Does Pharma Need Patents?

Talha Syed

Pharmaceuticals are the sector most widely thought to be in need of strong patent protection in order to sustain a robust level of innovative activity. This Feature seeks comprehensively to revisit that assessment. It argues that a proper understanding of the actual informational resources at play in drugs reveals that pharmaceutical innovation can, significantly does, and entirely should proceed without any role played by patents.

The foundational plank of the argument is to underline how innovation in pharmaceuticals consists of not one but two distinct information goods: (1) knowledge of a chemical or biological compound (the "compound information good"); and (2) knowledge of its safety and efficacy for use in humans, as validated by clinical trial data (the "data information good"). It is the latter information good, not the former, that is both the driver of the economics in this sector and the apt focal point of innovation policy rules. Indeed, a close examination of how the doctrines of patent law map onto the pipeline of pharmaceutical innovation reveals a set of radically sector-specific doctrines that confer little protection during the preclinical research that generates the compound information good, contrary to the common view. Meanwhile, for the clinical testing that generates the data information good, revised regulatory-exclusivity rules can and entirely should suffice. Indeed, the protection presently afforded this good by patents is indirect, incomplete, and—owing to a basic misalignment between the patent system's focus and sensible goals for innovation policy in this sector—haphazard and highly costly.

Consequently, simply by phasing out patent protection for drugs and replacing it with a revised form of regulatory exclusivity, we would reap large gains in social welfare: better-tailored incentives, reduced access and duplication costs, and significantly curbed wastes from gaming of the present system. Much of these costs stem from the widespread phenomena of "evergreening" practices and "me-too" drugs, which have come in for sharp criticism. The present analysis offers a deeper diagnosis of the causes and extent of these problems, and it proposes more effective, because better-tailored, solutions.

This same analysis should also reorient broader debates in patent theory and innovation policy more generally—by revising our understanding of the special case posed by drugs for innovation policy support. The conventional view that pharma presents an especially strong case for patent protection turns out to be triply wrong. First, the innovation taking pride of place in judicial and scholarly attention—the compound information good—poses no special case for patents. Second, the innovation that does pose a strong case for innovation policy support—the data information good—is both sidelined by the patent system and in any case ill-suited for patent protection. The special case posed by pharma, then, is not for patents but for an alternative innovation policy intervention. Finally, the basis of that special case for innovation policy support lies in a regulatory regime rather than generalizable economic or technological features of drugs.

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INTRODUCTION

Does pharma need patents? The consensus view among scholars is a resounding "yes." The pharmaceutical industry is widely agreed to be the sector most in need of strong patent protection to sustain a robust level of innovative activity.[1] Study after study of the effects of patents on

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[1] *See, e.g.,* Richard Posner, *Why There Are Too Many Patents in America*, ATL. (July 12, 2012), https://www.theatlantic.com/business/archive/2012/07/why-there-are-too-many-patents-in-america/259725 [https://perma.cc/SR4L-W5DD] ("[P]harmaceuticals are the poster child for the patent system. But few industries resemble pharmaceuticals[.]"); William W.

innovation—be they empirical surveys asking firms in different industries what they rely on to appropriate the benefits of innovation, historical studies of long-term patterns of innovation and patent protection, or synthetic theoretical-empirical treatments of the aggregate costs and benefits of the patent system as a whole—agree that, whatever other conclusions may be reached regarding the overall case for patent protection across the economy, such protection is crucial for innovation in drugs.[2] This conviction holds not only for those who most strongly endorse the patent system as a whole,[3] but also for those more uncertain about the overall merits of patent protection.[4] Indeed, the point also holds true even for those most skeptical of patents in general, as even the system's staunchest critics accept that pharma remains a crucial exception.[5]

This Feature seeks comprehensively to revisit that assessment.[6] It argues that a proper understanding of the actual informational resources at play in drugs reveals that pharmaceutical innovation can, considerably does, and entirely should proceed without any significant role played by patent protection.[7] The foundational plank of the argument is to underline how innovation in pharmaceuticals consists of not one, but *two separate information goods:* (1) knowledge of a new

Fisher III, *Intellectual Property and Innovation: Theoretical, Empirical, and Historical Perspectives*, *in* INDUSTRIAL PROPERTY, INNOVATION, AND THE KNOWLEDGE-BASED ECONOMY, 37 BELEIDSTUDIES TECHNOLOGIE ECONOMIE 47, 57 (2001) ("the pharmaceutical industry […] has traditionally—and properly—been seen as the field in which the argument in favor of intellectual-property rights is the strongest.").

