. cases, the theory was that combining the introduction of a reformulated product with the withdrawal of the branded (not generic) original version could result in consumer coercion by interfering with drug substitution regulations. Therefore, in the U.S. cases, the courts draw the line at whether or not the prior version of the drug was removed from the market when the new version was introduced.⁷⁵ In *AstraZeneca*, however, the ancillary conduct at issue is an action by the firm within the regulatory scheme that has implications for regulatory recognition of the original version.

The connections between the approach taken in *AstraZeneca* and innovation policy issues are two-fold. First, the fact that the case was pursued as the first abuse of dominance case in pharmaceuticals, when viewed in combination with the Commission's publicly expressed concerns over reduced rates of novel drug introduction,⁷⁶ suggests that the Commission views the two phenomena as being related. The arguments made by the Commission in the case support this reading—that this type of regulatory gaming is particularly troubling when it is used as a means of avoiding competition in innovation with other originators. For example, in responding to AZ's contention that generic competition was "parasitic", the Commission asserted that "[t]he threat of the entry of generic products forces companies to innovate..."⁷⁷ The second way in which this case has implications for innovation policy is that, despite the fact that one of the primary motivations for bringing the case was to ensure sufficient pressure on originators to engage in novel drug innovation, the way that the theory of harm was framed minimizes the negative impact on incentives for legitimate, pro-competitive incremental innovation. It is much simpler to evaluate the effect on competition resulting from a specifically regulatory action that impacts generics directly because there is no need to make a definitive conclusion as to precisely what extent the market is functioning as it should. This is largely attributable to the fact that the approach of the General Court, as compared to the U.S. approach, relies upon more readily accessible evidence and avoids the very difficult process of attempting to measure the value of a particular innovation, and therefore is less likely to result in a false positive.

According to the U.S. cases, where the original version of the product is removed, the conduct is assessed according to the rule of reason test articulated in *Microsoft*.⁷⁸ The *Microsoft* court set forth a three-step test: the plaintiff must demonstrate an anticompetitive effect, at which point the burden shifts to the defendant to proffer a pro-competitive justification for the conduct.⁷⁹ If the plaintiff offers such a justification, the burden shifts back to the plaintiff to either rebut the justification or establish that "the anticompetitive harm for the conduct outweighs the pro-competitive benefit."⁸⁰ Therefore, the court continued, if an anticompetitive harm is established, "that harm will be weighed against any benefits presented by Defendants."⁸¹ Thus, cases which are not screened out by the second step of the analysis require a very complex balancing effort which demands very detailed information about the nature of how the market operates—information that is not generally susceptible to observation or definitive answer.

By contrast, in the *AstraZeneca* framework courts and enforcement agencies are not faced with the task of deciphering whether the complexities of the pharmaceutical market leave sufficient room for meaningful consumer choice. In that sense, this approach might be thought of as "pure" regulatory gaming since it really focuses in on specifically regulatory conduct (See Figure 4.1). Narrowing the scope of inquiry and isolating the regulatory action in this way simplifies the inquiry, which makes it less likely to lead to reduced incentives for legitimate innovation than the product substitution theory. There are two primary virtues to the approach in *AstraZeneca* from the standpoint of error costs. First, the anticompetitive harm alleged is both more severe and its boundaries better defined than that which was asserted in the U.S. cases. In *AstraZeneca*, withdrawal of the market authorizations prevented, or at least significantly delayed, generic entry and parallel imports, thereby eliminating the possibility for consumer choice in favor of generics. In the U.S. cases, on the other hand, where market entry by generics was not prevented (only entry as a direct generic substitute to the reformulated product), commentators have criticized the decision as making the "true gravamen of... [the] allegations... not that consumer choice... was restricted but that an overt choice was required" (See Figure 4.2).⁸²

⁷⁴ *AstraZeneca*, *supra* note 6 at ¶646.

⁷⁵ *Walgreens*, *supra* note 73 at 151.

