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Annals OF Health Law

ADVANCE DIRECTIVE

The Student Health Policy and Law Review of
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THE HEALTH POLICY AND LAW REVIEW OF LOYOLA UNIVERSITY CHICAGO SCHOOL OF LAW

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ANNALS OF HEALTH LAW
Advance Directive

THE *STUDENT* HEALTH POLICY AND LAW REVIEW OF
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BRINGING YOU THE LATEST DEVELOPMENTS IN HEALTH LAW

Beazley Institute for Health Law and Policy

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CONTENTS

ANNALS OF HEALTH LAW
Advance Directive

Editors' Note

The *Annals of Health Law* is proud to present the Seventeenth Issue of our online, student-written publication, *Advance Directive*. *Advance Directive* aims to support and encourage student scholarship in the area of health law and policy. In this vein, this issue explores a variety of areas that focus on innovations and incentives in life sciences. Life sciences research, concerning the study of living organisms, including biology, botany, zoology, microbiology, physiology, biochemistry, and related subjects, is at the forefront of creating new innovative methods to increase patient access to quality treatments. This issue explores legal, regulatory and policy issues in the life sciences arena, focusing on past, current and future trends and the incentives and innovation that will get us there. Here, the authors examine a variety of topics on the issue of innovations and incentives in life sciences, ranging from the Precision Medicine Initiative for personalized medicine to drug compounding facilities as an alternative to skyrocketing drug prices.

This issue begins with a discussion of the Precision Medicine Initiative and its focus on developing diagnostic and preventive treatment options that are tailored to individual needs. The author suggests that insurers should provide reimbursements for these treatments because they will reduce long-term costs in the long run by preventing, mitigating, and treating expensive health conditions.

Our discussion then turns to a discussion on the Food, Drug, and Cosmetic Act and the impact of the FDA Modernization Act of 1997, federal cases regarding the First Amendment rights of drug makers to promote off-label drugs and the relaxation of administrative guidance from the FDA regarding "scientific exchange." The author argues that while the FDA plays a critical role in ensuring that patients and physicians have confidence that prescribed medicines are safe and effective for their approved uses and protecting the public health through rigorous clinical standards and administrative safeguards, the practice of modern medicine demands a more flexible framework of information sharing, pharmaceutical use, and discernment regarding prescriptions.

Next, the discussion turns to the newly instituted hospital-acquired condition penalty and the implications for disproportionate share and academic hospitals. The author proposes that the penalty would be more efficient if it was changed in two ways: first, if implemented as a function of hospital-acquired conditions per patients treated, and second, excuse disproportionate share hospitals and academic hospitals from the penalty altogether. The author notes that incentivizing hospitals to reduce hospital-acquired conditions can be effective, but that penalizing Medicare

payments could pose to large a financial risk for hospitals that rely heavily on government funded health plans.

Finally, we end our issue with a discussion of the rising prices of drugs. The author proposes that market-based solutions are the best mechanism to combat increased drug prices, and particularly, that compounded drugs could be a viable option. The author discusses the current problems that arise in drug compounding, and proposes solutions to allow for safe and effective methods of drug compounding. The author argues that while this method may be controversial, improvements to the process could increase patient access to affordable medications.

We would like to thank Kaitlin Lavin, our Technical Production Editor, because without her knowledge and commitment this Issue would not have been possible. We would like to give special thanks to our *Annals* Editor-in-Chief, Dennis Pangindian, for his leadership and support. The *Annals* Executive Board Members, Alanna Kroeker, MaryKathryn Hurd, Mandy Bast, and Kaitlin Lavin, and the *Annals* Senior Editors, Lindsey Croasdale, Xavier Vergara, Marika Iszczyszyn, Laura Doyen, and Mel Gaddy provided invaluable editorial assistance with this Issue. The *Annals* members deserve special recognition for their thoughtful and topical articles and for editing the work of their peers. Lastly, we must thank the Beazley Institute for Health Law and Policy and our faculty advisors, Professor Lawrence Singer, Megan Bess, and Kristin Finn for their guidance and support. We hope you enjoy our Seventeenth Issue of *Advance Directive*.

Sincerely,

Erica Jewell
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A Value-Based Approach to Insurer Coverage and Reimbursement for Molecular Diagnostic Tests

Megan Harkins[*]

I. INTRODUCTION

Healthcare is a constantly evolving industry, especially with regards to how physicians and other health care providers test, diagnose, and treat patient conditions.[1] Precision medicine is not a new endeavor,[2] but in the wake of President Obama's 2015 State of the Union Address, the push for more specific tests, more immediate diagnoses, and more targeted treatment approaches have been reinvigorated.[3]

Often, insurers are the last to adapt to changes within health care testing, diagnostics, treatment, and reimbursement decisions because of a lack of clinical utility, or evidence of a test's medical benefit.[4] However, with the

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1. Becki Rupp, *Health Care Industry Evolution and Trends: Reflections from an Insurance Veteran Part 1*, THE BENEFITS GUIDE (Sept. 21, 2015), https://thebenefitsguide.com/health-care-industry-evolution-trends-reflections-insurance-veteran-part/ (describing the expansion of coverage, evolution of the payer and provider relationship, and a shift in customer focus as major developments in health care in the past five years).

2. John R. Christiansen, *The Precision Medicine Initiative: Background and Issues for Participating Healthcare Organizations*, 28 NO. 1 HEALTH L. 38, 38 (2015) (stating that precision medicine has impacted medicine for years, primarily in the diagnosis and treatment of cancer and cardiology conditions).

3. Press Release, National Institutes of Health, NIH Awards $55 Million to Build Million-person Precision Medicine Study (July 6, 2016), https://www.nih.gov/news-events/news-releases/nih-awards-55-million-build-million-person-precision-medicine-study (explaining that the PMI is a longitudinal research project focused on improving disease prevention and treatment based on individual differences. Collaborations between data and research support centers, participant technology centers, healthcare provider organizations, and biobanks are several vital components to the PMI).

4. Patricia A. Deverka & Jennifer C. Dreyfus, *Clinical Integration of Next Generation Sequencing: Coverage and Reimbursement Challenges*, 42 J.L., MED. & ETHICS 22, 22 (2014); Anya E.R. Prince, *Prevention For Those Who Can Pay: Insurance Reimbursement of Genetic-Based Preventative Interventions in the Liminal State Between Health and Disease,* 2 J.L. &

support and the push for a more "targeted" approach to health care, insurers should change their approach to coverage and reimbursement for innovative diagnostic tests, such as molecular diagnostics.[5] Insurers should also provide greater coverage and reimbursement for tests that carry greater clinical utility and adjust coverage and reimbursement rates incrementally based on the available research. This should occur regardless of the presence of signs, symptoms or Food and Drug Administration (FDA) approval.[6] This innovative change in insurance coverage would reduce health care costs and continue to incentivize personalized medicine initiatives.[7]

The Precision Medicine Initiative (PMI)[8] reignited a focus in developing prevention, diagnostic, and treatment approaches that are tailored to the individual.[9] The PMI is a government funded initiative that requires a million person volunteer research cohort who will provide a detailed medical history, blood samples, and personal information to better understand how to improve diagnosis and treatment of diseases.[10] One notable PMI incentive involves lowering overall healthcare costs through early detection, prevention, and greater efficiencies in care delivery.[11] Precision medicine uses molecular

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BIOSCIENCES 365, 373 (2015).

5. Deverka & Dreyfus, *supra* note 4, at 23 (referring to coverage as the services a payer will pay for and under what circumstances and reimbursement at "the level of payment"); BRUCE QUINN, COVERAGE AND REIMBURSEMENT FOR MOLECULAR DIAGNOSTICS: CURRENT ISSUES AND OPTIONS, 8 (2009) (ebook).

6. PERSONALIZED MED. COAL., THE CASE FOR PERSONALIZED MEDICINE 22–23 (2014), http://www.personalizedmedicinecoalition.org/Userfiles/PMCCorporate/file/pmc_case_for_personalized_medicine.pdf [hereinafter CASE FOR PM] (noting that the FDA takes a tiered approach to regulation of lab-developed tests, with riskier clinical decisions taking longer to approve).

7. *See generally* CASE FOR PM, *supra* note 6, at 27–29 (explaining the incentives of personalized medicine); Deverka & Dreyfus, *supra* note 4, at 27 (explaining that long-term payment stability will ensure sufficient investment in newer technologies).

8. Robert Pear, *Uncle Sam Wants You—Or at Least Your Genetic and Lifestyle Information,* N.Y. TIMES (July 23, 2016), http://www.nytimes.com/2016/07/24/us/politics/precision-medicine-initiative-volunteers.html?_r=1.

9. Sairamesh Jakka & Michael Rossbach, *An Economic Perspective on Personalized Medicine*, 7 HUGO J. 1, 1 (Apr. 19, 2013), https://thehugojournal.springeropen.com/articles/10.1186/1877-6566-7-1#Sec3; Christiansen, *supra* note 2, at 38–39.

10. Pear, *supra* note 8.

11. Jakka & Rossbach, *supra* note 9, at 1.

diagnostics to identify predisposition, diagnostic, prognostic, and predictive biomarkers.[12] Providers may use biomarkers for simple tests, such as pulse detection and blood pressure readings, or more complex tests, such as blood chemistry and tissue analyses.[13] As laboratory-measured biomarker uses develop, the relationship between biomarkers and the clinical or surrogate endpoints[14] will become more valid.[15]

This article argues that innovative, molecular diagnostic tests that carry greater clinical utility should be covered and reimbursed at greater rates and incrementally decreased as the clinical utility of the test decreases, regardless of the presence of signs or symptoms. The incentive to adopt this proposed change in reimbursement structure could reduce long-term insurance costs by preventing, mitigating, and treating expensive health conditions.

The article will first address how insurers currently operate at both the public and private levels, followed by a discussion on how coverage and reimbursement policies for genetic testing are formed. Then, an argument in favor of adopting a value-based approach to coverage and reimbursement policies for molecular diagnostic testing will be presented. The remainder of the article will address the incentives for insurers to adopt a value-based approach to policies regarding molecular diagnostic testing and the counterarguments for adopting a value-based approach to cover and reimburse molecular diagnostic tests.

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12. *See generally* Kyle Strimbu & Jorge A. Tavel, *What are Biomarkers?*, 5 CURR. OPIN. HIV AIDS 463 (2010), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3078627/pdf/nihms259967.pdf (explaining that a biomarker is "any substance, structure, or process that can be measured in the body or its products and influence or predict the incidence and outcome of disease").

13. *Id.*

14. *Id.* (defining clinical endpoints as a reflection of how a subject in a clinical trial feels, functions or survives; and surrogate endpoints as a substitute for clinically meaningful endpoints, which are often used to reference biomarkers that consistently and accurately predict clinical outcomes).

15. *Id.* (explaining that in order for a biomarker to serve as a surrogate endpoint, it has to provide clinically relevant information).

II. THE CURRENT INSURER APPROACH

Coverage and reimbursement determinations are the product of a variety of factors, including historical guidance regarding genetic conditions, clinical utility of the test, and individual circumstances.[16] For instance, private payer plans categorize benefits and services, in addition to listing exclusions.[17] However, the Patient Protection and Affordable Care Act (ACA) implemented dramatic changes to the way policies now define coverage, and what is included within them.[18]

In response to the need to reduce healthcare costs, public insurers have moved toward payment models that drive improvements in health care quality and efficiency.[19] Alternative payment models (APMs) demonstrate the goal to increase quality of care by reimbursing providers based on the value of care provided.[20] If properly implemented, APMs may support the growth of personalized medicine, in addition to reducing the cost of health care.[21]

Historically, Medicaid covered some genetic testing, mainly for molecular diagnostic tests for cancer.[22] Medicare typically covers and reimburses services similar to those that private insurers cover.[23] Most recently, the Medicare payment system was revised in regards to clinical diagnostic

16. Prince, *supra* note 4, at 379 (listing organizations such as the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention, the Health Resources and Services Administration, and the USPSTF).

17. QUINN, *supra* note 5, at 12.

18. CASE FOR PM, *supra* note 6, at 35; Prince, *supra* note 4, at 378–80 ("[P]rivate insurers must cover any prevention method that the USPSTF has reviewed and recommended . . . CMS holds discretion as to which USPSTF recommendations are included in coverage.").

19. CASE FOR PM, *supra* note 6, at 27–28.

20. *Id*. at 28 (explaining that APMs can increase quality in health care by encouraging physicians to adopt targeted therapies based on an individual's genetics).

21. *Id*. at 27.

22. Prince, *supra* note 4, at 372.

23. *Id.* at 371 ("Medicare covers services that are 'reasonable and necessary for the diagnosis or treatment of illness or injury' . . . excluding coverage for tests 'performed in the absence of signs, symptoms, complaints, or personal history of disease or injury.'").

laboratory tests (CDLTs).[24] These revisions included the FDA's approval of advanced diagnostic laboratory tests (ADLTs) and changes to the payment structure to equal the weighted median determined for the test based on private payer rates.[25] Additionally, Medicare created a pilot program called the Medicare Molecular Diagnostic Services Program (MolDx).[26] This program evaluates genetic tests and identifies and establishes coverage and reimbursement policies for molecular diagnostic testing.[27]

Private insurers rely on Medicare for guidance on reimbursement policies and cost,[28] and oppose investing in personalized coverage.[29] This reliance is due to a lack of clear evidence showing measurable medical benefits or clinical utility.[30] Similar to public insurers, private insurers generally take a reactionary approach[31] when it comes to coverage and reimbursement policies.[32] When private insurers decide whether to cover genetic testing, the

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24. Medicare Program; Medicare Clinical Diagnostic Laboratory Tests Payment System, 81 Fed. Reg. 41,036, 41,036 (June 23, 2016) (to be codified at 42 C.F.R. pt. 414) (defining CDLTs as tests that are created and sold by a single laboratory, have been cleared or approved by the FDA, and are paid under the Clinical Laboratory Fee Schedule (CLFS) prior to January 1, 2017).

25. *Id.* at 41,098 (defining ADLTs as a subcategory of CDLTs covered under Medicare Part B, is created and sold by a single laboratory, and the test either (1) analyzes multiple biomarkers to yield a patient-specific result; (2) has been approved by the FDA; or (3) meets similar criteria established by the Secretary).

26. Sarah H. Beachy et al., Board on Health Sciences Policy Institute of Medicine, *Roundtable on Translating Genomic-Based Research to Health*, in ASSESSING GENOMIC SEQUENCING INFO. FOR HEALTH CARE DECISION MAKING: WORKSHOP SUMMARY 55 (2014).

27. Regence, *Genetic and Molecular Diagnostics - Single Gene or Mutation Testing*, MEDICARE ADVANTAGE POL'Y MANUAL 2 (Sept. 15, 2016), http://blue.regence.com/medicare/gt/m-gt20.pdf (indicating that MolDx has not been adopted by all contractors in all states and confirming that molecular diagnostic tests continue to exclude testing in the absence of signs or symptoms).