[2] For empirical surveys noting the especial importance of patents to pharmaceutical firms, see C.T. TAYLOR & Z.A. SILBERSTON, THE ECONOMIC IMPACT OF THE PATENT SYSTEM: A STUDY OF THE BRITISH EXPERIENCE 199, 263-65 (1973); Edwin Mansfield, Mark Schwartz & Samuel Wagner, *Imitation Costs and Patents: An Empirical Study*, 91 ECON. J. 907, 915-17 (1981); Edwin Mansfield, *Patents and Innovation: An Empirical Study*, 32 MGMT. SCI. 173, 174-75, 180 (1986); Richard C. Levin, Alvin K. Klevorick, Richard R. Nelson & Sidney G. Winter, *Appropriating the Returns from Industrial Research and Development*, 3 BROOKINGS PAPERS ON ECON. ACTIVITY 783, 796-97, 818 (1987); and Wesley M. Cohen, Richard R. Nelson & John P. Walsh, *Protecting Their Intellectual Assets: Appropriability Conditions and Why U.S. Manufacturing Firms Patent (or Not)*, 2-3, 9, 23 (Nat'l Bureau of Econ. Rsch., Working Paper No. 7552, 2000). For theoretical-empirical syntheses of aggregate costs and benefits singling out pharmaceuticals as the strongest case for protection, see ADAM B. JAFFE & JOSH LERNER, INNOVATION AND ITS DISCONTENTS 39-41 (2004); and JAMES BESSEN & MICHAEL J. MEURER, PATENT FAILURE: HOW JUDGES, BUREAUCRATS AND LAWYERS PUT INNOVATORS AT RISK, 13-18, 27, 88-89 (2008). For historical studies of long-term patterns coming to an overall ambivalent conclusion, but without specific reference to pharmaceuticals, see generally ELIZABETH PENROSE, THE ECONOMICS OF THE INTERNATIONAL PATENT SYSTEM (1951); STAFF OF SUBCOMM. ON PATENTS, TRADEMARKS & COPYRIGHTS OF THE S. COMM. ON THE JUDICIARY, 85TH CONG., AN ECONOMIC REVIEW OF THE PATENT SYSTEM, STUDY NO. 15 (Comm. Print 1958) (prepared by Professor Fritz Machlup); Josh Lerner, *Patent Protection and Innovation Over 150 Years* (Nat'l Bureau of Econ. Rsch., Working Paper No. 8977, 2002); and Petra Moser, *Patents and Innovation: Evidence from Economic History*, 27 J. ECON. PERSP. 27 (2013).

[3] *See, e.g.,* Richard A. Epstein & Bruce N. Kuhlik, *Is There a Biomedical Anti-Commons?*, REGUL., Summer 2004, at 54, 56 (arguing that "strong" protection should be "the dominant approach in patent law," one that "take[s] on special urgency in connection with pharmaceutical products"); ROBERT P. MERGES, JUSTIFYING INTELLECTUAL PROPERTY 2-3, 282 (2004) (advancing non-utilitarian justifications for "the necessity and importance of IP law" in the face of general empirical uncertainty, while emphasizing that the empirical case remains strong for pharmaceuticals).

[4] *See* the empirical surveys and theoretical-empirical syntheses cited *supra* note 2.

[5] *See* MICHELE BOLDRIN & DAVID K. LEVINE, AGAINST INTELLECTUAL MONOPOLY 212-42 (2008) (in a book-length attack on IP rights, devoting a special chapter to more moderate treatment of pharmaceuticals); *cf.* Posner*, supra* note 1.

