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Reducing the Regulatory Role of the FDA: Promoting Patient Autonomy to Choose Avastin and Other Cancer Drugs Note

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Note

REDUCING THE REGULATORY ROLE OF THE FDA: PROMOTING PATIENT AUTONOMY TO CHOOSE AVASTIN AND OTHER CANCER DRUGS

SARA J. RAY

On November 18, 2011, the Food and Drug Administration (FDA) revoked accelerated approval of the breast cancer indication for Avastin, a cancer drug manufactured by Genentech. The FDA claims that Avastin, when used to treat metastatic breast cancer, does not provide a benefit that justifies the serious and potentially life-threatening risks associated with its use. The agency concluded that there was insufficient evidence that Avastin would help women with breast cancer live longer or improve their quality of life. This decision has sparked controversy and debate among women who want to keep Avastin available as an option to treat their breast cancer and view this decision as a death sentence.

This Note discusses the importance of keeping Avastin available as a treatment option for women with metastatic breast cancer and the propriety of the FDA's authority to remove approval of its use in the treatment of this life-threatening disease. In this Note, I will argue that there are wide-ranging problems resulting from the current system in which the FDA is able to regulate serious cancer drugs like Avastin. I further argue that these problems demonstrate that the FDA should no longer be the sole regulatory authority for cancer drugs like Avastin and propose an alternative system of regulation that is better aligned with the principle of patient autonomy.

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REDUCING THE REGULATORY ROLE OF THE FDA: PROMOTING PATIENT AUTONOMY TO CHOOSE AVASTIN AND OTHER CANCER DRUGS

SARA J. RAY*

I. INTRODUCTION

The American Cancer Society has estimated that this year in the United States about 226,870 new cases of invasive breast cancer will be diagnosed in women, 63,300 new cases of carcinoma in situ (the earliest form of breast cancer) will be diagnosed, and 39,510 women will die from breast cancer.¹ Excluding skin cancers, “[b]reast cancer is the most common cancer among American women,” with a woman having slightly less than a one-in-eight chance of developing invasive breast cancer during her lifetime.² With breast cancer being the second leading cause of cancer death in women, breast cancer holds a prominent place in public health with a national focus on early detection initiatives, increasing awareness, and improving treatment.³

In addition to providing general information about breast cancer, the American Cancer Society provides information on treatment options based on the opinions and professional experience of the doctors and nurses serving on its Editorial Board.⁴ Among some of the available treatments are surgery, radiation therapy, chemotherapy, hormone therapy, and targeted therapy.⁵ Many Americans are familiar with radiation and chemotherapy as cancer treatment options, but “[a]s researchers have learned more about the gene changes in cells that cause cancer, they have been able to develop newer drugs that specifically target these changes. These targeted drugs work differently from standard chemotherapy

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¹ *Breast Cancer: What Is Breast Cancer? Topics: What Are the Key Statistics About Breast Cancer?*, AM. CANCER SOC’Y, <http://www.cancer.org/Cancer/BreastCancer/DetailedGuide/breast-cancer-key-statistics> (last visited July 21, 2012).

² *Id.*

³ *See id.* (discussing decreasing fatality rates from breast cancer since 1990).

⁴ *Breast Cancer: Treating Breast Cancer Topics: How is Breast Cancer Treated?*, AM. CANCER SOC’Y, <http://www.cancer.org/Cancer/BreastCancer/DetailedGuide/breast-cancer-treating-general-info> (last visited July 21, 2012).

⁵ *Id.*

drugs . . . [and] are most often used along with chemotherapy.”⁶ Although targeted drugs are a more recent development, targeted therapy is an attractive treatment option available to those threatened with more serious and advanced cases of breast cancer.

One such targeted therapy treatment for advanced breast cancer is Bevacizumab, more commonly known as Avastin.⁷ Avastin, produced by the pharmaceutical company Genentech, “first received accelerated approval by the [FDA]” in 2008 to treat metastatic breast cancer.⁸ The data backing the FDA’s approval for the drug indicated that combining Avastin with chemotherapy extended the time it took for the disease to progress when compared to chemotherapy treatments alone.⁹ “As part of the accelerated approval process, Genentech agreed to conduct further studies” of the drug to determine whether women taking Avastin indeed lived longer as a result.¹⁰

Although Genentech’s research and development of Avastin to treat metastatic breast cancer has been ongoing, an advisory committee to the FDA voted unanimously to remove approval of Avastin for this indication because recent studies did not show the drug to be safe and effective.¹¹ The 6-0 vote caused the FDA to rescind its approval,¹² which was granted “under a system” allowing for promising drugs that treat serious diseases “to [reach the] market more rapidly,” subject to further studies.¹³ Even though the approval of Avastin for breast cancer has been rescinded, the drug can still be prescribed “off-label” to treat breast cancer. Insurers, however, are now less likely to pay for the drug, “which can cost \$88,000 a

⁶ *Breast Cancer: Treating Breast Cancer Topics: Breast Cancer Targeted Therapy*, AM. CANCER SOC’Y, <http://www.cancer.org/Cancer/BreastCancer/DetailedGuide/breast-cancer-treating-targeted-therapy> (last visited July 21, 2012).

⁷ *Id.*

⁸ Rebecca V. Snowden, *FDA Advisory Panel Votes Against Avastin for Advanced Breast Cancer*, AM. CANCER SOC’Y (July 20, 2010), <http://www.cancer.org/Cancer/news/News/fda-advisory-panel-votes-against-avastin-for-advanced-breast-cancer>.

⁹ *Id.*

¹⁰ *Id.*; see also Hal Barron, Letter to the Editor, *Judging a Cancer Drug: Avastin’s Story*, NYTIMES.COM, (June 1, 2011), <http://www.nytimes.com/2011/06/02/opinion/102avastin.html> (“We continue to study Avastin . . . [and] believe that women who are trying to control their disease should retain the autonomy to decide, based on the facts, whether Avastin is right for them.”). Hal Barron is the chief medical officer and head of global product development for Genentech. *Id.*

¹¹ Andrew Pollock, *F.D.A. Panel Rejects Use of Avastin for Breast Cancer*, NYTIMES.COM (June 29, 2011), <http://prescriptions.blogs.nytimes.com/2011/06/29/f-d-a-panel-still-sees-no-benefit-of-avastin-for-breast-cancer/?scp=1&sq=f.d.a.%20panel%20rejects%20use%20of%20avastin&st=cse> [hereinafter *F.D.A. Panel Rejects Use of Avastin for Breast Cancer*].

¹² U.S. Dep’t Health & Human Servs., *Commissioner Statement: FDA Commissioner Removes Breast Cancer Indication from Avastin Label* (Nov. 18, 2011), <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm279485.htm> [hereinafter *Commissioner Statement*].

¹³ Andrew Pollock, *Breast Cancer Patients Plead for Avastin Approval*, NYTIMES.COM, (June 28, 2011), http://www.nytimes.com/2011/06/29/business/29drug.html?_r=1&scp=1&sq=breast%20cancer%20patients%20plead&st=cse [hereinafter *Breast Cancer Patients Plead for Avastin Approval*].

year” for one patient.¹⁴ Many claim that this decision effectively results in a death sentence for women with metastatic breast cancer who “want every available weapon in [their] arsenal as [they] fight this devastating disease.”¹⁵

This Note discusses the importance of keeping Avastin available as a treatment option for women with metastatic breast cancer and the propriety of the FDA’s ability to remove approval for its use in the treatment of this life-threatening disease. It presents the wide-ranging problems that are raised by the current system of FDA regulation of serious cancer drugs like Avastin. It argues that these problems demonstrate that the FDA should no longer be the sole regulatory agency for cancer drugs like Avastin and proposes an alternative system of regulation that is more in line with American values, while preserving the legitimate purposes and goals of the FDA.

Part II discusses the history of Avastin in the marketplace and the authority of the FDA to regulate cancer treatments as a means of promoting public health. This Part looks at the development, approval, and regulation of Avastin for treatment of metastatic breast cancer, the current state of Avastin following the FDA’s decision, and the significant effects that removing FDA approval for Avastin has on women with metastatic breast cancer. This Part also introduces the current problems and debates in this area.

Part III analyzes the wide-ranging problems that are raised by FDA regulation of cancer treatments like Avastin. This Part begins by looking at the significant burdens placed on individual patient autonomy in choosing effective forms of treatment under the guidance of a physician. Second, this Part discusses how FDA regulations have raised political debate in health care reform by those claiming the government is engaging in health care rationing when it denies expensive medical treatments to individuals. Lastly, this Part shows how the FDA’s decision increases the costs of drug development, slows down the rate of adopting effective new uses of cancer drugs for serious diseases, and limits the ability of prescribing physicians to receive useful medical information from drug developers. This Part concludes that these problems collectively demonstrate that the FDA is not the proper body to regulate Avastin and should no longer have the sole authority to regulate this type of drug.

Finally, Part IV argues that the existing system for Avastin and other cancer treatments should be modified. This Part focuses on the purposes of the FDA to demonstrate that while the FDA may be well-suited to regulate cosmetic drugs, its purposes are frustrated when it regulates

¹⁴ *F.D.A. Panel Rejects Use of Avastin for Breast Cancer*, *supra* note 11.

¹⁵ *Breast Cancer Patients Plead for Avastin Approval*, *supra* note 13 (internal quotation marks omitted).

cancer drugs like Avastin. Therefore, an alternative system should be implemented. This Part presents three alternatives that could follow the implementation of relaxed licensing requirements: (1) reassigning the regulatory role to patients and physicians through the process of shared decision making; (2) regulating through voluntary private organizations; and (3) permitting insurance payors to take charge of regulating once Avastin passes initial threshold approval from the FDA. This Part concludes that these proposals better serve the purposes of public health and thus one of them should be adopted.

This Note concludes that there should be a new scheme enacted to regulate cancer drugs like Avastin after they satisfy initial threshold licensing approval by the FDA.

II. THE HISTORY OF AVASTIN AND FDA REGULATION

A. *The Development of Avastin for Treatment of Breast Cancer*

The pharmaceutical company Genentech developed the drug Avastin to treat individuals with metastatic cancers. Avastin is currently approved to treat metastatic colorectal cancer, advanced nonsquamous non-small cell lung cancer, glioblastoma, and metastatic kidney cancer.¹⁶ Avastin is not chemotherapy, but is a “tumor-starving therapy” designed to control cancer longer than with chemotherapy alone by prohibiting blood vessels from accessing a cancer tumor, making the tumor shrink, and keeping it from spreading.¹⁷ Studies have shown that compared with chemotherapy alone, people taking Avastin with chemotherapy are more likely to “[h]ave their tumors shrink[,] [k]eep their cancer controlled longer[,] [and] [l]ive longer.”¹⁸ Additionally, “[t]he most common side effects of Avastin are: nosebleeds, headache, high blood pressure, inflammation of the nose, too much protein in the urine, taste change, dry skin, rectal bleeding, tear production disorder, back pain, and inflammation of the skin.”¹⁹

The FDA approved Avastin for the treatment of metastatic breast cancer in 2008 based on a study in which the women who took Avastin along with chemotherapy experienced a longer duration of stalled cancer

¹⁶ AVASTIN: WHAT DOES AVASTIN TREAT?, <http://www.avastin.com/patient/index.html> (last visited July 21, 2012).

