INTELLECTUAL PROPERTY AND THE FREEDOM NEEDED TO SOLVE THE CRISIS OF RESISTANT INFECTIONS

Gregory Salmieri[*]

INTRODUCTION

The increasing prevalence of antimicrobial-resistant infections is a dire and well-known crisis.[1] This Article argues that one reason this problem persists is that existing law does not recognize, define, and protect an intellectual property ("IP") right that would enable innovators to profit from creating new antimicrobial drugs and creating and implementing the protocols and business practices needed to use these treatments wisely. The current patent regime under which the creators' rights to these drugs are protected recognizes only a fraction of the intellectual work that goes into creating and maintaining the value of these drugs. In particular, it fails to recognize that, unlike other patentable inventions, antimicrobial treatments require continued intellectual work to retain their effectiveness. Currently, there is no way for anyone to capture the value created by this continued intellectual work, and so creating and stewarding antimicrobials is unprofitable, with the result that there is little investment in these activities. This problem could be addressed by legally defining and implementing an IP right in such drugs that functions like a patent, except that it is renewable indefinitely so long as it can be demonstrated that the treatments remain effective.

Part I of this Article reviews the problem of antimicrobial-resistant bacteria and some of the existing proposals to address it. Part II argues that the problem has structural features that suggest the need to recognize a property right of the sort indicated in Part I. Part III then discusses how such a right might be defined and implemented and addresses how some difficulties with this proposal might be resolved.

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[*] Ph.D., Philosophy, 2008, University of Pittsburgh; B.A. 2001, The College of New Jersey. Fellow, The Anthem Foundation for Objectivist Scholarship; Lecturer, Philosophy Department, Rutgers University. The Author would like to acknowledge several friends for their help or inspiration on this piece: Jonathan Anomaly, for a discussion many years ago that first stimulated some of the thoughts expressed herein; Adam Mossoff, for a wealth of information on IP law, and for an invitation to the conference where an earlier version of this paper was presented; Amesh Adalja, for sharing his wisdom concerning the medical issues discussed herein; and Maryah Haidery, for assistance with research and fact checking.

[1] CTR. FOR DISEASE CONTROL & PREVENTION, U.S. DEP'T OF HEALTH & HUMAN SERVS., ANTIBIOTIC RESISTANCE THREATS IN THE UNITED STATES 6 (2013), https://www.cdc.gov/drugresistance/threat-report-2013/pdf/ar-threats-2013-508.pdf.

I. THE STATE OF THE CRISIS AND OF PROPOSED SOLUTIONS

According to a 2013 report by the Center for Disease Control ("CDC"), two million people in the United States annually contract infections that are "resistant to one or more of the antibiotics designed to treat those infections"; the result is at least 23,000 deaths and (direct and indirect) economic losses that have been estimated at $55 billion (in 2008 dollars).[2] The United Kingdom's Antimicrobial Resistance Review estimates that, worldwide, there will be as many as ten million deaths annually from such infections by 2050.[3] A 2017 report by the World Bank Group anticipates the financial toll:

> In the optimistic case of low AMR [antimicrobial resistance] impacts, the simulations found that, by 2050, annual global gross domestic product (GDP) would likely fall by 1.1 percent, relative to a base-case scenario with no AMR effects; the GDP shortfall would exceed $1 trillion annually after 2030. In the high AMR-impact scenario, the world will lose 3.8 percent of its annual GDP by 2050, with an annual shortfall of $3.4 trillion by 2030.[4]

There are two related aspects to this crisis: (1) bacterial populations are evolving resistance to the antimicrobial drugs currently in use, and (2) there are few new drugs in the developmental pipeline that promise to be effective against these bacteria.[5] It is widely understood that both aspects are caused or exacerbated by the economic incentives faced by the pharmaceutical industry and the healthcare industry more broadly.[6]

The eventual obsolescence of any conventional antimicrobial drug is inherent in its use, but it is hastened when the drug is liberally prescribed.[7] Such liberal prescription is driven by incentives for both physicians and pharmaceutical companies. Patients' expectations for prompt treatment sometimes lead doctors to prescribe broad-spectrum antibiotics in cases where it would be more prudent to await testing and prescribe a more targeted antimicrobial—or to prescribe antibiotics for viral infections where they are ineffective.[8] Pharmaceutical companies have an incentive to sell as much

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2 *Id.* at 11.

3 JIM O'NEILL, REVIEW ON ANTIMICROBIAL RESISTANCE, TACKLING DRUG-RESISTANT INFECTIONS GLOBALLY: FINAL REPORT AND RECOMMENDATIONS 1 (2016), https://amr-review.org/sites/default/files/160525_Final%20paper_with%20cover.pdf.