28. Prince, *supra* note 4, at 371–72; Deverka & Dreyfus, *supra* note 4, at 27.

29. Jakka & Rossbach, *supra* note 9, at 3.

30. Prince, *supra* note 4, at 373 (explaining that the gap between evidence of clinical use of genetic tests and evidence for insurance coverage can be explained by the lack of evidence regarding cost-effectiveness of the genetic tests because the tests screen for rare diseases that are not prevalent in society).

31. CASE FOR PM, *supra* note 6, at 9 (explaining that insurers frame coverage and reimbursement policies to address when an individual has received a diagnosis rather than focusing on preventing the disease in the first place); Jakka & Rossbach, *supra* note 9, at 1.

32. Jakka & Rossbach, *supra* note 9, at 2; Prince, *supra* note 4, at 366–70 (explaining that insurers typically provide coverage for treatment more often than for prevention and leave no

determining factor is often whether the proposed genetic test or intervention is medically necessary.[33] Moreover, private insurers determine coverage and reimbursement policies for molecular diagnostics through a wide range of assessment procedures.[34] The practice of using multiple assessments creates substantial inconsistencies in the insurer's reimbursement decisions and often leads to test manufacturers' or insured persons' inability to predict what molecular diagnostic tests would be covered and reimbursed.[35] Even when a private insurer provides coverage for genetic testing, the coverage determinations are often difficult to find within the policy.[36] The insured person could be faced with difficulties when he or she is interested in a particular genetic test, but is unsure of whether the private insurer provides coverage for the test.[37] This could deter the individual from receiving genetic testing at all or could require a drawn out process of further review by the private insurer to adjudicate the claim.[38] Moreover, private insurers explicitly exclude a genetic test if it is for informational purposes in the absence of a family history of a condition, or in the instance a minor is tested for an adult onset condition.[39]

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room for asymptomatic individuals to seek coverage for preventative interventions).

33. Prince, *supra* note 4, at 369–70, 375 (noting additional considerations for whether a private insurer decides to cover genetic testing include the clinical validity and clinical utility of the test and if the test would have a direct effect on treatment, or if it would prevent diseases in high-risk patient. Clinical validity is whether the test and the clinical outcome correlate. Clinical utility occurs when the information from the test provides greater incentives when compared with current management without testing); *see also* Deverka & Dreyfus, *supra* note 4, at 36 (noting recent success that some prenatal NGS tests have been assessed to be medically necessary).

34. Ildar Akhmetov & Rostyslav V. Bubnov, *Assessing value of innovative molecular diagnostic tests in the concept of predictive, preventative, and personalized medicine*, 6 THE EPMA J. 1, 7 (2015) ("[S]ome payers use up to seven assessment frameworks to reason their reimbursement decisions . . . while others give preference to only one or two.").

35. *Id*.

36. Prince, *supra* note 4, at 372.

37. DEP'T HEALTH & HUM. SERVS., SEC'Y'S ADVISORY COMM. ON GENETICS, HEALTH, & SOC'Y (SACGHS), COVERAGE AND REIMBURSEMENT OF GENETIC TESTS AND SERVICES 17 (Feb. 2006), http://osp.od.nih.gov/sites/default/files/CR_report.pdf.

38. *Id.*

39. Prince, *supra* note 4, at 372.

Innovations drive health care in a direction that makes "precise" care more cost-effective for both the consumer and the insurer.[40] However, inconsistent standards used to evaluate molecular diagnostic tests create an obstacle to implementing precision care.[41] Organizations, such as the Institute of Medicine (IOM) and the Centers for Disease Control (CDC), published guidance for minimizing inconsistent standards and effectively demonstrating a test's clinical utility.[42] The Evaluation of Genomic Applications in Practice and Prevention (EGAPP) also recently recommended several changes to the evaluation of genomic technology.[43] The EGAPP focuses on expediting the review process for genetic testing by triaging tests and eliminating those that are not currently reviewable, using and updating existing reviews, and using decision models to assess potential clinical utility when direct evidence is unavailable.[44] The current glacial pace at which genomic technology is evaluated[45] slows payer decisions about coverage and reimbursement for genetic testing because of a lack of the required evidence of clinical utility.[46] Therefore, the EGAPP recommendations would likely accelerate evaluations and provide payers with the necessary evidence of clinical utility in order to begin expanding

40. *See, e.g.*, *Id*. at 463 (explaining when LTDs lack FDA approval, CMS has been advised to consider Medicare reimbursement for genetic testing when strong evidence of improved health outcomes exists).

41. PERSONALIZED MED. COAL., THE FUTURE OF COVERAGE AND PAYMENT FOR PERSONALIZED MEDICINE DIAGNOSTICS 15, http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/pmc_the_future_coverage_payment_personalized_medicine_diagnostics.pdf (last visited Dec. 15, 2016) [hereinafter FUTURE OF COVERAGE].

42. David R. Parkinson et al., *Evidence of Clinical Utility: An Unmet Need in Molecular Diagnostics for Patients with Cancer*, 20 CLINICAL CANCER RES. 1428, 1432 (2014).

43. Deverka & Dreyfus, *supra* note 4, at 25.

44. *Id.* (explaining that payers have a 'de factor role of enforcing clinical utility standards' because no regulatory body has specific oversight).

45. ADVAMEDDX, A POLICY PRIMER ON DIAGNOSTICS 18 (2011), https://dx.advamed.org/sites/dx.advamed.org/files/resource/advameddx-policy-primer-on-diagnostics-june-2011.pdf (explaining that evaluation of new tests require direct evidence of patient outcomes, code assignment, and rate-setting that often disregards the test value, all of which slow down patient access to new diagnostic tests).

46. Deverka & Dreyfus, *supra* note 4, at 25 (noting that the EGAPP has issued only nine recommendations over the course of seven years).

coverage and reimbursement for more innovative and personalized health care.[47]

III. COVERAGE AND REIMBURSEMENT POLICIES FOR MOLECULAR DIAGNOSTIC TESTING: A VALUE-BASED APPROACH

Conceptually, payers favor personalized medicine because of the potential cost-effectiveness in treating an individual based on his or her molecular makeup.[48] Molecular diagnostic testing will likely require insurers to adopt an entirely new coverage and reimbursement paradigm.[49] Under the current cost-based reimbursement approach, the value and cost saving potential molecular diagnostics provide are not usually reflected in the reimbursement and deter investment in personalized medicine.[50] Payers should develop a value-based approach to coverage and reimbursement for molecular diagnostics[51] because precision medicine pushes for more targeted health care approaches[52] and access to clinical utility evidence for genetic testing is what drives payer coverage and reimbursement policies.[53] By shifting to a value-based insurance design (V-BID), providers would be encouraged to use high-value services, leading to a more targeted approach to health care.[54]

Medicare has begun adjusting the coverage and reimbursement system by implementing the MolDx Program in a number of jurisdictions to facilitate

47. Parkinson, *supra* note 42, at 1442 (noting that if payers prioritize tests of potentially high clinical utility and improve reimbursement for genetic tests, it would incentive private investors to continue investing in future genetic test development).

48. Deverka & Dreyfus, *supra* note 4, at 22.

49. *Id.* at 28 (suggesting molecular diagnostics be reimbursed based on the value of the test); W. Nicholson Price II, *Black-Box Medicine*, 28 HARV. J.L. & TECH. 419, 460 (2015).

50. Deverka & Dreyfus, *supra* note 4, at 28.

51. *Id.* (supporting that payers develop an approach that is at least "predictable, objective and appropriate third party reimbursement payment structure that will improve patient outcomes, support patient access, and ensure continued investment and innovation").

52. Christiansen, *supra* note 2, at 38.

53. Deverka & Dreyfus, *supra* note 4, at 25; FUTURE OF COVERAGE, *supra* note 41, at 16.

54. SUZANNE F. DELBANCO ET AL., URBAN INSTITUTE, VALUE-BASED INSURANCE DESIGN 3 (2016), http://www.urban.org/sites/default/files/01_value-based_insurance_design.pdf.

the incorporation of molecular diagnostic tests.[55] Due to the unique nature of molecular diagnostic tests, the MolDx Program strives to create consistency in coverage and pricing for these tests.[56] Additionally, BlueCross BlueShield (BCBS) Association's TEC has developed a similar assessment program for molecular diagnostics.[57] Programs like MolDx and BCBS Association's TEC help ameliorate barriers to the insurer's decision to cover and reimburse for molecular diagnostic testing by standardizing the process for evaluating molecular diagnostics.[58]

Medicare and BCBS have made efforts to standardize how molecular diagnostic tests are evaluated in order to make coverage and reimbursement decisions. However, both public and private insurers continue to face the issue of deciding which molecular diagnostic tests to cover. For molecular diagnostic testing, all insurers should provide greater levels of coverage and reimbursement for molecular diagnostics that have high clinical utility and provide lower levels of coverage and reimbursement for testing that has lower clinical utility, regardless of the presence of signs or symptoms.[59] Additionally, the ACA implements a value-based approach by offering value-based exchange plan options.[60] Further, the FDA takes a value-based approach when regulating lab-developed tests (LDTs)[61] by requiring that

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55. PALMETTO GBA, MOLECULAR DIAGNOSTIC PROGRAM (MOLDX) 1 (2016), http://palmettogba.com/Palmetto/moldx.Nsf/files/MolDX_Manual.pdf/$File/MolDX_Manual.pdf [hereinafter MOLDX WHITE PAPER].

56. *Id*.

57. Deverka & Dreyfus, *supra* note 4, at 28.

58. *Id*.

59. Wylie Burke et al., *Recommendations for Returning Genomic Incidental Findings? We Need to Talk!*, 15 GENETICS IN MED. (SPECIAL REPORT) 854, 856 (2013) ("It is an established precept of public health that screening should be instituted only when there is compelling evidence that it improves health outcomes in asymptomatic people.").

60. Magaly Olivero, *Obamacare: Which 'Metal' Tier is Right for You?*, U.S. NEWS & WORLD REP. (Nov. 14, 2014, 8:00 AM), http://health.usnews.com/health-news/health-insurance/articles/2014/11/14/obamacare-which-metal-tier-is-right-for-you (indicating that more comprehensive coverage accompanied the more expensive plans).

61. Gail H. Javitt & Katherine Strong Carner, *Regulation of the Next Generation Sequencing*, 42 J.L., MED. & ETHICS 9, 14 (2014) (explaining that LDTs are laboratory-assembled tests that use a patient specimen, issue a lab report with the test results, and are both

"tests linked to riskier clinical decisions" need longer to approve.[62] Value, in this instance, emphasizes the perceived or anticipated value the consumer seeks to gain, rather than the actual cost of the plan or test.[63] Typically, the most important factors in a public or private insurer's decision to cover molecular diagnostics are the "rate of payer adoption" and "the time that is needed for [the diagnostic] approval."[64] Regardless of the questionable authority the FDA has over LDT regulation,[65] the FDA favors tests with prognostic indicators over tests that influence clinical decisions.[66]

However, it is important to remember that insured persons are also are affected by insurer coverage and reimbursement decisions. Therefore, potential emotional and psychological responses of insured persons to coverage decisions should be considered when deciding whether to cover molecular diagnostic testing. With the PMI's goal of recruiting one million individuals as a volunteer group, what happens to an individual after learning about the presence of a genetic predisposition?[67] If an individual's insurance does not offer (or provides insufficient) coverage and reimbursement for follow-up treatment, individuals could be psychologically harmed.[68]

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developed and approved by the lab); Deverka & Dreyfus, *supra* note 4, at 24.

62. CASE FOR PM, *supra* note 6, at 22–23; Jakka & Rossbach, *supra* note 9, at 5 ("There is a trend towards outcome- and value-based pricing and reimbursement models in many countries and this greatly increases the financial value of P4 medicine, and . . . the incentives to invest in it."); *see* Price, *supra* note 49, at 458 (explaining how medical devices are classified by risk by the FDA).

63. Mark Haller & Avynash Gersappe, *Value-based Pricing: Putting the Customer at the Center of Price*, PWC (2014), https://www.pwc.com/us/en/advisory/customer/assets/value-based-pricing.pdf.

64. Jakka & Rossbach, *supra* note 9, at 5.

65. Javitt & Carner, *supra* note 61, at 14.

66. Jakka & Rossbach, *supra* note 9, at 5 (explaining that the FDA would request premarket approval for tests that directly influence clinical decisions, compared to prognostic indicator tests that may only need a 510 (k) approval).

67. National Institutes of Health, *Precision Medicine Initiative Cohort Program - Frequently Asked Questions*, https://www.nih.gov/precision-medicine-initiative-cohort-program/precision-medicine-initiative-cohort-program-frequently-asked-questions (last updated Oct. 7, 2016).

68. Prince, *supra* note 4, at 373–74 (explaining the psychological side effects of receiving genetic testing results including anxiety and depression).

Additionally, if the treatments are expensive and are not covered, low-income individuals could be disproportionally affected after learning of the presence of a genetic predisposition.[69] This potential for psychosocial harms may deter individuals from participating in the PMI, leading to restrictions in innovative healthcare diagnosis and treatment efforts.[70]

IV. INCENTIVES FOR INSURERS TO COVER AND REIMBURSE MOLECULAR DIAGNOSTICS

Both public and private insurer decisions are driven by incentives to reduce healthcare costs, especially as annual costs have grown significantly.[71] Cost savings related to molecular diagnostic testing is also often delayed.[72] However, the incentives accompanying the wait go far beyond the financial gains insurers could realize[73] if universal adoption of a value-based approach to coverage and reimbursement of molecular diagnostic testing occurs.[74]

Insurers are typically risk averse and coverage for newer tests are also considered risky.[75] One of the biggest risks is the cost-effectiveness of the tests compared with the benefits.[76] Often, it is difficult to identify which

69. Price, *supra* note 49, at 462 n.215.

70. *E.g.*, Prince, *supra* note 4, at 374 (noting that a person may have to resort to insurance appeals or litigation in order to secure coverage for preventative medical interventions after genetic testing).

71. NAT'L CTR. FOR CHRONIC DISEASE PREVENTION & HEALTH PROMOTION, DIV. CMTY. HEALTH, UNDERSTANDING VALUE-BASED INSURANCE DESIGN 1 (2015), https://www.cdc.gov/nccdphp/dch/pdfs/value_based_ins_design.pdf.

72. A. MARK FENDRICK & SEEMA S. SONNAD, VALUE-BASED INSURANCE DESIGN FOR DIAGNOSTICS, DEVICES, & PROCS. 24 (2012), http://vbidcenter.org/wp-content/uploads/2014/08/V-BID-and-Devices-InHealth.pdf (explaining that targeted services may increase short-term costs, but would likely lead to lower aggregate costs. It is the fear of the insurer that the benefits occur too far "downstream" to offset the initial costs of utilizing a targeted approach).

73. Akhmetov & Bubnov, *supra* note 34, at 2 (noting the economic impact of molecular diagnostic testing for variants that guide the initial dosing of warfarin have the potential to provide $1.1 billion in annual savings and prevent 17,000 strokes).