¹⁷ GENENTECH, AVASTIN: GETTING STARTED WITH AVASTIN, http://www.avastin.com/concatenate/Avastin_Patient_TearPad.pdf?srcUrl=http://prod.avastin.gene.s3.amazonaws.com/patient/pdf/20120220/Avastin-Getting-Started.pdf&srcUrl=http://www.gene.com/gene/products/information/pdf/avastin-prescribing.pdf (last visited Aug. 30, 2012).

¹⁸ *Id.*

¹⁹ AVASTIN: WHAT DOES AVASTIN TREAT?, *supra* note 16. More serious side effects include gastrointestinal perforation, slow or incomplete wound healing, and serious (sometimes fatal) bleeding. *Id.*

growth than women who underwent chemotherapy treatment alone.²⁰ In July 2010, new study results were presented that did not show the same benefit for women who took Avastin to treat their cancer.²¹ The FDA concluded from these results that the risks of the drug outweighed the benefits in the treatment of metastatic breast cancer and, on December 16, 2010, announced a plan to remove the breast cancer indication for Avastin.²² Genentech responded by calling for a hearing on the FDA's conclusion before the FDA Commissioner, Margaret Hamburg, was to issue a final decision.²³ Rescission of FDA approval means that Genentech can no longer market Avastin for breast cancer by telling physicians or patients that the drug may help treat breast cancer, but Avastin will still be available in the drug market to treat indications for which it remains approved, such as lung and colon cancers.²⁴ Oncologists will still be able to prescribe Avastin to treat breast cancer on an "off-label" basis. Insurance companies, however, are less likely to cover this type of use, thereby escalating the cost of Avastin to around \$88,000 a year for a typical breast cancer patient.²⁵ There are many who fear that this decision will greatly hinder the individual's access to treatment.²⁶

²⁰ Snowden, *supra* note 8.

²¹ U.S. Dep't Health & Human Servs., *FDA News Release: FDA Begins Process to Remove Breast Cancer Indication from Avastin Label* (Dec. 16, 2010), <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2010/ucm237172.htm>. The study showed that although Avastin seemed to slow cancer growth for some of the women, it did not help them live longer and they had much more severe side effects. *Id.*

²² *Id.*

²³ *Commissioner Statement, supra* note 12.

²⁴ Snowden, *supra* note 8. The deputy chief medical officer of the American Cancer Society, Len Lichtenfeld, MD, recommended women currently taking Avastin to talk to their oncologists about what course of action to take pending the decision from the FDA. He noted "[t]hese studies and recommendations do not have any impact on the use of [Avastin] in the treatment of other forms of cancer where the FDA has given approval, such as colon cancer and lung cancer This review applies only to the specific recommendation regarding the use of [Avastin] in the treatment of recurrent breast cancer." *Id.* (internal quotation marks omitted).

²⁵ Andrew Pollack, *F.D.A. Plans to Revoke Approval for Breast Cancer Drug*, NY TIMES: PRESCRIPTIONS, (Dec. 16, 2010), <http://prescriptions.blogs.nytimes.com/2010/12/16/f-d-a-revokes-approval-for-breast-cancer-drug> [hereinafter *F.D.A. Plans*]; see also Letter from Hal Barron, Chief Medical Officer and Head, Global Product Development, Genentech to Avastin Patient (Nov. 18, 2011), available at http://www.gene.com/gene/products/information/pdf/avastin_informationforpatient_s.pdf (informing patients that "[t]he FDA's withdrawal of approval means that some insurers may no longer pay for Avastin for breast cancer").

²⁶ See, e.g., Jason Millman, *Following Avastin Decision, Republicans Say FDA Rationing Care*, THE HILL: HEALTHWATCH (Dec. 16, 2010, 6:06 PM), <http://thehill.com/blogs/healthwatch/medical-devices-and-prescription-drug-policy-/134131-following-avastin-decision-republicans-say-fda-rationing-care-> (sharing breast cancer advocate Susan G. Komen for the Cure's desire "to be sure that women who are using Avastin, and for whom it is working, can continue to have access to it, that their insurers will continue to pay for it and that the drug's manufacturer, Genentech/Roche, continues making the drug available to women through its patient support programs" (internal quotation marks omitted)).

It is a rare occurrence for the FDA to remove approval of a drug that has received accelerated approval.²⁷ By contrast, “[e]uropean authorities have not revoked Avastin’s approval for” this indication.²⁸ This decision has been controversial as breast cancer patients and patient advocacy groups claim that by not keeping the drug approved the FDA “den[ies] patients a chance at . . . a life-saving therapy.”²⁹ Genentech appealed to the FDA to keep Avastin available as a treatment option, arguing that “approval should be retained while [they conducted another] clinical trial.”³⁰ The FDA responded that since it had already found that the “benefits of [the drug did not] outweigh the risks, retaining the approval” during a new study “would not be in the interest of the public health and would jeopardize the integrity of the accelerated approval program.”³¹ Ultimately, the accelerated approval that had been granted by the FDA for the breast cancer indication was revoked by the Commissioner.³²

There are advocates on both sides of the Avastin debate. Some have urged the FDA “to revoke the approval to maintain the integrity of the accelerated process.”³³ On the other hand, there were “[a]bout a dozen

²⁷ *F.D.A. Plans*, *supra* note 25.

²⁸ Julian Pecquet, *FDA Defends Restrictions on Avastin Cancer Drug*, THE HILL: HEALTHWATCH (Jan. 7, 2011, 12:47 PM), <http://thehill.com/blogs/healthwatch/medical-device-and-prescription-drug-policy/136617-fda-defends-restrictions-on-avastin-cancer-drug>. European authorities, however, “have recommended restricting” Avastin to be “only used [with one specific] type of chemotherapy, paclitaxel.” *Id.*; see also *Breast Cancer Drug ‘Still Safe’ for Aussie Women*, ABC NEWS (July 22, 2010), <http://www.abc.net.au/news/2010-07-22/breast-cancer-drug-still-safe-for-aussie-women/914514> (noting that Avastin has remained available in Australia and “continues to be an option for women” with metastatic breast cancer).

²⁹ *F.D.A. Plans*, *supra* note 25. Some have called the FDA’s decision “cost control” or “rationing” “under the new health care law.” *Id.*

³⁰ Andrew Pollack, *Genentech to Appeal to F.D.A. for Breast Cancer Drug*, NYTIMES.COM (June 26, 2011), <http://www.nytimes.com/2011/06/27/health/27drug.html> [hereinafter *Genentech to Appeal*] (arguing that “[e]ven where [the] F.D.A. determines that confirmatory trials do not establish clinical benefit, withdrawal is not required” (internal quotation marks omitted)).

³¹ *Id.* (internal quotation omitted).

³² *Commissioner Statement*, *supra* note 12. According to the Commissioner: “[Avastin] has not been shown to provide a benefit, in terms of delay in the growth of tumors, that would justify its serious and potentially life-threatening risks. Nor is there evidence that use of Avastin will either help women with breast cancer live longer or improve their quality of life.” *Id.* However, Commissioner Hamburg did “encourage Genentech to consider additional studies to identify if there are select subgroups of women suffering from breast cancer who might benefit from this drug.” U.S. Dep’t Health & Human Serv., *FDA News Release: FDA Commissioner Announces Avastin Decision* (Nov. 18, 2011), <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm280536.htm> (internal quotation marks omitted). In fact, Genentech chief medical officer and head of Global Product Development, Hal Barron, M.D., said that “[d]espite today’s action, we will start a new Phase III study of Avastin in . . . previously untreated metastatic breast cancer and will evaluate a potential biomarker that may help identify which people might derive a more substantial benefit from Avastin.” Genentech, *FDA Commissioner Announces Final Decision on Avastin for Metastatic Breast Cancer* (Nov. 18, 2011), available at <http://www.gene.com/gene/news/press-releases/display.do?method=print&id=13687> (internal quotation marks omitted).

³³ *Genentech to Appeal*, *supra* note 30.

women with breast cancer” who came to Genentech’s hearing in front of the FDA to testify that “the [drug] does help some women” and “should [remain] available to them.”³⁴ As the *New York Times* reported: “Representatives of advocacy groups for patients with ovarian, kidney and colon cancer and melanoma also spoke in favor of retaining the breast cancer approval, saying, among other things, that revocation could discourage drug development.”³⁵ Some advocates for the drug have called the hearing a “death trial, not of Avastin but of [the] women who rely on Avastin to stay alive.”³⁶ As one physician noted prior to the decision, “[t]he FDA’s decision is not going to be an easy one. It is our hope they will make that decision with full consideration of the science and the interests of the public, and the women who have been and will continue to be diagnosed with metastatic breast cancer.”³⁷

In a society where progress in medicine and the development of innovative treatments are not just encouraged, but praised, it is hard to believe that a promising drug like Avastin has sparked so much debate and controversy. The choice by the FDA to follow the panel’s recommendation is a setback for both the development of Avastin and “the treatment of advanced metastatic breast cancer.”³⁸ This decision is particularly troublesome when one considers the significant effect that breast cancer has on women throughout the nation.³⁹ The unyielding views on both sides of the Avastin debate indicate that there are significant policy themes underlying this issue.

B. *The FDA’s Authority to Regulate*

The Federal Food, Drug, and Cosmetic Act (“FDCA”) of 1938 was a “complet[e legislative] overhau[l of] the public health system . . . authori[z]ing the FDA to demand evidence of safety for new drugs, issue standards for food, and conduct factory inspections.”⁴⁰ The FDCA has a substantial impact on food and drug products in the United States today,

³⁴ Andrew Pollack, *Cancer Survivors Appeal to F.D.A. over Avastin*, NY TIMES: PRESCRIPTIONS (June 28, 2011, 1:27 PM), <http://prescriptions.blogs.nytimes.com/2011/06/28/cancer-survivors-appeal-to-f-d-a-over-avastin>.

³⁵ *Id.*

³⁶ *Id.* (internal quotation marks omitted).

³⁷ Dr. Len, *FDA Advisors Vote Unanimously That Avastin Approval Should be Withdrawn, and You Could Hear the Pain*, AM. CANCER SOC’Y: DR. LEN’S CANCER BLOG (June 29, 2011), <http://www.cancer.org/AboutUs/DrLensBlog/post/2011/06/29/FDA-Advisors-Vote-Unanimously-That-Avastin-Approval-Should-Be-Withdrawn-And-You-Could-Hear-The-Pain>.

³⁸ Todd Zwillich, *FDA Panel Opposes Avastin for Breast Cancer: Advisory Panel Recommends That Avastin be Dropped as a Breast Cancer Drug*, WEBMD HEALTH NEWS (June 29, 2011), <http://www.webmd.com/breast-cancer/news/20110629/fda-panel-opposes-avastin-for-breast-cancer>.

³⁹ See *supra* notes 1–3 and accompanying text.

