The Generic Challenge

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Understanding Patents, FDA and Pharmaceutical Life-Cycle Management (Sixth Edition)

Martin A. Voet

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Dedication

I would like to dedicate this Sixth Edition to my Dutch immigrant parents, Andries and Henriette Voet, who *first* had the foresight to board a boat to America in early 1939 ahead of the German invasion of Holland, thereby allowing me the privilege of being born in America; and *second*, when I was wondering what to do with myself after graduating UC Berkeley with a degree in chemistry that I did not want to pursue further, suggested that perhaps I could be a patent attorney.

"The desire to take medicine is perhaps
the greatest feature which distinguishes man from animals"
Sir William Osler, M.D.

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This book is intended to provide information about the subject matter covered. It is sold with the understanding that the publisher and author are not engaged in rendering legal services or providing legal advice. If legal advice is required, the services of a competent legal adviser should be obtained.

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Acknowledgments

I have not attempted to cite in the text all of the authorities and sources consulted in the preparation of this book. To do so would make the book cumbersome and probably unreadable to the non-professional. Besides, I wanted to write an enjoyable book that would be easy to read and understand and by implication, that means no footnotes.

A special thanks to my long time good friend and teaching colleague, George Lasezkay, for encouraging me to write this book, whose genesis was a chapter outline sketched out on a yellow legal pad in the spring sunshine of Sun Valley, Idaho between ski runs on Baldy.

About the Author

Martin A. Voet was formerly Senior Vice President and Chief Intellectual Property Counsel for a Fortune 500 pharmaceutical company with over twenty-five years' experience in pharmaceutical intellectual property practice. He is currently a consultant in intellectual property management and pharmaceutical product exclusivity and Adjunct Professor of Law at the University of San Diego Law School.

He graduated from the University of California at Berkeley with a B.S. in Chemistry; received an M.B.A. from Pepperdine University School of Business and Management and was awarded a J.D. with Honors from the George Washington University National Law Center. He is a member of the State Bar of California.

He has been a contributor to the Practicing Law Institute's *Global Intellectual Property* Series and its annual *Patent Litigation* series, contributor and member of the Editorial Board of *Managing Intellectual Property*, speaker at ACI's annual *Maximizing Pharmaceutical Patent Life Cycles* in New York and co-chaired ACI's West Coast conference on *Paragraph IV Disputes*.

He recently published an article in the American Bar Association IP Journal *Landslide* Magazine with Louis Cullman titled "*Re-Purposing and Enforcement during Patent Term Extensions for Pharma Products*", July/August 2016.

Preface to the Sixth Edition

The FDA is approving new drugs at a record pace as advances in biotechnology and genetics are enabling drug companies to obtain approvals of breakthrough drugs sooner. While the US Food and Drug Administration (FDA) approved just 22 new molecular entity (NME) drugs in 2016, it approved 46 in 2017, 59 in 2018 and 45 in 2019. In 2018, more than half the approved NMEs targeted rare (orphan) indications, three-quarters benefitted from priority review and one-quarter had breakthrough designations. Also in 2018 there were over 7,000 Investigational New Drug filings (INDs) on the FDA's books, which suggests abundant potential new drug approvals in future.

On the darker side, patient safety advocates argue that speed comes at a price and that studies show that medicines approved on a faster timeline are more likely to have safety issues after they become available or offer fewer benefits than anticipated.

While the Trump administration has focused on reducing regulations, the FDA's newfound efficiency is primarily based on user fees in return for firm deadlines and programs providing incentives for drug developers to develop products for patient groups with critical unmet needs and for rare (orphan) conditions.

Spending based on list prices of the top five brand name U.S. prescription drugs for 2018 (in *billions* of dollars) were as follows:

AbbVie's *Humira* for arthritis and psoriasis	$19.9
BMS' and Pfizer's *Eliquis* for reducing risk of stroke	9.9
Celgene's *Revlimid* for cancer treatment	9.7
Merck's *Keytruda* for cancer immunotherapy	7.2
Amgen's *Enbrel* for arthritis and psoriasis	7.1

Note *all* of these mega-successful drugs are biotech drugs. This dramatic change of leading drugs from chemically manufactured conventional small molecule drugs to biologically produced large molecule biotech drugs is the most important current and future trend in the pharmaceutical industry. In addition, the FDA has been active in approving new "biosimilars"—essentially generic equivalents of biological drugs. In addition, FDA has published a "Biosimilars Action Plan" intended to provide clarity to biosimilar applicants on a variety of issues.

As of the end of 2019, The FDA Purple Book, which lists all approved biological drugs, now lists 24 approved biosimilars. Discounts from list prices of the branded versions of these drugs ranges from 15–33%, though market share is currently relatively small. This is in contrast with conventional drugs where generics dominate the market at substantially reduced prices once the patents on the brand name drugs have expired. This is partially a result of the fact that biosimilars are not *interchangeable* with their corresponding branded products. But from an economic point of view, the more biosimilars approved for a product, the more prices should fall. However without mandatory substitution, biosimilars will likely only capture more market share if health care professionals make the conscious decision to start new patients on the corresponding approved biosimilar.

The European Union (EU) was well ahead of the US by having approved 54 biosimilars as of 2019 for a number of important disease conditions. They currently sell for 20–30% below the list prices of the name brand versions of these drugs.

An issue you often see mentioned, especially around election time, is overcoming the high price of new drugs by importing

cheaper drugs from Canada. The U.S. Supreme Court ruled in 2017 in *Impression v. Lexmark* that any authorized sale of a patented product by the patent owner anywhere in the world exhausts all patent rights in the product sold. As a result, the patent owner can no longer enforce post sale restrictions through patent infringement suits if its patented product is sold in a foreign country. This decision should help open the legal door to importation of drugs from Canada. But that is only the beginning in this regulated world.

In late 2019, the US Department of Health and Human Services (HHS) and the FDA issued a notice of proposed rulemaking and a draft guidance for the importation of certain prescription drugs—a move which would clear the way to import some prescription drugs from Canada. Also in 2019, Florida became the fourth state to pass a bill allowing for the importation of prescription drugs from Canada. This follows the Trump administration's announcement to that effect in July of 2019. It remains to be seen if any of this will come to pass and it could take years to implement, if ever.

It is my hope that this sixth edition at the start of a new decade will be a useful update of the book as the laws and regulations and court decisions affecting this fascinating subject continue to evolve.

Martin A. Voet
March 1, 2020

Preface to the First Edition

A horse walks into a bar and the bartender says, "Why the long face?" Why indeed. The pharmaceutical industry should be on top of the world with innovative discoveries and development of so many fantastic new drugs for treating life-threatening illnesses, while often avoiding expensive surgeries. There are targeted new drugs for treating once deadly cancers and for preventing blindness; wondrous new life-saving biotech products for treating stroke and multiple sclerosis; amazing new lifestyle enhancement drugs from growing hair and erasing wrinkles to maintaining sexual vigor; yet the pharmaceutical industry is trashed nightly as being second only to the tobacco industry in the corporations-we-hate-most department.

Politicians sensing this are quick to lay blame, announce conspiracies, demand lower prices and push for re-importation of low-priced drugs from foreign countries. African countries blame them as if they started the AIDS epidemic, instead of coming up with promising treatments. Generic drugs are thought to be the answer to what is wrong with healthcare, while innovators are viewed at best with a jaundiced eye. In this charged and decidedly unfriendly environment, why write this book?

In fact there is nothing wrong with generics and they are a valuable and necessary part of a good health care system. However, there would be no generics without the innovators and I am worried that the public has lost sight of this truism. This book is intended to encourage the innovators to persevere in the