⁷⁶ Sector Inquiry Report, *supra* note 3 at ¶14.

⁷⁷ *AstraZeneca*, *supra* note 6 at ¶644.

⁷⁸ *Abbott Labs*, *supra* note 73 at 422.

⁷⁹ *Id.* at 422 *citing* *United States v. Microsoft Corp.*, 253 F.3d 34 (D.C.Cir.2001).

⁸⁰ *Id.*

⁸¹ *Id.*

⁸² Guy V. Amoresano, *Branded Drug Reformulation: The Next Brand vs. Generic Antitrust Battleground*, 62 *FOOD & DRUG L.J.* 249, 254 (2007).

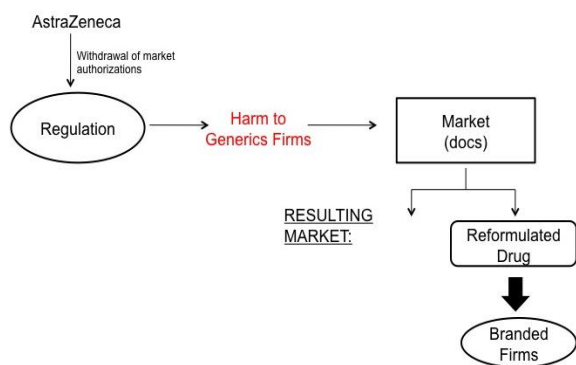


Figure 4.1: “Pure” Regulatory Gaming Theory (EC)

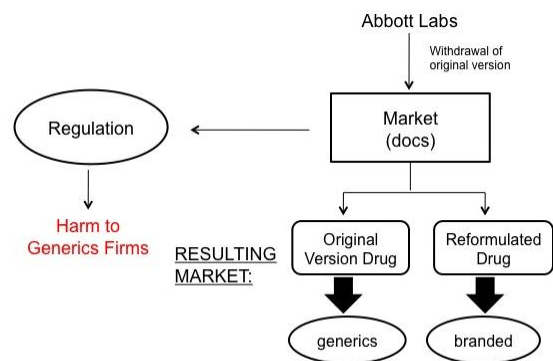


Figure 4.2: Product Substitution Theory of Gaming (U.S.)

The second primary advantage of this approach is that the evidence required to assess whether or not the regulatory action by the firm was justified is more readily available and susceptible to consistent, accurate, and objective evaluation. This arises from the fact that the conduct being assessed is an interaction directly with a regulatory agency, and not an action that is generally considered to be a “business judgment”. The value of this approach is demonstrated by the way in which the court assessed AZ’s (ultimately unsuccessful) argument that the pharmacovigilance requirements⁸³ associated with maintaining market authorizations were onerous and an objective driver of their decision to withdraw the authorizations in the countries they did. To assess the efficacy of this claim, the Commission and the General Court were able to look at AZ’s own conduct—particularly whether AZ’s conduct with respect to the regulation was consistent across the markets in which it marketed the drugs at issue. Furthermore, the regulatory agency in charge of oversight for the regulation that was allegedly gamed has a special competence in gauging the burdens of a particular regulation because of its accumulated experience, both across firms and over time.

A primary problem with the U.S. approach of balancing the value of the specific innovation is that in many product switch scenarios, there will be some basis upon which to argue that the reformulated product is superior to the prior version of the drug,⁸⁴ and therefore many product hopping cases will not be screened out by the second step, as was the case for many of the product designs at issue in *Microsoft*.⁸⁵ As mentioned previously, these reformulated products often involve improved delivery methods and dosing protocols, and often the use of drugs for new indications. There is research to support the conclusion that these reformulations “can...generate substantial health benefits.”⁸⁶ These benefits may take the form of “improved patient compliance, greater efficacy as a result of pharmacokinetics, reduced adverse effects or the ability to effectively treat new patient populations.”⁸⁷ Likewise, there may also be good reasons for withdrawing an older version of a product from the market when introducing a new one. “It reduces consumer confusion and support costs and focuses retailers on the objective of promoting the new product, all of which can generate consumer benefits.”⁸⁸ Finally, because of the procedural posture of the U.S. cases, we also have no clear picture of what this third step in the analysis would look like in the case of a legitimate product improvement.⁸⁹

