



CRA Insights: Life Sciences

CRA Charles River
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Incremental pharmaceutical innovation and antitrust concerns

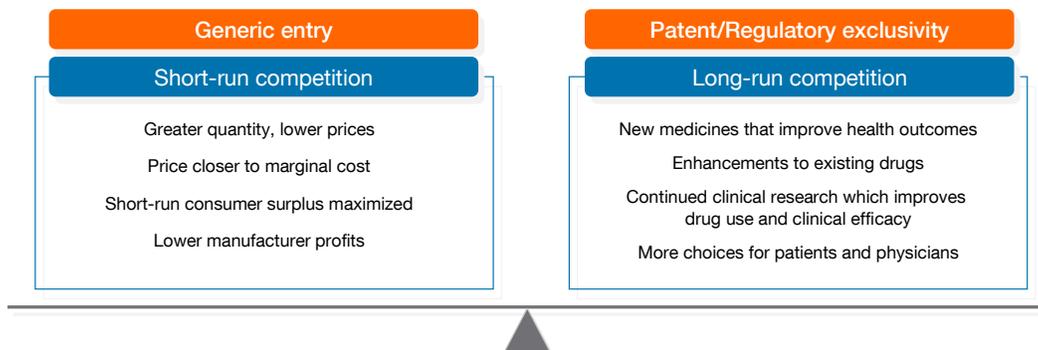
Many pharmaceutical innovations are improvements on existing drug therapies as opposed to entirely new molecular or biologic entities. Such “incremental innovation” has been at the center of a range of legal disputes in the pharmaceutical industry. In antitrust cases concerning the drugs BuSpar, Nexium/Prilosec, and DDAVP, among others, plaintiffs have challenged the validity of patents relating to incremental innovations asserted against potential generic entrants.

The US Food and Drug Administration (FDA) designates new non-biologic drugs with active ingredients that have never been approved in the US in any form as NMEs.¹ From 1995 to 2009, the FDA approved an average of 92.3 new drugs (including modified drugs), including 27.6 new medicines (NMEs or new biologics) per year. During this period, there were 1,385 new drug approvals in the US, 414 (30%) for NMEs or new biologics and 971 (70%) for modified versions of existing drugs.² Incremental innovations to existing drugs also account for a significant portion of industry revenues. From 1995 through 2000, modified drugs launched since 1995 accounted for \$16.8 billion in retail spending versus \$26.5 billion for NMEs.³

Assessment

When might incremental innovation be inefficient, potentially even raising antitrust concerns? A balance between promoting the development of new and improved drugs and the greater savings available from lower-priced generics is achieved by patent law, antitrust law, and the industry’s regulatory structure.

Figure 1: Tradeoff between innovation and competition



¹ FDA, “Drugs@FDA Glossary of Terms,” <http://www.fda.gov/Drugs/informationondrugs/ucm079436.htm>.

² FDA Website, “Drug and Biological Approval Reports,” available at www.fda.gov.

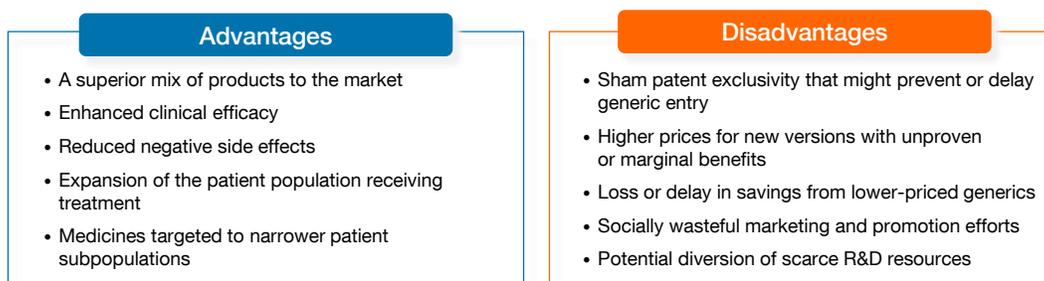
³ “Changing Patterns of Pharmaceutical Innovation,” *National Institute of Health Care Management*, 2002, p. 13.

