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Combating Antimicrobial Resistance: Regulatory Strategies and Institutional Capacity

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TULANE LAW REVIEW

VOL. 84

MARCH 2010

NO. 4

Combating Antimicrobial Resistance: Regulatory Strategies and Institutional Capacity

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David A. Hyman†

Amnesia is a common, important, but rarely noted side effect of antibiotics. Apart from medical historians, few recall the severe morbidity and mortality once associated with acute bacterial infection. However, decades of antibiotic overuse and misuse have compromised the long-term availability and efficacy of these life-saving therapies. If designed and implemented appropriately, regulation can reduce the risk of bacterial infection, reserve antibiotics for circumstances where they are necessary, and rationalize the use of the most powerful agents. Regulation of antibiotic resistance can be justified, and should be guided, by both efficiency and fairness. A range of regulatory options are available—some information-based, some incentive-based, some command-and-control—each of which has indications, strengths, and weaknesses. A desired set of regulatory strategies must then be matched with the appropriate legal and regulatory institutions. A renewed focus on regulatory and institutional design has significant potential to reduce antibiotic-resistant bacterial infections and increase the effective life of existing and new antibiotics.

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I. INTRODUCTION

Amnesia is a common, important, but rarely noted side effect of antibiotics. Apart from medical historians, few recall the severe morbidity and mortality once associated with acute bacterial infection. Some may know that pneumonia was once called “the old man’s friend,” but who remembers that William Osler described it as the “captain of the men of death”?¹ Puerperal (childbed) fever used to kill thousands of women every year, but is now largely a historic curiosity.² People with a persistent cough do not consider which sanatorium they should go to for a rest cure, or worry that they have received a death sentence, even though in 1900, pneumonia and tuberculosis were two of the leading causes of death in the United States.³

Before the rise of antibiotics, the risks of an early death lurked around every corner. In 1924, President Calvin Coolidge’s son died of sepsis when he got a blister on his foot after playing tennis on the White House lawn.⁴ Twelve years later, President Franklin Roosevelt’s son developed a “septic sore throat.”⁵ He was treated with a newly discovered sulfa-based antibiotic and recovered.⁶

1. WILLIAM OSLER, *THE PRINCIPLES AND PRACTICE OF MEDICINE* 38 (Henry A. Christian ed., D. Appleton-Century Co. 15th ed. 1944) (1892) (“One of the most widespread of acute diseases, pneumonia has become the ‘captain of the men of death’ among acute infections, to use the phrase applied by John Bunyan to consumption.”).

2. See IRVINE LOUDON, *THE TRAGEDY OF CHILDBED FEVER* (2000).

3. *Achievements in Public Health, 1900-1999: Control of Infectious Diseases*, 48 *MORBIDITY & MORTALITY WKLY. REP.* 621 (July 30, 1999), <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm4829a1.htm> [hereinafter *MMWR*].

4. ROBERT BUD, *PENICILLIN: TRIUMPH AND TRAGEDY* 4 (2007).

5. *Prontosil*, *TIME*, Dec. 28, 1936, available at <http://www.time.com/time/magazine/article/0,9171,771900,00.html>.

6. *Id.*

The first civilian life was saved by penicillin in 1942 after all other treatments had failed.⁷ Penicillin allowed a Connecticut woman named Anne Miller to live another fifty-seven years.⁸ First-generation cephalosporins were introduced in the mid-1960s; broader spectrum second- and third-generation cephalosporins followed.⁹

These drugs transformed the treatment of bacterial infection. In 1969, William H. Stewart, the U.S. Surgeon General, reportedly declared, “The time has come to close the book on infectious diseases.”¹⁰ Life before the discovery and commercialization of antibiotics now seems as distant as the Jurassic Era. Unfortunately, persistent misuse and overuse of antibiotics places our future at risk, as antibiotic resistance has become a major public health threat.¹¹

Although methicillin-resistant *Staphylococcus aureus* (MRSA) attracts most of the media attention,¹² serious risks are raised by other

7. See MMWR, *supra* note 3.

8. See Cesar A. Arias & Barbara E. Murray, *Antibiotic-Resistant Bugs in the 21st Century—A Clinical Super-Challenge*, 360 NEW ENG. J. MED. 439, 439 (2009).

9. STEPHEN C. STEARNS & JACOB C. KOELLA, *EVOLUTION IN HEALTH AND DISEASE* 129 (2008).

10. Ross Upshur, *Ethics and Infectious Diseases*, 86 BULL. WORLD HEALTH ORG. 654, 654 (2008) (book review), available at http://www.scielo.org/scielo.php?pid=S0042-96862008000800024&script=sci_arttext (“In an oft-quoted statement, the Surgeon General of the United States of America, William Stewart, said in 1967: ‘The time has come to close the book on infectious diseases. We have basically wiped out infection in the United States.’”). Interestingly, the U.S. Public Health Service Historian believes the quote is apocryphal. See The Office of the Pub. Health Serv. Historian, *Frequently Asked Questions*, <http://hncbc.nlm.nih.gov/apdb/phsHistory/faqs.html> (last visited Jan. 18, 2010).

A less famous, but equally optimistic quote came in July 1938 from Dr. Edward Mellanby, who discovered Vitamin D. *BUD*, *supra* note 4, at 22. Dr. Mellanby stated that within fifty years, a hospital would no longer be required to treat infections, although it may “be full of motor accidents (laughter); or it may be full of very old people whiling away their last years of life in peace and happiness.” *Id.* (internal quotation marks omitted).

11. See generally Infectious Diseases Soc’y of Am., *Bad Bugs, No Drugs* (2004), available at <http://www.idsociety.org/badbugsnodrugs.html> (commenting that antibiotic resistance is a growing threat to public health and that a “frightening twist” in the problem is that research and development for new antibiotics is not keeping pace with this resistance); STUART B. LEVY, *THE ANTIBIOTIC PARADOX: HOW THE MISUSE OF ANTIBIOTICS DESTROYS THEIR CURATIVE POWERS* (2d ed. 2002) (arguing that widespread and inappropriate use of antibiotics has threatened the healthcare system’s ability to cure common infections); Ruth L. Berkelman & James M. Hughes, *The Conquest of Infectious Diseases: Who Are We Kidding?*, 119 ANNALS INTERNAL MED. 426 (1993) (noting that the current array of available antibiotics has declined in effectiveness); REPORT ON INFECTIOUS DISEASES 2000: OVERCOMING ANTIMICROBIAL RESISTANCE, <http://www.who.int/infectious-disease-report/2000/> (last visited Jan. 30, 2010) (focusing on how the “disturbing development” of antibiotic resistance is threatening the ability to fight infection in both developed and developing nations); Gary Taubes, *The Bacteria Fight Back*, 321 SCI. 356 (2008) (arguing that bacteria “seem to be wining” the fight against antibiotics).

12. See, e.g., Ranit Mishori, *A Deadly Bug Invades Our Towns*, PARADE, Dec. 7, 2008, available at http://www.parade.com/articles/editions/2008/edition_12-07-2008/2Staph_

drug-resistant organisms, including vancomycin-resistant *enterococci* (VRE), *Clostridium difficile*, and multiple-drug-resistant *Klebsiella*.¹³ Barring significant changes, we run a substantial risk of returning to a world where bacterial infection causes tens of thousands of premature deaths.

Federal and state regulators have not ignored these issues, but they have had limited success in solving them. A March 2008 U.S. Government Accountability Office (GAO) report stated that it was

Epidemic. The *Seattle Times* did a multipart series on MRSA in 2008. Michael J. Berens & Ken Armstrong, *Culture of Resistance*, SEATTLE TIMES, Nov. 16-18, 2008, <http://seattletimes.nwsourc.com/html/mrsa/>. One of the authors of the *Seattle Times* series did a series of articles for the *Chicago Tribune* six years earlier about the infection epidemic. Michael J. Berens, *Infection Epidemic Carves Deadly Path*, CHI. TRIB., July 21, 2002, at 1, available at <http://www.chicagotribune.com/news/chi-0207210272jul21,0,2177158.story>; Michael J. Berens, *Lax Procedures Put Infants at High Risk*, CHI. TRIB., July 22, 2002, at 1, available at <http://www.chicagotribune.com/news/chi-0207220180jul22,0,2046086.story>; Michael J. Berens, *Drug-Resistant Germs Adapt, Thrive Beyond Hospital Walls*, CHI. TRIB., July 23, 2002, at 1, available at <http://www.chicagotribune.com/features/health/chi-0207230231jul23,0,5055330.story>.

Other recent articles and commentary on the issue include: *Our View on Protecting Patients: Lax Attitudes Help Spread Deadly Hospital Infections*, USA TODAY, <http://blogs.usatoday.com/oped/2009/01/our-view-on-pro.html?loc=interstitialskip> (Jan. 27, 2009, 12:22 EST); Jerome Groopman, *Superbugs*, NEW YORKER, Aug. 11, 2008, available at http://www.newyorker.com/reporting/2008/08/11/080811fa_fact_groopman; Laura Landro, *Curbing Antibiotic Use in War on "Superbugs,"* WALL ST. J., Sept. 3, 2008, at D1, available at <http://online.wsj.com/article/SB122039916170892933.html>; Kevin Mayhood & Suzanne Hoholik, *Over-Prescribing Boosts Superbugs*, COLUMBUS DISPATCH, Oct. 20, 2007, at A1, available at http://www.dispatch.com/live/content/local_news/stories/2007/10/20/superbug.ART_ART_10-20-07_A1_MT881Q7.html?sid=101; Erin Donaghue, *Pressure Is on Hospitals To Stamp Out Bacterial Bugs*, USA TODAY, Oct. 16, 2007, at D7, available at http://www.usatoday.com/news/health/2007-10-15-catheter_N.htm; Will Dunham, *Hospitals Use More Antibiotics Despite Concerns*, REUTERS, Nov. 10, 2008, <http://www.reuters.com/article/idUSTRE4A97BX20081110>; Lindsey Tanner, *Staph Fatalities May Exceed AIDS Deaths*, WASH. POST, Oct. 17, 2007, available at <http://www.washingtonpost.com/wp-dyn/content/article/2007/10/17/AR2007101700311.html>; Sabin Russell, *Bacteria Race Ahead of Drugs*, S.F. CHRON., Jan. 20, 2008, http://articles.sfgate.com/2008-01-20/news/17151270_1_resistant-antibiotics-viral-infection; Christopher Lee, *Studies: Hospitals Could Do More To Avoid Infections*, WASH. POST, Nov. 21, 2006, <http://www.washingtonpost.com/wp-dyn/content/article/2006/11/20/AR2006112001122.html>. For a collection of media coverage on this issue, see Consumers Union, http://www.safepatientproject.org/topic/hospital_acquired_infections/ (last visited Jan. 18, 2010).

13. Ciarán P. Kelly & J. Thomas LaMont, *Clostridium Difficile—More Difficult Than Ever*, 359 NEW ENG. J. MED. 1932 (2008); Scott K. Fridkin et al., *The Effect of Vancomycin and Third-Generation Cephalosporins on Prevalence of Vancomycin-Resistant Enterococci in 126 U.S. Adult Intensive Care Units*, 135 ANNALS INTERNAL MED. 175 (2001); Tara Parker-Pope, *Stomach Bug Crystallizes an Antibiotic Threat*, N.Y. TIMES, Apr. 13, 2009, at D1, available at <http://www.nytimes.com/2009/04/14/health/14well.html>; Andrew Pollack, *Rising Threat of Infections Unfazed by Antibiotics*, N.Y. TIMES, Feb. 26, 2010, at B1, available at <http://www.nytimes.com/2010/02/27/business/27germ.html?em>; Janis Wiener et al., *Multiple Antibiotic-Resistant Klebsiella and Escherichia Coli in Nursing Homes*, 281 JAMA 517 (1999).

difficult to be certain about the scope of the problem (which is itself a problem) and that federal efforts were uncoordinated and had not effectively addressed healthcare-associated infections (HAIs).¹⁴ A subsequent GAO report cataloged reporting initiatives at the state level and efforts by individual hospitals.¹⁵ In response, the U.S. Department of Health and Human Services (DHHS) announced a national action plan, extending and revising a similar plan announced seven years earlier.¹⁶ Other recommendations have been made by professional societies, public health organizations, and think tanks, and various efforts are underway within particular communities and internationally.¹⁷ Law professors have written on these subjects as well.¹⁸

Prompt action in many legal and policy arenas is necessary, and it is natural and proper that these endeavors begin in familiar territory. To select the most effective methods, however, it is important to survey

14. HEALTH-CARE-ASSOCIATED INFECTIONS IN HOSPITALS: LEADERSHIP NEEDED FROM HHS TO PRIORITIZE PREVENTION PRACTICES AND IMPROVE DATA ON THESE INFECTIONS, GAO-08-283 (Mar. 2008) [hereinafter LEADERSHIP NEEDED], available at <http://www.gao.gov/new.items/d08283.pdf>.

15. GAO, HEALTH-CARE-ASSOCIATED INFECTIONS IN HOSPITALS: AN OVERVIEW OF STATE REPORTING PROGRAMS AND INDIVIDUAL HOSPITAL INITIATIVES TO REDUCE CERTAIN INFECTIONS, GAO-08-808 (Sept. 2008) [hereinafter STATE REPORTING PROGRAMS], available at <http://www.gao.gov/new.items/d08808.pdf>.

16. The most recent action plan was announced in September 2008, but has not yet been publicly released. For details on the earlier plan, see Public Health Action Plan To Combat Antimicrobial Resistance, <http://www.cdc.gov/drugresistance/actionplan/html/index.htm> (last visited Jan. 18, 2010) [hereinafter Action Plan].

17. See *supra* note 11 and accompanying text; see also RAMANAN LAXMINARAYAN & ANUP MALANI, EXTENDING THE CURE: POLICY RESPONSES TO THE GROWING THREAT OF ANTIBIOTIC RESISTANCE (2007); Alliance for the Prudent Use of Antibiotics, <http://www.tufts.edu/med/apua/> (last visited Jan. 18, 2010); ReAct: Action on Antibiotic Resistance, <http://www.react-group.org/dyn/3,,.html> (last visited Jan. 18, 2010); Roger Finch, *Innovation—Drugs and Diagnostics*, 60 J. ANTIMICROBIAL CHEMOTHERAPY (SUPP.) i79 (2007); Pew Charitable Trusts, Human Health and Industrial Farming, <http://www.saveantibiotics.org/> (last visited Jan. 18, 2010); ELIAS MOSSIALOS ET AL., LONDON SCHOOL OF ECONOMICS AND POLITICAL SCIENCE, POLICIES AND INCENTIVES FOR PROMOTING INNOVATION IN ANTIBIOTIC RESEARCH (2009), <http://www2.lse.ac.uk/ERD/pressAndInformationOffice/PDF/PoliciesandIncentivesforpromotinginnovationinantibiotic.pdf>; J. Coast, R.D. Smith & M.R. Millar, *An Economic Perspective on Policy To Reduce Antimicrobial Resistance*, 46 SOC. SCI. & MED. 29 (1998).

18. Kevin Outterson & Aaron Kesselheim, *Fighting Antibiotic Resistance: Innovative Strategies To Promote Continued Antibiotic Effectiveness* (2009) (unpublished manuscript); Kevin Outterson, *The Legal Ecology of Resistance: The Role of Antibiotic Resistance in Pharmaceutical Innovation*, 31 CARDOZO L. REV. (2010) [hereinafter Outterson, *Ecology of Resistance*]; Richard S. Saver, *In Tepid Defense of Population Health: Physicians and Antibiotic Resistance*, 34 AM. J.L. & MED. 431 (2008); Eric Kades, *Preserving a Precious Resource: Rationalizing the Use of Antibiotics*, 99 NW. U. L. REV. 611 (2005); Kevin Outterson, *The Vanishing Public Domain: Antibiotic Resistance, Pharmaceutical Innovation, and Intellectual Property Law*, 67 U. PITT. L. REV. 67 (2005) [hereinafter Outterson, *Antibiotic Resistance*].

the forest of options that regulatory theory makes available, as well as to examine the individual trees represented by existing programs and institutions.

Our goal in this Article is to provide policymakers with both a map of the regulatory landscape and a compass for using particular institutions to address antibiotic resistance. We do not attempt to summarize the massive clinical and economic literature on antibiotic resistance, nor do we argue for a specific reform strategy as a “magic bullet.” Instead, we seek to provide a theoretical and practical framework for choosing among regulatory strategies and for matching strategies with institutional capacity.

