U.S. Senate Special Committee on Aging
Testimony of Terry G. Mahn
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"From Joint Pain to Pocket Pain: Cost and Competition Among Rheumatoid Arthritis Therapies."
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Chairman Collins, Ranking Member Casey and members of the Committee, thank you for the opportunity to appear before you today.

My testimony today will focus on intellectual property – patents to be more precise – and the important role that they play in driving the discovery and development of new drugs and medical therapies. I will try to relate how patent protection can impact the cost of drugs and health care generally, and I will offer some insights on how these forces are kept in balance.

A small caveat before I begin: all of my remarks today represent my views only and are not intended to represent the views of Fish & Richardson or any of its clients.

Every Spring, I co-teach a 3-day patent course on the Hatch-Waxman Act and the law of "biosimilars." I always begin by pointing out two related statistics that frame the issues for the course: the first statistic underscores the low probability of success associated with new drug discoveries; and the second statistic highlights the extraordinarily high cost of bringing a new drug discovery to market. First the probabilities – according to the Pharmaceutical Research and Manufacturers Association, for every 5K-10K newly discovered compounds with therapeutic potential, only 250 will make their way into pre-clinical testing, only 5 will qualify for clinical trials, and only one will result in an approved new drug. Second the costs – according the Tufts University, which has modeled the cost of developing new drugs for well over a decade, in 2015, the fully loaded cost of bringing a new drug to market exceeded $2.5 billion. Any way you look at this data, the facts are indisputable -- drug development is an enormously costly and risky business.

Because the pharmaceutical business is essential to our public health, however, our legal system must properly incentivize and appropriately reward its risk-takers. This is where patent system come in; in exchange for publicly disclosing new drug discoveries, the law grants patent owners a monopoly on those discoveries (or inventions) for a limited time. Ideally, this should only be long enough for patent owners to recover their investment and return a reasonable profit. After that, these new drug developers should be willing to face market competition so that the public will benefit from lower cost medications.

In fact, this was one of the important goals of the 1984 Hatch-Waxman Act, and after 34 years of tinkering – the Act has been amended about a dozen times – many would argue that Congress now has it just about right. Today, 85% of prescriptions are filled with generic drugs, 35% of industry revenues go to generic manufacturers, yet brand investment in new drug R&D is at an all-time high exceeding more than $100 billion annually. More tellingly perhaps, in 2017 FDA approved more novel drugs than in any year over the previous decade. So, from the data, it looks like this legislation is working well for the American public.

Still, achieving that brand/generic balance has not been the smoothest of roads. At its core, Hatch-Waxman radically simplifies the drug approval process by allowing generic applicants to "piggyback" on proprietary clinical data strictly required for brand drug approval. In return, the generic must await the expiry of brand patents (which are listed in the FDA's Orange Book) or it must challenge those patents for earlier market entry. If challenged, however, Hatch-Waxman affords the brand an opportunity to litigate its patents prior to generic launch.

The math then, becomes simple – the more patents obtained for a drug, the longer the litigation and the slower the entry of generic drugs. Even after a generic drug is approved for launch, if patent litigation is ongoing the potential damages for infringement can be enormous (lost profits) – a risk that is too great for most generics to bear. Thus, under the original Hatch-Waxman scheme, brand manufacturers were incentivized to list as many patents as possible in the Orange Book and then litigate them aggressively as a business strategy to slow down competition and preserve market share. This patent gathering tactic was pejoratively known as "ever-greening."

Both Congress through legislation and FDA through various rulemakings have taken deliberate steps to stop patent ever-greening. But those efforts have only been partially effective. A recent study by The Hastings College of Law examined the types of patents submitted for Orange Book listing between 2005 and 2015 and concluded that ever-greening is still alive. For example, the study found that:

- 74% of the patents listed over this period were for previously-approved drugs;
- 80 of the 100 top selling drugs listed a new patent at least once; and 50 listed a new patent more than once; and
- 40% of <u>all drugs</u> listed new patents, with 80% of those listing patents more than once and some as many as 20 times.

In addition, brands have ventured to assert their patents in other ways to slow down generic competition, including the patenting of FDA-required REMS programs, entering into "pay for delay" settlement agreements and implementing so-called "product-hopping" strategies. Nonetheless, and despite anecdotal evidence to the contrary, all the available data seems to

indicate that the Hatch-Waxman balance is working as intended, as both the new drug and generic businesses appear to be thriving.

But what about on the biologic drug side? Until 2010, the US drug laws did not provide an abbreviated approval pathway for "me-too" biologics, known as biosimilars. The Affordable Care Act sought to change that with new rules for the approval of biosimilar drugs that were loosely modeled on the Hatch-Waxman scheme. Yet, stark differences remain. Most biologic drugs are produced by living organisms and thus, are very large molecules that are difficult to characterize and almost impossible to duplicate, even from batch to batch. For this reason, biosimilars must be studied more carefully than smaller molecule generics to determine their "therapeutic equivalence" to the brand. Clinical trials and detailed scientific analyses are required for biosimilars resulting in an approval process that is slower and much more expensive than for generic drugs. Moreover, full substitutability of a biosimilar for the brand biologic – automatic in generic world – requires separate FDA licensing, a process that has yet to be fully developed or understood. Accordingly, only the most financially well-healed manufacturers can afford to enter the biosimilar space which, understandably, severely limits future competition. Still, the rewards are tantalizing: in 2015, for example, nine of the top ten best-selling drugs in the world were biologics that averaged over $8 billion in annual sales.

As one would expect, patents also play an important part in the development of biologic drugs and the market entry of biosimilars – only more so when compared to small molecule generics. First, due to the complexity of these large molecules and the processes required to grow them, many more opportunities exist for securing patent protection. Take Humira for example. In 2015, we counted 76 patents protecting this $16 billion annual franchise; by 2017, the number was over 100 and still growing. Second, the biosimilar legislation created an elaborate scheme involving two potential "waves" of patent litigation prior to biosimilar launch. Although the Supreme Court ruled last year that the first litigation wave is optional, that does not diminish the fact that a large portfolio of patents presents can an equally large barrier to biosimilar entry.

As of this date, FDA has approved only nine biosimilar drugs (five in 2017 alone), three of which are now on the market. Patent litigation is tying up 18 other biosimilar applicants with approved or pending applications. Early pricing shows only a 15% discount off the price of the brand biologic with 35% discounting in the case of a second approved biosimilar to Remicade. Several reasons are given for these smaller discounts than what has been seen on the generic side: much higher regulatory costs to market entry; fewer anticipated competitors; no assurances of automatic substitution thus, requiring much higher direct marketing costs to physicians and hospitals; and significant higher manufacturing costs as compared to small molecule generics. The current situation in Europe, which is ahead of the US in biosimilar approvals, may be illustrative. There, three biosimilars to Remicade are competing on the market yet the discount from the brand is only 45%. The comparable discount for a three-competitor generic drug would be in the vicinity of 85%.

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I have attached to my testimony a year-end blog prepared by my law firm that contains additional relevant information about biosimilar market entry and pricing which should be helpful to the Committee. Thank you again for this opportunity to appear before you and I will be happy to try to answer any questions that Committee members might have.

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