Undermining the accurate weighing of these competing considerations is the fact that these cases require the balancing of the harm to generic competition, which is purely price competition, against the consumer benefit from the reformulated drug product—which is generally non-price competition. The likely or actual impact on drug prices is readily measurable, whereas the benefit from the innovative contribution of the reformulated drug are only partially observable or predictable at the time of product introduction and are almost impossible to quantify in the same manner. On the one hand, it may be possible to measure, or at least estimate, increased utilization of a reformulated drug, which is associated with health and economic benefits.⁹⁰ Thus, one

⁸³ Pharmacovigilance requirements generally impose ongoing reporting and updating requirements on drug manufacturers for any health or safety issues related to the drug that might become apparent over the drug’s product life. See *AstraZeneca*, *supra* note 6 at ¶690.

⁸⁴ It is worth noting, however, that there is some ongoing debate as to what should be considered an “objective improvement” in the context of pharmaceuticals. In *Walgreens* the plaintiffs argued that the reformulated version was in no way pharmacologically better in treating the relevant condition. Thus, the fact that drug quality is a multidimensional issue may also inform the analysis.

⁸⁵ In *Microsoft*, Microsoft did not offer justifications for many of the product designs at issue in that case and therefore the DC Circuit did not have to proceed to the third step of the analysis.

⁸⁶ Berndt et al., *supra* note 25 at 71.

⁸⁷ *Id.*

⁸⁸ Gilbert, *supra* note 33 at 71.

⁸⁹ Dogan & Lemley, *supra* note 34 at 716 (noting that the *Abbott Labs* opinion leaves open the issue of “how a fact finder should go about balancing the precompetitive and anticompetitive effects of a change in formula”).

⁹⁰ Berndt et al., *supra* note 25 at 73.

metric by which the net benefit of a reformulation can be measured is by the increase in consumer welfare when the drug reaches a broader patient population, facilitates increased compliance with dosing regimens, or otherwise improves a consumer's experience in taking the drug. These can be thought of as direct contributions to welfare. But this is not the only metric we must examine when assessing the benefits of these reformulations.

As mentioned in Section II above, a significant level of knowledge spillovers characterizes the pharmaceutical industry.⁹¹ This means that the R&D from these reformulations may also benefit consumers indirectly by contributing to the effort to develop or improve other drugs. The impact of these spillovers are much more difficult to measure or estimate because they tend to be a long-run benefit, thus raising the possibility that they will be discounted in a competition analysis where the benefits are almost entirely realized in the short-term.⁹² Therefore objectively and accurately distinguishing between a pro-competitive withdrawal, which is meant to support the introduction of a new, innovative version of the drug, and an anti-competitive withdrawal meant only to impede generic substitution, is far more difficult. Because these problems tend to artificially tip the scales in favor of finding a violation, incentives for innovation are potentially negatively impacted.

Even if we were to disregard the possibility of spillover effects, the introduction of a reformulation with only marginal benefits over a prior version cannot be assumed to be indicative of anticompetitive intent. Though certainly less risky an endeavor than developing a novel drug,⁹³ it is not always possible to predict ex ante the benefits that will accrue to consumers from an effort to improve a drug. Nonetheless, it will still be rational for an originator to introduce the drug so long as profits exceed marginal cost (which is nominal for drug production), because most of the costs are sunk by the time a drug proceeds through testing.⁹⁴ Furthermore, “[t]here are legitimate reasons for a manufacturer to stop selling and even recall older products. It reduces consumer confusion and support costs and focuses retailers on the objective of promoting the new product, all of which can generate consumer benefits.”⁹⁵