In general, patent rights can allow for increased product variety, higher quality products, and/or more efficient production, all of which raise consumer welfare in the long run. Accordingly, limiting competition through the assertion of patent rights is protected by patent law and is not generally considered to violate antitrust laws.⁴ Sham patents or other abuses of the patent system are considered exceptions that cause harm to competition in the short run (reduced output, higher price), outweighing gains from innovation.

Some have suggested that incremental pharmaceutical innovation likewise may harm competition. In general, concern arises when the effect of incremental innovation arises mainly from limiting short-run competition with existing products rather than from delivering greater consumer benefits over the longer term. In these situations, the immediate “static losses” from higher prices outweigh the future “dynamic gains” from new or improved products.

There are both advantages and disadvantages potentially associated with incremental drug innovations, as noted in Figure 2.

Figure 2: Advantages and disadvantages of incremental drug innovations



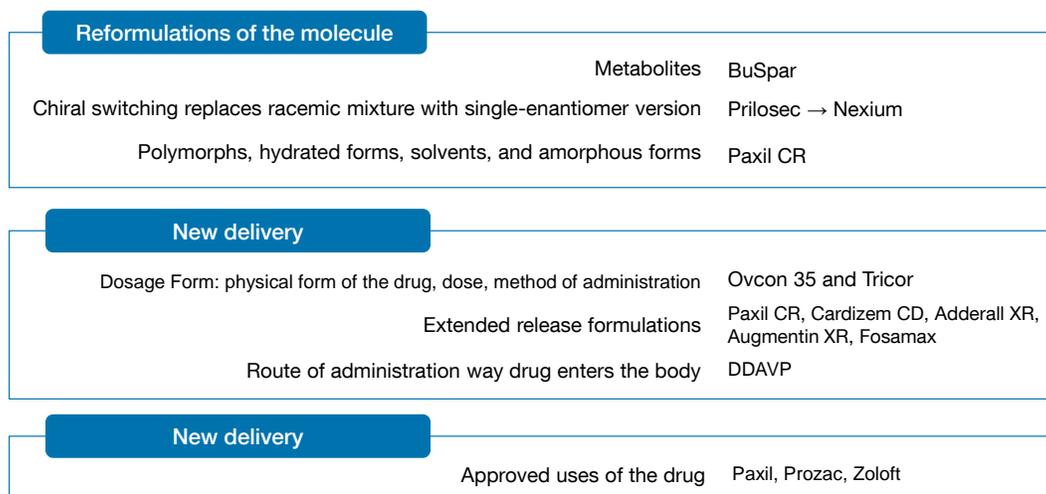
By extending the life of the product family, incremental pharmaceutical innovation delivers benefits through continued clinical research into existing and new uses of the drug. This can improve clinical knowledge and treatment regimens, e.g., the discovery of new uses or a greater understanding of negative side effects. Thus, incremental drug innovations may be an appropriate part of a product lifecycle management strategy. By delivering a superior drug therapy, physicians and patients may be convinced to shift their prescriptions to the new version of the drug, with the innovator maintaining a greater share of its sales in the face of competition from generic versions of the old drug. This might effectively extend the commercial life of the drug franchise and, in doing so, add significantly to the total returns to the innovator.

Other benefits to the branded drug manufacturer inherent to such strategies derive from weakening potential competition, such as delaying entry or otherwise restraining generic drug sales. For example, removing the older version of a drug from the market may preclude generic versions of that drug from being identified in the pharmaceutical distribution system as a bioequivalent drug appropriate for generic substitution. As discussed below, such actions may eliminate the generic drug's ability to compete in the market. Manufacturers may undertake costly but marginal innovations where the costs outweigh the added consumer value from the innovation as a tactic to limit or weaken a competitor's ability to market its product. There may also be socially wasteful marketing and promotional efforts that, in a similar fashion, do not add consumer value.

Figure 3 summarizes different types of incremental drug innovations and provides examples in which the innovation and accompanying conduct have raised concerns regarding effects on competition.