Part II provides an abbreviated primer on the problem of antibiotic resistance. Part III examines the case for regulation of antibiotics to address resistance. Part IV lays out a broad range of regulatory options. Part V analyzes the public and private institutions through which these regulatory reforms could be deployed and offers some suggestions for matching regulatory strategies with institutional capacity. Part VI concludes.

II. ANTIBIOTIC RESISTANCE 101

Like most biological processes, the problem of antibiotic resistance is complex and multifactorial.¹⁹ From an evolutionary perspective, the use of antibiotics creates selection pressure for the development of resistance, although a variety of factors influence the degree of resistance that develops, the speed with which it emerges, and the extent to which resistance is transferable across classes of pathogens.²⁰ The pathogens that are a problem in institutional settings

19. MOSSIALOS, *supra* note 17, at 26 (“Antibiotic resistance, a complex process which results from the use and misuse of antibiotics, is a process by which bacteria change and develop properties that make the drugs used to treat them ineffective.”); Barry M. Farr et al., *Can Antibiotic-Resistant Nosocomial Infections Be Controlled?*, 1 *LANCET INFECTIOUS DISEASES* 38, 38 (2001) (“The common wisdom is that antibiotic resistance is a natural consequence of antibiotic use and, as such, really cannot be controlled to any meaningful degree. . . . The clearest elucidation of why antibiotic resistance increases so much in hospitals was, ironically, offered by someone who never heard of antibiotics; Charles Darwin observed that competition occurs in every environment and that nature selects the strain or species most suited to survive within a particular environment.”).

20. See I.M. Gould, *A Review of the Role of Antibiotic Policies in the Control of Antibiotic Resistance*, 43 *J. ANTIMICROBIAL CHEMOTHERAPY* 459, 463 (1999) (“While it is true to say that there is no absolute proof of a causative association between antibiotic use and resistance, most authorities believe the association to be ‘virtually certain.’ . . . Given the recent worldwide escalation in resistance and the overwhelming evidence of much over-use of antibiotics (and thus unnecessary resistance), the pragmatic and essential approach to the

(hospitals and nursing homes) are not the same as those that are a problem in the community. The consequences of antibiotic resistance vary greatly, depending on the particular pathogen, the nature of the infection (merely colonized versus topical infection versus systemic infection), the availability and cost of alternative treatments, and patient compliance. Resistance can be drug-specific or it can be for an entire class of drugs. Any sensible regulatory response must take account of these biological realities.

Despite these variations, the long-term trends are clear: over the last half-century, a wide array of pathogens have developed resistance to a wide array of antibiotics. Consider *Staphylococcus aureus* (staph aureus), the bacteria that killed President Coolidge's son in 1924 and almost killed President Roosevelt's son in 1936.²¹ Sulfa-based drugs, like the one given President Roosevelt's son, worked reasonably well on staph aureus, but not always.²² When penicillin became available in 1941, it became the treatment of choice for staph aureus.²³ However, penicillin-resistant strains of staph aureus emerged within a few years and by the early 1950s were linked to deaths.²⁴ In 1960, methicillin became available and became the treatment of choice for penicillin-resistant staph aureus.²⁵ MRSA emerged in the 1970s in Europe, and shortly thereafter in the United States.²⁶ In U.S. hospitals, the frequency of MRSA exploded, growing from 2.4% of staph aureus infections in 1975 to 29% in 1991 and almost 60% in 2003.²⁷ Vancomycin became the treatment of choice for MRSA, but widespread usage predictably led to the emergence of vancomycin-resistant staph aureus (VRSA) and VRE.²⁸ One can tell a similar story about other pathogens and other antibiotics.

Why should anyone care? The death rate from infectious diseases was dropping steadily before the emergence of antibiotics.²⁹

control of antibiotic resistance is to control antibiotic use. The important question is how, not whether.”).

21. BUD, *supra* note 4, at 4; *Prontosil*, *supra* note 5.

22. *Prontosil*, *supra* note 5.

23. LAXMINARAYAN & MALANI, *supra* note 17, at 25.

24. *Id.*

25. *Id.*

26. *See id.*

27. *See id.* at 25-26; *see also* R. Monina Klevens et al., *Invasive Methicillin-Resistant Staphylococcus Aureus Infections in the United States*, 298 JAMA 1763, 1770 (2007) (“[I]nvasive MRSA disease is a major public health problem and is primarily related to health care but no longer confined to acute care.”).

28. *See* VISA/VRSA: Vancomycin-Intermediate/Resistant *Staphylococcus Aureus*, http://www.cdc.gov/ncidod/dhqp/ar_visavr.html (last visited Jan. 18, 2010).

29. *See* LAXMINARAYAN & MALANI, *supra* note 17, at 26 fig.11.

Antibiotic resistance may even create an incentive for further innovation by clearing the market of competitors for newly developed antibiotics.³⁰ We consider the justification for regulation of this area in more detail below, but it is important to understand that modern medicine is based on the availability of effective antibiotics. As a recent article in the *New England Journal of Medicine* observed, “It is difficult to imagine undertaking today’s surgical procedures, transplantations, cancer chemotherapy, or care of the critically ill or HIV-infected without effective antimicrobial agents.”³¹ A patient with an antibiotic-resistant infection faces a lengthier hospitalization, increased healthcare spending, and an increased chance of death.³² The problem of antibiotic resistance has now moved outside the hospital, and otherwise healthy individuals are being affected.³³ These developments raise an obvious risk of a public panic when the issue periodically attracts public attention.³⁴ Any one of these issues would

30. See Outterson, *Ecology of Resistance*, *supra* note 18.

31. Arias & Murray, *supra* note 8, at 439.

32. See LAXMINARAYAN & MALANI, *supra* note 17, at 28-34. To be sure, there are methodological challenges in estimating the number of individuals who die of an antibiotic-resistant infection that would not have otherwise died. See *id.* at 28-30; see also Michael R. Eber et al., *Clinical and Economic Outcomes Attributable to Health Care-Associated Sepsis and Pneumonia*, 170 ARCHIVES INTERN. MED. 347 (2010) (“[H]ealth care-associated sepsis and pneumonia impose substantial clinical and economic costs.”); Marin H. Kollef & Victoria J. Fraser, *Antibiotic Resistance in the Intensive Care Unit*, 134 ANNALS INTERNAL MED. 298, 299-300 (2001) (“In general, infections caused by antibiotic-resistant bacteria are associated with higher in-hospital mortality rates and longer lengths of hospital stay. . . . The overall annual national cost of control and treatment of infections caused by antibiotic-resistant bacteria has been estimated to be between \$100 million and \$30 billion, including the cost of development of new antibiotics.”); Pew Charitable Trusts, Human Health and Industrial Farming, Antibiotic Resistant Bacteria in Animals, <http://www.saveantibiotics.org/ourwork.html> (last visited Jan. 18, 2010) (“These impacts on human health can result in both higher frequency and longer duration of hospitalizations, raising the cost of healthcare. Estimates of the extra costs to the U.S. healthcare system due to antibiotic-resistant bacteria range from 4 to 5 billion dollars per year.”); ReAct-Action on Antibiotic Resistance, ReAct Facts, Economic Aspects of Antibiotic Resistance 2-3 (May 2008), <http://soaping.icecube.snowfall.se/stroma/BoR%20Economic%20Aspects.pdf> (summarizing literature on economic consequences of antibiotic-resistant infections).

33. See Elizabeth A. Bancroft, *Antimicrobial Resistance: It's Not Just for Hospitals*, 298 JAMA 1803, 1804 (2007) (“The reports in this issue of *JAMA* reveal that infections with significant antimicrobial-resistant pathogens, the types formerly seen only in hospitals, now have onset in the community. Old diseases have learned new tricks.”).

34. Panic might seem like too strong a word, but we are not the first to use the word, with regard to both MRSA and extremely drug-resistant tuberculosis (XDR-TB). See Nina Burleigh, *Medical Fugitive*, PEOPLE, June 18, 2007, available at <http://www.people.com/people/archive/article/0,,20061197,00.html>; Christopher J. Harrison, *In Fight Against MRSA, Panic Is Unwarranted*, INTERNAL MED. NEWS, Jan. 1, 2008, at 9, available at http://findarticles.com/p/articles/mi_hb4365/is_1_41/ai_n29432716/.

justify further attention to the problem of antibiotic resistance; in combination, they provide a compelling argument to do so.

III. THE CASE FOR ANTIBIOTIC REGULATION

What, exactly, makes antibiotics an appropriate subject for government intervention? Antibiotic regulation is most often justified on efficiency grounds, implying that current practices fail to achieve socially optimal outcomes. An analogy can be made to pollution control: government is asked to curtail or modify beneficial private activity to prevent spillover public harms. Moreover, as with pollution control, there is an important aspect of distributional fairness in reducing infectious disease by preserving antibiotic effectiveness. Other recognized social values, such as individual liberty and social solidarity, are also relevant to the analysis. Finally, a compelling argument for new regulation is that a huge amount of healthcare regulation already exists—and often creates perverse incentives for antibiotic overuse and misuse, undermining the preservation of antimicrobial effectiveness.

A. *Demand-Side Efficiency*

The fading effectiveness of antibiotic drugs against disease-producing bacteria is typically framed as a problem of social inefficiency. In a formulation that obscures almost as many issues as it clarifies, it is said that we engage in “unnecessary” use of the antibiotics we have, while failing to develop new ones. In utilitarian terms, this implies that a different allocation of society’s protective and curative resources would provide greater total benefit in the fight against infectious disease.

From an analytical perspective, antibiotic resistance is the result of interactions among five distinct efficiency-based problems: misuse, overuse, containment, prevention, and use in food production. These problems are not all under the control of healthcare providers, and they result from a mix of individual information shortfalls, agency failures, collective action problems, and externalities. The following discussion focuses on the demand side (infection and antibiotic use), after which we comment briefly on the supply side (antibiotic development).

1. Misuse

Antibiotic misuse is widespread and imposes both direct harms on treated patients and spillover harms on future patients.³⁵ Misuse takes various forms, the most common of which is physicians prescribing antibiotics when they are useless—most often because the patient suffers from a viral rather than bacterial infection.³⁶ Another form of misuse is prescribing the wrong antibiotic for the bacteria infecting the patient. A third is prescribing the right antibiotic in the wrong dose. The risk of creating drug resistance is increased by both extended exposure and subtherapeutic dosing or duration of treatment.³⁷ Patients can contribute to this problem by failing to complete the specified course of treatment (if it is science-based) or, at least as often, by completing that course (if the prescribed treatment is based on habit, superstition, or is excessive).

Misuse generally arises from faulty individual decision making, typically caused by lack of information, cognitive misperceptions of risks and benefits, or some combination thereof. Misuse attributable to noncompliance is particularly difficult to address, because direct monitoring of compliance is impractical, and the behavior of the physician and patient is often based on guesses made about the other's motives and conduct.

2. Overuse

Overuse of powerful antibiotics harms current and future patients with serious infections. Consider the use of “big-gun” antibiotics against routine organisms or at sites of infection that could be effectively treated with more ordinary drugs. Using powerful agents such as vancomycin or ciprofloxacin on bacteria susceptible to penicillin or tetracycline risks the development of resistance to the former, with potentially disastrous consequences for other patients suffering from rare but life-threatening diseases. However, successful application of narrow-spectrum or weaker drugs often requires sensitivity testing, which delays patient care and adds expense (offset to some extent if a cheaper drug can ultimately be employed).

In these situations, individual and collective efficiency may diverge, as a strong antibiotic may indeed be preferable for the treatment of each particular infected patient, even if it results in

35. See ReAct—Action on Antibiotic Resistance, *supra* note 32.

36. Kades, *supra* note 18, at 617-18.

37. *Id.* at 618; Saver, *supra* note 18, at 435-36.

adverse consequences for future patients. There are also strategic incentives for immediate, indiscriminate antibiotic use: the glass-half-full belief that one's own failure to conserve is riskless if everyone else acts properly (as with refusing vaccination), and the glass-half-empty belief that there is no point to one's acknowledging the need for long-term availability if everyone else ignores it (as with dirtying a public restroom).

3. Containment

Preventing the spread of drug-resistant organisms is an essential strategy in controlling antibiotic resistance. Hospitals and nursing homes routinely house both patients infected with resistant bacteria and noninfected (but susceptible) patients while frequently failing to observe basic principles of infection control such as hand washing, wearing gowns, sterilization of equipment, and physical separation of those infected with antibiotic-resistant bacteria.³⁸ Adherence to such protocols reduces the need for antibiotic treatment, the emergence of resistant strains, and the transfer of resistance from one strain to another.

Some of these process improvements require reconfigurations of physical space and protocols for sharing equipment and other medical resources, while others require behavioral changes among physicians, nurses, and other staff. Healthcare facilities vary in the degree to which they have addressed these issues. Although institutions suffer from some of the same collective action and externality problems that drive overuse, collectively beneficial choices may also be individually rational for institutions because they make decisions on behalf of groups of patients. This is particularly true if the payment system for medical care creates incentives for hospitals to keep patients free from infection—which, in general, it currently does not.

4. Prevention

A prevented primary infection requires no treatment, which of course lowers the risk of bacteria later developing antibiotic resistance. Occasionally, preventable infections occur because medical care was not sought early or because the wrong care was administered. More often, such events are a matter of public health, such as dirty water, contaminated food, inadequate sanitation, poor hygiene, and so on.

38. See LEADERSHIP NEEDED, *supra* note 14; STATE REPORTING PROGRAMS, *supra* note 15.

Environmental factors of this sort are seldom under the control of medical providers. Many represent failures of collective action, not faulty individual decision making. Funding for public health is often suboptimal because of political factors, even if there is bona fide social consensus regarding its importance. As a result, effective measures to prevent infections are likely to require cooperation between generally well-paid healthcare professionals and facilities, and typically cash-strapped departments of public health and safety-net providers.

5. Use in Food Production

Antibiotics have long been used in food production in the United States to promote growth and reduce illness/spoilage.³⁹ Strikingly, estimates of antibiotic usage for food production “range from 30 to 70 percent of all antibiotics and related drugs sold in the U.S.”⁴⁰ There is evidence supporting the efficacy of antibiotic usage in promoting growth and reducing illness/spoilage, which explains why we have not categorized agricultural usage as misuse or overuse. However, there is also convincing evidence that such usage encourages antibiotic resistance.⁴¹

As with prevention, antibiotic use in food production is an environmental factor that is not under the control of medical providers. Such use falls within the regulatory jurisdiction of the U.S. Department of Agriculture (USDA), which has historically been a strong advocate for the economic interests of farmers and ranchers.⁴² Although the USDA is quite concerned about the food safety implications of antibiotic usage, it will predictably give less weight to the indirect systemic risks that might result from the same usage.⁴³ Finally, the values at stake are, in important respects, incommensurable: how should one compare the benefits of cheap food for today’s consumers against the costs of a marginal decrease in antibiotic

39. Pew Charitable Trusts, *Antibiotic-Resistant Bacteria in Animals and Unnecessary Human Health Risks*, <http://www.saveantibiotics.org/resources/PewHumanHealthEvidencefactsheet7-14FINAL.pdf> (last visited Jan. 18, 2010).

40. *Id.*

41. *See* ANTIBIOTIC RESISTANCE: FEDERAL AGENCIES NEED TO BETTER FOCUS EFFORTS TO ADDRESS RISK TO HUMANS FROM ANTIBIOTIC USE IN ANIMALS, GAO-04-490 (Apr. 2004), <http://www.gao.gov/new.items/d04490.pdf> [hereinafter ANTIBIOTIC USE IN ANIMALS].

42. *See id.* at 15, 27-32 (discussing the roles, responsibilities, and surveillance activities of the USDA to ensure food safety in the United States).