[6] For an important partial revisiting, see Rachel E. Sachs, *The Uneasy Case for Patent Law*, 117 MICH. L. REV. 499 (2018). Based on a searching case study of the relative unavailability of patents for microbiome-based therapies, Professor Sachs suggested that "[p]erhaps scholars should reconsider, *if only selectively*, our focus on patents as an irreplaceable driver of pharmaceutical innovation." *Id.* at 500 (emphasis added). The present analysis reinforces Professor Sachs's conclusions by pointing to systematic misalignments between patent protection and pharmaceutical innovation in general, so as to make out a comprehensive case for phasing out patent protection for all drugs.

[7] That all "innovations" are properly conceived as "information goods" from an innovation-policy point of view is an insight going back at least to Kenneth Arrow's foundational work. *See* Kenneth Arrow, *Economic Welfare and the Allocation of Resources for Invention, in* THE RATE AND DIRECTION OF INVENTIVE ACTIVITY: ECONOMIC AND SOCIAL FACTORS 609, 609 (Richard R. Nelson ed., 1962) ("Invention is here broadly interpreted as the production of knowledge."). For systematic development of the point, see generally Yochai Benkler, *Intellectual Property and the Organization of Information Production*, 22 INT'L REV. L. & ECON. 81 (2002); Hal R. Varian, *Markets for Information Goods* (Bank of Japan Inst. for Monetary & Econ. Stud., Discussion Paper No. 99-R-9, 1998), https://www.imes.boj.or.jp/research/papers/english/99-E-09.pdf [https://perma.cc/BR43-25F2]. For further discussion of the point in connection with the present argument, *see infra* Section I.A and text accompanying notes 65-67.

chemical or biological compound; and (2) knowledge of the safety and efficacy of that compound for use in humans, as validated by clinical trials.[8] Moreover, not only is the latter information good a separate innovation from the former, it is one *very distinct* in its risk and cost profile, diverging sharply in those technical and economic features that are relevant to innovation policy analysis. What these features reveal is that the first information good likely poses no stronger case for patent protection than innovation in most other sectors, while fitting quite well a model of decentralized, competitive development. Meanwhile, the second information good does require strong innovation policy support, while better fitting a model of centrally-coordinated development.

Two fundamental implications follow from this theoretical distinction. First, the distinction reveals a new understanding of existing patent practice in the pharmaceutical industry. Applying the insight of two information goods discloses a dramatically new picture of how patent and related laws map onto the pipeline of pharmaceutical innovation, including by revealing a set of highly sector-specific patent doctrines applicable only to pharma. The upshot of this picture is that patents provide only partial—and largely unnecessary—protection over the first innovation and indirect—and highly misaligned—protection over the second. Second, these explanatory implications of the distinction justify a deep reform of pharmaceutical innovation policy. A better innovation policy for this sector would be to phase out patents altogether and replace them with an alternative form of innovation policy intervention, one better suited to the distinctive technological and economic features of the second information good: a revised system of "regulatory exclusivity."[9]

At the heart of pharmaceutical innovation lie two information goods. The first is knowledge of a new drug product, which we may call the "compound information good."[10] The second is knowledge of that drug's safety and efficacy for humans as evinced by clinical-trial data, which we may call the "data information good."[11] Generating the compound information good involves the exploration of a highly uncertain possibility frontier: each step involves many risks—only about one in a thousand candidate compounds make it through the drug-discovery phases of