4 WORLD BANK GROUP, DRUG-RESISTANT INFECTIONS: A THREAT TO OUR ECONOMIC FUTURE xviii (2017), http://documents.worldbank.org/curated/en/323311493396993758/pdf/114679-REVISED-v2-Drug-Resistant-Infections-Final-Report.pdf.

5 Katherine H. Luepke et al., *Past, Present, and Future of Antibacterial Economics: Increasing Bacterial Resistance, Limited Antibiotic Pipeline, and Societal Implications*, 37 PHARMACOTHERAPY: J. OF HUM. PHARMACOLOGY & DRUG THERAPY 71, 73 (2016).

6 *Id.*

7 *Id.* at 75.

8 *See* Scott Fridkin et al., *Vital Signs: Improving Antibiotic Use Among Hospitalized Patients*, 63 CDC MORBIDITY & MORTALITY WEEKLY REPORT 194, 195 (2014), https://www.cdc.gov/mmwr/pdf/wk

volume as possible in the period between the drug's Food and Drug Administration ("FDA") approval and the end of its twenty-year patent term.

The problem of liberal prescription of antibiotics has been much discussed in medical and policy circles.[9] It is widely agreed that an important part of the solution is antimicrobial stewardship, which the Infectious Diseases Society of America defines as follows:

> Antimicrobial stewardship refers to coordinated interventions designed to improve and measure the appropriate use of antimicrobials by promoting the selection of the optimal antimicrobial drug regimen, dose, duration of therapy, and route of administration. The major objectives of antimicrobial stewardship are to achieve optimal clinical outcomes related to antimicrobial use, to minimize toxicity and other adverse events, to reduce the costs of health care for infections, and to limit the selection for antimicrobial resistant strains.[10]

The most dramatic outcome thus far of the policy discussion, in the United States at least, is that the Centers for Medicare and Medicaid Services updated its "Conditions of Participation."[11] These updated "Conditions of Participation" (issued as a result of an executive order by President Obama in 2014) require all hospitals participating in Medicare and Medicaid to establish and maintain "antibiotic stewardship programs."[12] These conditions are already in effect for acute care hospitals and are expected to go into effect generally by the end of 2018.[13]

An additional incentive for too liberal use of antibiotics comes from outside of the healthcare industry. These drugs are useful as a growth promoter for livestock, and it has been shown that this use can lead to the growth

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9 *See generally National Action Plan for Combating Antibiotic-Resistant Bacteria*, THE WHITE HOUSE, https://obamawhitehouse.archives.gov/sites/default/files/docs/national_action_plan_for_combating_antibotic-resistant_bacteria.pdf (last visited June 25, 2018); *Joint Commission Joins White House Effort to Reduce Antibiotic Overuse*, JOINT COMM'N (2015), https://www.jointcommission.org/issues/article.aspx?Article=EqU%2FoSnu4hkAXIwCvF1YSDJ0WYDkPhDcUx31eV%2FmOnM%3D; Fridkin, *supra* note 8.

10 Brad Spellberg et al., *Combating Antimicrobial Resistance: Policy Recommendations to Save Lives*, 52 CLINICAL INFECTIOUS DISEASES S397, S413 (2011); *see also* sources listed *supra* note 9.

11 Zahra Kassamali, *Antimicrobial Stewardship Standards: A Comparison of Centers for Medicare & Medicaid Services and Joint Commission Requirements*, CONTAGION LIVE (Jan. 1, 2017), http://www.contagionlive.com/publications/contagion/2016/december2016/antimicrobial-stewardship-standards-a-comparison-of-centers-for-medicare--medicaid-services-and-joint-commission-requirements?p=1.

12 For President Obama's executive order, see Combating Antibiotic-Resistant Bacteria, Exec. Order No. 13,676, 79 Fed. Reg. 56,931 (Sept. 18, 2014). For the updated Conditions of Participation, see Medicare and Medicaid Programs, 81 Fed. Reg. 63,859 (Sept. 16, 2016) (codified in scattered sections of 42 C.F.R. ch. IV (2017)) and Medicare and Medicaid Programs Correction, 81 Fed. Reg. 80,594 (Nov. 16, 2016) (codified at 42 C.F.R. §§ 482–85).

13 Kassamali, *supra* note 11.

of resistant bacteria, which can then infect human beings.[14] Such use of most antibiotics is now banned in the European Union member states, Mexico, New Zealand, and South Korea.[15] In the United States and Canada, regulatory agencies have issued guidelines against this use of antibiotics that are deemed medically important.[16]

The second aspect of the crisis is the dearth of new antimicrobial drugs in development. A 2017 World Health Organization report projects that approximately ten new antibiotics and biologicals will be approved in the next ten years but warns that "these new treatments will add little to the already existing arsenal" because most of them will be "modifications of existing antibiotic classes," which are "only short term solutions as they usually cannot overcome multiple existing resistance mechanisms and do not control the growing number of pan-resistant pathogens."[17]