⁴⁰ U.S. Dep’t Health & Human Servs., *Regulatory Information: Legislation*, <http://www.fda.gov/RegulatoryInformation/Legislation/default.htm> (last visited July 21, 2012).

regulating \$1 trillion worth of products per year.⁴¹ Under the authority of the Act, the FDA governs how pharmaceutical drugs like Avastin acquire approval to be sold and how they are subsequently regulated in the marketplace.⁴² The FDCA prohibits the introduction of any new drug into interstate commerce unless the drug has been filed with and approved by the Secretary of Health and Human Services.⁴³

The Act establishes the power of the FDA⁴⁴ and authorizes the Secretary “to conduct examinations and investigations for the purposes of [the Act] through officers and employees of the Department.”⁴⁵ A “drug” under the Act is broadly defined as “articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease . . . intended to affect the structure or any function of the body.”⁴⁶ One who uses drugs in violation of the Act is subject to penalties, such as the seizure and destruction of the drugs,⁴⁷ injunctions against further use of the drugs,⁴⁸ fines, or imprisonment.⁴⁹ The FDA has thus been conferred broad authority under the FDCA to regulate in this area.

The U.S. Food and Drug Administration’s Center for Drug Evaluation and Research (“CDER”) “promotes and protects the health of Americans by assuring that all prescription and over-the-counter drugs are safe and effective.”⁵⁰ The CDER has the important task of evaluating all new drugs before they enter the market and monitoring more than 10,000 drugs currently on the market to make sure they continue to meet high standards.⁵¹ The Center’s evaluations provide doctors and patients with information that enables them to use medicines wisely, and the CDER continues to develop its drug safety program to ensure that drugs are used safely once they are approved.⁵² The Center also ensures that both brand-name and generic drugs work correctly and that their health benefits outweigh their known risks.⁵³

Under the FDCA, a new drug is approved for a specified and intended

⁴¹ *Id.*

⁴² Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 301–399 (2006).

⁴³ *Id.* § 355(a)–(b).

⁴⁴ *Id.* § 393.

⁴⁵ *Id.* § 372.

⁴⁶ *Id.* § 321(g)(1).

⁴⁷ *Id.* § 334.

⁴⁸ *Id.* § 332.

⁴⁹ *Id.* § 333(a)–(b).

⁵⁰ DEP’T HEALTH & HUMAN SERVS.: FOOD & DRUG ADMIN., IMPROVING PUBLIC HEALTH: PROMOTING SAFE AND EFFECTIVE DRUG USE, PUBLICATION NO. FS 01-3 (Aug. 2003) [hereinafter PROMOTING SAFE AND EFFECTIVE DRUG USE] (emphasis omitted).

⁵¹ *Id.*

⁵² U.S. FDA, *Drugs: CDER: The Consumer Watchdog for Safe and Effective Drugs*, U.S. DEP’T HEALTH & HUMAN SERVS., <http://www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm143462.htm> (last visited July 21, 2012).

⁵³ *Id.*

use after a manufacturer provides sufficient evidence that the drug is safe and effective for the medical condition prescribed, recommended, or suggested on the label.⁵⁴ Drug companies seeking to sell and distribute a drug must undergo a rigorous two-step approval process: an Investigational New Drug (“IND”) application followed by a New Drug Application (“NDA”).⁵⁵ This process first requires a drug manufacturer to conduct investigations on the effect of the drug on animals to discover how the drug works and whether it is likely to be safe and effective for humans.⁵⁶ Once this is shown, the drug can then be tested for safety in human clinical trials after the manufacturer submits the IND application.⁵⁷

Once an IND application is approved, the drug must undergo clinical trials. Tests are performed to establish whether the drug will safely treat a disease and whether it will provide health benefits.⁵⁸ Once testing is completed, the drug manufacturer may then submit an NDA to introduce a new drug product into the U.S. market.⁵⁹

Drug companies who wish to market, sell, and distribute a drug in the United States must “test it and submit evidence [to the CDER] that it is safe and effective” for its intended use.⁶⁰ The Center then employs its own team of physicians, statisticians, chemists, pharmacologists, and other scientists to review the company’s data and proposed labeling.⁶¹ This process is designed to be an independent and unbiased review of the test data to establish that a drug’s health benefits indeed outweigh its known risks; however, the Center does not itself test drugs.⁶² The Center instead conducts research into the drug’s quality, safety, and effectiveness before permitting testing in humans. After human testing is completed, if the drug meets all of the Center’s standards, it is then approved for marketing, sale, and distribution in the United States, subject to the Center’s determination about what the label should say about directions for use, side effects, and

⁵⁴ 21 U.S.C. § 321(p)(1) (2006).

⁵⁵ See U.S. FDA, *Drugs: Development & Approval Process (Drugs): How Drugs Are Developed and Approved*, U.S. DEP’T HEALTH & HUMAN SERVS., <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/default.htm> (last visited July 21, 2012) [hereinafter *How Drugs Are Developed and Approved*] (discussing the process of drug development).

⁵⁶ U.S. FDA, *Drugs: Development & Approval Process (Drugs)*, U.S. DEP’T HEALTH & HUMAN SERVS., <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/default.htm> (last visited July 21, 2011) [hereinafter *Development and Approval Process*].

⁵⁷ *How Drugs Are Developed and Approved*, *supra* note 55.

⁵⁸ *Development and Approval Process*, *supra* note 56.

⁵⁹ *How Drugs Are Developed and Approved*, *supra* note 55.

⁶⁰ *Id.*

⁶¹ *Id.*

⁶² *Development and Approval Process*, *supra* note 56.

warnings.⁶³

Although the CDER asserts that it “continues to facilitate development of new drugs and new uses for already-approved drugs,” in 2002 the approval of truly new drugs was at its lowest level in a decade.⁶⁴ In response to these figures, the Center took steps “to remove barriers to innovation in drug development and to facilitate the modernization of American drug manufacturing” by launching new initiatives.⁶⁵ Specifically in the area of cancer drug approvals, the FDA’s Office of Oncology Drug Products “is committed to facilitating rapid development, review, and action on promising new cancer therapies . . . [providing] the basis for accelerating introduction of new treatments for cancer into practice.”⁶⁶ The FDA also recognizes that “[s]peeding the development and availability of drugs that treat serious diseases benefits everyone, especially when the drugs are the first available treatment or have advantages over existing treatments.”⁶⁷

The FDA is mindful of the fact that it can take a long time—often years—to study a new drug and discover whether it provides a real benefit, such as living longer or feeling better.⁶⁸ Thus for certain serious or life-threatening diseases, the FDA has the power to grant accelerated approval for a drug under the Accelerated Approval regulation, which allows for drugs that treat serious diseases to receive earlier approval, based on a “surrogate endpoint.”⁶⁹ Post marketing clinical trials must then verify the predicted clinical benefit for the FDA to grant traditional approval for the drug.⁷⁰ By using the surrogate, the drug’s approval process can be shortened considerably, saving valuable time instead of waiting to learn if a drug actually extends one’s survival.⁷¹ If the confirmatory trial does not

⁶³ U.S. FDA, *Drugs: New Drug Application (NDA)*, U.S. DEP’T HEALTH & HUMAN SERVS., <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/NewDrugApplicationNDA/default.htm> (last visited July 21, 2012).

⁶⁴ PROMOTING SAFE AND EFFECTIVE DRUG USE, *supra* note 50.

⁶⁵ *Id.*

⁶⁶ *How Drugs are Developed and Approved: Cancer Drug Approvals*, *supra* note 55.

⁶⁷ U.S. FDA, *For Consumers: Consumer Information by Audience: For Patients and Patient Advocates: Speeding Access to Important New Therapies: Fast Track, Accelerated Approval and Priority Review*, U.S. DEP’T HEALTH & HUMAN SERVS., <http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/SpeedingAccessstoImportantNewTherapies/ucm128291.htm> (last visited July 21, 2012).

⁶⁸ *Id.* (“This real improvement is known as a ‘clinical outcome.’”).

⁶⁹ *Id.* A surrogate endpoint is not conclusive of a drug’s benefit, but “represents a clinically meaningful outcome, such as survival or symptom improvement. The use of a surrogate endpoint can considerably shorten the time required prior to receiving FDA approval.” *Id.*

⁷⁰ *Id.*

⁷¹ *Id.*

show the drug provides a clinical benefit, the FDA can then remove the drug from the market under its regulatory procedures.⁷²

The FDA has several policies and procedures that give the public the impression that it is dedicated to medical progress, such as the accelerated approval process. This commitment is particularly noteworthy in the FDA's Office of Oncology, which helps oversee Avastin for breast cancer. The current discussion around Avastin seems to be contrary to the FDA's philosophy, however, as its recent decision halts the development and manufacturing of Avastin for metastatic breast cancer. The effect of the FDA's decision ultimately is to hinder innovation in the development of this drug for that indication and cripple its manufacturing by Genentech. While the FDA claims to be justified in its reasons, this action is contrary to its advertised commitment to "facilitating rapid development, review, and action on promising new cancer therapies."⁷³

III. PROBLEMS RAISED BY FDA REGULATION OF AVASTIN

A. *Limitations on Patient Autonomy and the Problem of Paternalism*

The principle of autonomy is one of self-rule or self-determination, which regards individuals as the sole and exclusive owners of their person.⁷⁴ Put another way, autonomy allows an individual to use his or her body and natural faculties in ways that do not infringe on the autonomy or liberty of others.⁷⁵ There has been a longstanding tension between individual autonomy and social control because a rigid adherence to the principle of autonomy inhibits the ability of the state to organize the provision of public goods.⁷⁶ While government regulations deal with many public goods and common problems, the principle of autonomy influences "the decisions that individuals make over their own bodies" and has been used by patients to guide decisions regarding medical treatments, particularly in the area of life-threatening illnesses like metastatic breast cancer.⁷⁷

There are two components of patient autonomy: rejection and acceptance of medical treatment. Judge Benjamin Cardozo famously described this principle nearly a century ago when he wrote:

Every human being of adult years and sound mind has a right

⁷² *Id.*

⁷³ See *supra* note 66 and accompanying text.

⁷⁴ Richard A. Epstein, *The Erosion of Individual Autonomy in Medical Decisionmaking: Of the FDA and IRBs*, 96 GEO. L.J. 559, 564 (2008) [hereinafter *Of the FDA and IRBs*].

⁷⁵ *Id.* at 565.

⁷⁶ Richard A. Epstein, *Against Permittitis: Why Voluntary Organizations Should Regulate the Use of Cancer Drugs*, 94 MINN. L. REV. 1, 1 (2009) [hereinafter *Against Permittitis*].

⁷⁷ *Id.* at 2.

to determine what shall be done with his own body; and a surgeon who performs an operation without his patient's consent commits an assault, for which he is liable in damages This is true, except in cases of emergency where the patient is unconscious, and where it is necessary to operate before consent can be obtained.⁷⁸

Individuals may use the principle of personal autonomy defensively to refuse medical treatment that others conclude will benefit them. By contrast, the offensive use of autonomy—or “the right to accept treatment with consent—has been widely rejected today.”⁷⁹ As Professor Epstein observed, “[the] ability to reject treatment [is] in . . . tension with claims for modest paternalism on the ground that health, not [individual patient] autonomy, is the paramount social end.”⁸⁰ While a mentally competent adult patient has a near absolute right to refuse treatment where there is no harm to others,⁸¹ no individual has a right to demand whatever medical treatment or drugs he wishes to receive. The FDA must license a drug before it can be made available for general sale or use by the public.⁸² The distinction between the patient's right to accept or reject treatment is what shapes the role of the FDA in American law today.⁸³

Respect for a patient's autonomy in making medical decisions is a fundamental value in bioethics. This is so because the field of bioethics developed alongside a conceptual shift away from paternalism and towards respect for patient autonomy as the center of the physician-patient relationship.⁸⁴ One manifestation of the right to reject medical treatment was the rise of the doctrine of informed consent. Today, decision-making power has shifted from physicians to patients, who obtain medical information to guide their decisions on what procedures to undergo, what risks to accept, and what pain to endure.⁸⁵ This doctrine has longstanding roots found in the visions of autonomy articulated by political theorists:

In the conduct of human beings towards one another, it is necessary that general rules should for the most part be observed, in order that people may know what they have to expect; but in each person's own concerns, his individual

⁷⁸ *Schloendorff v. Soc'y of N.Y. Hosp.*, 105 N.E. 92, 93 (N.Y. 1914) (citations omitted).