[8] This insight has been implicit in the work of a number of scholars, needing only explicit crystallization and systematic development. The foundational work here is that of Rebecca Eisenberg. *See* Rebecca S. Eisenberg, *The Shifting Functional Balance of Patents and Drug Regulation*, 20/5 HEALTH AFFS., Sept.-Oct. 2001, at 119 (2001) [hereinafter Eisenberg, *The Shifting Functional Balance*]; Rebecca S. Eisenberg, Lecture, *Patents, Product Exclusivity, and Information Dissemination: How Law Directs Biopharmaceutical Research and Development*, 72 FORDHAM L. REV. 477 (2003) [hereinafter Eisenberg, *Patents, Product Exclusivity*]; Rebecca S. Eisenberg, *The Problem of New Uses*, 5 YALE J. HEALTH POL'Y. L. & ETHICS 717 (2005); and Rebecca S. Eisenberg, *The Role of the FDA in Innovation Policy*, 13 MICH. TELECOMM. & TECH. L. REV. 345 (2007) [hereinafter Eisenberg, *The Role of the FDA*]. For subsequent scholars developing related insights, see Valerie Junod, *Drug Marketing Exclusivity Under United States and European Union Law*, 59 FOOD & DRUG L. J. 479, 479-80 (2004); Stuart Minor Benjamin & Arti K. Rai, *Who's Afraid of the APA?: What the Patent System Can Learn from Administrative Law,* 95 GEO. L. J. 269, 307 (2007); Benjamin N. Roin, *Unpatentable Drugs and the Standards of Patentability*, 87 TEXAS L. REV. 503 (2009); and Talha Syed, *Should a Prize System for Pharmaceuticals Require Patent Protection for Eligibility?* (Incentives for Glob. Health Discussion Paper No. 2, 2009).

[9] The detailed contours of such a system of "regulatory exclusivity" are set out *infra* Section III.B(2). Briefly, it involves making three significant adjustments to the present form of "data exclusivity" currently conferred upon drug products: (1) *Tailoring* the scope of protection afforded to both new molecular entities (NMEs) and incrementally modified products (IMPS) to address (a) access concerns from "evergreening"; and (b) duplication wastes from "me-too" drugs. (2) Providing a new form of "*testing exclusivity*" for drug candidates that no longer avail themselves of patent protection, to coordinate clinical testing in the hands of a single applicant so as to avoid wastefully duplicative clinical trials. (3) Finally, requiring *data transparency* after the period of "data exclusivity" has expired.

[10] A breakdown of the different kinds of pharmaceutical innovations that fall under the "compound information good" rubric—and the different forms of product or process patents they may be eligible for—is provided *infra* text accompanying note 78.

[11] A breakdown of the different kinds of clinical information that fall under the "data information good" rubric—and the different forms of regulatory requirements and data exclusivity that may pertain to them—is provided *infra* text accompanying notes 84-86, 126-127.

"search, synthesis, and screening" to enter clinical trials[12]—so as to warrant comparatively low expenditures per step.[13] By contrast, generating the clinical information good is a comparatively low-risk, high-cost endeavor: roughly one out five to ten drugs that enter clinical trials successfully navigate the process of testing and refinement to receive Food and Drug Administration (FDA) approval,[14] while the costs of phase 1, 2, and 3 trials dwarf those of each step of preclinical drug discovery.[15] This sharp divergence in the risk/cost profiles of these information goods bears two sets of crucial implications for their apt innovation policy treatment.

First, from a purely *economic* point of view, it is the data information good—not the compound information good—that is the driver of the industry's innovation costs. While the cost of drug development remains a topic of fierce controversy,[16] what is not controversial is that clinical-trial expenditures comprise the lion's share of the costs, running between sixty and seventy percent according to the industry's own preferred studies,[17] and even higher for others.[18] Indeed, a 2021 metareview of twenty-two studies of drug-development costs conducted over the past four decades found that over half (thirteen) of the studies reviewed did not even consider preclinical drug-discovery expenditures significant enough to factor in as a part of total costs.[19]

A second pair of implications flows out from the fact that, in addition to their very different economic significance for pharmaceutical innovation, these information goods also sharply differ in the *technological* features of the respective innovation processes that generate them. Preclinical drug discovery, with its high risks and lower costs, is well-suited for a decentralized search, where "many minds" are given free rein to explore various different avenues, even at the risk of a fair bit of overlapping, duplicative activity.[20] Clinical trials, on the other hand, with their lower risks and high costs, are better suited for coordinated development, to curb duplicative efforts that would be highly wasteful at this stage.[21] In other words, preclinical research should be a nonexclusionary zone, to enable many-minded exploration unencumbered by proprietary barriers. For clinical trials, on the other hand, some mechanism is needed to call off the innovation race at their outset.