Few new antimicrobial drugs are in development because there is a low return on the investment needed to discover such drugs and shepherd them through the approval process. This is the reason why Aventis, Bristol-Myers, Squibb, Eli Lilly, GlaxoSmithKline, Proctor and Gamble, Roche, and Wyeth all "greatly curtailed, wholly eliminated or spun off their antibacterial research" between 1999 and 2003.[18] The already low return on investment will dwindle as stewardship guidelines are adopted and the drugs are prescribed more judiciously.[19]

The Chatham House Working Group on New Antibiotic Business Models summarizes the situation thusly:

> Today, few large pharmaceutical companies retain active antibacterial drug discovery programmes. One reason is that it is scientifically challenging to discover new antibiotics that are active against the antibiotic-resistant bacterial species of current clinical concern. Another core issue, however, is diminishing economic incentives. Increasingly, there are calls to conserve the use of truly novel antibiotics, which might limit sales severely and discourage greater investment in R&D. Meanwhile, unless they see evidence of superiority, healthcare payers are unwilling to pay prices that would directly support the cost of development, provide a

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14 RAMANAN LAXMINARAYAN ET AL., ORG. FOR ECON. CO-OPERATION & DEV., TRADE & AGRIC. DIRECTORATE, COMM. FOR AGRIC. GLOBAL ANTIMICROBIAL USE IN THE LIVESTOCK SECTOR 4 (2015).

15 *Id.*

16 *Id*; *see also* CTR. FOR VETERINARY MED., FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY NO. 213, NEW ANIMAL DRUGS AND NEW ANIMAL DRUG COMBINATION PRODUCTS, ADMINISTERED IN OR ON MEDICATED FEED OR DRINKING WATER OF FOOD-PRODUCING ANIMALS 4 (2013), https://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM299624.pdf; U.S. DEP'T OF AGRIC., ANTIMICROBIAL RESISTANCE ACTION PLAN 4 (2014), https://www.usda.gov/sites/default/files/documents/usda-antimicrobial-resistance-action-plan.pdf.

17 DEP'T OF ESSENTIAL MEDS. & HEALTH PRODUCTS, WORLD HEALTH ORG., ANTIBACTERIAL AGENTS IN CLINICAL DEVELOPMENT: AN ANALYSIS OF THE ANTIBACTERIAL CLINICAL DEVELOPMENT PIPELINE, INCLUDING TUBERCULOSIS 8, 35 (2017), http://www.who.int/medicines/areas/rational_use/antibacterial_agents_clinical_development/en/.

18 Steven J. Projan, *Why Is Big Pharma Getting Out of Antibacterial Drug Discovery?*, 6 CURRENT OPINION MICROBIOLOGY 427 (2003).

19 *Id.* at 428.

> competitive return on investment and reflect the value to society of maintaining a portfolio of antibiotics adequate to overcome growing resistance.
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> A principal reason for this is the mismatch between the current business model for drugs and combating resistance. The current business model requires high levels of antibiotic use in order to recover the costs of R&D. But mitigating the spread of resistance demands just the opposite: restrictions on the use of antibiotics. Economic incentives play a key role in the global resistance problem, leading to overuse of these precious drugs at the same time as companies are abandoning the field; and the increasing restrictions on inappropriate use of antibiotics make them relatively unprofitable compared with other disease areas.[20]

There has been much recent discussion of what changes to public policy might lead to the development of new business models for the development of antimicrobial drugs—models that would make this research profitable while eliminating the pharmaceutical companies' incentives to encourage the too liberal use of their antimicrobial products.[21] Most of the proposals that have been made fall into two broad categories. Proposals of the first sort involve a government or multi-national organization directly rewarding pharmaceutical companies for developing new antimicrobial drugs. The rewards are designed to offset the research and development costs, and on most versions of the proposal, the reward is tied to the company's acceptance of terms designed to promote good stewardship of the drug. "For example, companies would agree to restricted marketing of their drug, transparency of sales volumes, geographic scope of availability, and . . . the per unit price of the antibiotic."[22] In most versions of this approach, the company is awarded a cash prize, either upon market entry or at some other point (or points) in the research and development process.[23] Other variants of this approach involve awarding the company a "transferable exclusivity voucher" (or "wildcard patent") that would extend the company's period of market exclusivity for one of its other (non-antimicrobial) products, thereby enabling it to recoup the money lost on developing an antimicrobial through prolonged exclusive sales of a higher volume and more profitable product.[24]

Such proposals (especially those involving cash prizes) are often described as "delinking" the revenues a company derives from developing an

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20 CHATHAM HOUSE WORKING GROUP ON NEW ANTIBIOTIC BUSINESS MODELS, TOWARDS A NEW GLOBAL BUSINESS MODEL FOR ANTIBIOTICS: DELINKING REVENUES FROM SALES vii (Charles Clift et al. eds., 2015) [hereinafter Clift].