74. DELBANCO, *supra* note 54, at 3 (indicating benefits, such as improving customer health through beneficial, high-value services, reducing wasteful spending, and aligning patient needs with provider initiatives to improve the quality of care and make it more affordable).

75. Jakka & Rossbach, *supra* note 9, at 3.

76. *Id.*

genetic tests will save money, as savings are often not known until after the test has been on the market for an extended period of time.[77] Additionally, no structure currently exists for insurers to assess the cost savings from prognostic and preventative diagnostic testing.[78]

However valid insurer risk adversity may be, the incentives and benefits for insurers to cover and reimburse molecular diagnostic testing far outweigh the costs.[79] A prevention approach, compared to a reaction approach, would likely lead to short-term costs,[80] but would lead to long-term savings by utilizing a targeted approach for diagnosis, testing, and treatment.[81] For instance, if a preventable disease were diagnosed at an individual's young age, cost savings would likely be realized in adulthood.[82]

Several benefits of using biomarkers when treating individuals include decreased hospital admission costs and reduced prescription costs.[83] Adverse drug reactions are costly to treat,[84] but biomarkers can enhance drug-related safety in patients who may have otherwise experienced an adverse reaction.[85] For example, clinical trials for a new medicinal treatment may have been found to be a success if twenty-five percent of participants benefitted from

77. *Id.* at 2–3.

78. *Id.* at 3.

79. *See generally* CASE FOR PM, *supra* note 6, at 27–29 (explaining the incentives of personalized medicine).

80. Jakka & Rossbach, *supra* note 9, at 3 (noting that cost savings are often not known until after the test has been on the market for an extended period of time which make it difficult to identify which tests and technologies will truly save costs).

81. CASE FOR PM, *supra* note 6, at 8, 29.

82. *Id.* at 8.

83. *Id.* at 12–13; *see, e.g.*, Debra Hughes, *Consortium Antidepressant Guidelines Represent a 'Template for Psychiatric Precision Medicine,'* MONTHLY PRESCRIBING REFERENCE (Sept. 2016) (illustrating the potential benefits precision medicine could provide to patients by recognizing inherent genetic variations and recommending physicians consider alternative medications based on an individual's genetic make-up).

84. Elizabeth Burke et al., *Pharmacogenetic Testing: Application in Mental Health Prescribing*, 22 J. AM. PSYCHIATRIC NURSES ASS'N 185, 185 (2016) ("Every year in the United States, the cost of treating medication-related adverse events reaches $76 billion.").

85. CASE FOR PM, *supra* note 6, at 12; Jakka & Rossbach, *supra* note 9, at 2 ("30-40% of patients receive ineffective drugs; which can lead to adverse reactions that are costly to treat.").

the treatment.[86] However, if a person's genetic make-up was considered, treatment for the other seventy-five percent of patients could be tailored to his or her genetic profile, leading to greater efficacy of medicinal treatment.[87] Furthermore, pharmaceutical companies have implemented biomarker development in clinical trials after recognizing the value of personalized medicine and molecular diagnostic testing.[88]

Additionally, trial and error dosing and prescription of medications could be minimized, or even eliminated, with an increased use of biomarkers in treatment.[89] Compliance with medication would then likely increase with the use of genetic diagnostics.[90] Often, individuals do not comply with their medication because of the side effects.[91] For others, their body metabolizes the drug too rapidly for the medication to work.[92] Molecular diagnostics can improve a physician's understanding of individual genetic variations, which would help mitigate side effects through individualized dosing and would also help avoid prescribing medications that would be ineffective. Thus, potential cost savings for insurers serve as an incentive to use genetic testing and offer coverage and reimbursement policies that reflect those cost savings.[93]

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86. Antoinette F. Konski, *Personalized Medicine: Insights Into Current Legal Issues*, Personalized Medicine Bulletin (Sept. 18, 2016), https://www.personalizedmedicine bulletin.com/2016/09/18/personalized-medicine-insights-into-current-legal-issues/.

87. *Id.*

88. Akhmetov & Bubnov, *supra* note 34, at 3 (explaining that fifty percent of clinical trials conducted by pharmaceutical companies have focused on biomarker development).

89. CASE FOR PM, *supra* note 6, at 13.

90. *Id.* at 14 (regarding treatment for hypercholesterolemia, "patients with a genetic diagnosis have shown more than 86% adherence to treatment program after two years, compared to 38% prior to testing").

91. *Id.*

92. *Id.* at 13.

93. *See, e.g.*, Konski, *supra* note 86 ("By way of example, it has been projected that the frequency of chemotherapy could be decreased by thirty-four percent in women with breast cancer if they all received genetic testing prior to treatment.").

V. CONCLUSION

A value-based approach to healthcare is not a novel concept. However, the application of a value-based approach to coverage and reimbursement policies for molecular diagnostics is a newer concept that should be explored. Although insurer costs may increase due to a change in reimbursement policies, the overall health insurance market may see cost savings as chronic diseases are prevented and the current problem of paying for prevention is minimized.[94] Coverage and reimbursement policies must adapt to the ever-changing needs of the healthcare industry, especially in light of the expanded use of molecular diagnostics and the reinvigorated emphasis on personalized precision medicine.

94. Prince, *supra* note 4, at 390; *see also* Akhmetov & Bubnov, *supra* note 34, at 3 (stating that molecular diagnostic testing have contributed to 30–50 percent reductions in hospital and outpatient charges); *see, e.g.* THE KAISER FAMILY FOUND., *Snapshots: How Changes in Medical Technology Affect Health Care Costs* (Mar. 2, 2007), http://kff.org/health-costs/issue-brief/snapshots-how-changes-in-medical-technology-affect/ (highlighting that new vaccines may be costly at first, but often lead to cost savings if the vaccine results in fewer people seeking expensive treatment).

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Misbranded/Misled: Chipping Away at the Food, Drug, and Cosmetics Act & the Future of Off-Label Promotion

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Prior to marketing any drug or device, Federal law requires manufacturers to prove to the Food and Drug Administration's (FDA) satisfaction that their product is safe and effective for its intended uses.[1] If the FDA discovers the manufacturer intends other, unapproved uses[2]—also referred to as "off-label" uses—sales of the drug or device are determined to be illegal and the manufacturer may be charged in violation of the Food, Drug, and Cosmetic Act (FDCA).[3] The drug approval process serves as the FDA's primary means of protecting the public health by ensuring the safety, efficacy, and security of all pharmaceuticals and medical devices in the U.S. and prohibiting false advertising on the part of manufacturers.[4] Yet that mandate has been steadily undercut over the past thirty years on multiple fronts, eroding the balance

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1. 21 C.F.R. § 860.7(g)(1).

2. *See* Randall S. Stafford, *Regulating Off-Label Drug Use — Rethinking the Role of the FDA*, 358 NEW ENG. J. MED. 1427 (2008) (describing how off-label use arises through many pathways, including use for unapproved clinical indications (e.g., the antipsychotic Seroquel prescribed for depression) or in unapproved populations (e.g., Paxil for depression in children)).

3. Under the FDCA, the FDA must license any "new drug" before it may be *marketed*, not used. The approval process begins with the submission of an Investigational New Drug Application (NDA). If the application is approved, the sponsor may proceed with animal testing, then clinical trials on human subjects. A drug may only be marketed and labeled for the uses for which it received approval from the FDA. If a manufacturer promotes without going through the NDA, then the Department of Justice may charge them in violation of the FDCA. Richard C. Ausness, *"There's Danger Here, Cherie!": Liability for the Promotion and Marketing of Drugs and Medical Devices for Off-Label Uses*, 73 BROOK. L. REV. 1256, 1257 (2008).

4. U.S. FOOD & DRUG ADMIN., *What We Do*, USFDA, http://www.fda.gov/aboutfda/whatwedo/default.htm (last updated Oct. 24, 2016).

between commercial speech and the FDA's important public health policy goals. Statutory, judicial, and administrative challenges to the FDCA present a serious threat to the FDA's authority, as well as its traditional approach to regulating the safety and efficacy of pharmaceuticals sold in the U.S. The result is a growing protection for manufacturers to defend themselves from liability for off-label promotional speech altogether—or at least where it is "wholly truthful and non-misleading."[5] This article traces the arc of the FDCA from the FDA Modernization Act of 1997 (FDAMA),[6] to a number of Federal courts asserting a First Amendment right for drug manufacturers to promote their products off-label,[7] and finally to the relaxation of administrative guidance from the FDA regarding "scientific exchange."[8]

I. THE FDA'S TRADITIONAL APPROACH TO OFF-LABEL PROMOTION

Under the FDCA,[9] the FDA is authorized to regulate and control the labeling of drugs.[10] It is under this authority that the FDA acts as a gatekeeper to the pharmaceutical market as a whole, dictating which drugs are marketed

5. *See infra* Part I (discussing the traditional FDA approaches)*; see also* Proposed Jury Instructions, *U.S. v. Vascular Solutions, Inc.*, Cr. No. 14-926 (W.D. Tex. 2016) ("It is also not a crime for a device company or its representatives to give doctors wholly truthful and non-misleading information about the unapproved use of a device.").

6. Food and Drug Administration Modernization Act of 1997, 21 U.S.C. § 2201 et seq. (1997) [hereinafter FDAMA].

7. *See, e.g.*, Thomas Sullivan, *The Impact of Caronia Case: What Happens Next?*, POL'Y & MED. (Jan. 17, 2013), http://www.policymed.com/2013/01/the-impact-of-caronia-case-what-happens-next.html; *see also* Jeffrey Chasnow & Geoffrey Levitt, *Preemption of Non-Federal Restraints on Off-Label Product Communications*, 71 FOOD & DRUG L.J. 249 (2016).

8. FDA's regulations regarding the promotion of investigational drugs states that they are not "intended to restrict the full exchange of scientific information concerning the drug" but rather "to restrict promotional claims of safety or effectiveness of the drug . . . and to preclude commercialization of the drug before it is approved." 21 C.F.R. § 312.7.

9. Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 301-399(f) (2012).

10. FDA-required labeling is generally approved by the FDA before distribution with the product; promotional labeling is not reviewed by the FDA before it is distributed, but is defined as any written, printed, or graphic matter that bears a "textual relationship" with a drug or device. Therefore, although a pamphlet sent to a physician's office may not carry a "physical attachment" to the specific drug, it is still considered to be promotional labeling due to a textual relationship with the drug. U.S. FOOD & DRUG ADMIN., *Drug advertising: a glossary of terms* (June 19, 2015), http://www.fda.gov/Drugs/ResourcesForYou/Consumers/PrescriptionDrugAdvertising/ucm072025.htm [hereinafter *Drug advertising: a glossary of terms*].

and sold in the US.[11] Only after the FDA has approved a pharmaceutical product's indications, through rigorous phases of testing and approval of marketing materials, is the manufacturer then free to label, promote and distribute its product.[12] The indication approval process is the product of significant administrative effort—for decades, the FDA has required that the labels of approved drugs follow the format contained in its "Uniform Labeling Requirements."[13] Among the subjects to be included in a drug's label are its "indications and usage" information which is derived directly from the seller's approved New Drug Application (NDA).[14] This information cannot be unsubstantiated hearsay. As part of the NDA approval process, the manufacturer's products must be proven safe and effective for all indications, on the basis of "substantial evidence" from well-controlled clinical studies submitted to the FDA for independent review.[15] Given the cost of well-controlled clinical studies and the fees associated with NDAs, manufacturers must often decide which possible indications, among many, to pursue.[16] Therefore, the decisions a pharmaceutical company makes in the pre-market period regarding which indications are the focus of its clinical trials in large part determine the approved labeled indications and usage.[17]

The FDA's authority over pharmaceutical labeling and marketing is absolute. However, regulating the prescribing decisions of physicians is

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11. DANIEL CARPENTER, REPUTATION AND POWER: ORGANIZATIONAL IMAGE AND PHARMACEUTICAL REGULATION AT THE FDA 114, 613 (2010).

12. *Id.* at 591; *see also* 21 C.F.R. § 201.1 et seq. (2016).

13. CARPENTER, *supra* note 11, at 614-15.

14. 21 C.F.R. § 314.81(b)(2)-(3).

15. Promotion of Unapproved Drugs and Devices: Hearing Before the Senate Committee on Labor and Human Resources (1996) (testimony of William B. Schultz, Deputy Commissioner for Policy, Food and Drug Administration) http://www.fda.gov/newsevents/testimony/ucm115098.htm [hereafter Schultz Testimony].

16. Joseph A. DiMasi et al., *Innovation in the pharmaceutical industry: New estimates of R&D costs*, 47 J. OF HEALTH ECON., 20, 32 (2016) (finding that by the time a drug has made it through clinical testing and the FDA approval process, the cost to the pharmaceutical company is around $2,870 million).

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

beyond its mandate, due to statutory and constitutional limitations.[18] As a consequence, the agency has taken a strong stand against off-label promotional activities on the part of manufacturers as a way of ensuring that doctors can be confident that a product is safe and effective for its indications.[19] Patients, in turn, can have confidence in the quality of the products they are receiving and the public health is best served.[20] The FDA originally took the position that *any* claim from a manufacturer that a drug could be "safe and effective" for an off-label use was always "false or misleading," although more recently it retreated from that strong position.[21] Since then, the FDA has created a pathway through which additional indications can be approved, added to the drug's label, and then promoted.[22] Companies can file Supplemental New Drug Applications (sNDAs) following an earlier approval for the purpose of adding additional indications.[23] Between 2000 and 2006, there were 294 sNDAs filed for additional indications, although that number was only about two percent of

18. 21 U.S.C. § 396 (1997) ("Nothing in this Act shall be construed to limit or interfere with the authority of a healthcare practitioner to prescribe or administer any legally marketed device to a patient for any condition or disease within a legitimate healthcare practitioner-patient relationship."). In the FDA's guidance to physicians prescribing off-label, the agency states they have the responsibility to be well informed about the product, on the basis of "firm scientific rationale and on sound medical evidence." U.S. FOOD & DRUG ADMIN., OFF-LABEL AND INVESTIGATIONAL USE OF MARKETED DRUGS, BIOLOGICS, AND MEDICAL DEVICES - INFORMATION SHEET (2014) [hereinafter OFF-LABEL AND INVESTIGATIONAL USE]; *see also* Marcus v. Specific Pharms. Inc., 77 N.Y.S.2d 508, 509-10 (N.Y. App. Term. 1948) (stating that a physician may still be liable for failing to warn patients of the potential hazards and defects associated with prescribed medications).

19. *See* OFF-LABEL AND INVESTIGATIONAL USE, *supra* note 18; *see also* Schultz Testimony, *supra* note 15.

20. *See* OFF-LABEL AND INVESTIGATIONAL USE, *supra* note 18; *see also* Schultz Testimony, *supra* note 15.

21. Jerry Avorn et al., *Forbidden and Permitted Statements about Medications—Loosening the Rules*, 373 NEW ENG. J. MED. 967, 968 (2015).