⁷⁹ *Against Permittitis*, *supra* note 76, at 2.

⁸⁰ *Of the FDA and IRBs*, *supra* note 74, at 567.

⁸¹ Mary Ann Baily, *Futility, Autonomy, and Cost in End-of-Life Care*, 39 J.L. MED. & ETHICS 172, 172 (2011).

⁸² *Against Permittitis*, *supra* note 76, at 2–3.

⁸³ *Of the FDA and IRBs*, *supra* note 74, at 570.

⁸⁴ See Baily, *supra* note 81, at 172 (discussing the conceptual shift from paternalism to patient autonomy in the physician-patient relationship).

⁸⁵ *Of the FDA and IRBs*, *supra* note 74, at 568.

spontaneity is entitled to free exercise. Considerations to aid his judgment, exhortations to strengthen his will, may be offered to him, even obtruded on him, by others; but he himself is the final judge. All errors which he is likely to commit against advice and warning, are far out-weighed by the evil of allowing others to constrain him to what they deem his good.⁸⁶

While informed consent promotes the second part of individual autonomy—the right to accept potentially harmful medical treatments—there is currently an uneven acceptance of this part of the autonomy principle that has manifested in the area of drug regulation. FDA regulation of Avastin is an example of this problem.

It is argued herein that the FDA regulation of drugs restricts one's personal liberty. The FDA has the power to keep cancer drugs off the market, "thereby limiting the scope of autonomous choices" for individuals with this disease.⁸⁷ The normal principles of individual autonomy do not apply until a drug makes it to the marketplace; no individual is entitled to use any drug unless the FDA has approved it for sale and distribution.⁸⁸ Once a drug enters the market, however, it may be used for any purpose for which it has not received FDA approval because the FDA does not have the power to regulate the practice of medicine. The FDCA provides that the FDA does not have the authority to "limit or interfere with the authority of a health care practitioner to prescribe" any medication that has received FDA approval.⁸⁹ Such uses are considered "off-label" and are the only kind for which Avastin may be used to treat advanced breast cancer.⁹⁰

Although the FDCA allows a physician to prescribe Avastin for an off-label use, the Act still prohibits drug manufacturing companies like Genentech from promoting Avastin for that purpose, which is illegal under the Act.⁹¹ The law even goes as far as to prevent drug companies from warning physicians and the public about any negative side effects of their products, in hopes that the warning will not be misconstrued as implied approval from the FDA to use the drug.⁹² Such regulations impair both patients and physicians from gathering the necessary information to make informed treatment decisions together.

Arguably, patients have the right to determine their medical treatment based on the doctrine of informed consent. Under this doctrine, a patient

⁸⁶ *E.g.*, JOHN STUART MILL, ON LIBERTY AND OTHER ESSAYS 85 (1991).

⁸⁷ *Against Permittitis*, *supra* note 76, at 3.

⁸⁸ *Of the FDA and IRBs*, *supra* note 74, at 570.

⁸⁹ 21 U.S.C. § 396 (2006).

⁹⁰ *F.D.A. Plans*, *supra* note 25.

⁹¹ *Of the FDA and IRBs*, *supra* note 74, at 571.

⁹² *Id.*

should be able to choose his or her medical care “if given sufficient information to understand the consequences, risks and benefits, and alternatives to the chosen medical treatment.”⁹³ But under present rules, informed consent is insufficient to allow the distribution of experimental drugs outside the clinical testing context; therefore, patients cannot choose to take a potentially life-saving drug like Avastin—despite being fully informed of its consequences, risks, and the alternatives—simply because the FDA has not approved it.⁹⁴ The FDA’s response to criticisms of this policy is that they regulate drugs to protect the public.⁹⁵ The FDA thus takes a paternalistic role when it chooses for patients whether the benefits of Avastin sufficiently outweigh the risks to justify its accessibility for their condition. But such a paternalistic approach denies patient autonomy.⁹⁶

The FDA justifies its restrictive policies as necessary to ensure that a drug’s benefits outweigh its risks before granting approval for sale and distribution. Some argue that the FDA goes too far when it errs on the side of safety in regulating drugs.⁹⁷ One critic describes the FDA’s risk-adverse behavior:

If [FDA officials] approve a drug and one person in a million dies of it, they get the blame. But if they keep [the drug] off the market and a thousand people die for lack of it, they will still be seen as just doing their job, and groups . . . will still hail them for “protecting Americans from unsafe and ineffective drugs.”⁹⁸

For this reason, the FDA does not have an incentive to allow patients to take their chances with drugs like Avastin, but it has every incentive to deny patients access to the drug, even when the potential benefits to the individual are high.⁹⁹ This directly conflicts with the central belief of the autonomy principle that competent individuals, with the advice of their families, friends, and professionals, can “make better decisions about their own health care than any government agency that seeks to protect them from their mistakes.”¹⁰⁰

The present debate in modern drug regulation centers on whether the

⁹³ Thad Brady, Note, *Paternalism vs. Patient Autonomy: Is the FDA’s “Mothering” Smothering Grandma’s and Grandpa’s Choice of Prescription Drugs?*, 14 ELDER L.J. 393, 405 (2006).

⁹⁴ *Id.*

⁹⁵ See *How Drugs Are Developed and Approved*, *supra* note 55 (stating that the FDA’s mission “is to ensure that drugs marketed in this country are safe and effective”).

⁹⁶ Brady, *supra* note 93, at 405.

⁹⁷ *Id.* at 406.

⁹⁸ *Id.* (citation omitted).

⁹⁹ *Id.*

¹⁰⁰ *Against Permittis*, *supra* note 76, at 3.

FDA should continue in its role as a public gatekeeper, or be given a more modest role where it merely certifies drugs like Avastin as “safe and effective.”¹⁰¹ This change would remove the FDA’s monopoly position over potentially life-saving cancer treatments, while maintaining its ability as an agency to provide advice on which drugs to use and which to avoid.¹⁰² The effect of such a change would be to inhibit government agencies from blocking voluntary personal decisions.¹⁰³ Although FDA regulations are directed at pharmaceutical companies like Genentech, their effects are felt by the individuals who can no longer purchase and use drugs. The FDA thus substitutes its own judgment for that of individuals when it prevents them from assuming the risks of certain treatments in the hopes of receiving some health benefit.¹⁰⁴

Why should the FDA not loosen its controls on the initial licensing, marketing, and use of drugs like Avastin to encourage the sharing of information between drug manufacturers, physicians, and patients? This would in turn speed up the process by which more and improved drugs enter the market.¹⁰⁵ The FDA should not be able to ban drugs, but should instead be in the business of warning consumers. This is because banning drugs requires the FDA to make judgments about risks and benefits that apply to everyone, regardless of individual circumstances.¹⁰⁶ The government should not be in the business of life and death decisions; rather citizens, as autonomous individuals, should be free to make treatment decisions for themselves.¹⁰⁷ Individuals’ autonomy rights should be given the same level of respect whether they are requesting or rejecting treatment because the FDA cannot determine the odds of health benefits better than individual patients equipped with their physician’s advice.¹⁰⁸

The challenge to individual autonomy and problem of paternalism that is raised by FDA regulation of cancer drugs suggest that the current system is inadequate for the regulation of Avastin. American Cancer Society statistics show that despite widespread use of the proven therapies of surgery, radiation, chemotherapy, and hormone therapy, 1,500 people will die of cancer every day.¹⁰⁹ The FDA’s current policy objective is to guarantee that cancer sufferers only employ so-called “proven methods” of

¹⁰¹ *Id.* at 3–4 (internal quotation marks omitted).

¹⁰² *Id.* at 4.

¹⁰³ *Id.* at 5.

¹⁰⁴ *Id.*

¹⁰⁵ *See Of the FDA and IRBs*, *supra* note 74, at 573 (arguing that “the existence of [the] off-label market is . . . strong evidence that the entire system of direct regulation is misguided”).

¹⁰⁶ *Id.* at 574.

¹⁰⁷ *Id.*

¹⁰⁸ *Id.* at 580.

¹⁰⁹ Michael E. Horwin, “War on Cancer”: *Why Does the FDA Deny Access to Alternative Cancer Treatments?*, 13 ALB. L.J. SCI. & TECH. 681, 696 (2003).

treatment and are not tricked into using non-approved drugs that can be potentially dangerous.¹¹⁰ As former Senator Bob Dole stated, “In a free market system, it seems to make sense to make available non-harmful alternative medical treatments to individuals who desire such treatments, without the Federal Government standing in the way.”¹¹¹ There seems to be an inherent injustice in denying cancer patients the medical liberty to attempt to save their own lives. To promote autonomy and justice for individuals, the current system needs to be modified so the FDA no longer has sole regulatory power over Avastin and other cancer drugs.¹¹²

B. *The Health Care Rationing Debate*

Historically, the three pillars of comprehensive health care reform have been access, quality, and cost. Current health reform politics have focused on cost by framing the issue as “getting good value for the money spent.”¹¹³ Rationing has always been present in the health care system. Some rationing is inevitable because of limited resources; it is reasonable to manage collective resources when most people believe that there is no benefit of a certain treatment.¹¹⁴ Bioethicists argue that when the judgment that a treatment provides no benefit is not unanimous, the denial of care results not from the elimination of harmful care, but from rationing.¹¹⁵ A claim of government rationing is thus raised when the FDA claims Avastin does not provide a health benefit to women with metastatic breast cancer, while women who suffer from the disease advocate that it could provide a benefit in their individual case.

Rationing has been defined as a “method of allocating resources.”¹¹⁶ This definition, however, does not reflect the way in which the term is currently used by health reformers. Today, the use of the term in politics refers to some type of patient harm that occurs by denying resources to patients.¹¹⁷ Claims that rationing is taking place in “death panels” are hotly debated today.¹¹⁸ As one scholar put it:

The current clinical and political fears about rationing are that efforts to slow the rate of growth in health care expenditures will harm patients. Under this scenario,

¹¹⁰ *Id.* at 695 (internal quotation marks omitted).

¹¹¹ *Id.* (internal quotation marks omitted).

¹¹² *See infra* Part IV.

¹¹³ Baily, *supra* note 81, at 178.

¹¹⁴ *Id.* at 176.

¹¹⁵ *Id.*

¹¹⁶ ALAN EARL-SLATER, *DICTIONARY OF HEALTH ECONOMICS* 127 (1999).

¹¹⁷ *See* David C. Goodman, *Preventing Ruin, or the Ruin of United States Health Care?: A Requiem for Rationing*, 32 J. LEGAL MED. 61, 62 & n.7 (2011).