21 *See* Christine Årdal et al., *Pull Incentives for Antibacterial Drug Development: An Analysis by the Transatlantic Task Force on Antimicrobial Resistance*, 65 CLINICAL INFECTIOUS DISEASES 1378, 1379 (2017) (discussing various public policy incentives that governments worldwide are exploring to increase antibacterial drug development).

22 *Id.* at 1378–81.

23 Gregory W. Daniel et al., *Addressing Antimicrobial Resistance and Stewardship: The Priority Antimicrobial Value and Entry (PAVE) Award*, 318 J. AM. MED. ASS'N 1103, 1103–04 (2017).

24 *See* Kevin Outterson & Anthony McDonnell, *Funding Antibiotic Innovation with Vouchers: Recommendations on How to Strengthen a Flawed Incentive Policy*, 35 HEALTH AFFAIRS 784, 784–90 (2016) (discussing several such proposals, their defects, and how these might be partially remedied).

antibiotic from the volume of the antibiotic's sales.[25] But what these proposals have in common is not just the goal of delinking, but the means of accomplishing this via a public policy whereby a government or intergovernmental body devoted to public health awards prizes of some sort to the pharmaceutical companies.

More recently, FDA Commissioner Scott Gottlieb proposed delinking revenues from prescriptions in another way: by moving to a licensing model for certain antimicrobial drugs whereby "the acute care institutions that are most likely to prescribe these medicines would pay a fixed licensing fee for access to the drug, which would offer them the right to use a certain number of annual doses."[26]

The second broad category of proposals involves simply lengthening the term of market exclusivity for antimicrobial drugs. A version of this proposal was implemented in 2012 in the form of the Generating Antibiotics Incentives Now ("GAIN") Act,[27] under which the FDA grants to the creators of antimicrobial drugs intended to treat serious or life-threatening infections five years of market exclusivity beyond the end of the product's patent term. (This is achieved by withholding FDA approval of generic versions of the drugs.[28])

Early indications suggest that the GAIN Act has led to an increase in the number of clinical trials for qualified antimicrobial agents; however, more than half of these trials are for reformulations of old drugs, and it is not clear that the Act has stimulated research in new classes of antimicrobials with new mechanisms of action.[29] Indeed, as of October 2017, five drugs had been granted market exclusivity under the Act, and none of them had a novel mechanism.[30] But it is precisely new classes of drugs and new mechanisms that need to be developed to combat the resistance crisis. (The GAIN Act could, perhaps, be made more useful in this respect, if it were altered so that only the most critically needed drugs qualified for the benefits; proponents of various means of incentivizing antimicrobial development have drawn this

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25 *See* Årdal et al., *supra* note 21; Daniel et al., *supra* note 23.

26 *Statement from FDA Commissioner Scott Gottlieb, M.D., on FDA's Efforts to Foster Discovery and Development of New Tools to Fight Antimicrobial-Resistant Infections,* FOOD & DRUG ADMIN. (June 12, 2018), https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm610503.htm [hereinafter Statement of Gottlieb]. See Part II, *infra*, for suggestions of other means by which delinking might occur.

27 Food and Drug Administration Safety and Innovation Act, Pub. L. No. 112-144, 126 Stat. 993 (2012) (codified in scattered sections of 21 U.S.C. ch. 9 (2012)).

28 *Id.*

29 *Generating Antibiotic Incentives Now*, DEP'T OF HEALTH & HUM. SERVS., 12 (Feb. 2018), https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM595188.pdf; (last visited Jun 25, 2018); Jonathan Slater, *What Is There to GAIN?*, PHARMA INTELLIGENCE (July 12, 2017), https://pharmaintelligence.informa.com/resources/product-content/what-is-there-to-gain.

30 Årdal et al., *supra* note 21.

lesson from the Act and have proposed ways of targeting their incentives accordingly.[31])

The policy solutions discussed so far deal with the two aspects of the resistance problem separately. Some proposals aim to promote better stewardship of existing drugs; others, to incentivize the development of new drugs. The solutions are connected in that some of the rewards proposed to incentivize drug development are made conditional upon pharmaceutical companies accepting conditions or policies aimed at promoting good stewardship, but the specific content of these conditions or policies is unrelated to the incentives themselves.

This Article suggests another sort of solution, which might be described as a way of incentivizing, by means of a single policy change, both the development of new antimicrobials and the responsible stewardship of these drugs. In its simplest form, the solution is to make the patent terms on these drugs extremely long. The solution has been proposed in this form by Professor John Horowitz and Brian Moehring[32] as well as Professor Eric Kades,[33] and it is occasionally mentioned in the existing literature.[34] However, the case for this broad sort of solution has not been adequately articulated or appreciated. The next Part develops the case for a solution of this sort and proposes an alternative version of the solution that is better tailored to the problem and better situated within a theory of IP. Finally, Part III addresses some concerns faced by any solution of this sort.