Furthermore, measuring the impact on prices may not as simple as estimating what the price would have been if the reformulation had not entered the market. The *Abbott Labs* court, looking to *Berkey Photo*, concludes that deference to product designs and improvements is not warranted where consumer coercion is present.⁹⁶ But there are good reasons to doubt that the consumer coercion discussed by the *Berkey Photo* court can be equated with what is being alleged in drug reformulation cases. *Berkey Photo* involved purely complementary products and so the coercion concern was that demand for one product drives demand for another product, and therefore consumers who wish to have the one product are limited in their choice for the second product. The nature of coercion the *Abbott Labs* court impliedly equates to this is different. As mentioned in Section III, generics can be thought of as a substitute product with characteristics of a complementary product due to the imposition of drug substitution rules. As confirmed in *Walgreens*, the notion is that consumer choice is limited by the originator removing the old version from the market. But in both *Abbott Labs* and *Walgreens*, the older version was still available in generic form on the market. And in at least one very important respect, generics and branded drugs are much more like substitutes than complements—selection of drugs is still driven by quality and cost considerations, and not by possible interoperability concerns as may be the case with true complements. “At bottom, it appears that the true gravamen of Teva’s allegations in *Abbott Labs* was not that consumer choice (through the prescribing physician) was restricted but that an overt choice was required.”⁹⁷ Therefore, to the extent that markets may not efficiently choose between the branded reformulation and the generic version of the original, it is likely mostly due to information asymmetries and agency problems as opposed to coercion, in the traditional sense. Even if the concept of coercion is expanded to encompass this effect, the degree of the anticompetitive effect would be less than the more direct form of coercion, but given the vagueness of the notion it is difficult to estimate how much less. Without a clear notion of the impact of this broadened sense of coercion we do not really know how heavy the anticompetitive effect side of the scale is.

Some have argued that balancing tests in general are inappropriate for antitrust analyses of innovation. In a recent article, Geoffrey Manne and Joshua Wright argued that antitrust enforcement actions in the context of innovation generally “create[] a special opportunity for antitrust error.”⁹⁸ Their rationale is that false positives are more costly than false negatives because in the former, “successfully challenging...product innovations is likely to dampen innovation across the economy, whereas Type 2 errors are at least mitigated in part by entry and other competition.”⁹⁹ Others have argued that the stakes associated with error in an innovation case are

⁹¹ See e.g., Magazzini et al., *supra* note 7; Sternitzke, *supra* note 14.

⁹² Gilbert, *supra* note 33 at 72.

⁹³ Comanor, *supra* note 23 at 64.

⁹⁴ See *supra* notes 20–21 and accompanying text.

⁹⁵ Gilbert, *supra* note 33 at 71.

⁹⁶ See *supra* note 73 and accompanying text.

⁹⁷ Amoresano, *supra* note 82 at 254.

⁹⁸ Geoffrey A. Manne & Joshua D. Wright, *Innovation and the Limits of Antitrust*, J. COMPETITION L. & ECON. 153, 164 (2010).

⁹⁹ *Id.* at 167.

“much higher” because “most innovation is beneficial”.¹⁰⁰ Richard Gilbert, in his analysis of the various potential tests a court could use to identify so-called “predatory innovation”, concluded that “all of [the] tests are likely to produce false positives that chill incentives for beneficial investments in research and development.”¹⁰¹ Manne & Wright have even suggested that there is a bias against innovative products and practices because “courts and economists’ initial understanding of these practices” is usually limited, which skews attitudes in favor of enforcement.¹⁰²

These critiques make the U.S. product substitution theory of harm particularly problematic. Attempts to objectively administer a balancing test to determine the legality of a product withdrawal are prone to erring on the side of finding a violation and therefore condemning what may be a procompetitive innovation. Whereas the costs and benefits of a decision to take a particular regulatory step are usually readily estimable, product introduction and withdrawal is generally a business judgment. Therefore objectively and accurately distinguishing between a “pro-competitive” withdrawal, which is meant to support the introduction of a new, innovative version of the drug, and an “anti-competitive” withdrawal meant only to impede generic substitution, is far more difficult.