¹¹⁸ *See id.* at 62 (internal quotation marks omitted).

rationing need not be explicit Should rationing occur, it is likely to be from inaction without the fingerprints of any specific actor . . . with myriad effects on different populations.¹¹⁹

Such rationing can be seen in the FDA's decision to deny approval of Avastin for breast cancer.

Rationing can be described as both "explicit" and "implicit." Implicit rationing is a result of government accident or inaction, while explicit rationing occurs by design.¹²⁰ When the government acts in a way that prevents a medical care transaction from taking place that otherwise would have, it generates harm to a patient.¹²¹ There is, therefore, the potential for patient harm under both explicit and implicit rationing when cost is a factor in denying treatment.¹²² Some consider the denial of insurance payment for Avastin to be rationing under this view.¹²³ The FDA, in denying approval of Avastin for the breast cancer indication, effectively gives insurance companies reason to deny payment for this treatment option. Women are then forced to pay for this costly drug out-of-pocket, inhibiting the medical care transaction that would have occurred from taking place for all but a select few who can afford it.

By contrast, some do not consider this rationing because they do not agree there is patient harm in denying a treatment that has failed to show definitive net benefits in clinical trials.¹²⁴ Under this view, rationing is achieved explicitly by price. Insurance payors effectively tell patients "[y]ou want [Avastin] for your breast cancer, but this insurance plan does not cover an ineffective and potentially harmful drug."¹²⁵ Without proven health benefits, these individuals do not see this as creating patient harm, which they consider necessary for rationing to occur.¹²⁶

The flaw in this reasoning is that it associates the requisite patient harm needed for rationing to occur with a denial of the benefits of a treatment. Since no benefits have been proven in clinical trials, denial of insurance payment for Avastin is not rationing in their eyes.¹²⁷ The group that views the FDA decision as rationing is correct, however, when one considers that the actual patient harm in this instance is not the denial of a treatment with unknown or unproven benefits, but rather the denial of the autonomous decision of the patient to assume the risk of taking Avastin to

¹¹⁹ *Id.* at 64–65.

¹²⁰ *Id.* at 64.

¹²¹ *Id.* at 62.

¹²² *See id.* at 64.

¹²³ *F.D.A. Plans*, *supra* note 25.

¹²⁴ *See id.* at 63.

¹²⁵ *Id.* at 63, tbl.1 (internal quotation marks omitted).

¹²⁶ *Id.*

¹²⁷ *Id.* at 63.

pursue a chance at survival.

By removing its approval of Avastin, the FDA is engaging in implicit rationing and furthering the occurrence of explicit rationing by insurance companies. Denial of approval for Avastin is implicit rationing because the FDA's inaction in not approving the drug for breast cancer affects those whose insurance will in turn refuse to cover treatment payments. The FDA additionally incentivizes insurance payers to engage in rationing when a patient wants to take Avastin off-label to treat her breast cancer, but her insurance plan "does not cover an ineffective and potentially harmful drug."¹²⁸

Private insurers are forced to ration care because they have limited resources in a society of virtually boundless demand. No private insurer can survive without engaging in rationing because "[t]he essence of [managed care] is that salaries and profits are limited by the [managed care organization's] fixed membership fees."¹²⁹ As one scholar noted, "[t]he problem of [a] fixed revenue" stream is further exacerbated by "failure to effectively address limitless demand."¹³⁰ As a result, private insurers attempt to coerce physicians into limiting the treatment options they make available to their patients.¹³¹ Government and private insurers who cannot afford to pay high prices for treatments are thus in constant conflict with patients who desire to consume expensive care.¹³² The government and insurers need to develop alternative approaches to rationing that incorporate greater process for those who are denied access to medical care, since rationing restricts the individual's liberty interest of being able to choose any treatment option for one's condition.

Because the United States is a market-based system, rationing is achieved primarily by allocating resources like Avastin to those who are most willing to pay.¹³³ This effectively forces those who are unable to pay the high price of these treatments out of the market, denying them access to the drugs they need. Rationing by price is an effective means of rationing medical care because it excludes individuals from participating in market transactions, but limits consumption against the patient's will.¹³⁴

A better method of rationing is rationing by quantity, which focuses on limiting access to treatments like Avastin over time. Under this system, the government or private insurers set limits on an individual's access to care options "by artificially limiting the quantity of that care available for

¹²⁸ See *id.* at 63, tbl. 1.

¹²⁹ *Pegram v. Herdrich*, 530 U.S. 211, 220 (2000).

¹³⁰ Meir Katz, *Towards a New Moral Paradigm in Health Care Delivery: Accounting for Individuals*, 36 AM. J.L. & MED. 78, 83 (2010).

¹³¹ *Id.*

¹³² *Id.* at 83–84.

¹³³ *Id.* at 86.

¹³⁴ *Id.*

consumption.”¹³⁵ Price rationing permits the wealthy to have access to drugs that may have little benefit to them relative to their cost while denying the poor this same option. A system of rationing by quantity, however, gives preferential treatment to procedures that maximize public health relative to their costs.¹³⁶ Under this form of rationing, the government sets clear limits on the amount of consumption per individual without engaging in a cost effectiveness analysis.¹³⁷ This system reflects the value underlying recent health care legislation that all individuals should have access to health care, not just those who can afford it.

FDA approval of Avastin for the breast cancer indication would not result in wasteful spending by insurance payers in a quantity rationing system because insurance payers could still place limits on the amount of treatment available per individual. In a price-rationing system, medical allocations are effected by the government, resulting in reduced consumption of health care by those with insufficient insurance. By contrast, quantity rationing occurs when the private sector sets limits on an individual’s access to high-cost drugs like Avastin “by artificially limiting the quantity of . . . care available for consumption.”¹³⁸ Quantity rationing is thus more justified than price rationing by “controlling total expenditures” rather than “excluding a class of individuals from coverage entirely.”¹³⁹

Many scholars have theorized about whether all members of society should have access to “very expensive life-extending care at the end of life.”¹⁴⁰ Avastin, which costs up to \$90,000 per treatment, is estimated to add “only an additional 1.5 months” to one’s life expectancy, making it cost approximately \$720,000 per year of life.¹⁴¹ This high cost raises the question of whether medical spending at the end of life is justified or should be viewed as “unconstrained.”¹⁴² A moral dilemma is raised as to what a “just” and “caring” society ought to do when we have the medical technology that can add time to an individual’s life, “but that technology is

¹³⁵ *Id.* at 88.

¹³⁶ *Id.*

¹³⁷ *Id.*

¹³⁸ *See id.* at 88, 91 (critiquing the processes of rationing by quantity and rationing by price).

¹³⁹ *Id.* at 88.

¹⁴⁰ *See, e.g.,* Paul T. Menzel, *The Value of Life at the End of Life: A Critical Assessment of Hope and Other Factors*, 39 J.L. MED. & ETHICS 215, 216 (2011) (discussing whether such care “should be included in a ‘basic minimum’ of services to which everyone in . . . society ought to have affordable access”); *see also* Leonard M. Fleck, *Just Caring: Health Care Rationing, Terminal Illness, and the Medically Least Well Off*, 39 J.L. MED. & ETHICS 156, 156 (2011) (analyzing what it means “to be a ‘just’ and ‘caring’ society in meeting the health care needs of the terminally ill” and “how high a priority ought the health care needs of persons who are terminally ill” should be “[r]elative to all the other health care needs [of] society”).

¹⁴¹ Menzel, *supra* note 140, at 216.

¹⁴² *Id.* (internal quotation marks omitted).

not affordable to [those] who [require] that care.”¹⁴³ As one scholar asked, “[a]re we morally obligated as a just and caring society to provide access at social expense to these cancer drugs for all these terminally ill cancer patients? How high a priority (morally speaking) ought funding these drugs have . . . ?”¹⁴⁴

We should not accept the view that “we [have a moral obligation] to spend any amount of money to save all lives or life-years that medical technology permits.”¹⁴⁵ This would not be just or compassionate in a society of limited resources that needs “to meet virtually unlimited health care needs.”¹⁴⁶ But this does not mean that patients do not have a right to the health care treatments they need. It is not immoral to ration the health care that society provides to terminally ill patients.¹⁴⁷ But since the need for health care rationing cannot be avoided, “it is morally better [for society] that [these] decisions be visible and rationally self-imposed,” rather than imposed by the FDA. It is better for society to make these decisions using “rational and fair processes of democratic deliberation.”¹⁴⁸

There are certain limits to patient autonomy. It is undisputed that there is an ethical difference between refusing and demanding treatment—individuals do not have “unlimited choice [to receive care] at the expense of other[s].”¹⁴⁹ But the problem of rationing arises when the FDA substitutes its judgment for that of the public in determining what standard of care should be available to all. Since individual values and preferences differ, society needs to develop a consensus and compromise on what options to provide under a “cost-conscious standard of care.”¹⁵⁰ There is no definitive substantive standard to settle the conflicting judgments about whether certain treatments are sufficiently cost-worthy to be covered by insurance.¹⁵¹ A fair process would consider insurance coverage in light of a drug’s effectiveness and expense.¹⁵² These processes should be “fair,” “open,” and allow decision makers “to hear the case for all [the different] views.”¹⁵³

Society should not let “the emotional power and sympathy that surrounds . . . the end of life” or “the insurance effect” cause it to place a high value on “all demands and desires for life extending care at the end of

¹⁴³ Fleck, *supra* note 140, at 158 (internal quotation marks omitted).

¹⁴⁴ *Id.* at 161.

¹⁴⁵ *Id.* at 162.

¹⁴⁶ *Id.* at 156, 162.

¹⁴⁷ *Id.* at 156.

¹⁴⁸ *Id.* at 156–57.

¹⁴⁹ Baily, *supra* note 81, at 181 (emphasis omitted).

¹⁵⁰ *Id.*

¹⁵¹ Menzel, *supra* note 140, at 222.

¹⁵² *Id.*

¹⁵³ *Id.*

life.”¹⁵⁴ Rationing decisions are more legitimate when it is acknowledged that terminally ill patients “represent our future possible selves,” and decisions are “public” and “self-imposed.”¹⁵⁵ To achieve “fair rationing,” society should deliberate through the democratic process, instead of blindly relying on the FDA’s licensing decisions to determine rationing outcomes.¹⁵⁶ The FDA is therefore not the proper agency to be regulating drugs like Avastin.

C. Costly Information and Burdens on Physicians

The FDA’s decision to remove its approval of Avastin to treat metastatic breast cancer results in reduced use of Avastin for that indication because physicians now must prescribe the drug off-label to the patients that desire this treatment option. While no law prohibits physicians from prescribing drugs off-label, “drug manufacturers may not [legally] promote their products for off-label uses.”¹⁵⁷ Such a ban on off-label promotion raises social policy concerns as it increases the costs of drug development, slows down the rate of adopting effective new uses of Avastin for serious diseases, and limits the ability of patients and prescribing physicians to receive useful medical information from drug developers like Genentech.¹⁵⁸

Off-label uses of drugs are both widespread and beneficial in modern medicine. Such use occurs when a physician prescribes a pharmaceutical product at a dose and/or for a condition that the FDA has either not reviewed or not approved.¹⁵⁹ Manufacturers are regulated in the type of promotion for off-label uses they are permitted to engage in because off-label drug use imposes enhanced risks without proven benefits.¹⁶⁰ So while the FDA cannot restrict physicians from prescribing drugs like Avastin to their patients off-label, they do have the authority to forbid drug companies from promoting their drugs for off-label purposes.¹⁶¹ The FDCA does not address the practice of off-label promotion; however, the

¹⁵⁴ *Id.*

¹⁵⁵ Fleck, *supra* note 140, at 168.