43. *See, e.g.*, Nat’l Inst. of Food & Agric., *Food Safety & Biosecurity*, http://www.csrees.usda.gov/nea/food/in_focus/safety_if_national.html (last visited Jan. 18, 2010).

efficacy at some uncertain point in the future for an unidentifiable future patient with an unspecified bacterial infection?⁴⁴

B. *Supply-Side Efficiency*

Incentives to develop and market new methods for preventing and treating infectious disease are influenced by intellectual property rights, regulatory approval processes, private health insurance practices, and government-administered pricing in public programs. Pharmaceutical, medical device, and biotechnology companies are sources of medical innovation, which gives rise to new vaccines, antibiotics, diagnostic tests, and infection-control devices. In the absence of intellectual property rights (principally patents), innovation is a public good that will be underproduced by private actors. However, patents do not fully solve incentive problems in healthcare. Products typically require government approval, and demonstrating safety and effectiveness to the Food and Drug Administration (FDA) is time consuming, which imposes direct and opportunity costs while eroding the patent term.⁴⁵

Medical suppliers respond by focusing their efforts on products that will appeal to a broad market of paying customers. Because most antibiotics are prescribed for a short course of treatment, the range of use must be substantial to generate the same revenue stream as a product for the treatment of a chronic illness. Broad-spectrum antibiotics are therefore attractive from a business perspective, while constraints on their use to avoid breeding resistance are not.⁴⁶

Somewhat different problems apply to vaccines. Vaccines are administered to a large and otherwise healthy population, so they are strictly scrutinized for possible safety hazards. However, the price that can be charged tends to be far less than the cost of the suffering they help avoid, although the large market allows development expenditures to be recouped from a large population.

44. ANTIBIOTIC USE IN ANIMALS, *supra* note 41, at 1 (“While antibiotic use in animals poses potential human health risks, it also reduces the cost of producing these animals, which in turn helps reduce the prices consumers pay for food.”).

45. See Regulatory Information, <http://www.fda.gov/RegulatoryInformation/default.htm> (last visited Jan. 18, 2010). For a detailed discussion of the way intellectual property law affects pharmaceutical development, see Outterson, *Antibiotic Resistance*, *supra* note 18.

46. Of course, one could compensate for the short-course problem by increasing the price per dose, and there are biologic cancer treatments that cost tens of thousands of dollars per dose. But there is significant public resistance to unit prices at that level, and a rational pharmaceutical company could easily decide that it is not worth the push-back to price its products in that fashion and search for greener fields elsewhere.

C. *Distributional Issues*

Fairness considerations are often lost in discussions of market failures and their associated inefficiencies. Yet equity should enter the debate over antibiotic resistance at several junctures. Poorer individuals are often most exposed to infectious agents and have the least access to healthcare. In the short run, efforts to reduce antibiotic overuse may further compromise such individuals' likelihood of receiving treatment and reduce the benefits of treatment if it is received. Expensive infection-control measures may also be economically infeasible for providers serving the poor. Over the long run, preservation of therapeutic effectiveness may offset these regressive effects if older, cheaper drugs retain their efficacy.

Thinking about fairness also helps bring structure to valuation issues that are sometimes finessed in efficiency discussions. Eliminating pure waste, such as the use of antibiotics for infections that are obviously of viral origin, is of universal utility. By contrast, imposing restrictions on one person's antibiotic use in order to keep antibiotics available for another person raises questions about distributive justice (for example, who should sacrifice how much and for whose benefit).⁴⁷ Should one account for the subjective value of reassurance associated with taking a very powerful drug or only the objectively demonstrable potential for the drug to effect a cure? What discount rate should be applied to costs and benefits that occur at very different times—likely across generations? Should fairness focus on preserving the rights of the very poor or of the very sick, understanding that there is substantial but not total overlap between those groups? And, given our usual belief in sparing no expense to save identified lives, what value should attach to preserving access to treatment that is truly life saving?⁴⁸

47. See generally Joshua P. Metlay et al., *Tensions in Antibiotic Prescribing: Pitting Social Concerns Against the Interests of Individual Patients*, 17 J. GEN. INTERNAL MED. 87 (2002) (discussing physician attitudes regarding restricting the use of antibiotics).

48. See Clark C. Havighurst et al., *Strategies in Underwriting the Costs of Catastrophic Disease*, 40 LAW & CONTEMP. PROBS. 122, 141 n.81 (1976) ("It is difficult to improve significantly on the more commonplace observations that human beings cannot empathize with faceless abstractions and that 'squeaking wheels'—the complaints of known victims, such as the very vigorous lobbying of kidney-disease patients—not the silence of statistical unknowns, will get the government grease. Spending millions of dollars to save a fool who has chosen to row across the Atlantic has external benefits lacking from highway safety spending." (internal quotation marks omitted)).

D. *Liberty and Community Considerations*

Liberty is one of the founding principles of the United States, and it has independent ethical and constitutional importance. As with equity, liberty and efficiency are typically aligned when pure waste is eliminated, but not when one person is made to sacrifice for another's benefit. Recently, for example, courts and legal scholars have debated whether an individual's right to self-protection might trump the government's authority to restrict access to medical care, even if those restrictions are imposed for collective social benefit.⁴⁹ Although the government's lawful police power to curtail liberty in order to contain infectious disease is clearly established, traditional public health measures tend to mandate therapy rather than restrict access to it. Denying people something they want and can afford to purchase is a different type of incursion on liberty than compelling them to receive something they do not desire. This is especially true when the negative results of the denial may be immediately visible—such as a patient who fails to recover after receiving a less powerful drug—while the positive aspects to preserving drugs for the future seem distant and speculative.

On the other hand, efforts to preserve antibiotic effectiveness are likely to resonate with supporters of communitarian conceptions of government, who view the proper regulation of common resource pools as a politically important commitment, as well as one that produces a long-term efficiency gain.⁵⁰ One can also frame the antibiotic-resistance issue as a global public good involving norms of international governance.⁵¹ Such theories emphasize the importance of

49. See generally *Abigail Alliance for Access to Developmental Drugs v. von Eschenbach*, 495 F.3d 695 (D.C. Cir. 2007) (holding that patients had no fundamental right of access to experimental drugs not yet approved for public use); Eugene Volokh, *Medical Self-Defense, Prohibited Experimental Therapies, and Payment for Organs*, 120 HARV. L. REV. 1813 (2007) (discussing the right to self-protection and its interaction with regulation of the medical industry).

50. See generally Garrett Hardin, *The Tragedy of the Commons*, 162 SCI. 1243 (1968) (discussing regulatory challenges presented by common pool resources); David M. Patrick & James Hutchinson, *Antibiotic Use and Population Ecology: How You Can Reduce Your "Resistance Footprint,"* 180 CAN. MED. ASSOC. J. 416 (2009) (discussing common pool resource problems created by antibiotic use); Kevin R. Foster & Hajo Grundmann, *Do We Need To Put Society First? The Potential for Tragedy in Antimicrobial Resistance*, 3 PLOS MED. 177 (2006), <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1325265/pdf/pmed.0030029.pdf> (asking if improper use of antibiotics has created a tragedy of the commons); Howard H. Hiatt, *Protecting the Medical Commons: Who Is Responsible?*, 293 NEW ENG. J. MED. 235 (1975) (discussing common pool resource problems present in medical regulation).

51. Richard D. Smith & Landis MacKellar, *Global Public Goods and the Global Health Agenda: Problems, Priorities, and Potential*, 3 GLOBALIZATION & HEALTH 9, Sept. 22,

deliberative processes that involve communities in projects of self-governance and safeguard common resources from exploitation. Protection from infections fits this category, particularly as it relates to future generations, social stability, and long-term economic prosperity. Terms that often attach to improving antibiotic potency, such as stewardship and sustainability, invoke this political and regulatory tradition.

E. Improving Existing Regulation

Modifying the regulatory strategies that have brought us to the current state of antibiotic affairs would undoubtedly have broader consequences, not all of which can be anticipated. However, doing so is an important and necessary part of forestalling the development of widespread antibiotic resistance and of improving the treatment of infectious disease in the United States.

Skeptics regarding government intervention often point to the inefficiencies and maldistributions that existing healthcare regulation creates, either because it was enacted at the behest of special interests or because it has been poorly designed and administered.⁵² In addition to providing a valuable caution for new regulation, this perspective offers an independent justification to those pursuing a reform agenda.

Many characteristics of the extensive regulation that currently exists predispose the U.S. healthcare system to rampant antibiotic resistance. Unlike European healthcare systems that accept constraints in order to achieve universality, the principal commitment of government policies in the United States has been to promote the supply of healthcare services through subsidies for physician training, hospital construction, and both private and public health insurance.⁵³ By and large, physicians are granted exclusive prerogative to access these physical and financial resources, are spared the need to organize their fragmented business structures, and are urged to follow an ethic of single-patient advocacy rather than social stewardship.⁵⁴ Direct government control over medical practice is rare, notwithstanding the fact that government purports to assure the safety of medical products.

2007, <http://www.globalizationandhealth.com/content/3/1/9>. Effective antibiotics are a common pool resource, but not a public good (at least in the formal economic sense) because they are rivalrous.

52. Lawrence R. Jacobs, *Politics of America's Supply State: Health Reform and Technology*, 14 HEALTH AFF. 143, 144-45 (1995).

53. *Id.*

54. See PAUL STARR, *THE SOCIAL TRANSFORMATION OF AMERICAN MEDICINE* (1982).

For example, the FDA permits most “off-label” use of drugs or medical devices by physicians (and such use is compensated by health insurance) even though initial marketing of a new product requires prior approval.⁵⁵

Payment methods for medical products and services are established by government in connection with public insurance programs such as Medicare and Medicaid and are heavily influenced by government even for private insurers. Healthcare providers (both physicians and hospitals) are almost always paid for what they do to a patient and not for health gains that they actually accomplish. When complications ensue, providers are routinely paid even more to remediate them.⁵⁶ Service providers and medical suppliers respond to these incentives by providing more units of care, preferably high-margin, technologically sophisticated items that can be administered repeatedly.

Indirect influences on medical practice include restrictions on who may deliver healthcare services (by placing physicians at the pinnacle of the health professions hierarchy and prosecuting the unlicensed practice of medicine) and mandates on what services must be covered by health insurance (through coverage laws). These regulatory requirements also tend to favor the provision of large numbers of poorly coordinated services, with a heavy emphasis on prescription medication. Monitoring of cost and quality has also been quite limited. The most visible form of lay review, malpractice litigation, paradoxically reinforces physicians’ habits of excess by judging poor outcomes in hindsight to determine where care might have been insufficient.

55. Shopper’s Guide to Prescription Drugs, “Off-Label” Drug Use (2007), <http://www.consumerreports.org/health/resources/pdf/best-buy-drugs/money-saving-guides/english/Off-Label-FINAL.pdf>.

56. See David A. Hyman & Charles Silver, *You Get What You Pay For: Result-Based Compensation for Health Care*, 58 WASH. & LEE L. REV. 1427, 1433-34 (2001). The recent debate over whether Medicare should pay hospitals for both admissions when patients are readmitted within a short time of a previous hospitalization is one of the many examples of the piecemeal incentives that still prevail within our payment system. See generally Stephen F. Jencks et al., *Rehospitalizations Among Patients in the Medicare Fee-for-Service Program*, 360 NEW ENG. J. MED. 1418, 1425-26 (2009) (discussing problems relating to readmissions under Medicare); Arnold M. Epstein, *Revisiting Readmissions: Changing the Incentives for Shared Accountability*, 360 NEW ENG. J. MED. 1457 (2009) (discussing same). The problem was noted twenty-five years earlier. See generally Gerard F. Anderson & Earl P. Steinberg, *Hospital Readmissions in the Medicare Population*, 311 NEW ENG. J. MED. 1349 (1984) (discussing problems relating to readmissions under Medicare).

IV. METHODS OF REGULATION

Regulation can take many forms, several of which are relevant to the problems of bacterial infection and antibiotic resistance. Politicians often talk about regulation as if it falls along a continuum of intrusiveness, with less intrusive forms inherently preferable. This rhetorical framing results from the primacy accorded individual freedom in American constitutional design and political rhetoric. As discussed below, the intrusiveness formulation is also the result of a preference for federalism, which favors localism over centralized direction. This Part of the Article discusses regulatory methods across a spectrum of government intrusion into private conduct. Information disclosure is less intrusive; financial incentives are moderately intrusive; command-and-control regulation and rationing are very intrusive. Our aims are to display the breadth of available regulatory strategies, to identify their strengths and weaknesses, and to explain why and how they are applicable to the problem of antibiotic resistance. We leave to policymakers the task of choosing among them.

A. *Information Provision and Disclosure*

Information provision is a common regulatory method. Although information provision imposes costs on regulated entities and taxpayers, it is generally considered less intrusive than other forms of government involvement. Information-based regulation appeals broadly across the political spectrum: conservatives regard it as respectful of private decisions and market processes, while liberals celebrate “transparency” and the “right to know.”⁵⁷ The desirability of informational regulatory strategies depends on production-related factors such as the quality of gathered information, its lack of availability without government intervention, and its nexus with the desired real-world objective. Also relevant are user-related factors such as its salience to recipients, its manageability, its likelihood of accurate comprehension, and the existence of paths by which recipients can act on that information.

57. See William M. Sage, *Regulating Through Information: Disclosure Laws and American Health Care*, 99 COLUM. L. REV. 1701, 1803-04 (1999).

1. Education on Antibiotic Use and Infection Control

A straightforward (and long-standing) approach to antibiotic resistance is for the government to produce and disseminate educational materials on the proper use of antibiotics and best practices for infection control. These materials can be directed at both expert and lay audiences. Material of this sort principally addresses failures of individual decision making, such as taking antibiotics for viral infections, and has been uncontroversial, albeit largely ineffective.⁵⁸ The FDA's February 2003 final rule requiring the labels of systemic antibacterial drugs to include information on antimicrobial resistance and prudent use exemplifies this approach.⁵⁹

Somewhat more difficult issues are presented if government-funded educational tools attempt to correct how individuals frame and value health risks and the associated benefits of prevention or treatment. Whether one chooses a strong antibiotic where a weaker one might well suffice can be seen either as a behavioral misperception (for example, an irrational overestimate of the likelihood of suffering from "flesh-eating bacteria" based on salient media coverage) or as one's personal preference that should be respected (for example, a desire to minimize all risks to health if it can be done without undue effort or personal cost). Controversy may also arise with respect to the appropriateness of government educational programs that are intended to inculcate social norms of collective cooperation regarding the preservation of antibiotic effectiveness. Conflict over such strategies can be minimized by using information disclosure primarily to encourage public discussion and by ensuring that all recommended behavioral changes have a strong scientific foundation.

2. Public Reporting/Disclosure

A different information-based strategy is to require individuals and entities to measure their degree of success or failure and publicize the results. Generally, public reporting/disclosure of adverse events focuses on outcomes (such as rates of postoperative infection), but it can also be used for process-based measures of performance (such as

58. Whether these strategies are uncontroversial because they are ineffective is a subject we leave for another day.

59. Labeling Requirements for Systemic Antibacterial Drug Products Intended for Human Use, 68 Fed. Reg. 6062 (Feb. 6, 2003) (to be codified at 21 C.F.R. pt. 201). Of course, the difficulty is that the label is aimed at the physician, but is likely to be reviewed, if at all, by the patient.

the number of people receiving vaccination against pneumonia). Historically, reporting (to government or self-regulatory organizations) and disclosure (to private parties) have been considered distinct forms of informational mandates, but the Internet has largely collapsed these functions into a unitary concept of transparency.⁶⁰ Disclosure can induce improvement by several mechanisms, each of which is associated with somewhat different requirements for the content, format, and manner in which information is produced and distributed. In addition, government can learn from the reports it receives—and from the public discussion that follows release of information—whether and how to implement more direct forms of regulation.

Information directed at consumers is intended to help them choose the healthcare that is best for them. Ranking hospitals according to their rates of avoidable infection, or of infections with drug-resistant organisms, may induce patients (or their physicians, or their health insurers or employers who sponsor coverage) to select “better” healthcare providers. The belief that this might happen (a demand-side effect) in turn motivates hospitals and physicians to do a better job in addressing these problems (a supply-side effect). Although the two are obviously interrelated, there is better evidence for supply-side effects than demand-side effects from information disclosure in healthcare.⁶¹

The effectiveness of a consumer-disclosure strategy depends on recipients of information being in a position to select among healthcare providers, receiving accurate information about those providers, and incorporating that information into their decisions. It is unlikely that information about infections or antibiotic use will be sufficiently meaningful to have a large effect on patients’ choice of hospital given the urgency and emotional impact of a decision to seek medical care. However, because resistant infections can be fatal, it is possible that poor infection control could be a salient enough headline issue to serve as a proxy for overall hospital quality.