The risk that a balancing test in this context could result in false positives condemning procompetitive reformulations and conduct related to those reformulations, may negatively impact incentives for both incremental and radical innovations. The impact on this form of incremental innovation would be direct. If drug reformulations must now not only be simply “improved”, but improved to a particular degree above the original version to avoid antitrust scrutiny, the risk profile of these efforts rises. This may also discourage this type of innovative effort by increasing the costs of developing and introducing such a reformulation. To assess the risk of antitrust enforcement action, firms may find it necessary to begin doing side-by-side testing with the original version to ensure a sufficient amount of objective improvement. This would raise the costs of engaging in product improvement.

An obvious counterargument to this is that according to the courts in *Abbott Labs* and *Walgreens*, these reformulations could be introduced without giving rise to an antitrust claim, so long as the previous version remains in the market. But it is precisely in these marginal cases that the rationale for removing prior versions from the market may be strongest. Where the immediate benefits from the improvements are more modest, and therefore the prices able to be charged are likewise modest, a firm may not be able to justify the effort and resources associated with supporting two products in the marketplace. Of course, in these same circumstances, a firm may likewise be more tempted to withdraw the old version for the sake of the benefits it may reap as a result of closing off the opportunity for generics to benefit from drug substitution mechanisms. Thus, we are left with conduct that is as readily explainable as pro-competitive as it is as anti-competitive, with no clear and reliable means for a court to choose between the alternate explanations.

Furthermore, it is possible that the opportunity for incremental innovation down the road contributes to the incentives to create novel drugs in the first place. This is the notion that when a firm, pharmaceutical or otherwise, invests resources in developing a product and introducing it to the market, there is an assumption that the firm would retain the opportunity to change and improve that product.¹⁰³

Another way to differentiate these two theories of harm is according to the contexts in which they may be used. The success of a product switch depends heavily upon the second-generation drug being brought to market before a generic version of the first product has been introduced.¹⁰⁴ The Pharmaceutical Sector Inquiry Report by the European Directorate General of Competition identified several strategies sometimes used by originator firms to bridge this potential time gap between introduction of a second-generation product and generic entry. Those strategies include strategic marketing efforts for both products, litigation against generics with respect to the first product, withdrawal of marketing authorizations for the first product, intervention at various regulatory bodies, and settlements with generic companies.¹⁰⁵ Unlike these strategies, however, withdrawal of the first product is not a bridging strategy because it requires that the second-generation product be ready to be introduced to the market.¹⁰⁶

Secondly, the evidence required to assess whether or not the regulatory action by the firm was justified is more readily available and susceptible to consistent, accurate, and objective evaluation. Unlike the product substitution theory where the impact of the action by the originator is filtered through the market, in pure regulatory gaming cases, the action at issue is ancillary to the product switch and therefore can be evaluated on its own.

¹⁰⁰ Gilbert, *supra* note 33, at 49.

¹⁰¹ *Id.* at 47.

¹⁰² Manne & Wright, *supra* note 98 at 166.

¹⁰³ Gilbert, *supra* note 33 at 57.

¹⁰⁴ Pharmaceutical Sector Inquiry Report, *supra* note 3 at ¶1010.

¹⁰⁵ *Id.* at ¶¶1037–1044.

¹⁰⁶ Although the Sector Report discusses withdrawal of the 1st generation product under the heading of “Practices Employed by Originator Companies to Facilitate the Switch,” this is somewhat misleading since the focus of the section is on the importance of the “timing of the launch of generics and of next generation originator products”. *Id.* ¶1032.