II. THE RIGHT TO THE VALUE CREATED BY RESPONSIBLE STEWARDSHIP

Consider how the two-fold problem of growing resistance to our current antimicrobial drugs and the dearth of new antimicrobials under development looks once the specifics are omitted. Forget for a moment that the subject is drugs and microbes—or even inventions as opposed to other sorts of property—and just focus on the structure of the predicament.[35] There is a resource of immense value that is being used myopically in a way that destroys

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31 Clift, *supra* note 20, at 12–13.

32 John B. Horowitz & H. Brian Moehring, *How Property Rights and Patents Affect Antibiotic Resistance*, 13 HEALTH ECON. 575, 578 (2004).

33 Eric Kades, *Preserving a Precious Resource: Rationalizing the Use of Antibiotics*, 99 NW. U. L. REV. 611, 654 (2005). Neither of these papers cite the other, so I expect the authors thought of the idea independently of one another, as this Author did before discovering their papers.

34 Kevin Outterson, Julie Balch Samora & Karen Keller-Cuda, *Will Longer Antimicrobial Patents Improve Global Public Health?*, 7 LANCET INFECTIOUS DISEASE 559, 562 (2007); Clift, *supra* note 20, at 4.

35 I am assuming here that IP is property in the same basic sense and for the same fundamental reasons as other forms of property. For a defense of this (admittedly controversial) assumption on the basis of the history of American patent law, see Adam Mossoff, *Commercializing Property Rights in Inventions: Lessons for Modern Patent Theory from Classic Patent Doctrin*e, *in* COMPETITION POLICY AND PATENT LAW UNDER UNCERTAINTY 345 (Geoffrey A. Manne & Joshua D. Wright eds., 2011).

existing stocks of the resource, and little is being done to find or develop new stocks of it.

This is a pattern one expects to see with *unowned* resources, but not with *owned* ones. It is the classic "tragedy of the commons." When a patch of grazing land is owned in common by everyone—which is just to say it is *unowned*—everyone has an incentive to make what use of it he can, leading to its overuse and destroying its value. By contrast, an owner can use land judiciously in ways that preserve its value or even to invest in improving the land. This is possible because the owner has exclusive control of the land in the present and therefore can control its uses, and because the owner expects to reap the benefit of the land's future value. If deeds to land expired after twenty years, with the land reverting to the commons, land owners would have no financial incentives to preserve or enhance the land's value past the twenty-year window. In this scenario, they could not afford to forgo short-term gains that came at the expense of the land's later value. Nor could they afford to invest in long-term improvement projects, such as clearing new land for grazing. This is the predicament with antimicrobial drugs. The profligate use of such drugs in the present destroys their value in a future in which they are unowned.

This suggests the simple solution of extending the patent terms of antimicrobial drugs. So long as the drug remains under patent, the patent holder has both an interest in preserving its usefulness and the ability to control its use so as to preserve its value. How long should the patent term be extended? The five years of extra market exclusivity offered by the GAIN Act is calculated with a view to incentivizing companies to invest in developing new drugs. The aim of the present proposal is different. It is to enable the creators of drugs to profitably exercise their rights over the drugs in a manner that preserves the drugs' effectiveness over time—ideally into the indefinite future. This requires extending the term of exclusivity not just a few years or decades, but as far into the future as there is reason to hope that the drugs' effectiveness can be maintained.

There are various ways in which this suggestion could be further developed; perhaps the most promising is simply to allow patents on antimicrobial drugs to be renewed indefinitely, so long as the drugs' continued effectiveness can be demonstrated. (How exactly continued effectiveness should be demonstrated is a matter of detail, but likely by showing resistance to be below a certain threshold—perhaps 20 percent—in clinical isolates of interest.[36]) This would allow for a potentially infinite patent term. "Perpetual patents" have occasionally been proposed,[37] but the lack of a fixed term may do violence to the notion of a patent, so it may be better to conceive of this as a

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36 This was suggested to the author by Dr. Amesh Adalja, Senior Scholar at the Johns Hopkins University Center for Health Security.

37 Richard Gilbert & Carl Shapiro, *Optimal Patent Length and Breadth*, 21 RAND J. ECON. 106, 107 (1990); *see, e.g.*, John F. Duffy, *Rethinking the Prospect Theory of Patents*, 71 U. CHI. L. REV. 439, 448 (2004).

proposal for a new type of IP right that combines features of patents and trademarks. Conceptualizing the relevant right in this way highlights its basis. Like a patent, the right would pertain to an invention and would confer market exclusivity; like a trademark, however, it would be renewable in perpetuity on the grounds that the continued value of the property depends on the owner taking continuous action to maintain it. In the case of the right under consideration, the relevant actions would be those of stewarding the drug in such a manner as to prolong its continued effectiveness in the face of resistance.