60. Compare Kim Breen, *Information Is New Tool in Fight Against Hospital Infections*, DALLAS MORNING NEWS, May 3, 2007, http://www.dallasnews.com/shared/content/dws/news/localnews/stories/DN-infections_03met.ART.North.Edition1.431e1ac.html, with Molly Hennessy-Fiske, *State Lags in Listing Staph Rates*, L.A. TIMES, Feb. 24, 2008, at 1, available at <http://articles.latimes.com/2008/feb/24/local/me-infections24>, and Jessica Snyder Sachs, Editorial, *Hospitals Ought To Come Clean About Infections and What’s Causing Them*, NEWARK STAR-LEDGER, Nov. 12, 2007, at 15.

61. See Arnold M. Epstein, *Public Release of Performance Data: A Progress Report from the Front*, 283 JAMA 1884, 1885-86 (2000).

Patients want to know about their physicians. Unfortunately, information about the infection rate among individual physicians may not be useful, because practice size is often too small for statistical reliability. Although patients may wish to know if their physicians are prescribing antibiotics competently, that determination will likely be time consuming and controversial, because physicians will claim (sometimes correctly) that complex professional judgments are required. On the other hand, disclosure mandates can be used to help patients assess the reliability of their physicians' recommendations—by requiring, for example, that information about physicians' financial relationships with drug companies be made public. In the absence of direct regulation, consumer disclosure—perhaps in the form of a national publicly accessible database—may help discipline the terms of these arrangements.⁶²

On the whole, transparency is more likely to produce change through pathways other than consumer choice. Healthcare professionals take pride in their work and generally strive to improve their performance. Information can help motivate these efforts if professionals perceive it to be reliable and important. Reporting and disclosure requirements can also assist government by benchmarking current practices so that feasible direct regulation can be implemented if needed. For example, hospitals or nursing homes with low levels of acquired infections can set the standard for other facilities. Insofar as the voting public feels that public institutions and political leaders should be protecting its long-term collective interest in keeping effective antibiotics available, information about antibiotic use, infection control, and drug resistance also can help monitor the effectiveness of government itself at performing these tasks.

It is worth understanding, of course, that transparency can be a double-edged sword. It often induces “practicing to the rule,” even when doing so creates collateral problems or risks. For example, the adoption of a new quality measure—the time to first treatment with antibiotics for patients with community-acquired pneumonia—creates a substantial incentive for rapid administration of antibiotics,

62. CONFLICT OF INTEREST IN MEDICAL RESEARCH, EDUCATION, AND PRACTICE 170-83 (Bernard Lo & Marilyn J. Field eds., 2009) (calling for standardization and disclosure of certain information, and elimination of “problematic relationships” between physicians and industry). We are skeptical that “problematic relationships” can be easily defined or that the definition can be readily operationalized, particularly because the specifics of the relationships will be routinely revised in response to the announcement of new rules.

regardless of the degree of diagnostic certainty.⁶³ This approach may or may not constitute optimal care from the perspective of those treated, but it assuredly worsens the problem of antibiotic resistance in the long run.

3. Information Restrictions

Information-based regulation sometimes takes the form of restrictions rather than mandates. State attorneys general and the Federal Trade Commission routinely target false and deceptive advertising, such as “miracle cures.” Occasionally, regulation limits the dissemination of truthful information on the grounds that the intended audience is not a lawful user, as with marketing cigarettes to children, or that substantive regulation is being evaded, as with marketing off-label drug uses to physicians. These interventions must be carefully designed so as not to violate constitutional guarantees of commercial free speech.⁶⁴ Information restrictions may also be imposed to prevent an adverse inference being drawn from silence, perhaps in order to protect the privacy of the subject.

Restricting marketing of broad-spectrum antibiotics on the grounds they should be reserved for severe or hard-to-treat infections is likely to prove difficult, even though such use is an important contributor to overall antibiotic resistance. Because these antibiotics are FDA-approved, restrictions cannot be justified as necessary to protect the safety of specific individuals receiving the information, but require justification on collective grounds of public welfare. Such strategies can easily run afoul of constitutional limitations on the abridgement of freedom of speech.

B. Price Regulation and Financial Incentives

The information-oriented regulatory approaches discussed above are usually placed on the low end of the intrusiveness spectrum, with command-and-control strategies on the high end. This Part discusses incentive-based regulation, which occupies an intermediate position between advising people what to do and forcing them to do it. Incentives are usually applied through financial mechanisms that

63. Robert M. Wachter et al., *Public Reporting of Antibiotic Timing in Patients with Pneumonia: Lessons from a Flawed Performance Measure*, 149 *ANNALS INTERNAL MED.* 29, 30-31 (2008).

64. See Aaron S. Kesselheim & Jerry Avorn, *Pharmaceutical Promotion to Physicians and First Amendment Rights*, 358 *NEW ENG. J. MED.* 1727 (2008).

change the price of an activity. Implicit in this approach is the condition that the activity already be a subject of private transactions in an existing marketplace. When government is itself a very large buyer, as with Medicare and Medicaid, the structure of payments and the amount paid can act as de facto command-and-control regulation of the funded activity. Occasionally, as with pollution control permits, government actually creates both a marketplace and the products to be traded in it.

Price-based regulation has significant risks. As Friedrich Hayek observed, the “marvel” of the price mechanism in competitive markets is that it quickly conveys information about supply and demand among many decision makers without that information ever being gathered or consciously analyzed in one place.⁶⁵ Financial incentives that are justified by demonstrable inefficiencies in private markets may enhance welfare and often require altering only a subset of informational signals rather than subjecting an entire market to centralized planning through command-and-control regulation. However, price interventions that are not efficiency justified, or that create imbalances between supply and demand, can disrupt information flow in counterproductive ways.

On the other hand, medical prices in the United States are already higher than a competitive market would produce.⁶⁶ These prices are in part the result of long-standing regulatory restrictions on price competition and competitive entry, including licensing laws, corporate practice of medicine prohibitions, public purchasing practices, and private insurance mandates.⁶⁷ Not surprisingly, these limitations on price competition—and those that result from the existence of health insurance—produce competition along nonprice dimensions. In American medicine, this has usually taken the form of unverifiable professional assertions of “high quality” by individual physicians and investment in ancillary services (for instance, office-based procedures and imaging equipment), which lead in many cases to overuse of medical care and high rates of complications, including infection.

Third-party payment in healthcare raises an important question regarding price-based incentive mechanisms to control antibiotic use:

65. F.A. Hayek, *The Use of Knowledge in Society*, 35 AM. ECON. REV. 519, 527 (1945).

66. Devon M. Herrick & John C. Goodman, *The Market for Medical Care: Why You Don't Know the Price; Why You Don't Know about Quality; And What Can Be Done About It* (Feb. 2007), available at <http://www.ncpa.org/pdfs/st296.pdf>.

67. *Id.*

price to whom? Private and public health insurers pay for most big-ticket items involved in the antibiotic resistance debate: hospital care, “big-gun” antibiotics given during inpatient stays, and treatment of serious infectious complications. For uninsured patients, most of these costs are absorbed by the providers involved, which should reinforce incentives for hospitals to control infections. Individual insured patients, by contrast, pay for outpatient antibiotics either in full or through substantial co-payments and may incur significant financial harm from serious illness, but seldom bear the marginal costs of failing to prevent complications in a hospital setting.

Limitations on competitive entry create slightly different problems. Physicians in primary care settings must see large numbers of patients each day to achieve their target incomes, and giving a prescription (particularly an antibiotic) is a way to terminate a visit quickly without making the patient unhappy. Partly for this reason, settings that employ lower-cost nurse practitioners who can spend more time with each patient often generate fewer unnecessary prescriptions.⁶⁸ Excessive prescriptions can also result from poorly designed systems of government-administered pricing. In Japan, for example, artificially low government reimbursement for basic office visits resulted in physicians prescribing grossly inappropriate amounts of medication because they were permitted to dispense the drugs themselves at a substantial markup.⁶⁹

Encouraging price competition therefore is an important regulatory option—particularly if it triggers a restructuring of healthcare delivery to make inexpensive primary care widely available. Competitive pricing for basic medical care might well improve the rationality of individual antibiotic use, although it would not necessarily reduce true problems of collective action that increase bacterial resistance. A slight risk is that making healthcare more affordable might actually increase antibiotic overuse. Stated bluntly, a patient who receives an “unnecessary” prescription for an antibiotic is more likely to have it filled if it costs \$4 at Wal-Mart (or is free at a Giant supermarket) than if it costs \$25 at the local drugstore. Whether this turns out to be a serious problem depends on many factors, including the price of antibiotics; the rate of “unnecessary” prescrip-

68. James D. Woodburn et al., *Quality of Care in the Retail Health Care Setting Using National Clinical Guidelines for Acute Pharyngitis*, 22 AM. J. MED. QUALITY 457, 461-62 (2007).

69. Naoki Ikegami, *Japanese Health Care: Low Cost Through Regulated Fees*, 10 HEALTH AFF. 87 (1991).

tions; whether discounts apply to broad-spectrum, powerful antibiotics or only simpler drugs; the extent to which outpatient rather than inpatient use is the source of resistance; and the cost of infection prevention, diagnosis, and control in both of these settings. However, infectious disease specialists have expressed concern about reduced-cost prescription drug programs.⁷⁰

1. Pigovian Taxation of Externalities

Raising the price of a privately traded good to induce consumers to take full account of the cost associated with its use is perhaps the most common financial intervention. This so-called Pigovian taxation is most effective when demand is elastic, so that purchasing at the margin declines substantially for each increment in price.⁷¹ A second-best approach, valuable when demand is inelastic, is to apply revenue from a Pigovian tax to mitigate harms that result from overconsumption. This logic informs the efforts by public health professionals to use the amounts raised by taxes on tobacco to fund smoking cessation programs, health education, and smoking-related medical care.

Pigovian taxation is typically imposed when personal consumption inflicts harms on third parties. However, it can also supplement information disclosure when individuals misperceive risks to themselves or value them inaccurately. The politics of Pigovian taxation vary. Taxes on personal indulgences (such as smoking and

70. JoNel Aleccia, *Free Antibiotics May Have High Cost Later*, <http://www.msnbc.msn.com/id/29515330/> (last visited (Feb. 8, 1020) (“Offering free antibiotics to cash-strapped customers may have seemed like a good idea this dire winter, but supermarket chains are fielding a backlash from health experts who say the promotions may do more harm than good. Five large retailers have received letters from the federal Centers for Disease Control and Prevention and the Infectious Diseases Society of America cautioning that giving away antibiotics contributes to misuse of medication and the rise of increasingly drug-resistant bugs.”); *see also* Letter from Anne Gershon, President, Infectious Diseases Soc’y of Am., to Danny Wegman, Chief Executive Officer, Wegmans Food Markets, Inc. (Feb. 19, 2009), *available at* <http://www.idsociety.org/WorkArea/showcontent.aspx?id=13512>; Press Release, Infectious Diseases Soc’y of Am., Health Experts Urge Supermarket Pharmacies To “Get Smart” About Free Antibiotics (Feb. 25, 2009), *available at* <http://www.idsociety.org/Content.aspx?id=13514>; Posting of John Santa to Consumer Reports Health Blog, <http://blogs.consumerreports.org/health/2009/01/free-antibiotic.html> (Jan. 9, 2009); Alliance for the Prudent Use of Antibiotics Consumer Fact Sheet on Free or Discounted Antibiotic Promotions (Feb. 9, 2009), <http://www.tufts.edu/med/apua/Patients/consumerfactsheetfreeantibiotics2-09-09.pdf>.

71. For a general overview of Pigovian taxation, see William J. Baumol, *On Taxation and the Control of Externalities*, 62 AM. ECON. REV. 307 (1972); Rajeev K. Goel & Edward Wei-Te Hsieh, *Market Structure, Pigouvian Taxation, and Welfare*, 25 ATLANTIC ECON. J. 128, 128-38 (1997).

drinking) are more publicly acceptable than other explicit taxes, but have usually been enacted as revenue raisers (and regressive ones at that) rather than true deterrents.

Direct Pigovian taxes can be used to raise the price of antibiotics and reduce their use. Targeting assessments is likely to prove challenging, however. Tax rates should reflect the marginal disutility of particular drugs in particular situations and should be highest for high-harm uses. One strategy is to impose high tax rates on broad-spectrum or powerful antibiotics. In theory, this approach does not require government to tax more when benefit to the buyer is less (for instance, an antibiotic prescribed for a viral infection), because the consumer is assumed to balance personal benefit against personal cost. Still, a public process would be needed to determine which antibiotics would be subject to relatively more or relatively less tax, to decide which necessary uses would be exempt, and to determine (likely by trial and error) what tax rates are needed to change antibiotic consumption rates. Any given tax structure will be imperfect along some relevant dimensions, since clinical variation and informational asymmetries ensure that one size will not fit all.

Distributional consequences may also be material. With a uniform tax rate, less wealthy consumers are more likely to forgo necessary antibiotics, while wealthier consumers are likely to continue unnecessary overuse.

The level of trade at which the tax should be collected is also problematic. Should drug manufacturers, hospitals, physicians, or patients be assessed? Taxes are usually imposed in the manner that will generate the greatest compliance at the lowest enforcement cost and with the least political fallout. Price elasticities generally divide the economic burden (tax incidence) between sellers and buyers, regardless of where the locus of collection is placed. However, the number of payment intermediaries in healthcare makes the initial placement decision for any tax nontrivial.

2. Tradable Permits

Tradable permits are a theoretical alternative to Pigovian taxes. Permits are most useful when the public interest requires an aggregate reduction in consumption, the individual costs of reducing consumption vary widely, and price elasticities of demand are unknown. Government could establish a tradable permit system for certain high-value antibiotics, with large penalties applied to unpermitted uses. In concept, this is attractive because antibiotic

overuse and misuse are national problems, individual antibiotic prescriptions vary greatly in their likely effectiveness, and prescribers are better situated than regulators to know whether each prescription is strictly necessary.⁷²

Healthcare providers also have other means for reducing antibiotic use than forgoing prescription, such as improved infection control. In a permit system, hospitals that could prevent infections cheaply would sell permits to others that could not (such as providers located in communities with high infection rates), allowing overall antibiotic use to be reduced by the desired amount at the lowest possible cost. Because of enforcement costs, a permit system is most easily applied to a small number of participating users, such as large hospitals. As in all permit systems, leakage of antibiotics from regulated to unregulated sources must be policed, and regulators must be alert to unintended inequities and inefficiencies, such as "hot spots" for infection.

The initial allocation of the permits creates additional complexities, particularly the decision whether they will be sold at auction or assigned as allotments to existing users. Assignment reflects the reality that some hospitals and physicians treat patients with a greater risk of infection, but confers a valuable asset on institutions that currently have higher infection rates, some of which might be avoidable. An auction allows hospitals that value permits the most to secure them directly from the government, while simultaneously raising funds for the government that can be put to a variety of uses. However, hospitals that lack the resources to bid successfully for the permits might still have greater need for access to antibiotics, given the patient population they serve.

Finally, permits will be less effective if some jurisdictions do not adopt them or some uses within participating jurisdictions are exempted on political grounds. If this occurs, overall antibiotic use will not be sufficiently reduced and some antibiotic use by regulated sources will be converted into use by unregulated sources.

3. Subsidies

Public subsidies are a common fiscal-regulatory technique to encourage activities that are undersupplied by competitive markets.

72. See generally Richard D. Smith & Joanna Coast, *Controlling Antimicrobial Resistance: A Proposed Transferable Permit Market*, 43 HEALTH POL'Y 219 (1998) (proposing adoption of a tradeable permit system in order to reduce antimicrobial prescribing).

Many of these activities fall into the analytic category of public goods. The public subsidy can come in the form of cash transfers to those who provide the public goods, restricted vouchers given to those who need the services, or direct government provision of the services. All three strategies spread the cost of the subsidy among taxpayers, market participants, or both. Increased funding of public health activities directed at improved antibiotic use and infection prevention falls into this category.

Explicit subsidies can be used to alter relative prices and therefore consumer behavior. Subsidies for diagnostic tests are one possible intervention. Antibiotics are often needlessly prescribed because bacterial infection is never verified, or a more powerful antibiotic is given when testing would have revealed that a less powerful one would have been equally effective.⁷³ Subsidized testing might be particularly useful as an alternative to direct control of practice in widely dispersed settings, such as physicians' offices. Monitoring would be necessary to ensure that testing decreased antibiotic use, rather than merely adding another layer of cost between the time a patient seeks care and the time a prescription is generated.