¹⁵⁶ *Id.*

¹⁵⁷ John E. Osborn, *Can I Tell You the Truth? A Comparative Perspective on Regulating Off-Label Scientific and Medical Information*, 10 YALE J. HEALTH POL’Y L. & ETHICS 299, 305 (2010) (emphasis omitted). As a result of the FDA’s decision, “any language discussing a metastatic breast cancer indication must be removed from the package insert of the product.” U.S. FDA, *Questions and Answers: Removing Metastatic Breast Cancer as an Indication from Avastin’s Product Labeling*, U.S. DEP’T OF HEALTH & HUMAN SERVS., <http://www.fda.gov/NewsEvents/Newsroom/ucm280533.htm> (last visited July 21, 2012).

¹⁵⁸ Osborn, *supra* note 157, at 306.

¹⁵⁹ Aaron S. Kesselheim, *Off-Label Drug Use and Promotion: Balancing Public Health Goals and Commercial Speech*, 37 AM. J.L. & MED. 225, 225 (2011).

¹⁶⁰ *Id.* at 226–27.

¹⁶¹ *Id.* at 227.

FDA considers off-label promotion to be violative of the part of the Act that bans pharmaceutical manufacturers from introducing a new drug into interstate commerce unless it has received FDA approval.¹⁶²

When a drug label is based on clinical studies for specific indications, the possibility that the drug may work in other clinical situations is high; this is why off-label application is among the most prevalent in the treatment of cancer.¹⁶³ Off-label applications of cancer drugs have been called “the hallmark of state-of-the-art treatment.”¹⁶⁴ The National Cancer Institute and many publications encourage off-label use of cancer drugs as being reasonable, particularly in the cases of rare cancers where there is no existing treatment and when there is substantial evidence, but no FDA approval.¹⁶⁵ In instances where off-label use benefits patients, “off-label marketing [and promotion] may enable the greatest number of potential beneficiaries to [learn about the treatments that are] best suited to their needs.”¹⁶⁶

There are circumstances where off-label use to treat certain cancers is evidence-based. Sometimes, off-label use arises from post-marketing studies as physicians experiment with the drug after it is approved for the original indication.¹⁶⁷ If additional efficacy is shown, the drug label can be modified to reflect the new indication if the manufacturer submits a formal application to the FDA that justifies the new use with data.¹⁶⁸ Gaining FDA approval requires companies to invest in gathering evidence and conducting clinical trials, a process that involves significant cost and time.¹⁶⁹ Drug companies who fear that a bad review from the FDA will negatively affect their on-label prescription sales may be dissuaded from engaging in the process at all.¹⁷⁰ Even off-label uses that could generate a lot of revenue may not be pursued if the manufacturer does not want to risk these adverse effects. Such fears demonstrate that many off-label uses may

¹⁶² *Id.*

¹⁶³ Steven R. Salbu, *Off-Label Use, Prescription, and Marketing of FDA-Approved Drugs: An Assessment of Legislative and Regulatory Policy*, 51 FLA. L. REV. 181, 193 (1999). But, if a manufacturer wants an off-label use to be added to a drug’s labeling, it must apply to the FDA for approval as if it were submitting a new drug. *Id.* at 187–88.

¹⁶⁴ *Id.* at 193 (internal quotation marks omitted).

¹⁶⁵ Kesselheim, *supra* note 159, at 235.

¹⁶⁶ Salbu, *supra* note 163, at 194.

¹⁶⁷ Kesselheim, *supra* note 159, at 237.

¹⁶⁸ *Id.* This formal application is called a supplemental New Drug Application. *Id.*

¹⁶⁹ *Id.* “The administrative process at the FDA can take many months.” *Id.*; see also Salbu, *supra* note 163, at 188 (“[T]he manufacturer of a drug with potential multiple uses confronts the prospect of having to surmount the obstacles to FDA approval several times before it can exploit the full market potential of the drug.” Of course, inclusion of a new use in the drug’s labeling may not increase sales . . . [so] companies have little incentive to apply for labeling authorization under tedious and expensive FDA procedures.”).

¹⁷⁰ Kesselheim, *supra* note 159, at 237.

be beneficial even where they have not gained FDA approval.¹⁷¹

The FDA's policies are restrictive of drug companies like Genentech who need to promote their products directly to physicians and to patients in order to spur increased use of their products.¹⁷² A competitive market prompts manufacturers to initiate increased patient and physician use of their products to recover their costs of R&D and generate revenue for further development. Increased revenue gives manufacturers the ability not just to discover new drugs, but to develop those already present in the market for other indications as a way of promoting efficient development. Discussing their products with patients and physicians gives companies the ability to see how their products affect patients for these other uses, thereby reducing the costs of conducting additional clinical trials. Such work is desirable for patients who require a reactive and constantly improving drug market to treat their ever-changing needs.

Drug manufacturers fund the R&D of new drugs through high drug prices.¹⁷³ In order to offset the high costs of R&D and to generate funding to develop new drugs, drug manufacturers have an incentive to develop "blockbuster" drugs with high annual sales.¹⁷⁴ Biotechnology pharmaceutical companies are relatively new to the pharmaceutical industry, but experience the same challenges in researching and developing new drugs.¹⁷⁵ It has been estimated that the American biotechnology drug market exceeds \$60 billion annually.¹⁷⁶ However, this industry is perceived as dangerous for investors because many of these companies struggle to be profitable after they invest millions in researching new drugs.¹⁷⁷

The regulations imposed by the FDA are aimed at preventing drug companies from promoting unapproved uses of their products, as such uses

¹⁷¹ *Id.* Other examples where off-label use may be reasonable and beneficial are in cases where it is difficult to collect evidence.

For example, narrowly-defined populations including very young children, high-risk pregnant women, and patients with extremely rare diseases are not usually included in drug clinical trials because the numbers of patients might be too small, the patients may be unable or unwilling to provide informed consent, or the situation may be too unstable. Nonetheless, circumstances may arise where these patients must receive off-label prescriptions for their care.

Id. at 238.

¹⁷² *Id.* at 228.

¹⁷³ Paula Tironi, *Pharmaceutical Pricing: A Review of Proposals to Improve Access and Affordability of Prescription Drugs*, 19 ANNALS HEALTH L. 311, 324 (2010).

¹⁷⁴ *Id.* at 324.

¹⁷⁵ *See id.* at 324, 328.

¹⁷⁶ *Id.* at 328. Genentech is one biotech drug manufacturer that stands to be highly profitable, with Avastin costing \$4,400 per month. *Id.*

¹⁷⁷ *Id.*

may be dangerous or not based on complete evidence demonstrating efficacy.¹⁷⁸ The FDA has a legitimate, compelling interest in protecting the public health with off-label prescribing by ensuring that companies do not transmit false or misleading information or encourage such prescribing without an underlying medical basis.¹⁷⁹ Drug manufacturers should not be prohibited from promoting off-label use if the use is then “demonstrated to be scientifically reasonable through federal[] . . . research.”¹⁸⁰ Efficacy information for new drug approval is gathered in a very condition-specific process that results in a FDA decision on whether a drug is not just efficacious or safe enough to be allowed on the market, but whether these elements justify approval for the drug’s intended use.¹⁸¹ This evidence is gathered in adequate and well-controlled studies.¹⁸²

The FDA approved Avastin to treat patients with metastatic carcinoma of the colon or rectum in 2004, and to treat colon or rectal cancer and non-small cell lung cancer in 2006.¹⁸³ In 2007, one scientist experimented with a modified form of Avastin to treat neovascular age-related macular degeneration, a disorder of the retina causing vision loss.¹⁸⁴ Following this off-label experimentation, Genentech was uncertain of how to communicate with physicians about the off-label use.¹⁸⁵ From 2004 to 2007, Genentech struggled with their position as interest in the off-label use of Avastin increased, but the company did not know whether it could lawfully communicate with physicians regarding the safety information of the off-label use.¹⁸⁶ This is because the FDA’s interest in protecting the public health empowers it to prevent companies from transmitting false or misleading information and encouraging off-label prescribing of drugs at the risk of civil or criminal liability.¹⁸⁷

The problem this example illustrates is that the FDA does not consider whether or not scientific and medical information provided by a drug company is truthful and not misleading, or whether or not physicians prescribe a drug in a medically appropriate manner; the FDA is only

¹⁷⁸ Kesselheim, *supra* note 159, at 229; *see also* Salbu, *supra* note 163, at 187 (“The regulations are intended to ensure that the drugs and their promotional literature contain accurate and complete information regarding approved use and risks. Although the ultimate goal is consumer protection, prescription drug labels today are aimed at physicians, who have held a longstanding position in American jurisprudence as ‘learned intermediaries’ between manufacturers and users.”).

¹⁷⁹ Osborn, *supra* note 157, at 307.

¹⁸⁰ *See* Kesselheim, *supra* note 159, at 229 (questioning the propriety of the restrictions the FDA places on manufacturers).

¹⁸¹ *Id.* at 231.

¹⁸² *Id.* at 230.

¹⁸³ Osborn, *supra* note 157, at 336.

¹⁸⁴ *Id.*

¹⁸⁵ *Id.* at 337.

¹⁸⁶ *Id.* at 338.

¹⁸⁷ *Id.* at 307.

concerned with whether the indication in question has been approved. If it has not, and a company like Genentech communicates or conveys information to physicians on an unapproved indication, then the FDA will conduct an investigation and prosecute the company.¹⁸⁸ It is unclear under what circumstances a manufacturer will be permitted to express an opinion on off-label uses of its products without being subject to a billion-dollar investigation.¹⁸⁹ Drug manufacturers should be able to communicate truthful, non-misleading scientific and medical information that comports with sound medical practice.¹⁹⁰

Restricting off-label marketing ends a potential source of cost-containment. By subjecting all potential uses of a drug to FDA approval, the number of clinical trials conducted is increased, as well as the amount spent in R&D expenses.¹⁹¹ These costs are then passed to consumers through price increases, making treatments even more difficult to obtain.¹⁹² These resources could be saved or more appropriately used by the FDA if off-label treatments could be marketed without seeking FDA approval. By focusing instead on expediting approval of new drugs, the amount of money spent by the FDA could be reduced or spent processing new drug applications more quickly, benefiting consumers by expediting patient access to new treatments.¹⁹³

Knowledge is more readily collected and shared within the scientific and medical community without FDA intervention. Patients expect their physician to have the ability to learn of the most current scientifically valid information and incorporate it into the way they treat their patients.¹⁹⁴ Manufacturers are in the best position to keep physicians informed about the latest research findings that encourage “new and beneficial off-label uses of their products.”¹⁹⁵ Patients deserve to receive “better, potentially life-saving treatments before the completion of the lengthy approval process.”¹⁹⁶ In fact, drug companies frame the issue of off-label marketing in terms of whether they should be denied the freedom to provide doctors with “truthful information.”¹⁹⁷ The result of the FDA’s policies is that doctors and other health care providers may not be adequately informed. If the risks of treatment are clearly disclosed, reduced regulation by the FDA would increase social utility and benefit patients.