AZ unsuccessfully attempted to make such an argument. AZ asserted that the pharmacovigilance requirements associated with maintaining market authorizations were onerous and an objective driver of their decision to withdraw the authorizations in the countries they did. To assess the efficacy of this claim, the Commission and the General Court were able to look at AZ's own conduct—particularly whether AZ's conduct with respect to the regulation was consistent across the markets in which it marketed the drugs at issue. Furthermore, the regulatory agency in charge of oversight for the regulation that was allegedly gamed will have a special competence in gauging the burdens of a particular regulation because of its accumulated experience, both across firms and over time. AstraZeneca demonstrated this because the drug agency was able to contribute evidence that supported the notion that the burden pharmacovigilance requirements and the likelihood of a serious problem arising tended to decline significantly over time.

The objective justification test also sufficiently protects innovation incentives. If such an objective justification cannot be thoroughly established, then not only is the action presumptively anticompetitive, but it is also unlikely to affect the firm's decisions regarding developing improvements to existing drugs. Presumably, if a legal or functional connection could be established between a regulatory action and a pro-competitive, non-sham reformulation, that would constitute an objective justification.

C. Implications for Innovation Policy

Ultimately, despite the limited European case law on this form of regulatory gaming, *AstraZeneca* does offer some insights into the contours of the innovation-related thinking in the pharmaceutical sector. There seems to be an implicit presumption that radical innovation is significantly more important to overall competitiveness in the industry than is incremental innovation. By the same token, generic competition is viewed as being an essential source of pressure to drive originators back to competition in innovation post-patent lapse. Thus, while *AstraZeneca* constitutes a measured approach by refraining from broadly condemning product reformulations, the case suggests that actions which interfere with the standard model of upfront patent protection for novel medicines followed by vigorous competition by generics post-patent lapse to drive prices down, will be viewed with a healthy dose of skepticism.

V. THE *SYFAIT* CASES: THE DEBATE REGARDING INCENTIVES FOR INNOVATION, INDUSTRY-SPECIFIC CHARACTERISTICS & COMPETITION LAW ANALYSIS

A pair of relatively recent opinions, arising out of a conflict between GlaxoSmithKline and distributors in Greece who also engaged in parallel trading, brought the debate over two issues central to pharmaceutical innovation and competition law to the forefront.¹⁰⁷ The first is really a question that goes directly to the heart of the debate over pharmaceutical innovation policy—what is the relationship, if any, between parallel trading, firm revenues, and incentives to invest in research and development? The second issue over which these opinions clashed is a much broader question for competition law as a whole: what role should industry-specific characteristics have on the applicability of competition law rules? These opinions express vastly different perspectives on both questions, and this serves both to elucidate some of the points that an innovation policy must address, as well as to demonstrate that vast disagreement on many of those points is possible, and perhaps even likely.

A. Industry-Specific Characteristics

Up to this point, this paper has emphasized many unique characteristics of the pharmaceutical industry and the process of drug innovation. It is important to note, however, that the question of what role industry-specific characteristics should play in competition law analysis remains a matter of intense debate. The controversy is two-pronged. First, should unique industry contexts impact what conduct is considered abusive and/or should such characteristics constitute a legitimate source of for justification for certain types of allegedly abusive conduct? If this first question is answered in the affirmative, the second question is what is the burden faced by the parties for establishing that such characteristics exist and the nature of their effect on competition in the market? This issue has significant implications for innovation policy implementation through competition law because it defines the boundaries as to the extent to which competition rules can be tailored to suit the particularities of a given industry.

The *Syfait* cases involved attempts by GlaxoSmithKline to stem the tide of parallel trading in its pharmaceutical products out of Greece. In 2000, GSK stopped meeting the orders of Greek wholesalers who engaged in parallel trading of the drug products to other Member States, instead supplying hospitals and pharmacies directly. In 2001, GSK recommenced distribution to wholesalers, but limited the supplies distributed

¹⁰⁷ *Syfait I*, *supra* note 4; *Syfait II*, *supra* note 4.

to wholesalers to just above national market demand. Wholesalers claimed that these actions constituted an unjustifiable refusal to deal and therefore constituted an abuse of dominant position under Art.82 EC (now Art.102 TFEU). In the case, the Greek competition authority (the EA) identified a number of factors based on unique aspects of the pharmaceutical industry that it believed might impact whether or not the conduct at issue was objectively justified and made inquiry with the CFI as to whether they could play a role in justifying the conduct. The Commission argued that refusals to supply by a dominant firm could only be justified in a narrow set of circumstances and that none of the factors identified by the Greek competition authority were relevant considerations for justifying a refusal to deal.