Physician practices also tend not to make large capital investments. Subsidies for the acquisition of health information technology, including decision-support software, might encourage physicians to adopt these systems. Such systems have the potential to improve the use of antibiotics, as well as to facilitate compliance with an information reporting or disclosure regime if one were adopted.

Subsidies might also be offered for infection control systems in hospitals, although larger institutions probably do not require dedicated funds in order to afford such improvements. Unlike physician practices, enough money flows through the hospital sector that marginal incentives will seldom produce substantial effects. Hospitals will only alter their behavior if the financial implications are large.

One possible strategy is to condition the receipt of existing subsidies by hospitals (including the tens of billions of dollars they receive in exemptions from income and property taxes) on playing an active, verifiable role in improving infection control and treatment in their communities. Federal tax law already requires that hospitals perform a charitable function in their communities in order to retain

73. See Kades, *supra* note 18, at 617-18; Nat'l Inst. of Allergy & Infectious Diseases, NIAID's Role in Addressing Antimicrobial (Drug) Resistance: Causes, <http://www3.niaid.nih.gov/topics/antimicrobialResistance/understanding/causes.htm> (last visited Jan. 10, 2010).

their tax exemption.⁷⁴ Instilling in federal tax law a more detailed notion of community benefit as providing public goods as well as offering free or reduced-price medical care to indigent patients could induce hospitals to improve the use of antibiotics within their institutions, in the offices of physicians with admitting privileges at the hospital, and in their service areas generally.

An even more aggressive approach would be for Congress to tie its very large tax subsidy for employment-based health coverage to the adoption of explicit purchasing strategies designed to minimize antibiotic resistance. Once adopted, this approach would have both direct and indirect effects. The direct effect would be to revamp private insurance benefit packages and payment methodologies so as to reduce coverage of medical services that needlessly increase the risk of antibiotic resistance, and to expand coverage of interventions that might reduce resistance. The indirect effect would be to alter long-term incentives for suppliers of innovative products, whether vaccines, diagnostic tests, infection control systems, or new antibiotics.

Subsidies also raise obvious problems. Paying too little will result in an inadequate level of subsidized behavior, while paying too much will be wasteful. It is particularly difficult to determine the optimal level of the subsidized conduct (and hence of the subsidy) in the absence of the price signals delivered by a well-functioning market—but if there were a well-functioning market, there would be less need for a subsidy.

4. Prizes

A public monetary prize is a special form of subsidy designed to encourage and reward innovation without committing to an indefinite stream of payment or conferring an ongoing property right.⁷⁵ A novel prize recently added to federal food and drug law confers tradable “priority review vouchers” for expedited FDA review of unrelated

74. For a general overview of how a hospital qualifies for and maintains its tax-exempt status, see APPLYING FOR 501(C)(3) TAX-EXEMPT STATUS, <http://www.irs.gov/pub/irs-pdf/p4220.pdf> (last visited Jan. 30, 2010).

75. James Love & Tim Hibbard, *Prizes for Innovation of New Medicines and Vaccines*, 18 ANNALS HEALTH L. 155 (2009); James Love & Tim Hibbard, *The Big Idea: Prizes To Stimulate R&D for New Medicines*, 82 CHI.-KENT L. REV. 1519, 1528 (2007); Joseph E. Stiglitz, *Scrooge and Intellectual Property Rights: A Medical Prize Fund Could Improve the Financing of Drug Innovations*, 333 BRIT. MED. J. 1279, 1279-80 (2006).

products on companies that develop therapies for neglected (less profitable) diseases.⁷⁶

In addition to new antibiotics, prizes might be awarded for innovative ways to fight bacterial infections, or for replicable community strategies for prevention, detection, and control of spread. Prizes offer a more limited financial incentive than direct subsidies. On the other hand, the recognition and publicity associated with a substantial prize can help instill or reinforce professional and public norms about prudent stewardship of existing antibiotics. Prizes accordingly have the potential to encourage providers to adopt infection control strategies that less visible subsidies might not.

5. Property Rights

Subsidies can also be created or increased by operation of intellectual property law. Expanding the duration of patent protection for new types of antibiotics, for example, might lessen pharmaceutical manufacturers' incentive to promote immediate wide use of a drug and focus instead on marketing those drugs only for otherwise untreatable infections.⁷⁷ This approach would work best if only one company or one patent pool controlled all rights to a novel class of drug. An alternative strategy for restricting the use of new antibiotics to the most susceptible population is to award them orphan drug status, which confers preferential patent protection and other benefits as long as use is restricted.⁷⁸ At the same time, patent policy could promote greater use of ordinary antibiotics by granting earlier access to those formulas by generic manufacturers.

Changes in intellectual property rights are generally not well suited to the fine-tuning of public policy with regard to antibiotics, because any reform is certain to be both underinclusive and

76. Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, § 1102 (priority review for tropical diseases); *see also* David B. Ridley, Henry G. Grabowski & Jeffrey L. Moe, *Developing Drugs for Developing Countries*, 26 HEALTH AFF. 313 (2006) (proposing priority review vouchers).

77. *See, e.g.*, Kades, *supra* note 18.

78. Congress has already recognized this possibility. In the Food and Drug Administration Amendment Act of 2007, section 1112 requires the FDA to convene a public meeting "regarding which serious and life threatening infectious diseases, such as diseases due to gram-negative bacteria and other diseases due to antibiotic-resistant bacteria, potentially qualify for available grants and contracts under section 5(a) of the Orphan Drug Act . . . or other incentives for development." Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, § 1112, 121 Stat. 976 (2007). The FDA held this hearing on April 28, 2008. *See* Antimicrobial Resistance; Public Hearing; Request for Comments, 73 Fed. Reg. 20,309 (Apr. 15, 2008) [hereinafter Public Hearing].

overinclusive.⁷⁹ However, such strategies may be more politically attractive than direct subsidies because their costs do not appear in the federal budget. Regulatory relief, such as the “priority review vouchers” described above, is similarly off-budget.

6. Public Purchasing, Administered Pricing, and Price Controls

When most people think about price regulation, they imagine government directly setting prices or capping the amount that can be charged. In American healthcare, direct price controls of this sort are uncommon. On the other hand, because half of total health expenditures in the United States are paid by federal, state, and local government, government can implicitly regulate prices through its purchasing practices.⁸⁰ For political reasons, the prices at which government purchases healthcare are almost always set administratively (at first passively based on custom, now by statutory formula) rather than by competitive bidding. Private insurers routinely adopt similar methods or price in the shadow of public programs, taking account of local market conditions.

The substantive conditions of participation in Medicare and Medicaid, including compliance with administered pricing, can become de facto command-and-control regulation if the government’s role is so large that healthcare providers cannot survive without accepting publicly supported patients. Laws designed to protect the integrity of government purchasing also sometimes compel private conformity with public administered pricing. Fraud and abuse prohibitions, for example, make it difficult for healthcare providers to enter into many types of contractual arrangements with one another, or with third parties, even if those agreements do not specifically relate to federal health programs.

Medicare Part D, at least as it currently exists, represents an interesting example of public purchasing of pharmaceuticals because it builds on pricing models that were developed in the private sector, such as tiering of consumer cost-sharing by drug class.⁸¹ This is a

79. Kevin Outterson et al., *Will Longer Antimicrobial Patents Improve Global Public Health?*, 7 *LANCET INFECTIOUS DISEASES* 559, 561-64 (2007).

80. For an overview of healthcare expenditures by the U.S. government, see Ctrs. for Medicare & Medicaid Servs., *Medicare Modernization Update*, <http://www.cms.hhs.gov/MMAUpdate/> (last visited Jan. 18, 2010).

81. Medicare lacked coverage for outpatient prescription drugs until 2003. Under the Medicare Prescription Drug Improvement and Modernization Act, the drug benefit is administered through private insurers for all Medicare beneficiaries, not just those enrolled in

relatively hands-off approach compared to Medicare payment of physicians, hospitals, and durable equipment suppliers. It resulted from arguments made by the pharmaceutical and medical device industries to the enacting Congress that capping or benchmarking drug prices would discourage long-term innovation.⁸² Future Congresses attempting to close large budget deficits may be less receptive to this reasoning.

One can imagine using tiering strategies to address antimicrobial resistance, including greater consumer cost-sharing for antibiotics prescribed for marginal uses and substantial surcharges for nonconforming uses of drugs placed on a “reserve list” for serious infections.⁸³ At the same time, rewards to both pharmaceutical companies and physicians should be greater when the most powerful antibiotics are used on the sickest patients. However, it is impossible for antibiotic producers in a conventional market to receive more from a patient whose life is saved than from a patient who takes a product for a marginal or frivolous indication. An administered pricing system could redress this failure by ensuring higher reimbursement to the manufacturer or supplier for greater value received, with performance measured at the level of the health plan or the county, state, or country.

A tiering strategy would dovetail with existing initiatives to pay physicians based on their performance, while also maintaining the patient’s financial incentive to take antibiotics only to the extent they are clinically indicated. Although this strategy is intuitively attractive, it is at odds with larger market developments in the United States, which seek to lower the cost of pharmaceuticals across the board (including by offering free or extremely low-cost generic antibiotics at major retailers).⁸⁴

A different set of administered pricing policies governs reimbursement to hospitals for the cost of treating additional illnesses acquired during a hospital stay. The Medicare program and several private insurers have already limited or eliminated payment for treatment of obvious medical errors, including avoidable hospital-

HMOs, and the government is prohibited from negotiating prescription drug prices directly with pharmaceutical manufacturers. *See id.*

82. JOHN A. VERNON ET AL., ARE DRUG PRICE CONTROLS GOOD FOR YOUR HEALTH? (Dec. 2004), available at http://www.manhattan-institute.org/pdf/mpr_01.pdf.

83. Of course, these tiering strategies are not necessarily the optimal strategy for minimizing resistance. Design details matter in assessing the comparative performance of tiering versus alternative strategies.

84. *See supra* note 70 and accompanying text.

acquired infections.⁸⁵ The goal of these policies is to encourage hospitals to invest in early detection and control by removing revenue streams that previously made them financially indifferent to clinical complications arising from the care they provide. Conversely, if Medicare covers (and separately pays for) screening of newly admitted hospital patients for infection, such screening is likely to become prevalent, if not the standard of care.⁸⁶ If permitted by fraud and abuse law, hospitals might well adopt gain-sharing programs to encourage physicians to consistently order such screening, as well as to motivate compliance with antibiotic usage recommendations.

Finally, government can purchase antibiotics directly from manufacturers to be held in reserve rather than to be used. A strategic stockpile of effective antibiotics for use in case of widespread resistant infections is appealing at first glance and would build on the precedent of the Strategic National Stockpile.⁸⁷ However, as the negotiations over ciprofloxacin during the 2001 anthrax scare illustrate,⁸⁸ there may be a narrow window between the payment amount that would be sufficient to make the program attractive to the company whose product is picked, and the amount that the government can afford as an immediate, on-budget expense. There is also an important difference (both practical and perceptual) between the government stockpiling antibiotics so as to deal with short-term supply dislocations in the event of a public health emergency, and the government removing a

85. *But see* Nicholas Graves & John E. McGowan, Jr., *Nosocomial Infection, the Deficit Reduction Act, and Incentives for Hospitals*, 300 JAMA 1577 (2008) (critiquing this initiative); Peter D. McNair, Harold S. Luft & Andrew B. Bindman, *Medicare's Policy Not To Pay for Treating Hospital-Acquired Conditions: The Impact*, 28 HEALTH AFF. 1485 (2009) (estimating that payment reductions from this policy are likely to be negligible and unlikely to alter provider behavior).

86. We take no position on whether such screening is, in fact, efficient, and whether it should be performed on all admitted patients, or just those that are high-risk. For a collection of strategies to prevent HAIs, see Deborah S. Yokoe et al., *A Compendium of Strategies To Prevent Healthcare-Associated Infections in Acute Care Hospitals*, 29 INFECTION CONTROL & HOSP. EPIDEMIOLOGY (SUPP.) S12 (2008), and Paula Wilton et al., *Strategies To Contain the Emergence of Antimicrobial Resistance: A Systematic Review of Effectiveness and Cost-Effectiveness*, 7 J. HEALTH SERV. RES. & POL'Y 111 (2002).

More broadly, the economics of antibiotic resistance are complex and multifactorial. *See generally* David L. Smith et al., *Strategic Interactions in Multi-Institutional Epidemics of Antibiotic Resistance*, 102 PROCEEDINGS NAT'L ACAD. SCI. 3153 (2005) (discussing economics of antibiotic resistance); Shelby D. Reed et al., *Economic Issues and Antibiotic Resistance in the Community*, 36 ANNALS PHARMACOTHERAPY 148 (2002) (discussing same).

87. The United States maintains a stockpile of drugs, vaccines, and similar medical products to be relied upon in case of a bioterrorism attack or public health emergency. *See* 42 U.S.C. § 274d-6b (2006).

88. *See* Keith Bradsher, *A Nation Challenged: The Treatment*, N.Y. TIMES, Oct. 26, 2001, at A1.

class of antibiotics from the market entirely against the prospect of a new infection emerging that is resistant to all other antibiotics. In the former instance, the government is just another (bulk) purchaser of the products; in the latter, it is expropriating the entire value of the antibiotic over its useful life span, creating a taking that requires just compensation under the express terms of the Fifth Amendment.

C. Command-and-Control Regulation

Regulation that specifies permissible and impermissible conduct through the adoption and enforcement of substantive standards is often called “command and control.”⁸⁹ Although command-and-control regulation may be justified by reference to market imperfections of various sorts (such as lack of information), within its explicit scope it displaces rather than facilitates market transactions. Command-and-control regulation is often further divided into design standards that dictate structural or procedural details of private activities, and performance standards that set requirements for outcomes or outputs but allow them to be met using whatever method the regulated actor chooses.

Command-and-control regulators must also decide whether all activities of an industry or industrial sector should be subject to newly adopted or amended regulations, or whether the regulations should only apply to future products and production facilities (grandfathering). This decision is often a political one, but is sometimes linked to theories that emphasize precaution in the face of uncertain (unknown) risks or that recognize the potential for regulation to force the development and dissemination of new technology.

Command-and-control regulation requires a more extensive regulatory apparatus than other forms of government oversight. Legislatures generally delegate that responsibility to expert administrative bodies with rulemaking or adjudicative tools at their disposal. In healthcare, by contrast, self-regulation has been the predominant regulatory mechanism, based on widely held assumptions about the benefit to individual patients of medical expertise constrained only by professional ethics. Although these principles remain valid, an important question is whether medicine’s established self-regulatory capacity can deal effectively with a problem that was in

89. See Howard Latin, *Ideal Versus Real Regulatory Efficiency: Implementation of Uniform Standards and “Fine-Tuning” Regulatory Reforms*, 37 STAN. L. REV. 1267, 1267 n.2 (1985).

large part caused by decades of deference to physician and hospital self-regulation (see Part IV).

1. Design Standards

Several forms of design standards are potentially applicable to reducing bacterial resistance to antibiotics. One possibility would be to “schedule” antibiotics as controlled substances through the U.S. Drug Enforcement Agency (DEA) or a similar mechanism and therefore limit antibiotic use by regulating dispensing by pharmacies. Under such a regime, older and narrow-spectrum antibiotics could be prescribed freely by health professionals who enjoy that privilege under state law, while newer, broad-spectrum drugs could only be prescribed by infectious-disease specialists and others who applied for and received a special permit and who committed to filing paperwork documenting their decisions in particular cases. A few drugs might even be banned from private prescribing and held in reserve for emergency use on government order (with other regulation providing manufacturers with financial incentives to produce those drugs).

Similarly, the FDA could be given statutory authority to prohibit “off-label” prescribing of certain antibiotics, which would limit their use to the types of infections for which a New Drug Application had been approved. Much the same result would follow if the FDA manipulated other terms of drug approval. For example, if FDA only approved an injectable form of a particular antibiotic family, it would be prescribed much less frequently than would be the case if an oral formulation were available. Existing food and drug law would need to be amended for the FDA to “bank” a family of antibiotics in this way.

Another approach using design standards might specify the conditions under which each antibiotic, or any antibiotic, could lawfully be used. A regulatory body would list disease-causing organisms or sites and severities of infection, and would associate each with one or more allowed first-line therapeutic agents, procedures for granting exceptions, and prohibited treatments. Procedures for diagnosing bacterial infections and assessing sensitivity to particular antibiotics prior to treatment might also be required. Additional design standards could establish correct dosages, dosing schedules, and durations of therapy (unnecessarily prolonged exposure being a little-studied issue with considerable importance for the emergence of resistant strains). For very severe infections, monitored administration might be required, as is sometimes done for resistant tuberculosis today.