¹⁸⁸ *Id.* at 329.

¹⁸⁹ Kesselheim, *supra* note 159, at 252.

¹⁹⁰ Osborn, *supra* note 157, at 307.

¹⁹¹ Salbu, *supra* note 163, at 195.

¹⁹² *Id.*

¹⁹³ *Id.* at 195–96.

¹⁹⁴ *Id.* at 198–99.

¹⁹⁵ *Id.* at 199.

¹⁹⁶ *Id.* (internal quotation marks omitted).

¹⁹⁷ *Id.*

IV. ALTERNATIVES TO FDA REGULATION

The FDA has a policy “to ensure that cancer sufferers only employ the so-called ‘proven methods’ and are not deceived into using non-approved therapies that can be [totally] ineffective and potentially dangerous.”¹⁹⁸ However, this removes a patient’s autonomy to select a potentially life-saving treatment option, rations care through insurance companies’ denial of coverage for these treatments, increases costs of drugs to patients and of development to manufacturers, and reduces the information available to physicians to help their patients make informed decisions. Together, these problems indicate that the current system is inadequate and an alternative system of regulation for cancer drugs like Avastin should be implemented.

The FDA should no longer serve as a public gatekeeper for new cancer treatments, but should instead have the role of certifying these products as “safe and effective.”¹⁹⁹ They should no longer have control of the licensing of cancer drugs, but should act as a certification agency that offers advice on which drugs to use and which to avoid.²⁰⁰ Once initial clinical trials have been completed, patients and physicians should have the ability to choose a drug.²⁰¹ This would not only promote individual patient autonomy, but would also reduce fraud in the drug market. By denying approval for Avastin, the price of Avastin skyrockets for those without insurance to cover its cost. This in turn permits those producing counterfeit Avastin to have a market for their products, which are more affordable to those paying out-of-pocket. Such was the case where fake Avastin made it to the U.S. market in February, shortly after the approval for Avastin was removed by the FDA.²⁰²

The FDA should protect the public from treatments that have not passed any clinical trials, but should not be responsible for denying approval for drugs where it lacks the individualized calculation of whether patients have risk factors for particular treatments.²⁰³ Three alternative systems that could effectively regulate Avastin include: (1) shared decision making by patients and physicians; (2) regulation by private organizations; and (3) indirect regulation by insurance payors.

¹⁹⁸ Horwin, *supra* note 109, at 695. “FDA representatives have testified that they must play a crucial role in determining what drugs are made available so patients are ‘protected from untested and unproven products.’” *Id.* at 696.

¹⁹⁹ *Against Permittitis*, *supra* note 76, at 3–4.

²⁰⁰ *Id.* at 4.

²⁰¹ *Id.* at 23.

²⁰² Benoit Faucon & Jeanne Whalen, *Fake Avastin Took Murky Path to U.S.*, WALL ST. J., Apr. 5, 2012, at A1.

²⁰³ *Against Permittitis*, *supra* note 76, at 24.

A. Shared Decision Making

The first way that Avastin could be regulated subsequent to modifying the FDA's role from regulation to certification is through a process of shared decision making by patients and physicians. Experts have called shared decision making the "ideal model of treatment decision making in the medical [context]."²⁰⁴ Shared decision making reduces the imbalance between physicians and patients by increasing the information patients receive as well as their sense of having authority and control over their own treatment decisions.²⁰⁵ Support for shared decision making has risen as a result of informed consent being considered a patient right, the principle of informed choice gaining support, the consumer rights movement, and the changing nature of the medical practice from one of acute care to one of chronic care.²⁰⁶

Shared decision making is a process that occurs between a physician and patient, where both parties take steps to participate in the process of choosing a treatment.²⁰⁷ Essentially, both parties engage in information and value sharing and ultimately both parties agree on the final treatment decision.²⁰⁸ Physicians and patients participate in the treatment decision making process when they take several steps: first, the physician establishes a conducive atmosphere for the patient to feel their views about different treatment options are valued and needed; second, the physician elicits the patient's preferences so that the treatment options considered comport with their values; third, the physician explains the various treatment options, risks, and benefits to the patient in a clear and unbiased fashion; fourth, physicians help patients weigh the risks and benefits of each option and make sure the information they are basing their opinions on is accurate; and finally, the physician participates in the decision making by sharing his treatment recommendation and affirming the patient's treatment decision.²⁰⁹

The practice of medicine has changed over the last two to three

²⁰⁴ Cathy Charles, Amiram Gafni & Tim Whelan, *Shared Decision-Making in the Medical Encounter: What Does it Mean? (or it Takes at Least Two to Tango)*, 44 SOC. SCI. MED. 681, 681 (1997).

²⁰⁵ *Id.* at 682.

²⁰⁶ *Id.* at 681–82.

²⁰⁷ *Id.* at 685–86. Several physicians may participate in this process with a single patient, which could raise increased uncertainty and confusion for the patient if multiple treatment options are suggested. *Id.* at 685.

²⁰⁸ *Id.* at 687–88; *see id.* at 688 ("The test of a shared decision (as distinct from the decision-making process) is if both parties agree on the treatment option. This does not mean that both parties are necessarily convinced that this is the best possible treatment for this patient, but rather that both endorse it as the treatment to implement Through mutual acceptance, both parties share responsibility for the final decision.").

²⁰⁹ *Id.* at 687.

decades, resulting in a shift to physicians managing illnesses instead of curing diseases.²¹⁰ In these instances, the physician-patient relationship can potentially last for many years or even a lifetime. The changing nature of the practice of medicine requires that physicians now work closely with patients to choose the best drugs to treat their individual condition.²¹¹ This process takes time, continuous monitoring, and adjustment of drug types and levels. For life-threatening conditions such as cancer, this process is thought to work best if both patients and physicians participate in key treatment decision points and selecting medication regimens, as the wrong decision may result in severe consequences for the patient.²¹² Since the choice of the best treatment for a particular patient requires value judgments, this decision is best made by patients and physicians.

The current problem is that a physician's experience, knowledge and expertise can be trumped by the FDA when they do not approve treatments like Avastin for new conditions.²¹³ A physician who has used a drug like Avastin becomes an expert on its application and use, even where the treatment is new and not routinely used.²¹⁴ One attorney made the case against FDA bureaucrats when he said, "Your physician may recommend an experimental drug, the corporate sponsor of that drug may agree to supply it, and the clinical investigator may agree to administer it, but if the FDA disagrees, you are out of luck."²¹⁵ Not all persons with cancer have the same circumstances surrounding their condition. It is therefore inappropriate for the FDA to choose the best cancer treatment for individuals because they are unaware of an individual's unique medical history.²¹⁶

The FDA takes the position that cancer patients may choose a harmful treatment or receive a harmful batch of medicine and therefore they must be protected from making wrong decisions; but this argument ignores the fact that a patient's physician is the best medical decision maker to assist individuals in these choices.²¹⁷ A physician may not be able to monitor drug production and distribution, but physicians are trained and licensed to give diagnostic and therapeutic assistance to their patients. Why then should a paternalistic government stand in the way of them rendering the best advice and treatments for their patient's needs? Patients should have the ability not just to choose their physician, but to expect that their physician will use his best judgment to help them choose the optimal

²¹⁰ *Id.* at 682.

²¹¹ *Id.*

²¹² *Id.*

²¹³ Horwin, *supra* note 109, at 708.

²¹⁴ *See id.* (calling this "the nature of medicine").

²¹⁵ *Id.* (citation omitted).

²¹⁶ *Id.*

²¹⁷ *Id.* at 709.

treatment for their particular needs.²¹⁸ There is no evidence that patients and physicians are more likely than the FDA to make mistakes if their cancer options go beyond surgery, radiation, chemotherapy and hormone therapy.²¹⁹

It is often the case that a patient with advanced cancer is willing to try any treatment, no matter what risks are involved, as a last ditch effort to try and save her own life. It makes sense for us to have a procedure in place for these patients to exercise their right to take on any risk to try and save their lives. Once a physician determines that a patient has reached a point in her disease where traditional treatments will be fruitless and she will otherwise die from her cancer, that physician should be able to prescribe Avastin so long as the patient is fully informed of all the risks involved. The FDA should clear the prescription of Avastin for such cases and permit issuance of the drug to those who have consented to the risks. The FDA could label the drug with these risks and as not having full approval. This would maintain the FDA's role as a protector of public health while promoting complete patient autonomy and informed consent.

Shared decision making can also be achieved through a bill like the Access to Medical Treatment Act ("AMTA").²²⁰ This bill, if passed, would "permit an individual to be treated by a health care practitioner with any method of medical treatment such individual requests, and for other purposes."²²¹ It would give the individual the right to be treated with medical treatments that are not approved, certified, or licensed by the Secretary of Health and Human Services.²²² It would allow cancer sufferers to choose the most appropriate medical treatment for their condition with the help of their physician.²²³ However, AMTA will not be passed so long as the FDA is permitted to trump the medical decisions of a patient's physician where cancer treatments are not "proven" by the FDA.²²⁴

AMTA takes a liberal approach to drug regulation by focusing on patient autonomy rather than FDA paternalism. If passed, it would allow cancer patients to consult with their physicians to discuss a variety of medical treatments, including Avastin.²²⁵ Under AMTA, a patient could

²¹⁸ *Id.* at 710.

²¹⁹ *Id.* "Even if one were to assume that the FDA was in the best position to make medical decisions for everyone, the FDA cannot play the role of physician to the half million cancer patients who will die this year." *Id.*

²²⁰ H.R. 2736, 112th Cong. (2011) [hereinafter AMTA].

²²¹ *Id.*

²²² H.R. 2736—*Access to Medical Treatment Act: Official Summary*, OPENCONGRESS, <http://www.opencongress.org/bill/112-h2736/show> (last visited July 21, 2012).

²²³ Horwin, *supra* note 109, at 696.

²²⁴ *Id.*

²²⁵ See Brady, *supra* note 93, at 411 (contrasting the paternalistic approach of the FDA with the liberal approach of AMTA in the area of drug regulation).

receive a treatment so long as a physician had no reason to conclude the treatment was dangerous to the patient. This would permit a patient to receive a treatment like Avastin in the early stages of development or before it underwent any clinical trials if the patient was fully informed and provided consent.²²⁶ This would dramatically increase patient autonomy under the FDA, making shared decision making possible for those suffering from cancer.

AMTA would also allow drug manufacturers to market drugs directly to patients and physicians without FDA approval.²²⁷ Drugs would still be regulated, but this would be accomplished by physicians, tort liability, and market factors, rather than by the FDA.²²⁸ Physicians would take on an increased role in protecting their patients from harmful drugs and treatments by becoming informed of the alternatives and shielding their patients from harmful drugs.²²⁹ Patients could also use the tort system against manufacturers who put out harmful products and against doctors who breached the standard of medical care.²³⁰ Lastly, the drug market would regulate manufacturers as harmful or ineffective drugs would not be profitable and would be forced out by drugs that are more effective.²³¹

The FDA is ill-suited to regulate cancer drugs like Avastin because of the threat raised to patient autonomy. While shared decision making is but one alternative to the current system, it is a preferable one because it allows patients and physicians to evaluate individual circumstances and make informed choices about the best possible treatments, something the FDA does not have the knowledge or resources to do.