This new sort of property right could, in principle, be applied to drugs that are already off patent or otherwise ineligible for patent protection. The Chatham House Working Group proposes granting "delinkage rewards" to "firms registering a new antibiotic without patent protection (such as new uses for old drugs),"[38] and it may be that the sort of IP protection proposed here would be applicable in such cases as well. If so, the right would be justified by the discovery of the new use for the drug and by the fact that intelligent management of this use is required for it to retain its value. A more difficult case is granting such rights to already known antibiotics that have gone off patent and are now available as generics. Removing these drugs from the commons would make it possible for an owner to profit by stewarding them responsibly. The difficulty here is determining who would own them. Professor Kades considers the possibility of granting a new patent to the original patent holder but suggests "auctioning the patent rights [to such drugs] to the highest bidder."[39] Both are plausible solutions. Another option, in light of the issue of cross-resistance (which will be discussed in Part III) would be to apportion the IP rights to the relevant drugs among the owners of other drugs with similar mechanisms of action.

Instituting the sort of property right described here (whether or not it is extended to drugs that are currently unpatentable and/or in the public domain) would create an environment in which pharmaceutical companies and other private entities can compete to develop new policies and business models that maximize the total value derived from antimicrobial drugs over time. An important advantage of this proposal is that it does not require policymakers (or authors of law review articles) to know in advance which specific practices would have this auspicious effect. However, some obvious possibilities suggest themselves.

Pharmaceutical companies could sell new antimicrobials at a price high enough to make it prohibitive to use them as anything other than treatments of last resort. In addition to extending the drugs' useful lives, the high prices would compensate for the lower initial volume of sales, and the drugs could eventually be repriced for wider use as second- and then first-line treatments. This repricing would have to be paced both to the growth of the resistant bacterial population and to the development of new antimicrobial drugs to

38 Clift, *supra* note 20, at 20.

39 Kades, *supra* note 33, at 653.

take their predecessors' place as treatments of last resort. One can imagine many variations of this strategy with different price points and development cycles.

Pharmaceutical companies could also extend the effective lifespan of their antimicrobials through contractual arrangements with healthcare providers, which restrict the latter's use of the drugs to certain protocols or best practices. Imagine the new business practices whereby pharmaceutical companies might profit from drugs that are never or hardly ever used. Licensing plans like the one proposed by Commissioner Gottlieb might be employed in innovative ways.[40] For example, healthcare providers or insurance companies might pay a monthly fee for the right to use these drugs should it ever become necessary to do so. Or the various parties might negotiate a system whereby a pharmaceutical company (or an entity that has licensed drugs from multiple companies) charges a fixed price for treatment in accordance with a proprietary antimicrobial protocol that makes use of several of their drugs, specifying which drugs can used under which conditions.

The suggestions in the last paragraph all amount to ways in which revenues from the creation of a new drug might be "delinked" from sales volume. In principle, this delinkage could occur simply through market forces, without any additional policy interventions, but since governments and multinational organizations account for most of the spending in the healthcare sector in much of the world, their adopting policies favoring delinkage would likely stimulate the development of these sorts of business models under an IP regime of the sort suggested. Indeed, such delinkage–promoting policies would likely fare better under the proposed IP regime than under the current IP system because, as the Chatham House Working Group observes, "patent expiry" creates some difficulties for such policies.

> Obligations for responsible use can be carefully crafted and functional when monopoly rights are in place, but are likely to fail once generic antibiotics are introduced upon the termination of the period of exclusivity. Generic manufacturers ordinarily rely on volume-based rewards, and low prices and large volume of sales without appropriate measures to conserve the antibiotics may be an important driver of indiscriminate use and resistance. A sustainable system will require controls on market entry after termination of the patent, and regulation of the way the generic products are marketed and prescribed.[41]

It bears emphasizing at this point that the best stewardship policies for antimicrobial drugs remain to be discovered. The Chatham House Working Group report (quoted several times above) represents the cutting edge of research on this issue, and it offers precious few details about the new "delinked" business model it says "needs to be developed." Successful business models are rarely if ever specified from on high by public policy makers. Securing a long-range IP right to antimicrobial drugs would create the conditions in which the healthcare industry as a whole could invest the resources

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40 Statement of Gottlieb, *supra* note 26.

41 Clift, *supra* note 20, at 24.

required to discover the practices, protocols, and business models that maximize the value of these substances. In addition, the ability to capture this value as profit would create an incentive to develop new drugs as needed.

IP rights, and patents in particular, are sometimes understood as bargains between creators and society. The proposal under consideration grants a lot more to the developers of any new antimicrobial drugs than they are granted under current law, but it asks a lot of these developers in return—for it requires them to become good stewards of their drugs by discovering and implementing the means necessary to preserve the drugs' value over time, so that the maximum potential benefit from them is realized.[42] This is work that needs to be done by someone, and the sort of IP regime proposed here would enable those people and firms most qualified to do this work to profit by doing it.