Infection control measures also can be instituted through design standards. Public health authorities could mandate screening newly admitted hospital patients for infection, and analogous requirements could be imposed on nursing homes, residential schools, and other community institutions. Within those institutions, specific measures to maintain hygiene and prevent the spread of infection could be required as well.

If delegated self-regulation is deemed preferable to direct government control for some or all of these functions, design standards can specify the structures and processes for conducting that oversight. For example, Joint Commission accreditation requirements and survey-and-certification criteria for hospitals and health facilities might specify that infection control committees draft plans for preventing the spread of resistant bacteria, and that pharmacy and therapeutics committees design and enforce drug formularies that reduce antibiotic resistance.

Financial relationships between healthcare providers and the pharmaceutical industry that create conflicts of interest are a qualitatively different regulatory problem, whose nexus with antibiotic resistance is less clear. If deemed useful, such relationships are amenable to modification through design standards. For example, one could flatly prohibit payments or gifts by drug companies to physicians in connection with the treatment of infectious disease. Promotional activities could also be regulated within the strictures imposed by the First Amendment.

2. Performance Standards

Performance standards are an alternative to design specifications for most of the regulatory approaches discussed above. Although the design-performance dichotomy is not absolute, performance standards are generally framed in terms of measurable outcomes for patients, facilities, or communities, rather than mandatory structures and processes. If a regulated entity failed to achieve those outcomes, one possible penalty for noncompliance would be to trigger a set of fallback design standards that would be more effective, albeit costlier, for the entity to implement.

Performance standards for the prevention or spread of drug-resistant infections could be as simple as setting benchmarks for acceptable and unacceptable infection rates or antibiotic sensitivity profiles. As with medical outcome measures generally, standards of this type require that outcomes be ascertainable with statistical

confidence. Similarly, the desired outcomes must be at least partially within the operational control of the regulated entity. Both of these preconditions favor application to hospitals, nursing homes, and large physician groups rather than small medical practices. Finally, fair comparison requires the development of valid risk- or severity-adjustment methodologies. There are various state and federal (Medicare) initiatives adopting this approach.⁹⁰

Performance standards are also valuable where the controlling governmental body considers it practically or constitutionally preferable to delegate specific decisions to smaller political subdivisions or community coalitions. In clean air regulation, for example, the federal government requires states to develop and enforce implementation plans to reduce specified pollutants below threshold levels of risk.⁹¹ A similar approach might induce key stakeholders within communities, such as groups of hospitals and physician practices, to formulate joint plans for controlling antibiotic resistance.

Performance standards can induce problematic adaptive responses if regulated entities have discretion to choose which activities will be assessed. If hospitals are punished for high infection rates, they will have an incentive to avoid more susceptible patients (for example, those who are immunocompromised), particularly if risk adjustment is imperfect. Similarly, regulators must decide whether to demand similar levels of performance from all types of regulated institution. For example, standards that reward improvement from baseline trends will have a very different impact than standards tied to an absolute level of performance.

3. New Source Standards

Substantive regulatory standards can be either implemented across the board or applied selectively to new technologies, services, or facilities. Existing practices are “grandfathered” for three main reasons: fairness (activities had been initiated without expectation of regulation), political support (incumbent firms prefer to selectively burden new entrants and thereby raise their rivals’ costs), and efficiency (new activities may create significant harm at the margin if a saturation point or threshold has been reached).

90. See *supra* notes 14-15 and accompanying text.

91. See John P. Dwyer, *The Practice of Federalism Under the Clean Air Act*, 54 MD. L. REV. 1183, 1190-99 (1995).

In some cases, it may make sense to impose restrictions mainly on newer antibiotics to which resistance has not yet developed, while in other cases it may be preferable to restrict older drugs (particularly ones that are no longer in widespread use because of unpleasant side effects) in order to restore their potential utility.⁹² For healthcare facilities, it may be pragmatic to impose infection control requirements that depend on significant capital investment, such as isolation systems, only for new construction because of the high cost of retrofitting existing structures. This would be especially true if new facilities significantly expand high-risk clinical services and therefore opportunities for infections to develop or spread. On the other hand, applying regulation only to new construction creates perverse incentives for regulated entities to keep older, less well-designed facilities in operation longer.

New source performance standards are worth considering for antibiotics mainly because the principal mission of the FDA is to screen novel drugs and medical devices for lack of safety or effectiveness. With enabling legislation, the FDA could use this authority to place conditions on approved indications for using new antibiotics, or to withhold approval from antibiotic molecules with sensitivity profiles no better than existing drugs that are likely to contribute to aggregate overuse or misuse. The former measure would be most effective if, unlike current FDA regulation but like the design standards discussed above, the FDA's determination limited actual use of antibiotics rather than merely prohibiting "off-label" marketing to physicians.

Analogously, the FDA could selectively relax standards for, or expedite approval of, new vaccines, diagnostic tests or medical devices

92. On whether antibiotic cycling is effective, see Robert G. Masterton, *Antibiotic Cycling: More Than It Might Seem?*, 55 J. ANTIMICROBIAL CHEMOTHERAPY 1, 4 (2005); Carl T. Bergstrom et al., *Ecological Theory Suggests That Antimicrobial Cycling Will Not Reduce Antimicrobial Resistance in Hospitals*, 101 PROCEEDINGS NAT'L ACAD. SCI. 13,285, 13,287-88 (2004); Scott K. Fridkin, *Routine Cycling of Antimicrobial Agents as an Infection-Control Measure*, 36 CLINICAL INFECTIOUS DISEASES 1438, 1443 (2003).

To be sure, although usage creates selection pressure for the development of resistance, it is less clear whether reducing antibiotic usage will restore the status quo ante once resistance has developed. See Bat Sheva Gottesman et al., *Impact of Quinolone Restriction on Resistance Patterns of Escherichia Coli Isolated from Urine by Culture in a Community Setting*, 49 CLINICAL INFECTIOUS DISEASES 869, 869 (2009) ("Although it is well accepted that resistance rates will increase with increasing antibiotic use, conflicting answers exist as to the question of whether susceptibility patterns will be restored once antimicrobial use is decreased, which has evolutionary importance. . . . In the present study, a decrease in *E. coli* resistance to quinolones was observed concomitantly with a decrease in quinolone use.").

intended to improve infection control.⁹³ This strategy is controversial, but it has been used in other areas where the perceived stakes are sufficiently high (such as AIDS research) to justify overriding the general preference among FDA personnel for prioritizing safety over early access to untested medication.⁹⁴

4. Technology Forcing Standards

Substantive regulation can induce investment in new ways to reduce the risks of harm from existing activities if compliance depends on adopting technology that is not yet commercially available. Ambitious performance standards can “force” technologic advances by penalizing continuation of the status quo, while leaving to the regulated entities the manner in which the underlying problems are fixed. By contrast, design standards typically entrench existing technology that is known to be affordable, chilling rather than spurring innovation, and at most can mandate widespread application of technology that is currently used only by particularly wealthy or progressive entities.

With respect to antibiotic resistance, technology-forcing strategies are most likely to pay dividends for infection control practices in healthcare facilities, where advanced diagnostics, monitoring systems, and disinfectant methods can significantly reduce spread. Technology forcing is probably less viable in office-based physician practices because of their limited financial resources, although it might be used to induce collective investment in health information technology.

D. Physical Rationing

Physical rationing represents highly intrusive government regulation, exceeded perhaps only by direct restriction of physical liberty such as quarantine.⁹⁵ Although quarantines (and less Draconian measures such as social distancing) are legitimate and occasionally

93. Paul H. Rubin, *The FDA's Antibiotic Resistance*, 27 REGULATION 34, 36-37 (2004).

94. For instance, the FDA relied upon its accelerated approval process in approving H1N1 influenza vaccines this past flu season. See Press Release, FDA Expands Use of CSL Limited's Seasonal and H1N1 Vaccines to Infants and Children (Nov. 12, 2009), <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm190359.htm>.

95. Some might object that physical rationing is indistinguishable in its effects from rationing by price, and so it should not be treated separately. Such objections ignore the history and rhetorical implications of the word “rationing” in common discourse. For better or worse, most people do not understand “rationing by price” to be rationing.

necessary public health measures to prevent the spread of disease, applying them to resistant infections would signal the failure of other regulatory measures and mark the triumph of the “superbugs.” Still, many of the possible interventions discussed in this Article aim to improve priority setting among uses and users of antibiotics in order both to promote long-term efficiency and to avoid manifest unfairness. Rationing merely does so explicitly and coercively.

Government generally plays a role in designing rationing systems for scarce resources when the price system that allocates and distributes most goods and services is deemed socially unacceptable. Rationing systems are typically made necessary by physical shortages, as for human organs for transplantation or in wartime, for civilian access to materials the majority of which must be used for military purposes. In a market economy, rationing goods and services that can be produced for a price is rare because all markets clear. Occasionally, however, price controls necessitate rationing because demand at the capped price will inevitably exceed supply, and formal rationing systems are perceived by those backing them as fairer or less socially wasteful than informal alternatives.

Rationing can be implemented explicitly by rule or implicitly through discretionary professional practices. Rationing schemes often have both allocative goals (ensuring that higher value uses get priority) and distributional goals (ensuring that everyone receives an acceptable amount). Unless allocation-oriented rationing can be governed by objective, scientific standards, attempts to set priorities through logical deliberation may provoke greater objection from the public than distributionally fair but seemingly random approaches such as lotteries and queuing. In socially contentious, constitutionally delicate areas such as health, the details of rationing may be delegated to private self-regulatory organizations (for example, the United Network for Organ Sharing and affiliated Organ Procurement Organizations) that are bound by professional ethics as well as by explicit rules.

Rationing because of antibiotic resistance would likely be applied only in extreme circumstances, such as managing a limited supply of effective drugs during an outbreak of resistant disease. The U.S. government currently has a physical rationing plan for dealing with pandemic flu, for instance.⁹⁶ However, rationing principles are relevant to curbing overuse and misuse of antibiotics generally. One can

96. Dep't of Health & Human Servs., H1N1 (Swine Flu) Immunization Campaign, <http://www.pandemicflu.gov/> (last visited Jan. 18, 2010).

imagine giving particular hospitals or nursing homes fixed budgets of particular drugs, which they would be responsible for rationing among potential users. A rationing system for antibiotics would be contentious, because medical criteria for which patients to treat first would inevitably blend scientific and social judgments about clinical benefit.⁹⁷ This concern has been ameliorated somewhat for organ transplantation because prioritizing the sickest patients does not seem to significantly disadvantage less sick individuals awaiting livers, and dialysis is available to those who require new kidneys.

Typically, rationing coupons are not tradable because exchange, while allocatively efficient, undercuts the commitment to fairness and shared sacrifice that often motivates public acceptance of rationing. However, as described briefly above with respect to tradable permits, this concern might be outweighed for antibiotics by the potential for exchange to motivate improvement in infection control and prevention at institutions that can do so inexpensively, so that ultimately few if any patients end up being denied medically necessary therapy.

V. MATCHING REGULATORY INTERVENTIONS TO INSTITUTIONAL CAPACITY

In addition to being theoretically sound and appropriately designed, effective regulation of antibiotic resistance must synchronize with existing laws and institutional capacities. Regulatory institutions in the United States are embedded in a complex federal system that divides authority both vertically between federal, state, and local governments, and horizontally among the administrative agencies at each level. In addition, the judicial branches of both federal and state government not only interpret legislative and administrative enactments, but also create law while adjudicating private disputes that can have systematic implications. These legal entities interact with a host of formal self-regulatory organizations, self-governing private organizations, and social and professional norms.

Failure to attend to institutional dynamics will doom any reform proposal, no matter how well intentioned or rationally constructed. Accordingly, this Part surveys the existing regulatory framework, identifies factors that should be considered before attempting to

97. For example, concerns about how "God Committees" were allocating access to dialysis led Congress to create special Medicare coverage for all individuals with chronic renal failure. See David Sanders & Jesse Dukeminier, Jr., *Medical Advance and Legal Lag: Hemodialysis and Kidney Transplantation*, 15 UCLA L. REV. 357, 378 (1968) ("The Pacific Northwest is no place for a Henry David Thoreau with bad kidneys.").

implement reform through a particular institution or set of institutions, and suggests potentially productive areas of focus based on the foregoing analysis of regulatory goals and methods. Our goal is to provide a reasonably comprehensive listing of the institutions with which the problem of antibiotic resistance can be attacked, and the comparative advantages (and disadvantages) of doing so using each.

A. Federal Government

Federal regulation has several functional characteristics relevant to addressing antibiotic resistance. One advantage of a national solution is that it helps limit interstate externalities when states might impose solutions that create internal benefits but increase external harms (such as tall smokestacks that send local pollutants into regional airsheds). Similarly, national solutions can reduce temptation by states to free-ride on other states' regulation, potentially promoting a "race to the bottom." Where regulation affects businesses that operate in many states, moreover, a uniform federal approach can reduce compliance and administrative costs and is often more politically transparent and less subject to interest-group influence.

States vary in wealth and administrative sophistication. The federal government has far greater fiscal capacity than the states and fewer constraints on borrowing, which allows it to redistribute resources among states and to make long-term investments in things other than physical infrastructure. The rise of the federal administrative state since the 1930s, moreover, allows federal regulation to work comprehensively across industrial sectors, reducing leakage of harm into unregulated activities.⁹⁸ Finally, federal regulation enjoys constitutional exclusivity in certain areas, such as negotiations with foreign nations and granting patent rights to inventors.

Federal regulation has disadvantages as well. Federal solutions are less attuned to local conditions. Federal authorities are remote, making enforcement difficult. Interventions often draw on federal fiscal capacity to the exclusion of other approaches, and regulatory design tends to be dictated by programs' large aggregate budgetary implications. Finally, certain local activities are beyond the constitutional reach of federal law, and the federal government is constitutionally prohibited from commandeering (but not from purchasing) assistance from state authorities.

98. See Dwyer, *supra* note 91, at 1183 n.1.

Several of these factors suggest a primary federal presence regulating antibiotic resistance. Resistance is fundamentally an externality problem, including internationally, making federal regulation attractive.⁹⁹ The long time horizon over which benefits will become manifest, likely encompassing generations rather than lifetimes, argues for a large federal component, as the federal government is better equipped to incur costs today for distant improvements that can be estimated only with ample provision for scientific uncertainty. Synergies between control of infectious disease and the bioterrorism and emergency preparedness aspects of national security argue for a federal role as well, although problems can arise when subtle, complex scientific problems are assigned to agencies with highly visible, quasi-military missions.

Compared to state licensing of health professionals and facilities, federal involvement with healthcare providers and suppliers is indirect (except for the armed forces and veterans' health) but nevertheless substantial, operating primarily through Medicare's (and to a lesser extent Medicaid's) payment formulas and insurance coverage determinations. Large federal grants-in-aid for various state health and safety programs, investment in biomedical science, and supply-side incentives through patent law and FDA oversight also weigh on the side of federal intervention. In addition, federal tax law offers a national platform for incentivizing healthcare providers, insurers, and employers. Finally, through the Employee Retirement Income Security Act (ERISA), the federal government can reach sources of private health coverage that are not subject to state insurance oversight, although this authority has not been exercised to influence clinical practice.¹⁰⁰

1. Medicare and Medicaid

The Medicare program, administered by the Center for Medicare and Medicaid Services (CMS), offers the longest lever for altering antibiotic usage and infection control patterns, primarily by refining its payment strategies or by amending its conditions of participation. Although Medicare's beneficiaries account for only about thirteen percent of the U.S. population, they account for a disproportionate

99. We do not address global strategies in this Article because the lack of centralized authority means that such strategies are more likely to be hortatory than regulatory. To be sure, the externalities from antibiotic resistance do not stop at national boundaries. Therefore, a role for global coordination undoubtedly exists.

100. See Sage, *supra* note 57, at 1713-14.

percentage of spending on hospital and physician services. Medicare's purchasing strategies can have a profound effect on the practice of medicine and can create positive (and negative) spillovers that affect the care received by the rest of the population. Medicare's influence over hospital practices is greater than its influence over physicians.