22. CARPENTER, *supra* note 11, at 613 (describing the primary reasons sNDAs have been filed since 1970, including chemistry revisions, manufacturing revisions, package changes, control supplements, labeling revisions (SLR), and other label changes).

23. Supplemental Indications for Approved Prescription Drugs: Hearing Before the H. Comm. on Gov't Reform and Oversight, Subcomm. on H.R. and Intergovernmental Relations (1996) (testimony of Michael Friedman Deputy Commissioner for Operations, Food and Drug Administration) http://www.hhs.gov/asl/testify/t960912a.html.

the total 14,000 sNDAs filed during the same years.[24]

However, from the manufacturer's perspective there are significant drawbacks to the sNDA system. Adding additional indications to the drug's label requires the submission of supplementary clinical data—collected on company time and expense—and FDA approval for an sNDA often takes as long as the original NDA.[25] The advantages are therefore typically outweighed by the costs and risks involved in applying for additional indications.[26] While the NDA and sNDA process protects the public health mission of the FDA through stringent regulation and a rigorous clinical testing process, it remains a burdensome obstacle for manufacturers who have to bear the additional fees, research costs, and scrutiny.[27]

II. STATUTORY LOOPHOLES AND THE FDAMA

Given the burdens of the NDA and sNDA process, manufacturers face the question of how to market their drugs for off-label use without triggering liability under the FDCA.[28] A critical question involves whether they can legally provide information to physicians on non-indicated uses of their drugs.[29] Prior to the FDAMA,[30] the FDA's answer was largely no.[31] However, FDA restrictions to provider-manufacturer communication came under attack from the American Medical Association (AMA) in the 1990s,

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24. *See* Avorn, *supra*, note 21, at 968 (indicating other causes for sNDA filing).

25. *See* Veronica Henry, *Off-Label Prescribing Legal Implications*, 20 J. LEGAL MED. 365, 368 (1999).

26. *Id*.

27. DiMasi et al., *supra* note 16.

28. Elizabeth Richardson, *Health Policy Brief: Off-Label Drug Promotion*, HEALTH AFF. 3-4 (Jun. 30, 2016), http://healthaffairs.org/healthpolicybriefs/brief_pdfs/healthpolicybrief_159.pdf.

29. *See, e.g.*, United States v. Caronia, 703 F.3d 149 (2d. Cir. 2012). As illustrated by the misbranding guilty plea of former Orphan consultant Dr. Gleason, physician consultants are often paid by pharmaceutical companies to speak about their drugs at various professional functions. These types of arrangements are commonplace in the healthcare industry; however, substantive conversations about off-label drug uses often cannot be had with pharmaceutical sales representatives for fear of triggering liability.

30. *See* 21 U.S.C. § 2201 et seq.

31. Avorn et al., *supra* note 21, at 967-68.

for limiting access to pharmaceutical research.[32] Congress responded with FDAMA, which, under Section 114, authorized manufacturers to distribute unabridged peer reviewed publications or reference materials to healthcare practitioners, pharmacy benefit managers, health insurers, and federal and state governments.[33] Though the FDA described implementing the new law as "one of the most demanding challenges faced by the Agency in its 92 year history,"[34] it nonetheless moved forward with regulations requiring the distributed materials to disclose the manufacturer as the source and to indicate specifically that the FDA had not approved the information.[35] Yet the effect of these changes was to allow for the broader distribution of research relevant to off-label use.[36] Direct marketing of off-label indications remained prohibited, but the dissemination of accurate scientific information by manufacturers was acceptable—albeit with two corollaries: first, the materials had to be provided to the FDA in turn, and second, the manufacturer had to verify its plans to seek approval for the new indications.[37] Strict compliance guaranteed a "safe harbor" from prosecution for engaging in false or misleading advertising.[38]

On its face, the new statutory pressure from FDAMA had not substantially altered the balance between commercial speech and the larger public health

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32. James M. Beck & Elizabeth D. Azari, *FDA, Off-Label Use and Informed Consent: Debunking Myths and Misconceptions*, 53 FOOD & DRUG L.J. 71, 103 (1998) (explaining that AMA representatives called for the FDA to permit physicians increased access to information about off-label uses by allowing manufacturers to distribute scientific studies to physicians).

33. *Id*.

34. FDAMA: Hearing Before the Senate Committee on Commerce (1998) (testimony of Michael A. Friedman, Acting Commissioner of Food and Drugs, Food and Drug Administration) http://www.fda.gov/NewsEvents/Testimony/ucm115096.htm.

35. 21 U.S.C. §§ 360aa, 551.

36. Robert I. Field, *The FDA's New Guidance for Off-Label Promotion Is Only a Start*, 33 HEALTH CARE & L. 220, 249 (2008).

37. 21 U.S.C. §§ 360aa, 551.

38. In 1998, the federal district court for the District of Columbia prohibited the FDA from enforcing the FDAMA conditions as requirements, on the grounds that they infringed on free speech rights. Washington Legal Foundation v. Friedman, 13 F. Supp. 2d 51 (D.D.C. 1998). In response to the court ruling, the FDA issued regulations adopting the FDAMA standards. 21 C.F.R. § 99.1 et seq.

mandate of the FDA. Direct marketing for off-label use remained prohibited and manufacturers seeking physicians to prescribe their products off-label had to essentially submit to the sNDA process or risk prosecution.[39] The FDAMA safe harbor had benefits too, promising greater patient access to new medical products and more effective management of the FDA's limited resources.[40] At the same time, FDAMA was also the first significant cession of the authority–previously absolute–granted by FDCA with regard to promotional labeling.[41] The exception it created was narrow: the FDAMA only relaxed off-label marketing rules with regard to physicians and other qualified health care professionals, theoretically, so that manufacturers could in fact monitor the flow of information themselves.[42] Still, the FDAMA safe harbor opened the door to attacks on the primacy of the FDA—it would take subsequent litigation to push it open further.[43]

III. THE RISE OF FIRST AMENDMENT PHARMACEUTICAL PROMOTION LITIGATION

In its creation of the FDAMA safe harbor, the FDA carefully skirted issues of commercial free speech in order to avoid triggering constitutional

39. *See* Washington Legal Foundation, *supra* note 38.

40. FDAMA: Hearing Before the Senate Committee on Health, Education, Labor and Pensions (1999) (testimony of Jane E. Henney, Commissioner of Food and Drugs, Food and Drug Administration) http://www.fda.gov/NewsEvents/Testimony/ucm115036.htm.

41. Jennifer Washburn, *Undue Influence*, THE AMERICAN PROSPECT (Dec. 19, 2001), http://prospect.org/article/undue-influence (explaining how FDAMA enhanced the pharmaceutical industry's marketing powers by abolishing absolute prohibitions against manufacturers disseminating information about unapproved uses and easing restrictions on advertising).

42. 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, 188 (1999).

43. It is worth noting that FDAMA's limitations on off-label promotion expired on September 30, 2006, and Congress has yet to reauthorize them. The FDA's draft guidance is an attempt to fill the void. The agency continues to require that materials be reprinted from bona fide independent peer-reviewed sources, but it omits mandates for prior agency approval and for manufacturers to verify their intent to conduct clinical trials of unapproved uses. *See generally* Robert I. Field, *The FDA's New Guidance for Off-Label Promotion Is Only a Start*, 33 PHARMACY & THERAPEUTICS 220 (2008).

challenges to the regulation.[44] Nevertheless, it was a dispute that would not be postponed for long. This tension between public health and truthful and non-misleading off-label promotion was elucidated by the United States Supreme Court's 2011 decision in *Sorrell v. IMS Health,* where a majority of the Court concluded that a state-imposed restriction on commercial speech was subject to a heightened standard of judicial review.[45] *Sorrell* involved a First Amendment challenge to Vermont's Act 80, which prohibited pharmaceutical companies from using "prescriber-identifying information" to market drugs to physicians.[46] Drug manufacturers purchase and use this data to more effectively promote drugs to physicians.[47] The Vermont legislature was concerned that prescriber-identifying information facilitated marketing tactics that caused physicians to prescribe more expensive brand name drugs over cheaper generic equivalents.[48] IMS Health, a physician prescribing data mining company, and the Pharmaceutical Research and Manufacturers of America challenged these restrictions as violating the Free Speech Clause and filed certiorari with the Supreme Court.[49] A six Justice majority led by Justice Kennedy struck down the law as unconstitutional due to what it characterized as unacceptable "viewpoint discrimination" aimed at suppressing the drug manufacturers' commercial message in favor of

44. Washington Legal Foundation v. Henney, 202 F.3d 331 (D.C. Cir. 2000) (re-framing the FDA's policies as ones in which manufacturer compliance with the FDA's safe harbors would not be used as evidence of misbranding—but that non-compliance could be used as such evidence—the government removed any constitutional issue; finding no constitutional controversy between the parties, the court vacated the district court's decisions and injunctions).

45. Sorrell v. IMS Health Inc., 131 S.Ct. 2653 (2011).

46. Prescriber-identifying information is data that pharmacies collect, pursuant to federal regulation, about customer prescriptions, including the identity of the prescribing physician. *Id.* at 2660.; *see* Andrew J. Wolf, *Detailing Commercial Speech: What Pharmaceutical Marketing Reveals About Bans on Commercial Speech*, 21 WM. & MARY BILL RTS. J. 1291 (2013)).

47. John N. Joseph et al., *Is* Sorrell *the Death Knell for FDA's Off-Label Marketing Restrictions?*, 5 J. HEALTH & LIFE SCI. L. 1, 5 (2012).

48. Sorrell, 131 S.Ct. at 2670.

49. *Id.* at 2662.

Vermont's message of cost effectiveness and balanced information.[50]

Notwithstanding the Court's conclusion that Act 80 should be reviewed under strict scrutiny,[51] the *Sorrell* majority decided that Act 80 would not survive even the lesser intermediate scrutiny test under *Central Hudson Gas & Electric Corp. v. Public Service Commission*, that is, whether the government's speech restriction directly advanced its asserted interest and was not more extensive than necessary.[52] Addressing Vermont's argument that promotional speech based on prescriber-identifying information undermined the doctor-patient relationship by influencing medical treatment decisions, the majority reasoned that "the fear that speech might persuade provides no lawful basis for quieting it."[53] The majority concluded that Act 80's restrictions did not directly advance the state's purported goals and was unconstitutional.[54]

As Justice Breyer warned in his *Sorrell* dissent, and as predicted by many commentators, it was not long before the pharmaceutical industry argued that the *Sorrell* rationale applied to FDA restrictions on truthful off-label promotional speech.[55] The Second Circuit's 2012 decision in the criminal case of *United States v. Caronia*[56] did just that, the first in a long line of cases spread of the "false and misleading" standard to the district court level. Alfred Caronia, a sales consultant for the pharmaceutical company Orphan

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50. *Id.* at 2663-64.

51. The court found that Vermont's law "enact[ed] content- and speaker-based restrictions . . ." since prescribing information could be used for any speech except promotional speech and the only prohibited speakers were pharmaceutical manufacturers and their agents. *Id.* at 2663. Strict scrutiny was therefore demanded. *See also* Reed v. Town of Gilbert, 135 S. Ct. 2218, 2228 (2015) ("A law that is content based on its face is subject to strict scrutiny regardless of the government's benign motive, content-neutral justification, or lack of animus toward the ideas contained in the regulated speech.").

52. Sorrell, 131 S.Ct. at 2667-68 (citing Central Hudson Gas & Elec. Corp. v. Public Serv. Comm'n of N.Y., 447 U.S. 557 (1980)).

53. *Id*. at 2670.

54. *Id.* at 2672.

55. *See* Sorrell, 131 S.Ct. at 2676-78; *see also* Joseph et al., *supra* 47.

56. U.S. v. Caronia, 703 F.3d 149, 154 (2d. Cir. 2012).

Medical, was caught on video promoting Xyrem for unapproved uses.[57] He was charged in the Eastern District of New York with introducing a misbranded drug into interstate commerce and conspiracy to introduce a misbranded drug into interstate commerce, both are violations of the FDCA.[58] Caronia appealed his conviction to the Second Circuit, arguing that the misbranding provisions of the FDCA prohibit off-label promotion, and therefore, unconstitutionally restrict speech.[59]

The majority, applying the reasoning from *Sorrell*, found that the FDA's position on misbranding imposed both content and speaker-based restrictions on off-label promotional speech—i.e., it allowed speech about government-approved uses while prohibiting speech about unapproved uses, targeting only one class of speakers (pharmaceutical manufacturers).[60] Additionally, the majority reasoned that the government's off-label speech restrictions did not advance a substantial interest because "even if pharmaceutical manufacturers are barred from off-label promotion, physicians can prescribe, and patients can use, drugs for off-label purposes."[61] The majority determined that restricting off-label speech by drug companies while allowing off-label uses by physicians "paternalistically interfered with the ability of physicians and patients to receive potentially relevant treatment information."[62] The Court also reasoned that the off-label restrictions were not narrowly tailored when there were multiple less restrictive means by

57. *Id.* at 156.
58. *Id.* at 159.
59. *Id.* at 160; Orphan pleaded guilty to a single count of introducing a misbranded drug into interstate commerce with the intent to defraud and mislead. It was ordered to pay $12,262,078 in restitution and $5 million in criminal fines. Dr. Peter Gleason, a physician paid by Orphan to promote Xyrem for off-label uses, pleaded guilty to a single count of misdemeanor misbranding and was sentenced to one year of probation. James E. Tysse et al., *Free Speech and the Future of Off-Label Pharmaceutical Marketing Regulation After* United States v. Caronia, LIFE SCI. L. & INDUSTRY REP., 7 LSLR 117 (2013).
60. Caronia, *supra* note 56, at 165.
61. *Id*. at 166.
62. *Id*.

which FDA could further its interests.[63] In short, the *Caronia* majority concluded that the misbranding provisions of the FDCA could not be interpreted as prohibiting truthful and non-misleading off-label promotion, because such an interpretation would run afoul of the First Amendment's free speech protections.[64]

Notwithstanding the *Caronia* majority's sweeping denunciation of the FDA's ban on truthful off-label promotional speech, the government elected not to seek rehearing or otherwise appeal.[65] In early 2013, an FDA official explained that the agency did not believe that the *Caronia* decision would significantly affect the agency, since the court acknowledged that even the First Amendment did not preclude an enforcement action based on false or misleading speech.[66] The government seemed to decide that attempting to narrow and distinguish the Second Circuit's holding was a better strategy than risking a potentially unfavorable final ruling from the Supreme Court.[67] However, truthful non-misleading speech in aid of off-label promotion did not stay out of the courts, and *Caronia* and *Sorrell*'s rationale proved influential.[68] While "false or misleading" speech is not an inviolable standard

63. *Id*. at 167-68 (suggesting that instead of restricting promotional speech on off-label uses, FDA could provide guidance to physicians and patients on how to distinguish between false or misleading information and truthful or non-misleading information).