While both the CFI and ECJ opinions acknowledge that in certain circumstances the features of a market rise to the level of creating a distinctive context that should be taken into account in assessing whether certain conduct can be justified, the opinions diverged considerably in their assessment of whether the pharmaceutical sector constitutes such an altered environment. In the CFI opinion, Advocate General Jacobs held that a refusal to supply “is capable of objective justification, and thus of not constituting an abuse, where the price differential giving rise to the parallel trade is the result of State intervention in the Member State of export..., given the combined circumstances of the European pharmaceutical sector at the current stage of its development...”¹⁰⁸ AG Jacobs went on to identify four factors in particular that make the pharmaceutical sector unique and are therefore relevant to determining whether a refusal to supply is justified: (1) the “pervasive and diverse State intervention in the pricing of pharmaceuticals”; (2) the regulation by the Community and the Member States of the distribution of pharmaceutical products establishing nationally demarcated obligations upon pharmaceutical firms; (3) the “potentially negative consequences of parallel trade for competition...and incentives to innovate”; (4) the fact that the end consumers of pharmaceutical products cannot be assumed to benefit from parallel trade.¹⁰⁹ What this holding clearly indicates is a willingness on the part of AG Jacobs to tailor a competition law analysis in a way that is “highly specific to the pharmaceutical industry in its current condition.”¹¹⁰

In *Syfait II*, however, AG Colomer took a very different view of the nature of the pharmaceutical industry in holding that GSK could not justify its policies against parallel trade. According to AG Colomer, the control and regulation of drug product prices by Member States “does not entirely remove the prices of those products from the law of supply and demand”¹¹¹ and therefore Art.82 cannot be applied differently in the pharmaceutical sector on that basis.¹¹² Although AG Colomer ultimately rejected all of the justifications proffered by GSK, he ultimately left the door open for justification analysis to take some account of the unique nature of price regulation in pharmaceuticals. Though he did not offer much in the way of specific guidance on how the analysis would work, he did note that “it cannot be ignored that...State intervention is one of the factors liable to create opportunities for parallel trade.”¹¹³

B. Relationship Between Parallel Trading and Innovation Incentives

Among the factors he found to be particularly relevant to the analysis of whether GSK’s conduct was justified, AG Jacobs found it “relevant to consider some of the economic factors affecting the commercial policy of pharmaceutical undertakings.”¹¹⁴ Because production in pharmaceuticals is characterized by high fixed costs and relatively low variable costs, by the time a drug reaches the market, most of the costs are sunk and it is therefore rational for a drug company to bring a drug to market so long as the price is above variable cost. Therefore, “[t]he mere fact that a product is marketed on a given market at a given price does not mean that a pharmaceuticals undertaking could recoup its total costs if that price were generalized across the whole of the Community.”¹¹⁵

According to AG Jacobs, this cost structure, together with the fact that pharmaceutical price and distribution are regulated in a nationally segregated manner, and that parallel trading, by definition, undermines national price differentials, suggests that parallel trading threatens to undermine incentives for pharmaceutical firms to invest in research and development.¹¹⁶ In other words, the fact that drug prices are regulated along national market lines allows firms to market drugs even in markets where the low prices established would not otherwise cover total costs, but parallel trading destabilizes this system by undermining the firm’s ability to make up in high price markets what is not covered by sales in low price markets. If a firm is unable to cover its total costs, it is unlikely to invest in developing the drugs in the first place. Therefore, according to AG Jacobs, a

¹⁰⁸ *Syfait I*, *supra* note 4 at ¶105.