This leads to a deeper point. Although IP rights are often understood as special privileges granted by a government and justified on utilitarian grounds, the dominant strand in early American jurisprudence, taking its inspiration from John Locke, regards all property rights as securing to a creator the fruits of his productive work.[43] Among the reasons why patents and copyrights are finite in duration, whereas rights to chattels or land can be passed on from generation to generation indefinitely, is that chattels and land generally need to be maintained in order to retain their economic value over time, whereas this is not true of the economic value of an artwork or a method.[44] But the case under consideration reveals that the continued economic value of certain methods does depend on an ongoing process of intelligent management by which one uses the method sparingly. It is this very fact that (according to this Part's argument) justifies extending the IP right to the drug indefinitely. This raises the question of whether there are structurally similar cases in other fields, where the continued commercial value of a potential invention depends on its judicious use. If so, it may be that there are other values being destroyed (or never created) because of tragedies of the commons that could be rectified by policies analogous to the one suggested here.

III. TWO COMPLICATIONS

Two complications pertaining to the proposal developed in the previous Part are worth considering. The first concerns cross-resistance, which was

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42 It should be acknowledged that there may be some cases in which the maximum benefit to be derived from a drug involves using it liberally for a period when there is a great need for it and letting it become obsolete quickly. If there are such cases, pharmaceutical companies would be free to discover and exploit them in the proposed regime.

43 *See* Mossoff, *supra* note 35, at 350.

44 Ayn Rand, *Patents and Copyrights*, *in* AYN RAND CAPITALISM: THE UNKNOWN IDEAL 125, 126, 127 (1966).

alluded to earlier. The second concerns the challenges posed by the fact that antimicrobial resistance is a global problem, which therefore cannot be adequately addressed by policy changes in any one country alone.

A. *Complication One: Cross-Resistance*

Antimicrobial drugs often have similar mechanisms of action, such that bacteria resistant to one will be resistant to others as well.[45] Professor Kevin Outterson, Dr. Julie Balch Samora, and Karen Keller-Cuda, lay out the complications this can raise for any attempt to use one's IP rights over a microbial drug to manage its use so as to maintain its effectiveness over time.

> Consider the difficulty when patents for drugs in an antimicrobial class are held by different owners, or when one or more of the drugs in class are off-patent. Joint property owners are exposed to the tragedy of the commons, and are thereby prone to waste. If the number of patent holders within the class is quite small, then perhaps private coordination can prevent overzealous marketing and delay resistance. Competition laws might need to be modified to permit this joint coordination among rival companies. When one or more drugs in a class are off-patent, private coordination cannot work, because there are reduced barriers to entry by a nonconforming and profit-maximising generic producer. A patent-based solution to these issues would require a very broad patent for the entire drug class to the first applicant. The first company to patent a new target or mode of action would have to control the licensing of all downstream innovation, and thus manage the entire class.[46]

Regarding the first of the objections raised in this passage—it is not clear why the ability for multiple firms to coordinate the exercise of their IP rights depends on the total number of firms being "quite small." If all the firms have property, the continued value of which depends on their finding a way to coordinate, why would not (say) a dozen firms or more be able to negotiate some sort of pooling arrangement to their mutual advantage? If the firms were not able to negotiate such an arrangement, and the value of their property was in jeopardy because of this, that would create incentives for some or all the firms to sell their rights to a small number of other parties who are capable of negotiating such an arrangement and who, therefore, could afford to buy the rights from each of the initial firms for a sum higher than the firm could otherwise expect to realize from the rights.

Turning now to the second objection—it is possible that some of the ways in which pharmaceutical companies might coordinate the sales of their products so as to maintain their value over time could be deemed "anticompetitive" under current antitrust laws. But, as Professor Outterson et al. note, the relevant laws could be modified or interpreted to permit these activities.

Regarding the third objection—generic drugs do pose a special challenge, and this is a reason to consider removing these drugs from the commons and putting them in the hands of an owner, ideally one who owns other

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45 *Cross Resistance to Antibiotics*, 148 J. AM. MED. ASS'N 470–71 (1952).

46 Outterson et al., *supra* note 34, at 563.

drugs of the relevant class. This could be accomplished through an auction or through a policy of awarding the rights to such drugs to the owners of similar drugs. Moreover, such a policy could be set up to encourage coordination among the several owners of the drugs of a given class. For example, the policy might provide that if, and only if, all the currently owned drugs of a given class are in the hands of a single party (including a consortium or holding company), the rights to currently unowned drugs of the same class will revert to that party. Alternatively, if some antimicrobials remain in the commons, then antimicrobials that belong to the same classes as these will be worth less than ones that belong to classes that have no members in the commons. This will create an additional incentive to develop new classes of antimicrobials with new mechanisms of action. This is the sort of drug of which too few are in development today.