64. The dissenting opinion took issue with the possible repercussions the majority's decision would have on FDA's drug-approval process, reading the majority's holding as allowing "any substance that may be legally sold for some purpose [to] be promoted by its manufacturer[s] for any purpose—so long as the manufacturer's statements are merely unsubstantiated, rather than demonstrably false or misleading." The dissent warned that such a reading would "invalidate the very definitions of 'drug' and 'device' that undergird the entire FDCA," and could render the FDCA unconstitutional. *Id*. at 168-69, 178.

65. Thomas M. Burton, *FDA Won't Appeal Free-Speech Marketing Decision*, WALL STREET J. (Jan. 23, 2013, 8:20 PM), http://www.wsj.com/articles/SB10001424127887324539304578260323575925896.

66. Jill Wechsler, *Tom Abrams: Caronia Won't Stop Off-Label Enforcement*, PHARMEXEC.COM (Jan. 29, 2013), www.pharmexec.com/tom-abrams-caronia-wont-stop-label-enforcement (quoting Tom Abrams, director of the Office of Prescription Drug Promotion in the Center for Drug Evaluation and Research).

67. *Id.*

68. *See, e.g.*, Caplinger v. Medtronic, Inc., 784 F.3d 1335, 1352 (10th Cir. 2015) (2016) (discussing the definition of misbranding in relation to FDCA); *see also* 1-800-411-Pain Referral Serv., LLC v. Otto, 744 F.3d 1045, 1054 (8th Cir. 2014) (discussing the application

across all jurisdictions, Federal courts in have increasingly adopted similar reasoning.[69] Pharmaceutical companies, citing *Caronia* and similar district court cases, petitioned the FDA to review its policies regarding communication of off-label or unapproved indications—resulting in a two-day conference in November of 2016 where the FDA heard public comments.[70]

Yet despite a shifting legal standard, the FDA's concerns about returning to the lawless "pre-1962 era"[71] endure. Although *Thompson* and *Sorrell* do not protect false or misleading commercial speech,[72] they invite a grim slippery slope argument: that judicial recognition of off-label promotion will inevitably lead courts to also strike down the FDA's entire premarket approval structure, chipping away at the mandate of the FDCA.[73] While it is possible the courts will articulate an "arbitrary but workable" status quo,[74]

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of Sorell).

69. *See* Allergan, Inc. v. United States, No. 1:09-cv-01879 (D.D.C. 2010) ("although the Government has significant interests that could justify some restrictions of off-label promotional practices, there is no need for . . . the blanket suppression of off-label speech."); *see also* Vascular Solutions, *supra* note 8; Amarin Pharma, Inc. v. U.S. Food & Drug Admin., 119 F. Supp. 3d 196, 227-28 (S.D.N.Y. 2015) (holding that the FDA could not pursue misbranding sanctions against Amarin for statements that were truthful and nonmisleading).

70. Toni Clarke, *Under pressure, FDA to hold public meeting on off-label use*, REUTERS (May 6, 2015 9:35 PM) http://www.reuters.com/article/us-fda-pharmaceuticals-constitution-idUSKBN0NS00F20150507.

71. Memorandum of Law in Opposition to Plaintiffs' Motion for Preliminary Injunction, at 1, Amarin Pharma, Inc. v. FDA, 119 F. Supp. 3d 1196, 2015 WL 4387279 (S.D.N.Y. 2015) (referring to Drug Efficacy Amendment, Pub. Law. No. 87-781, 76 Stat. 1040, signed into law in 1962, strengthening and standardizing the FDA's enforcement of drug trials and efficacy requirements).

72. *See*, e.g., U.S. ex rel. Cestra v. Cephalon, Inc., 2015 WL 3498761 (E.D. Pa. 2015). Because the relator in a qui tam action for False Claims Act violations had alleged that the off-label statements were false and misleading, the court rejected the defendant's motion to dismiss because *Caronia* did not control where the statements at issue may be false or misleading.

73. *See* Joseph et al., *supra* note 47, at 33 (noting the Government's "compelling" argument that off-label detailing exacerbates the health risk by increasing the number of people using drugs for off-label purposes); Christopher T. Robertson, *When Truth Cannot Be Presumed: The Regulation of Drug Promotion Under an Expanding First Amendment*, 94 B.U.L.R. 545, 554 (2014).

74. *See* Toni M. Massaro, *Constitutional Law as Normal Science*, 21 CONST. COMMENT. 547, 548 (2004) (describing the Supreme Court's preference for "seek[ing] to cabin the impact of any changes, and they [the Justices] emphasize the limited role that the Court realistically

the current judicial atmosphere seems to favor "wholly truthful and nonmisleading" commercial speech.[75] If the FDAMA safe harbor provision exposed vulnerabilities in the FDA's public health mandate, then the rise of judicial protection for off-label promotion took advantage of those vulnerabilities. However, as significant as the legislative and judicial challenges to the FDCA have been, they are further bolstered by administrative regulation.

IV. THE REGULATION OF "SCIENTIFIC EXCHANGE"

Even if the rise of First Amendment litigation regarding off-label promotion creates binding precedent where all truthful and non-misleading statements in off-label promotion are constitutionally protected, the FDA still has the regulatory power to assert that a given promotional message is false or misleading.[76] What constitutes false or misleading speech is a subjective and fact-driven determination of the FDA Office of Prescription Drug Promotion (OPDP).[77] Because the OPDP generally does not determine what promotional materials are false or misleading until after launch of the product, a drug manufacturer that promotes off-label indications risks having these materials deemed outside the protections of the First Amendment.[78] Given the FDA's opposition to off-label promotion, the agency may now be more apt to find promotional messages false or misleading.[79]

However, given the existing statutory and legislative protections for

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can, and constitutionally should, play in shaping public policy.").

75. Vascular Solutions, *supra*, note 5.

76. *See* 21 U.S.C. § 352 ("A drug or device shall be deemed to be misbranded . . . If its labeling is false or misleading in any particular.").

77. Vascular Solutions, *supra*, note 5.

78. Under 21 C.F.R. § 314.550, the manufacturer is required to submit all promotional materials for the first 120 days of the launch campaign to the FDA *during* the pre-approval review period. However, all promotional materials for after the 120 day launch period must be submitted to the FDA just 30 days before the intended time of initial dissemination.

79. Declaration of Janet Woodcock, M.D., Amarin Pharma, Inc. v. U.S. Food & Drug Admin., No. 1:15-CV-03588-PAE (Jun. 23, 2015) (describing the public health reasons for the FDA's opposition to limitless off-label promotion).

commercial speech, it seems unlikely the agency will enforce such a hard line.[80] The FDA is more likely to take another route, and continue to refine its distinction between "promotion" and "scientific exchange."[81] In response to both the FDAMA and the rise of First Amendment litigation, the FDA shifted its stance on commercial speech—part of which entails non-promotional information and research, conducted by individuals who are scientifically trained professionals and in a forum or context that is conducive and reflective of scientific discussion.[82] In 2009 and 2014, the FDA released guidance with updated standards for reprint practices related to journal articles, scientific or medical reference texts, and clinical practice guidelines.[83] The draft guidance further updated FDA's perspective on best practices for distributing scientific and medical publications on unapproved new uses.[84] In the case of the aforementioned guidance, it has echoed the FDAMA safe harbor provisions as well as the holdings of *Sorell* and *Caronia.* Additionally, it distinguished between the traditional "promotional"[85] speech and the dissemination of "wholly truthful and non-misleading" research for off-label uses.[86] In other words, while the former is still regulated in the traditional fashion, the latter has been deemed an

80. *Supra*, Part II, Part III.

81. *See* Communications and Activities Related to Off-Label Uses of Marketed Products and Use of Products Not Yet Legally Marketed; Request for Information and Comments, 76 F.R. 81508 (2011).

82. *See*, 21 C.F.R. § 312.7(a) (stating the administrative basis for scientific exchange safe harbor).

83. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: GOOD REPRINT PRACTICES FOR THE DISTRIBUTION OF MEDICAL JOURNAL ARTICLES AND MEDICAL OR SCIENTIFIC REFERENCE PUBLICATIONS ON UNAPPROVED NEW USES OF APPROVED DRUGS AND APPROVED OR CLEARED MEDICAL DEVICES (2009), http://www.fda.gov/RegulatoryInformation/Guidances/ucm125126.htm (writing to address the sunset of FDAMA in 2007, effectively ending the sNDA-specific provisions of Section 401); FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: DISTRIBUTING SCIENTIFIC AND MEDICAL PUBLICATIONS ON UNAPPROVED NEW USES—RECOMMENDED PRACTICE 2 (2014), http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm387652.pdf [hereinafter DISTRIBUTING SCIENTIFIC AND MEDICAL PUBLICATIONS].

84. DISTRIBUTING SCIENTIFIC AND MEDICAL PUBLICATIONS at 2.

85. Drug advertising: a glossary of terms, *supra* note 10.

86. DISTRIBUTING SCIENTIFIC AND MEDICAL PUBLICATIONS, *supra* note 83, at 6.

exception to FDCA under the administrative rulings of the FDA.[87]

Although not enforceable regulation, the guidance provides the FDA's perspectives on off-label information dissemination and promotion in the course of litigation.[88] And where the administrative guidance of the past ten years has complimented the legislative and judicial developments, it has cemented them. Certainly, there are benefits to the current FDA pre-approval system—it allows doctors and manufacturers to exchange information about unproven uses, maintaining clarity and as much informed consent as possible, while still giving an incentive for manufacturers to study pharmaceuticals more systematically.[89] In a system where it is unlikely that any individual patient or doctor could conduct scientific studies to determine safety and efficacy of drugs, it is important to the public health that there be some means of disseminating information in a flexible yet discerning way.[90]

However, achieving such an end through restricting the FDA's authority over off-label promotion risks undermining the FDA's regulatory regime as a whole.[91] The head of the Cleveland Clinic called the legitimation of off-label promotion "a potential catastrophe for patients" due to the public health impact.[92] In essence, courts and legislatures are putting a great deal of faith—first, in manufacturers *not* to conduct poor-quality studies for the purpose of showing products' utility for unapproved indications,[93] and second, in

87. *Id.*

88. *Id.*

89. Woodcock, *supra* note 79.

90. *Id.*

91. 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, 307 (2010).

92. Editorial, *The Limits of Free Speech*, NATURE (Dec. 19, 2012), http://www.nature.com/news/the-limits-of-free-speech-1.12062.

93. "There is no need for companies to design these studies to meet the FDA's standards for methodological rigor if the companies have no intention of submitting an application for approval of the new use, but rather intend to use the study findings only in marketing communications. Companies can design studies in ways that maximize the chances of obtaining a desired result and select which studies to emphasize in promotional communications, ignoring others that do not support their promotional message." Aaron S.

physicians to independently evaluate claims about off-label uses.[94] Ultimately, undermining the FDCA in this way undermines the authority and project of the FDA, threatening the public health mandate which is the heart of its mission.

V. CONCLUSION

The FDA plays a critical role in ensuring that patients and physicians have confidence that prescribed medicines are safe and effective for their approved uses, protecting the public health through rigorous clinical standards and administrative safeguards. Yet, the practice of modern medicine has demands a more flexible framework of information sharing, pharmaceutical use, and discernment regarding prescription.[95] As a result of judicial and regulatory shifts, the FDA stands at a crossroads when it comes to off-label promotion and communication by pharmaceutical manufacturers. Whatever framework is ultimately adopted will certainly be informed by *Caronia*, FDAMA, and the FDA's own administrative governance—however, such a framework must also preserve the necessary authority of the FDA. At the November 2016 public meeting to review the FDA's policies on off-label promotion, FDA Commissioner Robert Califf remarked that going forward, there may be room for both flexibility of information-sharing as well as faithfulness to the FDA's public health mandate.[96] Yet neither can be truly accomplished without the FDA acting to the extent of its authority as arbiter

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Kesselheim & Michelle M. Mello, *Prospects for Regulation of Off-Label Drug Promotion in an Era of Expanding Commercial Speech Protection*, 92 N.C. L. REV. 101, 144 (2014).

94. "Physicians must rely on their judgments of representatives' personal credibility. Some promotional claims may be inherently impossible for physicians to verify, such as a claim that other physicians are already widely prescribing the drug for a particular off-label use and have encountered no serious safety problems." *Id*. at 147.

95. James M. Spears et al., *Embracing 21st Century Information Sharing: Defining A New Paradigm for the Food and Drug Administration's Regulation of Biopharmaceutical Company Communications with Healthcare Professionals*, 70 FOOD & DRUG L.J. 143, 159-60 (2015).

96. Clarke, *supra* note 70.

of pharmaceutical safety and efficacy, and guardian of the U.S.'s long-standing regulatory framework. Any change—even a small change—has the power to influence what kind of information patients receive on drugs and devices, and the FDA alone has the ability and responsibility to ensure public health remains a priority.

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The Hospital-Acquired Condition Penalty: Well Intentioned, Poorly Implemented

Jordan Donnelly[*]

I. INTRODUCTION

The newly instituted hospital-acquired condition penalty would be more effective if changed in two ways: first, if implemented as a function of hospital-acquired conditions per patients treated, and second, if the Centers for Medicare and Medicaid Services excused disproportionate share hospitals and academic hospitals from the penalty altogether. Penalizing hospitals based on data that is published once a year does not effectively incentivize hospitals to improve consistently throughout the year.[1] Not only is the penalty inefficient and ineffective, but it is also unfairly applied to disproportionate share hospitals and academic hospitals because disproportionate share hospitals' patients are more likely to develop a hospital-acquired condition,[2] and hospital-acquired conditions are more likely to be noticed at academic hospitals.[3] Disproportionate share hospitals already face a stark financial picture and penalizing them further undercuts their ability to provide care to those who need it, but may not be able to afford

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1. Maureen McKinney, *Hospitals Question Whether Latest Penalty Program Will Help Them Improve Quality*, MODERN HEALTHCARE (Dec. 7, 2013), http://www.modernhealthcare.com/article/20131207/MAGAZINE/312079990.

2. David Richardson, *Reducing HACs Penalties for Hospital-acquired Conditions Cut into Bottom Line*, MANAGED HEALTHCARE EXECUTIVE 17, 18 (2015).

3. Jordan Rau, *How Medicare Penalizes Hospitals for Being Too Careful*, N.Y. TIMES, (Apr. 20, 2016), http://www.nytimes.com/2016/04/21/health/how-medicare-penalizes-hospitals-for-being-too-careful.html.

it.[4] Academic hospitals should not be penalized for treating some of the sickest patients in the country, and testing their patients more thoroughly.[5] Therefore, disproportionate share hospitals and academic hospitals should be exempt from the penalty.