¹⁰⁹ *Id.*

¹¹⁰ *Id.* at 101.

¹¹¹ *Syfait II*, *supra* note 4 at 1424.

¹¹² *Id.* at 1422.

¹¹³ *Id.* at 1425-26.

¹¹⁴ *Syfait I*, *supra* note 4 at ¶89.

¹¹⁵ *Id.*

¹¹⁶ *Id.* at ¶93.

pharmaceutical firm may be justified in making certain efforts to stem parallel trading. AG Colomer, however, entirely dismissed the argument that parallel trading may negatively affect incentives for research & development, stating that “no causal link between the repercussions of parallel trade on the revenues of pharmaceutical companies and those companies’ investments in research and development” had been established.¹¹⁷

Thus, while there seems to be some agreement on the principle that industry-specific characteristics may have a role to play in competition law analysis in certain circumstances, the fact that these two opinions articulate almost entirely contradictory perspectives on the pharmaceutical industry highlights one of the major obstacles to effectively incorporating industry-specific insights into legal rules and analysis. Economics does not always offer clear answers to what drives innovation.

Furthermore, at least in the pharmaceutical sector, the structure and process of R&D along with our understanding of it, is evolving in ways that may undermine the applicability of the standard narrative regarding what drives drug innovation that was laid out under 2.1. above. Indeed, in recent years there has been a trend towards disintegration in pharmaceutical R&D.¹¹⁸ An increasing number of innovations are originating outside of the major pharmaceutical firms, instead coming from smaller firms (especially biopharmaceutical outfits), with “the major drug companies only entering the process at the development and testing phases.”¹¹⁹ Another poignant example of this is the argument made by Boldrin & Levine in their book *Against Intellectual Monopoly*, questioning the almost universal assumption¹²⁰ that pharmaceutical innovation, more than innovation in almost any other industry, depends heavily upon strong patent protection.¹²¹ Thus, the fact that many of these issues remain in flux and a matter of sharp debate complicate their incorporation into a coherent, consistent approach to competition law analysis.

VI. Conclusion

Although this study is in no way exhaustive, it does provide some insights as to how the Commission and European courts are approaching innovation in this industry. First, the *Syfait* cases suggest that while industry-specific characteristics may have a role to play in narrow circumstances, the burden of justifying conduct on the basis of protecting incentives to invest in innovation will be high. Furthermore, there is vast disagreement over what drives investments in pharmaceutical R&D and the extent to which state intervention alters the competitive environment in the market. The limited context of regulatory gaming also contributes to our understanding of now prevailing pharmaceutical innovation policy in competition law. The Commission and General Court decision in *AstraZeneca* suggest a skepticism regarding the impact of incremental innovation in the form of reformulated drugs on consumer welfare. The very fact that the case was brought may reflect a judgment by the Commission that radical innovation is far more important to competition in the pharmaceutical sector and a concern that incremental innovation will draw resources away from novel drug development. Given that the Final Pharmaceutical Sector Report was released only just over a year ago, the prospect of increasing levels of enforcement in this industry, and the evolution of the structure of pharmaceutical R&D, we should expect ongoing development of these perspectives in coming years.

¹¹⁷ *Id.*

¹¹⁸ See *supra* notes 20–24 and accompanying text.

¹¹⁹ Comanor, *supra* note 23 at 67. See also Tijssen, R.J.W., *Is the Commercialization of Scientific Research Affecting the Production of Public Knowledge?: Global trends in the Output of Corporate Research Articles*, 33 RESEARCH POLICY 709 (2004).

¹²⁰ See Sector Inquiry Report, *supra* note 3 at ¶9.

¹²¹ Michele Boldrin & David K. Levine, *AGAINST INTELLECTUAL MONOPOLY* 212–38 (2008).