Medicaid is a state-administered health insurance program for low-income individuals, including the elderly, that is funded by both federal and state dollars (see state discussion below). Medicare exerts little direct oversight of long-term care facilities, which constitute a large reservoir of drug-resistant bacteria, but Medicaid pays for roughly half the nursing home care in the United States. States have considerable latitude to vary eligibility and benefits under Medicaid, but federal minimum standards must be met.

Medicare currently pays for care more or less regardless of its quality. By changing its payment system, Medicare more than any other program can create better global incentives to prevent infections, control their spread, and treat them appropriately. Medicare has recently taken tentative steps in this direction by identifying nosocomial infections for which it will not pay, including vascular catheter-associated infection, catheter-associated urinary tract infection, and certain surgical site infections. Although the total amounts at issue are modest, this approach marks a dramatic change in Medicare's payment philosophy.

Alternatively, Medicare can identify certain infection-control strategies that it believes should be used, and make the adoption of such strategies a condition of participation in Medicare. Once it does so, all providers who wish to contract with Medicare must adopt the specified practice. Historically, conditions of participation have focused on structural attributes of provider institutions, rather than details of clinical practice.

Priorities:

- Create financial incentives for hospitals to improve infection prevention and control
- Include specific infection-related practices in conditions of participation
- Expand reporting and disclosure for hospital infections

These three priorities will leverage CMS's purchasing power to address problems with antibiotic misuse and overuse by hospitals.

2. FDA

The FDA is a publicly visible watchdog for food and drug safety. It determines which drugs and medical devices may be sold in the United States. As part of the approval process, the FDA demands extensive information from drug and device developers on safety and efficacy.¹⁰¹ The FDA can specify the labeled uses for a drug or device, but it has essentially no control over how drugs or devices are actually prescribed by physicians once on the market. Unlike its substantive regulatory authority over drug sales, moreover, its ability to restrict marketing of off-label uses to physicians is limited by the First Amendment.

For approved drugs whose risks can be reduced by patient monitoring, the FDA can impose restrictions that affect how the product is distributed (the RiskMAP program).¹⁰² The FDA also engages regularly in public education campaigns and has already done so with respect to antibiotic overuse. It recently held hearings on antibiotic resistance,¹⁰³ and its Center for Drug Evaluation and Research is the focal point for FDA activities with regard to the problem.¹⁰⁴

The FDA can reduce inappropriate use of antibiotics by narrowing approved labeling or imposing conditions on distribution. However, the difficulty of obtaining FDA approval and the scope of approved uses affects the incentives of companies to develop, test, and market new drugs. As a result, FDA efforts to rationalize antibiotic use and improve long-term effectiveness of existing drugs are in tension with the desire to stimulate antibiotic development.

The FDA also regulates the amount of antibiotic residue that may be found in food products. However, a 2008 proposal to ban the use of cephalosporins in animal feed was withdrawn shortly before it was to go into effect.¹⁰⁵

101. See The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective, <http://www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm143534.htm> (last visited Jan. 10, 2010).

102. See Guidance for Industry Development and Use of Risk Minimization Action Plans, http://www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4136b1_03_Risk%20Minimization%20Action%20Plans.pdf (last visited Jan. 10, 2010).

103. See *Public Hearing*, *supra* note 78, at 20,310.

104. About the Center for Drug Evaluation and Research, <http://www.fda.gov/AboutFDA/CentersOffices/CDER/default.htm> (last visited Jan. 18, 2010).

105. FDA Revokes Order Prohibiting Extralabel Use of Cephalosporin (Nov. 25, 2008), <http://www.fda.gov/AnimalVeterinary/NewsEvents/CVMUpdates/ucm054431.htm>.

The FDA model can be contrasted with that of the DEA, which enforces federal laws concerning controlled substances. To date, the DEA's involvement with the practice of medicine has focused on the diversion and misuse of pain medication. Some of its efforts have been harshly criticized for targeting legitimate pain control practitioners.¹⁰⁶ Although antibiotics have never been treated as controlled substances, the DEA presents a cautionary tale of the consequences if there are doubts as to the merits of a regulatory regime, particularly if it relies on the criminal law to achieve its ends.

Priorities:

- Work with drug makers to develop voluntary codes regarding antibiotic marketing
- Produce more extensive educational materials for physicians and patients
- Work with USDA to reduce unwarranted use of antibiotics in food production¹⁰⁷
- Seek authority from Congress to directly control uses of antibiotics and other drugs where uncontrolled use compromises effectiveness

3. National Institutes of Health

The National Institutes of Health (NIH) is the primary federal agency for performing and supporting biomedical research. NIH is composed of twenty-seven Institutes and Centers, the most relevant of which to antibiotic resistance is the National Institute of Allergy and Infectious Disease (NIAID).¹⁰⁸ NIAID receives a budget of roughly \$4.7 billion per year, or roughly fifteen percent of the total NIH

106. See, e.g., Marc Kaufman, *DEA Revises Rule on Prescribing Painkillers*, WASH. POST, Sept. 7, 2006, <http://www.washingtonpost.com/wp-dyn/content/article/2006/09/06/AR2006090601756.html>.

107. We note that a similar recommendation was made by the Institute of Medicine in 1992. See EMERGING INFECTIONS: MICROBIAL THREATS TO HEALTH IN THE UNITED STATES 23 (Joshua Lederberg et al. eds., 1992) [hereinafter EMERGING INFECTIONS] ("The committee recommends that clinicians, the research and development community, and the U.S. government (Centers for Disease Control, Food and Drug Administration, U.S. Department of Agriculture, and Department of Defense) introduce measures to ensure the availability and usefulness of antimicrobials and to prevent the emergence of resistance. These measures should include the education of health care personnel, veterinarians, and users in the agricultural sector regarding the importance of rational use of antimicrobials (to preclude their unwarranted use), a peer review process to monitor the use of antimicrobials, and surveillance of newly resistant organisms.").

108. NIH Organization, <http://www.nih.gov/about/organization.htm> (last visited Jan. 18, 2010).

budget.¹⁰⁹ NIAID funds various grants and contracts to study antimicrobial resistance, including basic and translational research, and clinical trials.¹¹⁰ Concern has been raised that, in recent years, NIAID has been overly focused on research against bioterrorism, although NIAID representatives have asserted that additional funding for biodefense has complemented existing research work.¹¹¹

Priorities:

- Perform intramural research on antimicrobial resistance and infection control
- Refine resistance-related topics of interest for extramural research funding

4. Centers for Disease Control

The Centers for Disease Control (CDC) is the federal agency that identifies and addresses epidemics and outbreaks of infectious disease. Composed of six coordinating centers, it conducts epidemiologic investigations and develops and implements disease prevention and control campaigns.¹¹² The CDC also provides assistance to other countries experiencing outbreaks of communicable diseases.

The CDC is generally the lead agency on federal drug-resistance initiatives, including the interagency task force on the problem.¹¹³ In this role, it defines the standards for identifying healthcare-associated infections and collects data from hospitals that participate in the National Healthcare Safety Network.¹¹⁴ At present, roughly 1000 hospitals and outpatient dialysis centers voluntarily report outcome data on central line-associated bloodstream infections, surgical site infections, catheter-associated urinary tract infections, and

109. See FY 2010 Budget, <http://www3.niaid.nih.gov/about/whoWeAre/budget/PDF/FY2010CJ.pdf> (last visited Jan. 10, 2010).

110. NIAID's Role in Addressing Antimicrobial (Drug) Resistance, <http://www3.niaid.nih.gov/topics/antimicrobialResistance/> (last visited Jan. 18, 2010).

111. Open Letter in *Science* Regarding NIH Biodefense Funding (Mar. 17, 2005), <http://www3.niaid.nih.gov/news/newsreleases/2005/scienceletter.htm>.

112. See CDC Fact Sheet, <http://www.cdc.gov/about/resources/facts.htm> (last visited Jan. 18, 2010).

113. ANTIMICROBIAL RESISTANCE INTERAGENCY TASK FORCE 2007 ANNUAL REPORT (2008), available at http://www.cdc.gov/drugresistance/actionplan/2007_report/index.html; see also Action Plan, *supra* note 16.

114. See About NHSN, <http://www.cdc.gov/nhsn/about.html> (last visited Jan. 18, 2010). The NHSN started in 2005. It replaced the National Nosocomial Infections Surveillance System, which started in the 1970s.

pneumonia.¹¹⁵ The CDC releases results as aggregate rates for different types of infections and does not disclose hospital-specific information. Hospitals can risk-adjust their own results in order to see how they compare to other participating hospitals. The CDC also publishes guidelines for infection prevention and control,¹¹⁶ and maintains the strategic national stockpile of antibiotics and other medical supplies, to be used in the event of a public health emergency.¹¹⁷

Priorities.

- Coordinate regional infection control and treatment practices
- Refine infection reporting systems for hospitals, with possible public disclosure
- Expand public education efforts
- Maintain strategic drug stockpiles

5. Agency for Healthcare Research and Quality

The Agency for Healthcare Research and Quality (AHRQ) is the lead federal agency for issues of healthcare quality. Its goals include encouraging safety and quality (by promoting delivery of the best possible healthcare), improving effectiveness (by encouraging the practice of evidence-based medicine), and increasing efficiency in the delivery of healthcare services.¹¹⁸ It has funded research into improving the use of antibiotics, issued reports describing ways of improving antibiotic usage, and sponsored educational campaigns aimed at physicians and patients regarding the problem of antibiotic resistance.¹¹⁹ AHRQ also sponsors the Healthcare Cost and Utilization Project (HCUP), a compendium of healthcare databases.¹²⁰ HCUP has

115. See Jonathan R. Edwards et al., *National Healthcare Safety Network (NHSN) Report, Data Summary for 2006-2007, Issued November 2008*, 36 AM. J. INFECTION CONTROL 609, 610 tbl.1 (2008).

116. Infection Control Guidelines, <http://www.cdc.gov/ncidod/dhqp/guidelines.html> (last visited Jan. 18, 2010). These guidelines are developed with the help of an advisory group. See Healthcare Infection Control Practice Advisory Committee (HICPAC), <http://www.cdc.gov/ncidod/dhqp/hicpac.html> (last visited Jan. 18, 2010); see also Healthcare-Associated Methicillin Resistant *Staphylococcus Aureus* (HA-MRSA), http://www.cdc.gov/ncidod/dhqp/ar_mrsa.html (last visited Jan. 18, 2010).

117. See *supra* note 87 and accompanying text.

118. See What Is AHRQ?, <http://www.ahrq.gov/about/whatis.htm> (last visited Jan. 18, 2010).

119. See *id.*

120. See Overview of HCUP, <http://www.hcup-us.ahrq.gov/overview.jsp> (last visited Jan. 18, 2010).

been used to generate surveillance reports on antibiotic-resistant infections.¹²¹

Priorities:

- Fund comparative effectiveness research on avoiding, controlling, and treating drug-resistant infections
- Develop national data sets on causes and consequences of antibiotic resistance

6. Public Health Service

The Public Health Service (PHS) is composed of a Commissioned Corps of more than 6000 uniformed officers.¹²² PHS officers are health professionals who perform a wide variety of tasks and serve in many different settings, including direct provision of care to underserved communities and emergency response, such as outbreaks of communicable diseases. Roughly half the PHS Commissioned Corps is assigned to the CDC.

Priorities:

- Use PHS officers to assess antibiotic resistance patterns and associated infection control and treatment
- Work with local physicians and hospitals in PHS settings to coordinate and improve community practices

7. Veterans Health Administration

The Veterans Health Administration (VA) provides treatment for approximately 5.5 million military veterans through a network of hospitals and outpatient centers.¹²³ After years of periodic scandals regarding quality of care, the VA made substantial improvements during the 1990s.¹²⁴ Veterans generally remain in the VA system for many years, and care within the VA is more integrated than in much of the rest of the healthcare system. The VA can implement top-down

121. See, e.g., ANNE ELIXHAUSER & CLAUDIA STEINER, AHRQ, INFECTIONS WITH METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA) IN U.S. HOSPITALS, 1993-2005, STATISTICAL BRIEF #35 (2007), available at <http://www.hcup-us.ahrq.gov/reports/statbriefs/sb35.pdf>.

122. See About the Commissioned Corps, <http://www.usphs.gov/aboutus/questions.aspx#whatis> (last visited Jan. 10, 2010).

123. See VA Benefits & Health Care Utilization (Aug. 3, 2009), http://www1.va.gov/vetdata/docs/4X6_summer09_sharepoint.pdf.

124. See generally Gary J. Young, Martin P. Charns & Galen L. Barbour, *Quality Improvement in the US Veterans Health Administration*, 9 INT'L J. FOR QUALITY HEALTH CARE 183 (1997) (discussing quality improvement efforts within the VA).

strategies that are rarely available in private medical practice, such as strict limits on antibiotic usage and universal MRSA screening of patients admitted to specified clinical units.¹²⁵

Priorities:

- Serve as pilot site for infection-control innovations
- Serve as pilot site for health information technologies that monitor infection control and antibiotic use
- Develop systems to assess and address outpatient care practices and physician-hospital linkages
- Work with the Department of Defense (the Tricare program) on coordinated infection prevention and treatment practices for active duty military, military dependents, and veterans

8. Patent Law

The United States Constitution authorizes the issuance of patents to promote the progress of the “useful arts.”¹²⁶ The U.S. Patent and Trademark Office issues patents to individuals or entities that invent or discover “any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof.”¹²⁷ The patent term is generally twenty years from the date of application. A patent confers the right to “exclude others from making, using, offering for sale, or selling” the invention in the United States or “importing” the invention into the United States.¹²⁸ The patent holder is responsible for enforcing the patent. Both drugs and medical devices are routinely patented, although the usable term of the patent is much shorter than the statutory term after subtracting the time required to obtain FDA approval. As discussed above, patent law is a blunt instrument for making policy.

Priorities:

- Evaluate patent law changes to extend patent rights for narrowly marketed and used antibiotics

9. Internal Revenue Service (IRS)

The tax system creates financial incentives that shape various aspects of the healthcare marketplace. A tax credit for expenditures on

125. *VA National Campaign Takes Aim at Resistant Staph Infections*, MED. NEWS TODAY, Oct. 19, 2007, <http://www.medicalnewstoday.com/articles/86035.php>.

126. U.S. CONST. art. I, § 8, cl. 8.

127. 10 U.S.C. § 101 (2006).

128. 35 U.S.C. § 154(a)(1) (2006).

research and development induces companies to innovate. A tax exemption for nonprofit hospitals enables those institutions to provide community benefits. A tax exclusion for employment-based health coverage promotes risk pooling through one's employer and reduces sensitivity to rising medical costs. Because nonprofit hospitals play a central role in both breeding and controlling drug-resistant infections, tax law has the potential to increase private investment in improvement.

Priorities:

- Incorporate hospitals' efforts to prevent and control community-based infections into IRS standards for reviewing charitable activities of tax-exempt organizations

10. Department of Labor

Pursuant to ERISA, the U.S. Department of Labor (DOL) regulates employment-based health insurance. Employment-based coverage provides health insurance for roughly sixty percent of the U.S. population.¹²⁹ ERISA distinguishes between employee benefit plans that are self-funded by sponsoring employers and those that are insured by commercial insurance companies. Self-funded plans are regulated solely by the DOL, while both the DOL and state insurance commissioners regulate insured plans.

Priorities:

- Interface with state insurance departments to examine the relationship between health benefit design and infection prevention and treatment practices

11. Office of Personnel Management

The Office of Personnel Management (OPM) is responsible for handling personnel arrangements for roughly 2.7 million federal employees.¹³⁰ Through its administration of the Federal Employee Health Benefits Program, OPM can regulate the terms and conditions of the coverage made available to federal employees nationwide.

129. CARMEN DENAVAS-WALT ET AL., U.S. CENSUS BUREAU, INCOME, POVERTY, AND HEALTH INSURANCE COVERAGE IN THE UNITED STATES: 2008, P60-236(RV) 23 fig.7 (2008), <http://www.census.gov/prod/2009pubs/p60-236.pdf>.

130. FEDERAL CIVILIAN WORKFORCE STATISTICS, THE FACT BOOK: 2007 EDITION, <http://www.opm.gov/feddata/factbook/2007/2007FACTBOOK.pdf> (last visited Jan. 10, 2010).

Priorities.