II. BACKGROUND

When the Affordable Care Act (ACA) was enacted in 2010, Congress included a penalty for hospitals with a comparatively high frequency of hospital-acquired conditions in an attempt to incentivize high-quality care.[6] Beginning in fiscal year 2015, "subsection (d) hospitals" have been required to submit yearly reports on the number of hospital-acquired conditions observed at their respective hospital over the course of the fiscal year.[7] A "subsection (d) hospital" refers to any hospital in the United States that is not a psychiatric hospital, rehabilitation hospital, or children's hospital.[8] If a hospital is in the bottom quartile of all qualifying hospitals for hospital-acquired conditions at the end of the fiscal year, that hospital is penalized one percent of its annual Medicare payments.[9] The ACA gives the Secretary of the Department of Health and Human Services (DHHS) the power to determine what qualifies as a hospital-acquired condition.[10] Such conditions

4. Peter Cunningham & Robin Rudowitz, *Understanding Medicaid Hospital Payments and the Impact of Recent Policy Changes*, KAISER COMM'N ON MEDICAID AND THE UNINSURED 1, 6 (2016).

5. Rau, *supra* note 3.

6. Patient Protection and Affordable Care Act, 42 U.S.C. §1395ww(p)(1), (p)(2)(B)(i) (2010).

7. *See id.* §1395ww(p)(5) (hospitals are required to submit one report per year and whether the hospital is penalized is based solely off the single report).

8. *Id.* §1395ww(d)(1)(B).

9. *See id.* §1395ww(p)(2)(B)(i) (meaning they are among the worst performing hospitals in terms of hospital-acquired conditions).

10. *See id.* 42 U.S.C. §1395ww(p)(3). The Secretary can add any condition to the definition that has a high cost and/or high volume, results in the assignment of a case to a diagnosis-related group that has a higher payment when the code is present as a secondary diagnosis, or could reasonably have been prevented through the application of evidence-based guidelines.

may include catheter-associated infections, foreign objects retained after surgery, surgical site infections, falls and trauma, and pressure ulcers.[11]

Hospital-acquired conditions present a number of concerns. For example, preventable complications within a hospital, such as hospital-acquired conditions, cost hospitals an estimated $88 billion a year in the United States, and in 2007, they accounted for 12.2 percent of health care facilities' legal liability costs.[12] However, concerns related to hospital-acquired conditions are not limited to financial losses; hospital-acquired conditions also account for an estimated 100,000 deaths each year.[13] The penalty was introduced to both incentivize better care and to save hospitals money.

It is possible that the penalty will increase in the future. Before the ACA was passed, a proposed policy was circulated by the U.S. Senate Finance Committee requiring higher penalties than those that were ultimately enacted.[14] Experts predict that because the DHHS has the authority to expand the required reported conditions, and the continuing demand to "bend the cost curve," there will be pressure to increase the penalties and increase the number of conditions at issue.[15]

Financial incentives for hospitals to reduce hospital-acquired conditions have been effective in recent history, suggesting this penalty could be effective as well. Beginning in fiscal year 2009, hospitals no longer received

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11. U.S. DEP'T OF HEALTH & HUMAN SERVS., *FY 2013, FY 2014, and FY 2015 Final HAC List* (2015), https://www.cms.gov/medicare/medicare-fee-for-service-payment/hospitalacqcond/downloads/fy_2013_final_hacscodelist.pdf.

12. Kevin W. Lobdell et al., *Hospital-Acquired Infections*, 92 SURGICAL CLINICS OF N. AM. 65, 65 (2012).

13. Judith Graham, *New List Offers Hospital-Specific Data on Patient Safety*, L.A. TIMES, (Apr. 11, 2011, 2:56 AM), http://www.latimes.com/health/ct-met-hospital-errors-20110410-story.html.

14. Qian Gu, et al., *The Medicare Hospital Readmissions Reduction Program: Potential Unintended Consequences for Hospitals Serving Vulnerable Populations*, 49 HEALTH SERVS. RES. 818, 830–31 (2014).

15. *Id*. at 830.

payment for treatment of conditions not present at the time of admission.[16] During the same time period, public reporting of hospital-level results, technical assistance offered to hospitals, and the use of Electronic Medical Records were all implemented.[17] As a result of the numerous incentives, it is not clear which ones caused the subsequent improvement in hospital-acquired conditions.[18] The Agency for Healthcare Research and Quality reported a seventeen percent decrease in the number of hospital-acquired conditions between 2010 and 2014.[19] As a result, there were an estimated 87,000 deaths averted and a cost-avoidance of $19.8 billion between 2011 and 2014.[20] By broadly incentivizing higher quality care through a variety of efforts, the number of hospital-acquired conditions and their related costs can be effectively reduced. Additional incentives targeted specifically at hospital-acquired conditions, could encourage further improvement.

Clearly, incentivizing hospitals to reduce hospital-acquired conditions can be effective, but penalizing Medicare payments can be dangerous. Many hospitals are losing money on Medicare patients even before the penalty.[21] The Medicare Payment Advisory Commission found that "relatively efficient" hospitals only operate at a one percent margin for Medicare patients and most hospitals only aim to break even on Medicare patients.[22] Additionally, in terms of cost, Medicare only paid eighty-eight percent of

16. Melinda S. Stegman, *The Hospital-Acquired Condition Initiative: Two Years Later*, 13(2) J. HEALTH CARE COMPLIANCE 63, 63 (2011).

17. AGENCY FOR HEALTHCARE RESEARCH AND QUALITY, SAVING LIVES AND SAVING MONEY: HOSPITAL-ACQUIRED CONDITIONS UPDATE INTERIM DATA FROM NATIONAL EFFORTS TO MAKE CARE SAFER, 2010–2014, 1, 6 (2015).

18. *Id.*

19. David Carter, *Success Seen in Decline in Hospital-Acquired Conditions*, 116 AM. J. OF NURSING 17, 17 (2016) (seventeen percent decrease in hospital-acquired conditions per 1,000 discharges).

20. *Id.*

21. Chad Mulvany, *Margins Under Pressure*, 70(4) HEALTHCARE FINANCIAL MGM'T. 30, 30 (2016) ("average total Medicare margin for all hospitals in 2014 was minus 5.8 percent").

22. *Id.*

costs incurred by a patient whereas private insurers covered 144 percent of costs.[23] The average penalized hospital loses $480,000 per year in withheld Medicare payments, with some academic hospitals losing significantly more.[24] The penalty is further reducing income to hospitals as reimbursement payments continue to decline.[25] Hospitals' ability to cut costs is narrowing, making this issue even more worrisome when coupled with hospitals' already thin margins.[26] Penalizing hospitals for hospital-acquired conditions intensifies the reality of our healthcare system in which payers and the government ask hospitals to do more with less, when the hospitals are already operating on a tightrope.

III. PROPOSAL

The hospital-acquired condition penalty must be improved. The main problem with the penalty is that it does not distinguish between different types of hospitals.[27] Losing one percent of Medicare income affects hospitals differently—one percent of Medicare funding has a more significant impact on a hospital with a high proportion of Medicare patients than a hospital that primarily serves the privately-insured. Additionally, certain hospitals identify hospital-acquired conditions at a higher rate.[28] To counter this disparity, the penalty's structure should be adjusted. Currently, all subsection (d) hospitals that fall within the bottom quartile of hospitals in terms of hospital-acquired conditions are subject to a penalty of one percent of their

23. Cunningham & Rudowitz, *supra* note 4 at 3.

24. Rau, *supra* note 3 (for example, Northwestern Memorial Hospital was penalized $1.6 million dollars in Medicare payments).

25. Beth Kutscher, *Hospital Margins Slump Due to Squeeze From Volume, Rates, Investments*, 44 MODERN HEALTHCARE 8, 8 (2014) (hospital margins narrowed significantly despite an improving economy do to a decreasing ability to cut costs, low credit ratings, and a patient population delaying care due to high deductible health plans).

26. *Id.*; Mulvany, *supra* note 21.

27. 42 U.S.C. §1395ww(p).

28. Rau, *supra* note 3.

yearly Medicare income.[29] Hospitals file a report once per year and find out at the end of the fiscal year whether they will be penalized. Therefore, to make the penalty more equitable, rather than arbitrarily penalizing the bottom quartile, the penalty should be changed to a set threshold. This should be determined as a function of hospital-acquired conditions per patient treated, with an exemption for academic hospitals and hospitals that receive disproportionate share payments. The yearly reports go to the Secretary of the DHHS, who has the power to include or exclude conditions.[30] Since the Secretary has the authority and requisite information, the Secretary would be best suited to analyze the annual data, identify, and implement a specific threshold.

A. A Static Threshold Would Provide a Better Incentive for Improvement

The current penalty creates an uncertainty as to whether a hospital will be penalized.[31] There is no way for a hospital to predict whether it will fall in the bottom quartile of hospitals for hospital-acquired conditions and incur the penalty.[32] When a hospital is penalized based on performance relative to other hospitals, the inability to judge industry-wide performance creates a lack of incentive to alter behavior to avoid the penalty.[33] Grading hospitals on a curve eliminates a hospital's ability to identify if it will be subject to a penalty and make the requisite adjustments.[34]

Hospitals whose performances are on the verge of incurring the penalty would have a greater incentive to consciously take steps to improve if they knew where they fell on the scale. The CMS data shows that in fiscal year

29. 42 U.S.C. §1395ww(p)(5).
30. *Id.* §1395ww(p)(6)(A) (2010).
31. McKinney, *supra* note 1.
32. *Id.*
33. *Id.*
34. *Id.*

2015, there was a large concentration of hospitals at the threshold for the bottom quartile.[35] A score greater than seven incurs the penalty, and a total of 293 hospitals scored between 6.850 and 7.075.[36] A total of 220 of the 293 hospitals sustained the penalty.[37] There was a large number of hospitals on the verge of incurring the penalty, and if they had been aware of their proximity to a one percent penalty, more hospitals likely would have taken steps to avoid the penalty. Performance rankings are announced only once a year, so not only is there no incentive to improve performance, but there is an inability to effectively set and achieve goals because hospitals do not know how they compare to others. Increasing a hospital's ability to foresee a penalty as drastic as one percent of its yearly Medicare income would allow hospitals to proactively take steps to improve care and reduce hospital-acquired conditions.

It is unreasonable to expect hospitals to avoid the penalty when they do not know what level of performance will warrant a penalty. Of the 757 hospitals in the worst performing quartile in fiscal year 2016, approximately fifty-three percent were also in the worst performing quartile in 2015.[38] This could indicate that hospitals struggle to improve because they are unable to plan ahead due to the penalty's reliance on relative performance. Awareness of past performance is not helpful for a hospital when the level of performance that warrants the penalty varies year to year. The goal of the penalty is to deter hospital-acquired conditions through improvements in performance, but when hospitals do not know if they are performing well and

35. Charles N. Kahn III, et al, *Assessing Medicare's Hospital Pay-For-Performance Programs and Whether They Are Achieving Their Goals*, 34 HEALTH AFFAIRS 1281, 1285 (2015).

36. *Id.*

37. *Id.*

38. CTRS. FOR MEDICARE & MEDICAID SERVS., HOSPITAL-ACQUIRED CONDITION REDUCTION PROGRAM FISCAL YEAR 2016 FACT SHEET (Dec. 10, 2015), https://www.cms.gov/Newsroom/MediaReleaseDatabase/Fact-sheets/2015-Fact-sheets-items/2015-12-10-2.html.

are unable to effectively modify their performance, the penalty falls short of this goal.

A better approach would be to implement the penalty as a function of hospital-acquired conditions per patient—creating a static goal, which would allow hospitals foresee an upcoming penalty and incentivize them to improve care to avoid the penalty. This creates an incentive for hospitals that are on the cusp of incurring the penalty to proactively take steps to avoid it. Sometimes a change as simple as altering safety protocols or creating dialogue between staff members and their superiors make a significant impact on the quality of care provided.[39] For example, SynergyHealth in Wisconsin saw an eighty percent decline in hospital-acquired infections after giving nurses the authority, without physician approval, to remove urinary catheters as soon as the patient was appropriately stabilized.[40] This is an example of a simple step that, if aware of a looming penalty, a hospital could take in order to avoid the penalty. When hospitals are unaware of their performance in relation to the penalty, these additional steps may be overlooked or not taken. By implementing a per-patient standard, hospitals will be aware of their performance in relation to the penalty throughout the year and take the necessary steps to avoid it.

Applying the penalty to the bottom quartile is not an efficient or effective manner of minimizing hospital-acquired conditions. Altering the penalty to penalize hospitals that exceed a set threshold of hospital-acquired infections per patients treated would prevent the arbitrary punishment of a static number of hospitals. This eliminates the incentive for a hospital to make improvements throughout the year. The proposed changes provide hospitals the ability to evaluate their performance and improve throughout the year.

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39. Richardson, *supra* note 2 at 19.
40. *Id.* at 20.

B. Academic and Disproportionate Share Hospitals Should Not be Penalized

Academic and disproportionate share hospitals (DSHs) should be exempt from the penalty. Academic hospitals encounter some of the sickest patients and are more vigilant about hospital-acquired conditions and therefore test patients at a higher rate.[41] DSHs are more likely to incur the penalty, but are less likely to receive full reimbursement because their patient population is predominantly low-income.[42] As a result, DSHs and academic hospitals should be exempt from the hospital-acquired condition penalty.

1. Academic Hospitals are Unfairly Affected

The penalty unfairly affects academic hospitals.[43] Some of the most prestigious hospitals in the country have the highest rates of hospital-acquired conditions.[44] Institutions such as Stanford Hospital, the Cleveland Clinic, and Northwestern Memorial Hospital have all been subject to the penalty.[45] These hospitals have plenty of company—almost half of the country's academic hospitals were penalized in 2014.[46] Statistically, hospitals are penalized more often if they are larger, accredited with the Joint Commission, have a Level I trauma center, if they accept a greater number of patients, or have a higher nurse-to-bed ratio.[47] The penalty punishes institutions for

41. Rau, *supra* note 3; Ellen Jean Hirst, et. al, *Infection Rate Penalties Hit Chicago-Area Hospitals*, CHI. TRIB., (Dec. 20, 2014, 9:18 AM), http://www.chicagotribune.com/business/ct-hospital-infection-rates-1220-biz-20141219-story.html.

42. Kahn, *supra* note 35 at 1286; Cunningham & Rudowitz, *supra* note 4 at 2 ("The American Hospital Association (AHA) estimated that Medicaid payments to hospitals amounted to 90 percent of the costs of patient care in 2013, while Medicare paid 88 percent of costs; by contrast, hospitals received considerable overpayment from private insurers, amounting to 144 percent of costs").

43. Rau, *supra* note 3.

44. *Id.*

45. *Id.*

46. Hirst et. al, *supra* note 41.

47. Ravi Rajaram, et al., *Hospital Characteristics Associated with Penalties in the Centers for Medicare & Medicaid Services Hospital-Acquired Condition Reduction Program*, 314 J. OF THE AM. MED. ASS'N 375, 377–78 (2015).

treating more difficult patients.[48] Additionally, evidence shows that academic hospitals are more aggressive in screening patients for problems.[49] Another hypothesis is that academic hospitals perform procedures that are simply more prone to having adverse events than a typical hospital.[50] Regardless, it is likely that academic hospitals are taking aggressive steps to treat patients and are being unfairly penalized for it.

