The Paragraph Four Book

Gregory Glass

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This book is dedicated to my wife Susan and to the hundreds across the globe who subscribe to ParagraphFour.com

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Preface

This book is written for beginners as well as for those who have some degree of Paragraph IV experience, hence its light, informal tone. Paragraph IV veterans will find it to be a thorough and complete guide to the field.

I have been researching Paragraph IV patent cases since 2003. This research — housed at ParagraphFour.com — covers thousands of court cases and parallel activities (that is, Inter Partes Reviews [IPRs] and Citizen Petitions) that affect PIV court cases and their products. The insights revealed into "the Paragraph IV Market," and the value of those insights to various players in the PIV world serve as the basis for this book.

If you work at a generic drug company, you are familiar with your products and their paths through the ANDA process, how your company dynamics work, how your firm interacts with the FDA, and how decisions are made. But other companies may work differently; they take risks or identify opportunities that your company wouldn't. This book will help you see past the "bubble" of your own corporate environment.

A lawyer who has handled ten PIV cases in the past five years will have cultivated a great deal of expertise on the law, but consider that more than 300 PIV cases get filed each year. That lawyer might have little idea of how PIV cases behave in the aggregate. The context provided by this book's aggregate view will inform sounder legal strategies.

In both examples, the personal data points are just too small to provide an accurate picture of the PIV Market as a whole.

A comment made by an experienced PIV lawyer in *The Wall Street Journal* sums this up.[1] The article focused on how tough the PIV Market has become: "Today, four or more generic drug makers may launch a new generic at the same time, damping prices." The lawyer, given his personal experience, may have believed this to be true, but his statement did not reflect reality. A vast majority of generics entering the market through the PIV process had *fewer* than four competitors back in 2013 when the article was published, and this is still the case today. You have to count them all to know this fact instead of relying on the few data points you know.

The PIV Market is a puzzle that's missing a few pieces. While anyone who deals in this market will know *some* of the pieces, no one can possibly know *everything* about the PIV Market. That includes me.

Anyone who reads this book will learn something – from those with no knowledge of the PIV world to those with a great deal of experience.

If you **work for a generic drug company,** you will explore how PIV Market dynamics work. You'll make better portfolio decisions when it comes to choosing which products to pursue and when generic markets might emerge. Product selection, timing, and launch dates are critical to success. The PIV data show that some companies have figured out that working smarter (i.e. being more selective in their portfolios) is more productive than chasing down every possible opportunity, only to find out a dozen companies have also done the same thing. This book will be particularly helpful to those new to your business.

If you work at a brand-name pharmaceutical company, you will learn how generic drugs come to market using the PIV process. Did you know that 75% of brand products will not survive to the end of their patent terms? The data tell us this is true – and this likely includes your products. This book will help you make better, more informed lifecycle decisions whether they involve which indications and studies to pursue, how many promotional dollars to spend, and when is the best time to invest. Many companies view a PIV case as a "legal" problem. It's not. It's a "threat to revenue" business problem.

If you're a PIV attorney, this book will help you better serve your clients. Clients will be thirsty for information when they come to you for advice. They may ask, "If an IPR[2] is filed, how will that impact the PIV case or outcome?" You may have dealt with an IPR or two, but did you know that PIV data show that IPRs are more likely to fail than a PIV case/challenge? This is true, in spite of the fact that the legal proof standard is lower in an IPR. That one fact may enable better counsel and decision-making for your client — and there are many more gems in this book.

If you're an investor, you will develop a greater understanding of how the PIV Market operates so you can advise clients using data points and statistics. There are data behind *everything,* and the data reveal insights into how individual companies react to changes in the market. Using PIV data, you'll be able to discern what players' business strategies are and how successful they may become.

If you're an academic, you will become grounded in the PIV Market and understand the dilemmas players need to address before making decisions. This serves as a framework upon which you can examine research questions. There will always be unanswered questions about this market whether the implications are economic or related to public policy, firm behavior, brand management, or corporate strategy, to name a few.

On occasion, you may discover exceptions to the information I present. Standard disclaimer: this book cannot serve as legal advice nor substitute for legal counsel or answer specific questions about your product or PIV case.

This book is neither a footnote-heavy legal treatise nor a regulatory guide on preparing and filing an ANDA. That would make it technical, complicated, and boring. As such, while I cite a few sources at the end, I have avoided footnotes. Much of what is presented is either from legal or government sources or from my own extensive research.