- Work with private health plans to improve benefit design and provider oversight regarding infection prevention and control

B. State and Local Government

State and local government interventions typically have strengths and weaknesses inverse to those discussed above for federal regulation. States tend to have closer connections to the problems they regulate, which allow them to adapt to local conditions and to improve both compliance and enforcement. New approaches to national problems can be tested in state “laboratories.” This diversity of approach, however, can produce large disparities in outcomes across states and may motivate a “race to the bottom.”¹³¹ States are also limited in their ability to borrow, which increases pressure to cut spending in economic downturns. Because of the federal government’s fiscal advantages, state health insurance programs such as Medicaid and the State Children’s Health Insurance Program (SCHIP) are largely federally funded and are subject to federal minimum requirements while otherwise being defined and administered at the state level.

Insofar as genes for antibiotic resistance and resistant bacteria themselves can spread nationally and often internationally, states and localities would not seem a good fit for the problem. On the other hand, resistant infections often cluster within particular health facilities, with bacterial agents continually reintroduced from reservoirs in surrounding communities. Successful initiatives by hospitals working together in cities or counties to curb infections suggest that some resistance may be associated with “germsheds” analogous to the airsheds and watersheds routinely used to motivate and organize pollution-control efforts.

State governments also possess specific advantages for regulating infectious disease. Infection control is a core function of state departments of public health, which have in place a comprehensive legal mandate, physical infrastructure, and professional workforce for disease prevention, surveillance, detection, evaluation, and treatment. States, not the federal government, set and enforce licensing requirements—including drug prescribing privileges—for physicians, nurses, pharmacists, and other health professionals. Similarly, states

131. The empirical evidence on a race to the bottom in corporate governance is mixed; many scholars believe there is a “race to the top,” or a “race to nowhere in particular.” It is not obvious why a state would vie to have more antimicrobial resistance, since the costs would be disproportionately borne by its own citizens.

license and monitor hospitals, nursing homes, and other health facilities, often using periodic on-site inspections (called survey and certification). States also determine provider payment and benefit design for populations enrolled in Medicaid and SCHIP, accounting for large blocks of nursing home and obstetric care as well as substantial amounts of other health services. In addition, subsidized prescription drug programs for poorer residents give states significant influence over pharmaceutical practices. Finally, pursuant to the McCarran-Ferguson Act, states have primary regulatory authority over health insurance sold to state residents.¹³²

Priorities.

- Increase funding for state public health departments to develop, disseminate, and educate the public about infection prevention and control, including appropriate antibiotic use
- Focus state boards of medicine on educating physicians about antibiotic prescribing
- Develop and refine state department of health oversight of infection control in hospitals and other healthcare facilities, including public disclosure of reported infections
- Prioritize reducing infection risks in skilled nursing facilities as a state Medicaid initiative, perhaps with federal coordination and oversight
- Engage state insurance departments to work with one another and with the DOL on health insurance benefit design to reduce resistant infections

C. Self-Regulation

Self-regulation by the medical profession has been the dominant mode of health system oversight for over a century.¹³³ Federal and state healthcare regulation frequently occurs through or in conjunction with self-regulation, which has expanded beyond physicians to many other healthcare providers and suppliers. Self-regulation may be preferable to direct government control when technical expertise is required, cooperation from the regulated entities is important, or the regulated industry is undergoing rapid structural change. Self-regulation may be

132. See 15 U.S.C. §§ 1011-1015 (2006).

133. See generally Peter D. Jacobson, *Regulating Health Care: From Self-Regulation to Self-Regulation?*, 26 J. HEALTH POL., POL'Y & L. 1165 (2001) (providing an overview of the evolution of healthcare oversight in the United States and discussing arguments both for and against self-regulation).

cheaper than direct regulation if its compliance costs are lower, and always appears less expensive to taxpayers because it is off-budget. On the other hand, self-regulation is often insular, self-serving, and anticompetitive.

Notwithstanding these risks, medicine has historically enjoyed wide latitude to self-regulate because of deference to physician expertise and trust in professional ethics and the charitable mission of nonprofit hospitals. Even nominally governmental mechanisms, such as professional licensing boards, are routinely controlled (de facto, if not de jure) by the regulated entities or individuals. However, public demand for cost control has eroded these self-regulatory privileges to some degree in recent years.

Self-regulation takes various forms, all of which may have potential for attacking the problem of antibiotic resistance. Certification or accreditation systems can be used to implement information disclosure requirements or substantive design and performance standards relating to infection control and antibiotic use. A self-regulatory imprimatur from an accrediting body is typically used to convey information about superior quality or reliability to a purchaser, but can become a de facto minimum quality standard. The Joint Commission, for example, reviews hospital compliance with a host of structural and process measures of quality, and conducts periodic direct inspections. American hospitals are nearly universally accredited because Joint Commission review serves to verify compliance with federal conditions of participation in Medicare and Medicaid. Similar reviews occur for nursing homes, ambulatory surgical centers, and other health facilities, while managed care organizations undergo accreditation from the National Committee on Quality Assurance and other groups.

State licensing is necessary but not sufficient for modern medical practice. Advanced health professional certification operates through a parallel system of self-regulatory organizations, and focuses more on past training than on current practice environment or processes of care. Most U.S. physicians have specialty training, with credentials issued by medical specialty boards following examination, which occurs after completion of graduate programs that themselves are accredited by residency review committees. Additional certifications are available from a variety of organizations and attest to particular skills or education. Unlike medical licensure, none of these credentials have formal legal status, but physicians who lack them may find it difficult to secure admitting or procedural privileges in hospitals and to obtain

participating provider contracts from managed care organizations. Other health professionals and public health professionals have similar self-regulatory mechanisms in place.

Each of these mechanisms may be useful in reorienting health professional education toward proper use and stewardship of antibiotics. These mechanisms can also be used to improve infection control, both generally and for the purpose of designating specially trained individuals to whom use of the most powerful antibiotics might be entrusted.

Clinical practice guidelines are another common self-regulatory approach potentially adaptable to reducing antibiotic resistance. Traditions of physician autonomy and customized treatment were long considered incompatible with prescriptive approaches to medical management. However, research demonstrating unexplained (and almost certainly unwarranted) practice variation, coupled with pressure for cost containment, has greatly increased interest in guidelines. Guidelines are rarely mandatory, but are influential with patients, insurers, and policymakers. However, because competing guidelines are issued by generalist physicians, competing specialists, and insurance groups, even guided practice is strikingly variable.

Several well-respected entities have constructed guidelines (or issued reports similar to guidelines) that bear on antibiotic resistance.¹³⁴ Most recently, three epidemiological societies joined with the American Hospital Association and the Joint Commission on the Accreditation of Healthcare Organizations (JCAHO or Joint Commission) to issue a compendium of guidelines on ways to prevent infection.¹³⁵ The Joint Commission and its members have also developed several infection-control initiatives, including performing a root cause analysis of infection-control related sentinel events,¹³⁶ encouraging hand washing,¹³⁷ and preparing a compendium of strategies to prevent hospital-acquired infections.¹³⁸

134. See, e.g., EMERGING INFECTIONS, *supra* note 107 (reporting on antimicrobial resistance and recommending alternative courses of action).

135. Kevin Sack, *Infection Control Guidelines Issued*, N.Y. TIMES, Oct. 9, 2008, at A21, available at <http://www.nytimes.com/2008/10/09/us/09infection.html?ref=us>.

136. See generally Infection Control Related Sentinel Events (Jan. 22, 2003), http://www.jointcommission.org/SentinelEvents/SentinelEventAlert/sea_28.htm (detailing numerous strategic facilities implemented to reduce the risk of patients acquiring infections in a healthcare setting).

137. See MEASURING HAND HYGIENE ADHERENCE: OVERCOMING THE CHALLENGES 1-5 (2009), http://www.jointcommission.org/NR/rdonlyres/68B9CB2F-789F-49DB-9E3F-2FB387666BCC/0/hh_monograph.pdf.

138. See Yokoe et al., *supra* note 86.

Self-regulation often operates locally as well, with internal monitoring and compliance systems either being self-imposed or expressly required by government. Acute care hospitals are the most common sites for internal self-regulation, much of which is essentially made mandatory by Joint Commission accreditation standards.

Hospital credentialing is another important self-regulatory mechanism. Physicians undergo strict initial and periodic review in order to gain the right to admit patients to a given hospital, thereby joining the medical staff. Hospitals have internal oversight committees, composed of medical staff physicians and other expert professionals, to deal with avoidable morbidity and mortality, surgical facilities, infection control, and drug therapies—all of which have responsibility for areas that implicate antibiotic resistance. A secular trend away from “open” medical staffs (independent physicians practicing at several hospitals concurrently) and toward exclusive relationships between physicians and community hospitals, along with the emergence of “hospitalists” (who limit their practices to hospitalized patients and do not maintain private offices) is likely to increase the potential effectiveness of these institutional compliance systems over time.

Professional norms that influence rates of medical error have already begun to change, particularly for low-technology interventions such as proper patient identification. For example, norms regarding hand washing, use of sterile barriers for intravenous line placement, and care of indwelling catheters are all important to reducing resistant infections.¹³⁹ Other relevant norms are connected more to medical ethics than to microbiology. Notably, contemporary ethics that orient physicians only to the immediate benefit of the individual patient under their direct care may need to be modified, if not superseded, by

139. Unfortunately, those norms have historically been lacking. See Sack, *supra* note 135, at A21 (“Epidemiologists contend that the challenge in reducing hospital infections, which are said to attack one of every 22 patients, has not been a dearth of guidelines but a lack of adherence. A survey of hospitals last year by The Leapfrog Group, which advocates for health-care quality, found that 87 percent did not consistently follow infection-control guidelines. Studies have found that half of hospital workers do not follow hand-washing protocols. . . . ‘Too often where we fail is not in the knowledge but in the execution,’ said Dr. Patrick J. Brennan, chairman of the federal Healthcare Infection Control Practices Advisory Committee, which supports the effort.”); LORRAINE MOONEY & ROGER BATE, FIRST, DO NO HARM: THE TOLL OF UNHEALTHY HEALTH CARE PRACTICES, AEI HEALTH POLICY OUTLOOK NO. 13 (2007), http://www.aei.org/docLib/20071010_22255HPO13MooneyBate_g.pdf (“For too long, the medical and public health professions have regarded incidental infection as an acceptable side effect. Even now, the problem is obscured by language—nosocomial; iatrogenic; hospital- or health care-acquired infection—and by statistics which are difficult to put into context.”).

norms of population health management and stewardship of scarce resources.

Consumers and patients seldom have a direct voice in medical self-regulatory organizations, although they may be entitled to representation. Nonetheless, consumer and public interest groups can be important catalysts in addressing the problem of antibiotic resistance. Consumer groups that have issued statements or position papers on the problem of antibiotic resistance include Consumers Union,¹⁴⁰ the Center for Science in the Public Interest,¹⁴¹ and the Committee to Reduce Infection Deaths.¹⁴²

D. Private Tort Litigation

In the United States, an ad hoc mixture of public law (such as the Medicare program) and private law (such as litigation over contractual agreements or personal injuries) is used to accomplish healthcare oversight. Medical malpractice litigation is highly salient to American physicians, and therefore bears discussion in connection with alterations of their clinical practices. Product liability lawsuits are equally important to makers of drugs, medical devices, vaccines, and diagnostic tests.

Private tort litigation, under state law and generally in state court, might be initiated by individuals seeking compensation for negligent treatment. One set of claims could be based on a hospital's failure to protect the patient from contracting a drug-resistant infection or its failure to treat adequately an infection that occurred. Alternatively, claims might be brought against healthcare providers who exercise responsible stewardship of antibiotics, alleging that they negligently misdiagnosed what turned out to be a serious infection and therefore incorrectly withheld treatment with the most powerful drug possible. In cases like these, injured plaintiffs can recover both economic damages (lost earnings and cost of subsequent medical treatment) and noneconomic damages (pain and suffering). In theory, the obligation to compensate injured plaintiffs deters defendants from providing negligent treatment in the first place.

140. CONSUMERS UNION, STOP HOSPITAL INFECTIONS (2009), http://www.safepatientproject.org/cutting_surgical_infection.pdf.

141. Antibiotics in Jeopardy, http://www.cspinet.org/ar/antibiotics_jeopardy.html (last visited Jan. 18, 2010).

142. See Betsy McCaughey, *Doctors, Wash Your Hands*, L.A. TIMES, Feb. 3, 2007, at 19, available at <http://articles.latimes.com/2007/feb/03/opinion/oc-mccaughey3>.

Lawsuits against corporations such as pharmaceutical manufacturers are governed by similar standards, although punitive damage awards are more common than in claims involving individual physicians or hospitals. Unlike healthcare providers, product manufacturers are strictly liable for injuries arising from defects if they fail to provide adequate warning. Although the law continues to evolve, drug makers can be sued for failure to warn adequately even when a product has received FDA approval.¹⁴³ The National Childhood Vaccine Injury Compensation Act of 1988 protects vaccine manufacturers from litigation: before filing suit, persons injured by vaccines must seek no-fault administrative compensation through the DHHS, the Department of Justice, and the U.S. Court of Federal Claims.¹⁴⁴

Courts labor under significant institutional constraints that hinder their ability to address the problem of antibiotic resistance effectively.¹⁴⁵ Although some plaintiff lawyers advertise for clients injured by hospital-acquired infections,¹⁴⁶ and there have been some extremely large verdicts in cases involving MRSA infection,¹⁴⁷ relatively few lawsuits have been brought against healthcare providers despite considerable publicity and large numbers of affected patients. As a result, the cases that courts encounter are likely unrepresentative of the larger pool of injuries.

To bring a claim, an aggrieved patient must find a lawyer willing to take the case. Many of those injured by drug-resistant infections are elderly, resulting in lower damages, particularly in states with damages caps.¹⁴⁸ Most cases also raise difficult issues of causation and standard of care, including proving that a particular defendant is responsible for a particular infection. Tort cases are brought before nonspecialty courts, who view each case and the range of acceptable remedies in

143. See, e.g., *Wyeth v. Levine*, 129 S. Ct. 1187, 1191 (2009).

144. See 42 U.S.C. § 300aa-11 (2006).

145. Pamela Nolan, *Unclean Hands: Holding Hospitals Responsible for Hospital-Acquired Infections*, 34 COLUM. J.L. & SOC. PROBS. 133 (2000); Jennifer M. Miller, Commentary, *Liability Relating to Contracting Infectious Diseases in Hospitals*, 25 J. LEG. MED. 211 (2004).

146. See, e.g., Kershaw Cutter Ratinoff LLP, *Hospital Infections*, <http://www.kcrlegal.com/legalspecialties/medicalmalpractice/hospital-infections.asp> (last visited Jan. 18, 2010).

147. Poliakoff & Assoc., P.A., *MRSA Verdict Lowered Because of Tort Reform* (Mar. 7, 2009), <http://www.scnursinghomelaw.com/2009/03/articles/tort-reform/mrsa-verdict-lowered-because-of-tort-reform/>; Case Report: *Death from MRSA Results in Million Dollar Verdict* (Aug. 17, 2007), <http://legalmedicine.blogspot.com/2007/08/case-report-death-from-mrsa-results-in.html>.

148. David A. Hyman et al., *Estimating the Effect of Damages Caps in Medical Malpractice Cases: Evidence from Texas*, 1 J. LEGAL ANALYSIS 355, 356-57 (2009).

isolation. Defendants are often willing to pay more for a confidential settlement, which means that other injured persons and other healthcare providers may not receive information about risks and injuries.¹⁴⁹ Finally, the transaction costs of resolving disputes through the tort system are extremely high.

VI. CONCLUSION

Profligate use of antibiotics over the past several decades has created risks of resistant infection that affect everyone. No magic medical bullet exists to eradicate these risks; neither is there a magic regulatory bullet. Still, judicious regulation can help ensure that antibiotics are reserved for circumstances where they are needed, and that the most appropriate treatment is provided.

In our expensive and disorganized healthcare system, a multipronged approach to antibiotic resistance seems necessary. Priority should be given to measures that will also help improve the accessibility and cost-effectiveness of American healthcare more generally. Early experience with particular approaches, properly evaluated, should guide further regulation. Whatever regulatory strategy is pursued, it must synchronize with current and future institutional capacity for it to work effectively. Otherwise, it will be very difficult to implement, and equally difficult to make the numerous ongoing adjustments that will be necessary. Should that occur, we will soon experience a real tragedy of the commons.

149. Jack Dolan & Dave Altimari, *Court Order Silences Victims: Hospital Sues over Families' Comments*, HARTFORD COURANT, July 26, 2002, at A1.