2. Disproportionate Share Hospitals are Unfairly Affected

DSHs are hospitals that serve a large number of Medicaid and low-income uninsured patients.[51] These hospitals generally receive supplemental payments to compensate for treating patients who need care but are unable to pay for the hospital's services.[52] Problematically, the ACA decreased payments to DSHs based on expectations for an increased insured payer mix.[53] Many hospitals are now skeptical that the supposed increase in revenue created by the ACA Medicaid expansion will make up for the loss of Medicaid DSH funds.[54] In addition to being in a financially precarious position, hospitals with a disproportionate share payment patient percentage between 50-65 percent are 1.5 times more likely to be penalized for hospital-acquired conditions.[55] This is due to the prevalence of existing health issues that may show up during a hospital stay in patient populations that have limited access to healthcare.[56] Essentially, low-income patients are more likely to develop a hospital-acquired condition because of their reduced

48. Rau, *supra* note 3.
49. *Id.*
50. Hirst et. al, *supra* note 41.
51. Evan S. Cole et al., *Identifying Hospitals That May Be at Most Financial Risk From Medicaid Disproportionate-Share Hospital Payment Cuts*, 33 HEALTH AFFAIRS 2025, 2025 (2014).
52. *Id*.
53. *Id.* at 2026.
54. Cunningham & Rudowitz, *supra* note 4 at 6.
55. Kahn, *supra* note 35 at 1286.
56. Richardson, *supra* note 2.

access to care.[57] DSHs are tasked with treating patients who are more likely to develop a hospital-acquired condition and less likely to be able to pay for their care. This is an issue because DSHs' supplemental Medicaid funding is being reduced, and, on top of everything else, they may have to forfeit one percent of their yearly Medicare payments.

The penalty unfairly disadvantages DSHs that predominantly treat a low-income patient population. Regardless of whether the penalty impacts the quality of care, hospitals that treat the country's sickest and poorest patients should not be punished with additional payment reduction.

IV. CONCLUSION

The hospital-acquired condition penalty should be altered to be a static percentage of hospital-acquired conditions per patient treated and academic and DSHs should be exempt from the penalty altogether. The penalty is implemented in a manner that does not maximize a hospital's incentive to increase their quality of care and reduce hospital-acquired conditions. Further, it penalizes hospitals that have a higher likelihood of identifying hospital-acquired conditions as well as penalizing hospitals treating patients who have a higher likelihood of developing hospital-acquired condition. With these proposed changes, a hospital's ability to assess its performance in preventing hospital-acquired conditions would improve while removing an arbitrary penalization on hospitals that serve unique populations.

57. Richardson, *supra* note 39 at 18.

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Compounding Drugs: Using Market-Based Solutions to Respond to Patient Needs

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INTRODUCTION

Off-patent drug costs have soared over the past several years, causing patients to urge federal and legislative policy makers to create fast and cheap solutions.[1] For instance, drugs and medical devices such as Mylan's EpiPen surged in price from $10 to $600 after the company acquired the product in 2007.[2] In 2015, Turing Pharmaceutical's Daraprim increased in price from $13.50 to $750 seemingly overnight.[3] Though pharmaceutical companies are under scrutiny by lawmakers and the public for the soaring off-patent drug costs, the companies have not lowered their prices.[4] Off-patent prescription drug price increases are attracting national attention since the profits of these pharmaceutical companies come at the expense of the general health and welfare of the public.[5]

To better respond to patient needs and increase patient access to affordable medicine, the legal industry should examine the controversial process of drug compounding with proper safety regulation and examine new law implementation as an alternative source of obtaining essential medicines. Market-based solutions may be the easiest, most affordable way to combat

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1. Naren P. Tallapragada, *Off-Patent Drugs at Brand-Name Prices: A Puzzle for Policymakers*, J. L. & BIOSCIENCES 1, 2 (2016).
2. *Id.*; Rita Rubin, *EpiPen Price Hike Comes Under Scrutiny*, 388 LANCET 1266, 1266 (2016).
3. Tallapragada, *supra* note 1.
4. *Id.*
5. *Id.*

rising prescription drug costs.

This article will first provide an overview of the current drug compounding legal framework. It will then discuss controversies surrounding drug compounding and the adverse health effects that have occurred from the use of compounded drugs. Finally, this article will advocate for and propose changes to current drug compounding laws to better ensure patient safety and provide an affordable medicine alternative.

I. THE RISING COSTS OF MEDICALLY NECESSARY DRUGS

New inventions are granted patents, or a property right to the product.[6] This right includes the right to exclude others from making, using, offering for sale or selling the invention in the United States.[7] The development of new inventions is risky, expensive and time-consuming.[8] The right to exclude thus allows a monopolization of a drug or invention to permit inventors and businesses to recoup their research and development costs.[9] A patent encourages innovation by supplying inventors with a reward when they undergo risks in developing a drug or product.[10] Without generic competition, patients can expect newly patented brand-name drugs to be more expensive until the patent expires and generic competition enters the market.[11] However, older, off-patent drugs typically have generic competitors which lower the cost of the drugs.[12] Thus, recent price hikes for older, off-patent drugs has policymakers confounded.[13]

Off-patent drug companies have raised their prices through two avenues.[14]

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6. U.S. PATENT & TRADEMARK OFFICE, *General Information Concerning Patents*, (Oct. 2015) https://www.uspto.gov/patents-getting-started/general-information-concerning-patents.
7. *Id.*
8. *Id.*
9. *Id.*
10. *Id.*
11. Tallapragada, *supra* note 1.
12. *Id.*
13. *Id.*
14. *Id.*

First, by increasing rates for single-source drugs, pharmaceutical companies are able to monopolize the market.[15] In other words, with no generic competitors, companies for off-patent drugs are able to exponentially raise their prices since generic companies offer no cheaper alternatives.[16] Second, multisource drugs, and the companies that manufacture them, have undergone manufacturer mergers and manufacturing disruptions.[17]

Furthermore, some off-patent drugs with astronomical prices are classified by the World Health Organization (WHO) as "essential medicines."[18] The WHO recommends essential medicines be available in health systems at all times in adequate amounts, in appropriate dosage forms, with quality and at a price that the community can afford to pay.[19] Unfortunately, the WHO's recommendations have not been carried out. Included on the WHO's list of essential medicines for 2015 are off-patent epinephrine and Daraprim, both of which are monopolized by companies that have raised their prices to an unaffordable cost.[20]

The EpiPen, an off-patent auto-injector used to administer epinephrine for life-threatening allergic reactions, increased in price nearly 400 percent over the last three years.[21] While the auto-injector used to administer epinephrine is forty years old, and epinephrine itself is 100 years old, one EpiPen costs a patient over $600 today.[22] Efforts by generic companies to acquire FDA

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15. *Id.* at 3 (defining single source drugs as those with only one manufacturer as opposed to multi-source drugs with multiple manufacturers).

16. *Id.*

17. *Id.* (discussing how mergers can lead to single source drugs and further monopolization).

18. *Id.* at 5.

19. *Id.*; WORLD HEALTH ORG., *Essential Medicines*, http://www.who.int/medicines/services/essmedicines_def/en/. (last visited Mar. 31, 2017) (defining essential medicines as "those that satisfy the priority health care needs of the population").

20. *See generally* WORLD HEALTH ORG., *WHO Model List of Essential Medicines*, http://www.who.int/medicines/publications/essentialmedicines/EML_2015_FINAL_amended_NOV2015.pdf?ua=1. (last updated Nov. 2015).

21. Rubin, *supra* note 2.

22. *Id.*

approval have proved futile.[23] In October, 2015, the Auvi-Q injector was voluntarily recalled by Sanofi because of worries over inaccurate dosage delivery.[24] Another attempt by Israeli drug company Teva to produce an epinephrine auto-injector failed due to "major deficiencies" in its application.[25] Concerns over EpiPen's lack of competition led President Barack Obama to sign into law the School Access to Emergency Epinephrine Act to ease parents' anxiety about children with severe allergies going into anaphylactic shock while at school.[26] Although the Act is aimed at keeping children safe while at school, the President's endorsement of EpiPen may further monopolize the market, labeling EpiPen as the only trusted auto injector and discouraging new generic attempts to enter the market.[27]

II. DRUG COMPOUNDING AND THE ENDANGERMENT OF PUBLIC HEALTH

Physicians suggest that if worse comes to worse, a doctor can instruct patients how to use a simplified version of the EpiPen, a needle, a syringe and epinephrine.[28] Doctors can put these packs together for less than four dollars, although it carries risks of not meeting the "current standards of medicine."[29] A 2012 study on physician characteristics associated with off-label prescribing in primary care revealed that off-label prescribing is common, accounting for up to twenty-one percent of prescribed drugs.[30] This

23. *Id.*
24. *Id.*
25. *Id.*
26. *Id.* (statement of presidential adviser Valerie Jarrett) ("Under the law, the Department of Health and Human Services will give funding preferences to states for asthma-treatment grants if they maintain an emergency supply of epinephrine (EpiPens) and develop a plan to ensure that school personnel are trained and available to administer it."); *see also* School Access to Emergency Epinephrine Act, S. 1503, 113th Cong. (2013); Part of the reason for the price increase of Mylan's EpiPen may be due to its' program that offers free EpiPens to schools. Mylan, *EpiPen4Schools*, (2016), https://www.epipen4schools.com/.
27. *See generally* Rubin, *supra* note 2.
28. *Id.*
29. *Id.*
30. Tewodros Eguale et al., *Drug, Patient, and Physician Characteristics Associated with Off-Label Prescribing in Primary Care*, 172 ARCH INTERN MED 781, 781 (2012).

alarmingly cheap alternative begs the question of what the legal repercussions and risks would be if doctors were to make their own drugs and devices, otherwise known as "drug compounding" or "pharmacy compounding."[31]

Physicians have compounded drugs for patients well before the rise of mass-produced pharmaceuticals.[32] Compounded drugs represent one to three percent of all pharmaceuticals and are an important aspect for public health.[33] Pharmacy compounding refers to the process by which pharmacists combine drug ingredients to produce medicines tailored to the individual needs of each patient.[34] Often, drugs are modified to a lower dosage or are modified to omit an ingredient to which the patient is allergic.[35] Drug compounding can also take place when physicians produce drugs that are otherwise unavailable or are not being manufactured.[36] "Office-use" drugs that are produced in advance, without a prescription when physicians need them on-hand, are also considered compounded drugs.[37]

Over the past twenty to thirty years, drug compounding has seen significant growth and certain companies have begun producing drugs on a much larger scale.[38] Thus, the traditional role of compounding that occurred for centuries between doctor and patient has been blurred with the process of drug manufacturing.[39] However, because drug compounding is not required

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31. Carey B. Nuttall, *Pharmacy Compounding Issues in Today's Marketplace*, ASPATORE 1, 1 (2013).

32. T.R. Goldman, *Regulating Compounding Pharmacies*, HEALTH AFF. (May 1, 2014), http://www.healthaffairs.org/healthpolicybriefs/brief.php?brief_id=114.

33. *Id.*

34. Nuttall, *supra* note 31, at 1 (discussing modifying a drug based on a patient's allergies or need for a different dosage or form).

35. *Id.*

36. *Id.*

37. Goldman, *supra* note 32 (including dermatologists' salves and creams and cardioplegic surgical solution pumped into heart valves).

38. Nuttall, *supra* note 31, at 1.

39. Thomas Smith et al., *There Is No Such Thing as a Compounding Manufacturer! (Or Is There?)*, 27 HEALTH L. 1, 2-3 (2015).

to undergo the premarket approval process by the Food and Drug Administration (FDA), there have been various incidents of mass-manufacturing drug compounding pharmacies endangering patient health.[40]

In 2007, the Centers for Disease Control and Prevention reported a compounding pharmacy in Texas that did not adhere to the correct dosage for intravenous colchicine.[41] The incident resulted in three deaths from cardiac arrest and a recall of the medication.[42] Another adverse event occurred in Florida of August of 2011 when intravitreal injections of bevazicumab were used to treat macular degeneration.[43] Twelve patients were infected with Streptococcus and some lost their remaining vision.[44] In 2012, the worst compounding incident occurred when the New England Compounding Company (NECC) caused more than 438 cases of fungal meningitis and thirty-two deaths.[45] The NECC manufactured and sold vials of a bacterially contaminated steroid solution to physicians that were used on patients nationwide.[46] This tragedy led Congress to enact the Drug Quality and Security Act (DQSA).[47]

III. THE DRUG QUALITY AND SECURITY ACT

The NECC outbreak prompted the FDA and states to conduct inspections at compounding pharmacies which revealed objectionable conditions at more than sixty facilities.[48] House and Senate Committee hearings ensued to formulate a law that would prevent such a disaster from happening again.[49]

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40. Tyler Dinkelaker, *A False Sense of Safety: How The Drug Quality and Security Act Fails to Protect Patients from Harm*, 9 ST. LOUIS U. J. HEALTH L. & POL'Y, 329, 330 (2016).
41. Jennifer Gudeman et al., *The Potential Risks of Pharmacy Compounding*, 13 DRUGS IN R & D 1, 5 (2013).
42. *Id.*
43. *Id.*
44. *Id.*
45. Dinkelaker, s*upra* note 40, at 330.
46. *Id.*
47. *Id.* at 332-33.
48. Goldman, supra note 32.
49. *Id.*

On November 27, 2013, President Obama signed into law the DQSA to clarify FDA oversight of compounding pharmacies and to ensure the FDA could take action against compounding pharmacies that were not up to the standard of practice.[50]

The DQSA amends Section 503B of the Food and Drug Cosmetic Act (FDCA) to allow compounding pharmacies to voluntarily register as "outsourcing facilities" and subjects pharmacies to enhanced FDA regulation.[51] "Outsourcing facilities" can produce medications for patients without prescriptions.[52] Under the DQSA, these facilities may not make drugs that are "essentially a copy" of a drug commercially available and must undergo FDA inspections only if there is a health risk.[53] Outsourcing facilities also must submit information to the FDA about compounded products every six months, report product adverse events and pay an annual fee for inspection.[54] Compounders are permitted to produce products and sell unlimited quantities of drugs on the FDA's drug shortage list without requiring a preexisting prescription.[55] However, if a drug compounding

50. Dinkelaker, s*upra* note 40, at 349.

51. *Id.* at 350. (including the requirement to report adverse events); *see also* The Drug Quality and Security Act, H.R. 3204, 113th Cong. (2013).

52. *Id.*

53. *Id.* at 352. ("Essentially a copy" is defined by section 503B as "(A) a drug that is identical or nearly identical to an approved drug, or a marketed drug not subject to section 503(b) . . .," not on a list of drug shortages "at the time of compounding, distribution, and dispensing; or (B) a drug, a component of which is a bulk drug substance that is a component of an approved drug or a marketed drug that is not subject to 503(b) and not subject to approval in an application submitted under Section 503(b), unless there is a change that produces for an individual patient a clinical difference, as determined by the prescribing practitioner. "Health Risk" is based on the Secretary's inspection of outsourcing facilities "according to the known safety risks of such outsourcing facilities, which shall be based on the following factors: (i) The compliance history of the outsourcing facility. (ii) The record, history, and nature of recalls linked to the outsourcing facility. (iii) The inherent risk of the drugs compounded at the outsourcing facility. (iv) The inspection frequency and history of the outsourcing facility, including whether the outsourcing facility has been inspected pursuant to section 704 within the last 4 years. (v) Whether the outsourcing facility has registered under this paragraph as an entity that intends to H. R. 3204—6 compound a drug that appears on the list in effect under section 506E. (vi) Any other criteria deemed necessary and appropriate by the Secretary for purposes of allocating inspection resources.").