Having researched the PIV world since 2003, I have encountered many myths and misconceptions. I will describe these along the way.

This book offers a framework for understanding the PIV universe and how it works. For constantly updated information on PIV cases and issues, see ParagraphFour.com and FDAPetitions.com (dedicated to citizen petitions).

— Gregory Glass - September, 2020

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What is PIV?

In 1984, Congress passed a law that set out to establish a process for how drugs are approved and come to market. It was an amendment to an existing law called the "Food, Drug, and Cosmetic Act." Lawmakers in the U.S. like to give their proposed laws either stuffy and pretentious titles or ones that try to elicit support from regular people and their representative lawmakers so that they vote for them without actually understanding them.

This was the case here. The amendment was called the "Drug Price Competition and Patent Term Restoration Act." Who would vote against "drug price competition" or "restoring patent terms?" Not too many apparently, as the measure passed through Congress and was signed into law.

But nobody calls it the "Drug Price Competition and Patent Term Restoration Act." Instead, they refer to its two original

sponsors: Senator Orrin Hatch and Congressman Henry Waxman—who created the Hatch-Waxman Act. A few people like to be different and call it the Waxman-Hatch Act, but they are few and far between.

These two lawmakers did everyone a solid favor. The system they created for drug approval—particularly generic drug approval—works well and has stood the test of time. While it has been tweaked and improved over the years by other amendments and FDA regulations, it is essentially the same as it was back in 1984.

The Act set up a system for drug approvals, and it covered the interactions between the legal and regulatory rules governing pharmaceutical products and patent law. Patent law is administered by a separate government agency, the U.S. Patent and Trademark Office (USPTO). The Act connected patents with drugs which, of course, are patented and need to wind through the approval process with the U.S. Food and Drug Administration (FDA).

The Act devised an ingenious scheme for drug approvals. After a brand drug gets approved, it needs to list three types of patents in a book called the *Approved Drug Products with Therapeutic Equivalence Evaluations.* Back in 1984 and over the course of the next decade or so, the FDA actually *printed* the *Approved Drug Products with Therapeutic Equivalence Evaluations* periodically because the Internet, like cellphones, did not exist for regular people.

The cover of the *Approved Drug Products with Therapeutic Equivalence Evaluations* was orange. Hence, everyone called it "the Orange Book." FDA calls it "the Orange Book," too, and it is now available as *The Electronic Orange Book* at *FDA.gov*.

The Act requires a brand-name pharmaceutical company to list patents in *The Orange Book* to publicly "stake its claim" to the primary patents covering its product. The term "brand-name pharmaceutical company," (or "brand company") refers to those companies that make proprietary drug products that have a trade name such as "Lipitor"® or "Nexium."® These companies include GlaxoSmithKline, Johnson & Johnson, and Bristol Myers, for example. A brand product will often have dozens (even hundreds) of patents that reference it, including some the brand company owns and others they don't. The Act requires the brand company to list the molecule (or compound) patent, the formulation patent, and the method of use patent for each of its products. (More on this later.)

The term "generic drug company" (or "generic company") means those drug companies that make the non-patented version of the brand. These are called by their molecule, or generic, name like "atorvastatin" or "esomeprazole." As patents are listed in the Orange Book, generic drug companies know what patents they need to consider when developing generic versions of brand products. These are the patents that are most likely to be

infringed if the generic product is developed and approved and brought to market.

When a generic company files an application to make a generic version of Brand A, the Act requires it to certify against each patent listed in the Orange Book for Brand A. This basically means that the generic company includes a formal statement (the "certification") in its application regarding each patent.

The statute (the Act) lists four certification types as roman numerals. The first two types of certifications (I and II) don't matter for our purposes. The important certification types are III and IV.

If a generic company submits a Paragraph III certification against a patent, it is stating to the FDA, "We think this patent is valid and that we may infringe it. Please approve of our application (and generic product) as soon as this patent expires."

The Paragraph IV certification is different. When a generic company submits a Paragraph IV certification, it does not want to wait for the patent to expire. The PIV certification states to FDA, "We think this patent is invalid or unenforceable, or our product does not infringe it. Please go ahead and approve our generic product so we can get it to market as soon as possible." "As soon as possible," typically means *before* the patent expires.

When the PIV certification is submitted, it sets off a chain of events that, in effect, creates its own market. "The PIV Market" will be discussed in the next chapter.