Regarding the last of the objections raised by Professor Outterson et al.—if it turns out that the best stewardship policy for an antimicrobial drug requires one to have control of all the drugs of its class, and if there is a great need for development of new classes of antimicrobials, then there is something to be said for defining rights in this domain so that the first applicant to develop a drug's new mode of action has rights to the whole class of drugs based on that mode of action. But even if the rights are not defined in this way, it is likely that new classes of drugs based on new targets of modes of action will become owned by a single firm (or coordinated group of firms). Since each drug in the class will be most valuable if the whole class is controlled by a single party, the first party to develop a drug in the class will have an incentive to develop or purchase others, or else to sell its rights to some other firm that is better positioned to develop other drugs in the new class. Moreover, firms beginning their research on new modes of action will have incentives to conduct this research in such a manner as to maximize possible returns. This could mean researching modes of action that few competitors are researching, or perhaps developing agreements with competitors whereby the first to bring a drug of the relevant class to market has an option to buy the rights to subsequent drugs of the same class.

One can envision other possible arrangements as well, and it is a fool's errand to try to project from one's armchair precisely which business models for antimicrobial research would develop under any IP regime. But it is a principle that, when property rights are defined so as to recognize the people who create and maintain values as the *owners* of those values, the result is an environment that enables the discovery of new ways to create and maintain the relevant values. The business models that flourish in such an environment are often different from and better than any that could have been predicted from an armchair.

B. *Complication Two: Global Problem*

Consider now the second complication mentioned above: the challenges posed by the status of antimicrobial resistance make it a global rather than national problem. If an IP right of the proposed sort would enable a solution to the crisis of antimicrobial-resistant infections, then, of course, it would be best if this right were recognized the world over. But significant benefits could presumably be achieved even if it were instituted in the United States alone, given the size of the American pharmaceutical industry and the size of the American market (the same may apply to the European Union). That the GAIN Act has stimulated research[47] (though perhaps not in the intended areas) shows that even comparatively modest extensions to market exclusivity within the United States provide significant incentives for pharmaceutical development, and presumably they would incentivize stewardship as well. Of course, if antimicrobial drugs that were protected as IP in the United States were widely available as generics in other countries, this would thwart the ability of the drugs' owners to steward their use to preserve their value. However, this is unlikely to be an issue in the case of newly developed drugs, because before a drug can be offered for sale in a given country, it must be approved by that country's regulatory bodies, and the substantial cost of approving a drug is presently borne by the patent holder—the only party with a reasonable expectation of recouping those costs.[48] Thus, if a perpetual IP right to antimicrobial drugs is recognized in the United States alone, it is likely that any new drugs developed as a result of this right would simply not come to market in other countries. This has the significant disadvantage that new drugs would not be available in many places where they are desperately needed. However, at least the utility of these new drugs would not be undermined by irresponsible use of the drugs in these countries, so the drugs could be made available there eventually once a legal framework is put in place that makes it possible to offer the treatments there profitably and responsibly.

Proposals for global streamlined regulatory approval processes for antimicrobials are parts of plans for "delinkage" and stewardship,[49] so they are unlikely to be carried out in ways that lead to protected drugs becoming liberally available in other countries. And given the difficulties posed by generics to organizations attempting to promote "delinkage," it is likely that any such organization would rather deal with American IP holders than encourage the manufacture of generics. Moreover, even if generics were available in other countries, if they were used relatively judiciously there, the continued market exclusivity within the United States would likely enable owners of antimicrobials to profit from stewarding them well within the United States.

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47 Slater, *supra* note 29.

48 *See* Clift, *supra* note 20, at 18.

49 *Id.* at 26.

It is less likely that the ideas (considered above) for removing off-patent drugs from the commons could be implemented effectively in a single country. So, the main expected benefit of the proposed IP policy, if implemented by the United States alone (or any other country), would be its contribution to the creation and good stewardship of new antimicrobials and, especially, new classes of antimicrobials, rather than to the preservation of the value of existing antimicrobials.

CONCLUSION

No attempt has been made here to quantify the beneficial effects of the proposed IP policy (whether implemented in the United States alone or on an international scale). Quantifying the effects of such policies is notoriously difficult, even when one is armed with a great deal of quantitative data, and it is beyond the scope of this modest paper. The arguments offered here are philosophical in nature: The crisis of antimicrobial resistance has the structure of a tragedy of the commons, and such tragedies can in general be solved by defining and recognizing property rights that enable individuals (or firms) to capture some of the values they produce and maintain. The advent of such rights creates a social environment in which new, concrete solutions can be found—solutions that could not have been anticipated in advance or mandated by policymakers. It is just such solutions that are needed for the crisis of antimicrobial resistance—not only solutions in the form of new drugs, but also of new business models for creating and stewarding these drugs so as to fully realize their value.