⁴ Richard A. Posner, “Antitrust in the New Economy,” *Antitrust Law Journal*, 2001, pp. 930–31.

Figure 3: Types of incremental drug innovation



In these situations, a new drug based on an existing drug was introduced prior to (or around the time of) planned generic entry. The incremental innovation and associated conduct were suspected of foreclosing, limiting, or delaying competition from the generic drugs. Attempting to evaluate the benefits to patients from the incremental innovation directly can be challenging. Fortunately, there is generally no need to assess the clinical merits of a reformulation directly. Patients and physicians, as long as they are given the choice, will reveal through their choices whether or not they find an incremental innovation to be worthwhile. In addition, the decisions made by managed care organizations about how to reimburse the drug will reveal their views of the benefits of an incremental innovation.

Incremental drug innovations are not always successful. For example, Prozac Weekly garnered only a small fraction of sales relative to Prozac.⁵ In such an instance, the incremental innovation was rejected by patients, physicians, and payers as not being of sufficient value to warrant its cost. These experiences show that the market for pharmaceuticals is able to discriminate between worthwhile and ineffectual modified drugs.

The result is a guiding principle: *As long as choice is not being restricted, the market may be relied on to assess the value of incremental drug innovations.*

Incremental innovations could also raise questions about misuse of the regulatory system to inappropriately limit or deter generic competition. Consider the *TriCor* case in which the dose of the active ingredient, fenofibrate, was reduced and reformulated twice, first from 200mg capsules to 160mg tablets then to 145mg tablets. The manufacturer claimed that reducing the amount of the active ingredient while maintaining the drug's potency was advantageous to patients because it reduced unwanted side effects.⁶ The switch to the 145mg tablets involved one other change: the tablet could be taken without food. Both reformulations occurred just before generic versions of existing *TriCor* were about to enter the market. Usually, when a modified drug is introduced, the pre-existing version of the drug remains on the market. In *TriCor*, however, the manufacturer removed the old formulation from the distribution channel in both cases. In each instance, *TriCor* sales converted rapidly from the old to the new formulation, overall *TriCor* sales continued to grow, and generic sales were minimal.

Two questions could help to determine whether an incremental innovation constitutes an abuse of the system:

⁵ SDI/Verispan VONA, 1996–2003.

⁶ In both switches, the new drug was claimed to have the same therapeutic efficacy.

- Does the marketing of the new product effectively foreclose the distribution channel for competitors' products?
- Does the modified product expand or constrain the choices available to payers, physicians, and consumers?

In TriCor, the generic equivalents to the existing version of the drug effectively lost their ability to compete in the market. Generic drug sales are predicated upon being certified as bioequivalent to their reference drug by the FDA. This certification of bioequivalence is incorporated in the system for dispensing prescriptions by retail pharmacists and is essential to the generic substitution that typically occurs. Because the older version of the drug was removed from the market, the normal generic substitution could not occur. The choice set to patients and physicians was being restricted.

In cases where the new formulation competes against the old formulation and demonstrates its benefits to be worth any difference in price, the incremental innovation should not be condemned. However, when this competition does not take place, the market cannot render its judgment and any lessening of competition may be questioned as anticompetitive.

Conclusion

Over the last decade, incremental innovation has accounted for 70% of the new drugs approved in the US and a substantial portion of the industry's revenues. In this environment, concerns that reformulated drugs are being used to delay or preclude generic competition have given rise to a number of high-profile antitrust suits. Observers have questioned the clinical value and commercial success of reformulated drugs versus NMEs. Fortunately, when given a choice, the market for pharmaceuticals provides an assessment of the benefits of incremental drug innovations, including their efficacy and side effects. Antitrust concerns may be raised when the market is not given this choice. In determining whether or not incremental drug innovations will be found to be anticompetitive, there are two considerations: whether the new drug and/or actions associated with it will restrict the distribution channel for competing products and whether the drug or associated actions will constrain the choices available to consumers.

Contact

Andrew Tepperman, Principal
+1-416-413-4084, atepperman@crai.com

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