B. *Voluntary Private Organizations*

Another way to regulate cancer drugs like Avastin is through voluntary private organizations. This type of system is favored by those holding a presumption against the use of government power to regulate autonomous individuals.²³² The government must justify asserting power over individual decisions where a loss of personal liberty is involved. This burden is met where the government is trying to prevent harms that individuals may inflict on others; however, the threshold to justify government action is higher where the potential harm of an individual's decision is to himself.²³³ If one starts with a strong presumption against

²²⁶ *Id.* at 412.

²²⁷ *Id.* at 413.

²²⁸ *Id.* at 414.

²²⁹ *Id.*

²³⁰ *Id.*

²³¹ *Id.* at 416.

²³² *Against Permittitis*, *supra* note 76, at 40.

²³³ *Id.* at 6.

government regulation of autonomous decisions, the FDA does not have a sufficient reason to overcome the liberty interest of individuals in choosing for themselves the best treatment option.

Following this presumption, government coercion is not justified in the cancer context, where private groups can process information more efficiently for consumers at lower costs than the FDA.²³⁴ Professional intermediaries already administer cancer drugs, even with the FDA in place as a public gatekeeper.²³⁵ Voluntary methods of regulating cancer drugs will be more successful than the FDA because “[d]ecentralized bodies are more likely to make sound[] decisions.”²³⁶ The FDA is inferior to the private systems already in place, and such systems can advance when drug companies are permitted to engage in the distribution of information created by independent sources, something currently prohibited.²³⁷

Voluntary organizations that deal with oncology already exist; patients and physicians use them to connect to the manufacturers of cancer drugs.²³⁸ Voluntary organizations are usually nonprofit organizations that “collect, digest, and interpret material for their members in areas where there is an information shortfall.”²³⁹ Physicians benefit from the information these organizations communicate and the best practice standards they set.²⁴⁰ Private organizations compete to provide the best information. Physicians may “use information from such organizations” and then “report their own experiences [with a drug] back” to the organization, allowing for an ongoing updating of information that physicians can compare.²⁴¹ The FDA does not have a similar means of collecting and disseminating information; the fact that “the FDA lacks the resources [and] expertise . . . to evaluate cutting-edge . . . technologies” causes the regulatory power of the FDA to exceed its ability to discharge its obligations.²⁴²

The FDA should grant accelerated regulatory approval for cancer drugs like Avastin, especially when they have demonstrated efficacy for other indications. There should be reduced evidentiary requirements to justify certification from the FDA, which in turn would reduce the amount of money the FDA would have to spend.²⁴³ Such accelerated approval

²³⁴ *Id.* at 8 (“No grant of monopoly power is justified if private groups are able to provide better information to potential end users at lower costs than the state.”).

²³⁵ *Id.* at 41.

²³⁶ *Id.*

²³⁷ *Id.*

²³⁸ *Id.* at 25–26.

²³⁹ *Id.* at 26.

²⁴⁰ *Id.*

²⁴¹ *Id.*

²⁴² *Id.* at 35–36.

²⁴³ Kesselheim, *supra* note 159, at 255.

should then be followed by post-approval monitoring by private organizations for adverse effects. “[M]anufacturers would [then] have an accelerated pathway they could use to discuss [the benefits of the] off-label uses of their products” and disseminate information to consumers in need of life-saving therapies.²⁴⁴ Private organizations, unlike the FDA, have the resources to efficiently update information received from physicians using Avastin for off-label uses. It is inefficient for the FDA to continue regulating where a private body can achieve the same, if not better, results.

C. Insurance Payors

The last possibility for regulating Avastin subsequent to modifying the FDA’s role is through insurance payors. Under current law, the FDA cannot prohibit physicians from prescribing drugs off-label. Insurers, however, are able to discourage such applications by denying payment for these uses.²⁴⁵ Insurance plans dissuade physicians from prescribing off-label drugs by requiring evidence of the use’s quality and efficacy before providing payment for that use.²⁴⁶ It is undisputed that some off-label prescribing can provide important benefits to patients.²⁴⁷ Since physicians have the ability to practice medicine according to their best medical judgment, “there are inherent risks attached to” the unregulated practice of off-label prescribing.²⁴⁸ If the private market can address these risks better than the government, then regulation should be left to the private market. This makes sense where “[t]he FDA has limited resources to monitor the 11,000 drugs on the market,”²⁴⁹ let alone to regulate off-label applications.

If necessary, states could influence off-label drug use by requiring insurers to pay for off-label uses of certain drugs for which they would normally deny coverage. States also have the authority to ban off-label uses in their efforts to promote public health.²⁵⁰ Since the federal government is without authority in the practice of medicine, it does not make sense for the federal government to regulate off-label uses of drugs like Avastin. A system is already in place for insurance payors to regulate this market indirectly by denying coverage for drugs that lack evidence of quality and efficacy, supplemented by the states’ authority to establish off-label mandates in line with their policies.²⁵¹

²⁴⁴ *Id.* (internal quotation marks omitted).

²⁴⁵ Amy E. Todd, Note, *No Need for More Regulation: Payors and Their Role in Balancing the Cost and Safety Considerations of Off-Label Prescriptions*, 37 AM. J.L. & MED. 422, 428 (2011).

²⁴⁶ *Id.*

²⁴⁷ *Id.* at 430.

²⁴⁸ *Id.*

²⁴⁹ *Wyeth v. Levine*, 129 S. Ct. 1187, 1202 (2009).

²⁵⁰ Todd, *supra* note 245, at 429. Some states mandate insurance coverage of off-label treatment of conditions like cancer. *Id.*

²⁵¹ *Id.*

The best alternative to FDA regulation is a model that is flexible enough to allow physicians to prescribe drugs off-label where it is the best treatment for a patient's condition, while containing the possibility of patient harm.²⁵² Insurance payors, in their role as reimbursement agents, are capable of "discouraging harmful and non-beneficial off-label drug use" because they have an "incentive to eliminate unnecessary drug use[e]."²⁵³ Regulation at this level is achieved at a lower price because insurance payors already engage in this process. Insurance payor regulation of cancer drugs is thus a solution that promotes the autonomy of patients and physicians in choosing drugs like Avastin when they are the optimal treatment, while decreasing the risk of patient harm by not reimbursing unnecessary drug usage.

The effectiveness of the insurance payor as a regulator of drugs is undeniable. Physicians already make off-label prescribing decisions based on payor reimbursement decisions.²⁵⁴ If such a model already induces physicians to follow the standard of care, why should the government continue to regulate in this area? FDA oversight is duplicative where insurance payor regulation can facilitate evidence-based medicine at lower costs.²⁵⁵ Most insurance payors require a showing of safety and efficacy for off-label drug use before providing reimbursement. Almost all payors use medical evidence in these decisions.²⁵⁶ This alternative gives physicians and drug manufacturers a compelling interest in providing scientific evidence of a drug's capabilities before prescribing it off-label. Those who did not produce such evidence would face the risk of non-payment by insurance payors; such a prospect guides them in practicing evidence-based medicine so funds can be administered to them.²⁵⁷

The FDA approval process for cancer drugs like Avastin has strict requirements and is incredibly costly. The evidence required for payor reimbursement of off-label prescriptions is more relaxed than this process, but still guides medical decision making when physicians consider the safety of an off-label use and their chances of reimbursement.²⁵⁸ "In light of [insurance] payor's reliance on [actual] medical evidence when making reimbursement decisions for off-label [uses]," the need for costly clinical trials is reduced, which in turn "lower[s] the cost of evidence-based off-label prescribing."²⁵⁹ This model not only reduces costs for an already

²⁵² *Id.* at 433.

²⁵³ *Id.*

²⁵⁴ *Id.*

²⁵⁵ *See id.* ("Enforcement on the insurance level relieves the government from costs associated with enhanced regulation.")

²⁵⁶ *Id.* at 433–34.

²⁵⁷ *Id.* at 434.

²⁵⁸ *Id.* at 435.

²⁵⁹ *Id.*

overburdened government agency, but creates the flexibility needed to achieve physician and patient autonomy in medical decision making.

Once the federal government's regulatory role is reduced and the private industry takes over the bulk of the regulation of cancer drugs, states can replace federal oversight where public health or policy issues are raised. For example, states may choose to mandate private insurers to provide or deny coverage for off-label prescribing. In this way, the government can prevent insurance companies from denying reimbursement for off-label uses that patients need to treat their medical conditions or can discourage off-label prescribing.²⁶⁰ According to one researcher, "[m]ore than thirty states [require] at least some [insurance] coverage for off-label uses of drugs."²⁶¹ Such mandates enable states to compel insurance payors to cover certain costs when their cost-containment policies would harm patient's health needs. This measure would protect against health care rationing because insurance payors would no longer rely on the decisions of the FDA to deny coverage for potentially life-saving treatments; rather, insurance payors would be held accountable by the states with an interest in and the ultimate authority to promote the health and safety of the population.

V. CONCLUSION

The FDA claims that it is "committed to providing early access to promising, but unproven, medical treatments for seriously ill patients who might otherwise have no hope."²⁶² However, the FDA contradicts itself when it states that no matter how compelling a case may be, "the cost of providing individual access [to care] cannot be to sacrifice the system that ultimately establishes whether therapies are safe and effective."²⁶³ Such conflicting statements highlight the FDA's limitations: it is incapable of accomplishing its goals of both promoting public health through innovative treatments and protecting people from unproven therapies.

Since the FDA does not have sufficient resources to address both issues, it often fails in its first goal by sacrificing innovation and drug development to maintain the integrity of the agency. By removing the FDA as the sole regulatory authority for the approval and licensing of cancer drugs like Avastin, this problem can be avoided. The FDA continues to protect the public health by promoting drugs that pass Phase I clinical trials, but does not stand in the way of patient autonomy and drug development by engaging in subsequent approval of cancer drugs for all

²⁶⁰ *Id.*

²⁶¹ Leslie Pickering Francis, *Legitimate Expectations, Unreasonable Beliefs, and Legally Mandated Coverage of Experimental Therapy*, 1 *IND. HEALTH L. REV.* 213, 235 (2004).

²⁶² Horwin, *supra* note 109, at 712 (internal quotation marks omitted).

²⁶³ *Id.* at 712–13 (internal quotation marks omitted).

potential uses. More responsibility will be placed on patients who desire these treatments and the physicians who gather the necessary information to prescribe them. This is desirable in a country based on the democratic principle of free choice.

Although the FDA has an important role as a protector of the health and safety of the public at large, the solution proposed by this Note does not detract from this role nor does it challenge FDA authority in its traditional areas of regulation. This proposal merely recognizes that in an era where rapid development of new and promising drug therapies is prevalent, the FDA does not have adequate resources to keep up. This role should properly be transferred to patients, physicians, voluntary organizations, and insurance payors who can better bear the burden of information gathering, engaging in public discourse/debate, disseminating test results, and holding drug manufacturers accountable for the products they send into the market. For these reasons, Congress should modify the role of the FDA and allow the market to take control in the regulation of cancer drugs like Avastin.