54. *Id.*

55. *Id.*

company chooses not to register as an "outsourcing facility," the company is subject to all the requirements of the FDCA.[56] These requirements include seeking drug approval and including adequate directions for patient use.[57]

Although Section 503B attempts to ensure the safety of compounding manufacturers, concerns remain.[58] For example, the DQSA only applies to facilities that engage in the compounding of sterile drugs. Further, the DQSA allows outsourcing facilities producing sterile drugs to be compounded with or without a patient name and Section 503B's registration requirement is completely voluntary.[59] By not regulating non-sterile drugs, the FDA misses an opportunity to engage in strict oversight of a compounding drug company.[60] In addition, because these compounding facilities may still produce drugs without a patient name, manufacturers can produce drugs off-label without a patient prescription.[61] Further, since registration is voluntary, dangerous compounding companies may not register because of the requirements to which they must adhere.[62] This voluntary registration theory is contingent on two premises.[63] The first is that hospitals will only choose to buy from FDA approved outsourcing facilities and thereby provide an economic incentive for companies to register under Section 503B.[64] The second is the use of payment policies where insurers will only reimburse for compounded drugs from registered facilities.[65] These incentives are yet to be

56. *Id.* at 351.
57. *Id.*
58. *See* i*d.*
59. *Id*.
60. *Id.*
61. *Id.*
62. *Id.*
63. Erika Lietzen, *Pharmacy Compounding After the Drug Quality and Security Act*, 26 HEALTH L. 1, 5-6, 8 (2014).
64. The FDA has engaged in substantial outreach efforts to governors, health departments, boards of pharmacy and hospital purchasers asking that they support the FDA's goal to encourage outsourcing facilities to register. However, whether outsourcing facilities will continue to register remains unseen. If outsourcing facilities stop registering it could prompt additional legislation. *Id.*
65. *Id.*

proven effective in encouraging registration.[66]

Finally, one interpretation of the DQSA is that it actually undermines the authority the FDA had before the Act was enacted.[67] Not only is the registration voluntary, but one reading of the DQSA suggests that the FDA already had authority over these large scale pharmacy compounders prior to the enactment of the law.[68] This authority is evident by the agency's actions in response to the meningitis outbreak.[69] The DQSA may simply have made it completely legal for compounding companies to not register and continue to operate facilities that are not up to quality standards while simultaneously regulating the companies that were most likely already in close compliance with FDA requirements.[70] Companies with resources to comply with FDA safety requirements are likely to voluntarily sign up, while those who have not voluntarily signed up are likely non-compliant and free to compound, risking patients' health.

IV. ENHANCED PATIENT SAFETY MEASURES: MAKING COMPOUNDED DRUGS A VIABLE OPTION

Before compounded drugs can be a viable option for producing alternative,

66. *Id.*; FOOD & DRUG ADMIN., *Registered Outsourcing Facilities*, http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm378645.htm (last updated Dec. 2, 2016); As of December 2, 2016, sixty-seven compounding pharmacies have registered as "outsourcing facilities." Although this may seem like a lot, there may be many more eligible to register. It is unknown how many there are and there is no way to track because there is no federal licensing required. *Checking in on 503B: To Register or Not to Register?*, AM. PHARMACISTS ASS'N (Sept. 1, 2015) https://www.pharmacist.com/checking-503b-register-or-not-register-0.

67. Lietzen, *supra* note 63.

68. *Id.*

69. *Id.*; *The Fungal Meningitis Outbreak: Could It Have Been Prevented? Hearing before the Subcomm. on Oversight and Investigations of the Comm. On Energy and Commerce*, 112th Cong. (Nov. 14, 2012) (statement of Margaret A. Hamburg) http://www.fda.gov/NewsEvents/Testimony/ucm327664.htm (explaining that the FDA's far-ranging response to the outbreak includes, but is not limited to, coordinating with the state to conduct an investigation of the facility, conducting an investigation of NECC on October 1, 2012, issuing a MedWatch Safety Alert to health professionals, making available lists of customers who purchased NECC products on or after May 21, 2012 and conducting recall audit checks of NECC's customers).

70. Lietzen, *supra* note 63.

less expensive medication, there must be changes to the law to correct the serious public safety issues. For example, to ensure patient safety, the FDA could implement transparency in the drug supply chains of pharmacy compounders.[71] This would allow consumers to access information about the components and the final production of the prescription drug.[72] In addition, the FDA could rate compounding plants A, B, C, and D, for example, based on FDA inspections and any warning letters issued to the plant.[73] Consumers should then have access to this grading scale when purchasing prescription drugs.[74]

Although grading would be a valuable resource for consumers, there are of course drawbacks. Supply chain transparency, or the availability of information concerning the various levels of the supply chain, is critical for manufacturers to gain and maintain knowledge about their sources of supply and thus better control the quality of the drugs that are manufactured and sold to consumers.[75] Each supplier may have manufacturing sites around the world and manufacture in facilities that are run by subcontractors leading to a complex supply chain structure.[76] This complex structure, although important because it can identify risks when suppliers or subcontractors fail to meet regulatory requirements concerning product quality, is highly difficult to monitor. Furthermore, it is not simply sufficient to gather supplier information once, but it must be continually updated which requires time and resources.[77]

Another concern is that the FDA has limited resources, and requiring it to

71. MARK L. BAUM, PHARMACEUTICAL COMPOUNDING: AN ESSENTIAL PIECE OF THE HEALTHCARE REFORM PUZZLE 48 (2016).
72. *Id.*
73. *Id.*
74. *Id.*
75. *Id.*
76. *Id.*
77. *Id.*

take on additional tasks may be unrealistic.[78] Therefore, the FDA should acquire more funding to better monitor supply chain transparency. In addition, defining factors to create a grading system could prove difficult with such a vast amount of information that would take extensive time to gather and categorize. For instance, determining what factors would separate an A from a B pharmacy may be hard to distinguish. In addition, even an A graded pharmacy may not meet or exceed every FDA requirement or guideline, so there could still be potential safety risks associated with an A-rated pharmacy.

Further, Section 503B could be applied to non-sterile medications.[79] Non-sterile compounds, which include hormone, pain and pediatric medications are commonly used throughout the country and have the ability to be just as dangerous as sterile compounds when ill-prepared.[80] For example, a dose higher than three times the normal amount for non-sterile thyroid medication could result in cardiac arrest.[81] In addition, failure to monitor all aspects of a compounding pharmacy could result in facilities continuing their normal outsourcing practices without stricter scrutiny.[82]

This is the simplest solution to implement, although the FDA may struggle with resources to conduct screening of all non-sterile compounds as well. Another concern with making compounding drugs safer while simultaneously trying to provide a cheaper alternative is fear of making the compounding drug approval process just as long as the FDA's current approval procedures.[83] Currently, priority review takes about twelve

78. *Addressing the FDA's Resource Challenges,* NAT'L CTR. FOR BIOTECHNOLOGY INFO. (2007), https://www.ncbi.nlm.nih.gov/books/NBK52926/.
79. Dinkelaker, *supra* note 40, at 358.
80. *Id.*
81. *Id.*
82. *Id.*
83. *Id.*

months,[84] but if all drugs at compounding facilities are required to undergo thorough inspection, the same timing problem experienced with generic approval could undermine the alternative solution to lowering drug costs. However, considering that many high-priced prescription drugs are essential medicines, the solution is worth pursuing.

V. MOVING TOWARDS AFFORDABLE PRESCRIPTION DRUGS: PROPOSED AMENDMENTS TO THE DRUG QUALITY AND SECURITY ACT

Compounding companies have begun to take active steps to enter the pharmaceutical market which could aid in lowering prescription drug costs.[85] For example, Imprimis Pharmaceuticals, Inc. is taking affirmative steps to break down monopolized markets for Daraprim, a drug that fights a parasitic infection that affects HIV patients.[86] In December 2015, Imprimis announced a deal with Express Scripts Holding Co. to make a new version of Daraprim for just one dollar a capsule to compete with the current market price established by Turing Pharmaceuticals' Daraprim of more than $750 a capsule.[87] Imprimis operates facilities for individual patients and is building two outsourcing facilities.[88] The company fills prescriptions for patients every day and reports high regulation by the FDA.[89]

Although Imprimis may be able to provide a cheaper alternative, the option is not without its obstacles. First, in July 2016 the FDA provided further guidance on the statutory language in the DQSA which states that no compounded drug may be "essentially a copy" of a drug that is currently on

84. Michael Hiltzik, *The FDA Can Single-Handedly Reduce Drug Price Gouging. Why is it Waiting?*, L.A. TIMES (Jan. 5, 2016, 12:31 PM), http://www.latimes.com/business/hiltzik/la-fi-mh-the-fda-can-single-handedly-stop-20160105-column.html.

85. Steve Sternberg, *Can Compounding Pharmacies Circumvent Big Pharma?*, U.S. NEWS (Dec. 15, 2015, 2:14 PM), http://health.usnews.com/health-news/hospital-of-tomorrow/articles/2015-12-15/can-compounding-pharmacies-circumvent-big-pharma.

86. *Id.*

87. *Id.*

88. *Id.*

89. *Id.*

the market.[90] This makes it difficult for Imprimis to produce its version of Daraprim when the current monopolized drug is on the market.[91] Alternatively, the FDA could amend its definition of "essentially a copy" to better align a vision towards affordable prescription drugs. This provision is directly at odds with discouraging monopolized markets and could be amended to "exact copy" so that compounding pharmacies can alter a drug slightly, either by dosage or route of administration, and provide a cheaper and safe alternative.[92] However, if safety measures are not first implemented, then compounding companies will be free to produce a copy of a drug that without adequate standards of safety and efficacy.

Second, the FDA could redefine the term "drug shortages" in the DQSA.[93] The FDA defines a drug shortage as "a period of time when the demand or projected demand for a medically necessary drug in the United State exceeds its supply."[94] However, this definition is too narrow to allow compounding companies to compete with monopolized markets.[95] The definition could be construed more broadly to include economic factors.[96] By including economic factors in the definition, compounding pharmacies will be able to produce drugs that are off-patent on the "drug shortage list" due to lack of competition.[97] This is a simple market-based solution without resorting to price controls or more policy implementation.[98]

A major drawback to allowing compounding companies to make exact

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90. *Id.*

91. BAUM, *supra* note 71, at 26 (defining "essentially a copy" as a compounded drug that has the same active pharmaceutical ingredient, excipients, dosage form and strength and route of administration as a commercially available drug or FDA-approved drug).

92. *Id.*

93. *Id.* at 49.

94. U.S. FOOD & DRUG AMIN., *CDER Conversation: FDA's Drug Shortages Prevention Strategies*, http://www.fda.gov/drugs/newsevents/ucm432474.htm (last updated Feb. 5, 2015).

95. BAUM, *supra* note 71, at 49.

96. *Id.*

97. *Id.*

98. *Id.*

copies of a drug on the market is the negative effect such manufacturing could have on the generic market.[99] For example, allowing compounded drug products to be sold without full FDA approval could provide a disincentive for companies to take drugs through the generic drug approval process.[100] While generic drug manufacturers must go through a lengthy and expensive approval process, compounding companies need not go through bioequivalence trials or comply with significant safety standards, saving time and costs.[101] Therefore, amending the definition of "drug shortages" could provide a short term solution but in the long term may actually undermine affordability goals.[102]

Lastly, the FDA could allow drugs that have been off-patent for more than ten to twenty years to be compounded in 503B outsourcing facilities.[103] The Hatch-Waxman Act was implemented to bring competition for off-patent drugs but it has only been partially successful.[104] One consequence of the act has been to protect markets for old off-patent drugs whose markets are overlooked.[105] Interpreting the DQSA to permit outsourcing facilities to produce these off-patent drugs with no generic competition to make safe copies of the drugs would lower drug prices and permit companies to safely produce the drugs without fear of being shut down.[106]

One disadvantage is that expanding compounding beyond what is prescribed in the statute could weaken oversight.[107] Compounded drugs have

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99. *Why Drug Compounding is Not a Solution to High Drug Prices*, PEW CHARITABLE TR. (Feb. 4, 2016), http://www.pewtrusts.org/en/research-and-analysis/analysis/2016/02/04/why-drug-compounding-is-not-a-solution-to-high-prices [hereinafter *Not a Solution*].

100. *Id.*

101. *Id.*

102. *Id.*

103. BAUM, *supra* note 71, at 58.

104. *Id.* (enacting the Hatch-Waxman Act to encourage the manufacturing of generic drugs by pharmaceutical companies).

105. *Id.*

106. *Id.*

107. *Not a Solution*, *supra* note 99.

historically played a vital role in the nation's health care system, most notably by allowing a physician to order specialized medicines for patients.[108] This need for efficient, specialized medicine has exempted compounders from the normal drug approval process when compounding provides a significant difference to the patient.[109] Allowing compounded drugs for the sole purpose of providing a lower cost-alternative may go beyond the scope intended by the industry.[110] Essentially, compounding exemptions could eliminate the very competition for lower drug prices that it seeks to implement.[111] Efforts to facilitate patient access to affordable medicine should not undermine the significance of bioequivalence testing and quality standards that uphold the patient safety and drug efficacy that consumers rely on.[112]

VI. CONCLUSION

The high prices of off-patent, medically necessary drugs require innovative legal solutions. The controversial drug compounding industry may be a viable solution to increase patient access to affordable medicines. However, after the NECC meningitis controversy and other health incidents throughout the nation, addressing patient safety concerns should be the first priority for lawmakers and the FDA. The FDA should address patient safety issues by implementing transparency in drug supply chains and applying the DQSA rules to both sterile and non-sterile compounds. With improved safety, drug compounding using market-based solutions may be an effective way to address rising drug costs for off-patent, affordable prescription drugs. To address high-costs, several terms in the DQSA should be re-defined and

108. *Id.*
109. *Id.*
110. *Id.*
111. Rob Wright, *What is the Solution to the "High-Price" Drug Sticker Shock*, LIFE SCI. LEADER (Feb. 2, 2016), http://www.lifescienceleader.com/doc/what-is-the-solution-to-high-price-drug-sticker-shock-0001.
112. *Id.*

drugs that have been off-patent for ten to twenty years should be permitted to be produced in compounding facilities. However, none of these solutions are without obstacles. Encouraging compounding drugs, for example, could lead to decreased competition by eliminating the generic market. Drug compounding as a solution to high drug costs of off-patent drugs may be a great option, but actual viability is yet to be seen.