Integrating these distinct economic and technological features of the two innovations leads to the following pair of conclusions. First, the compound information good—generation of new knowledge of a chemical or biological product or process—poses no special incentive case for patent protection. Not only is its share of overall industry innovation costs relatively modest but, what is really the relevant focus for innovation policy analysis, the differential between its average innovation costs and risks and imitation costs and speed (i.e., the cost and time involved in reverse engineering and getting ready for manufacture a new or improved drug product or process) is likely

[12] *See* references and discussion *infra* note 130.

[13] For discussion of this point, *see infra* text accompanying notes 131-132.

[14] *See* references and discussion *infra* note 130.

[15] *See* discussion in following paragraph.

[16] The key sources and extent of the controversy are reviewed *infra* text accompanying note 97-101.

[17] Joseph A. DiMasi, Ronald W. Hansen & Henry G. Grabowski, *The Price of Innovation: New Estimates of Drug Development Costs* 22 J. HEALTH ECON. 151, 166 (2003); Joseph A. DiMasi, Henry G. Grabowski & Ronald W. Hansen, *Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs*, 47 J. HEALTH ECON. 20, 25 (2016).

[18] Michael Schlander, Karla Hernandez-Villafuerte, Chih-Yuan Cheng, Jorge Mestre-Ferrandiz & Michael Baunmann, *How Much Does It Cost to Research and Develop a New Drug? A Systematic Review and Assessment*, 39 PHARMACO-ECON. 1243, 1245-46 (2021).

[19] *Id.* at 1246.

[20] *See* Robert P. Merges & Richard R. Nelson, *On the Complex Economics of Patent Scope*, 90 COLUM. L. REV. 839, 873-74 (1990).

[21] *See* Edmund W. Kitch, *The Nature and Function of the Patent System*, 20 J.L. & ECON. 265, 278-79 (1977).

no greater than in many other sectors where a combination of first-mover advantages and secrecy suffice to ensure a relatively robust level of innovative activity.[22] In addition, patents also serve no useful "coordinating" function during the research phase leading to this innovation, owing to its comparatively high risks and low costs that make it suitable for competitive, decentralized search.

Meanwhile, the data information good—generation of new clinical results on a drug—*does* present a strong case for an innovation policy intervention, but it is one for which patents are a highly unsuitable instrument. That strong case stems from not only the large share of overall industry innovation costs taken up by this activity but, what is again the relevant focus, the large difference between its average costs and risks of generation and costs and speed of replication (with the latter massively reduced by regulatory permission of imitator piggybacking on innovator data).[23] Yet the patent system provides little to no direct protection over this information good, as its doctrines center on the results of preclinical research, not clinical testing.[24] And it is not only that patents currently sideline the protection of clinical data; they also *cannot* effectively provide such protection. Given the technological features of this innovation, it would be untenable to try to reform the patent system to protect it: inquiries into its desirability and validity are simply not ones that the patent system is well-suited to carry out.[25]

Consequently, the two primary functions that patents serve in pharmaceutical innovation—coordinating innovation races and incentivizing innovative activity—they do so only indirectly, with respect to an information good, clinical data, that they do not directly protect.[26] Meanwhile, for the information good that patents do directly cover—knowledge of the compound—they play little-to-no coordinating role and a secondary incentive one.[27] A sounder innovation policy would be to replace the primary, yet indirect, role played by patents over data information with a form of regulatory exclusivity that specifically attends to the distinctive features of this innovation, while at the same time phasing out the direct but secondary role patents play over compound information.

The point of doing so is to bring our system of innovation policy rules into better alignment with the underlying innovations that they seek to generate, such that the rules directly attend to the relevant features of the information goods they govern and, as a result, are better equipped to make the various tradeoffs facing any innovation policy. In particular, such a reform would significantly improve the performance of our innovation policy for drugs in tackling the two key tradeoffs facing incentives system that use exclusionary rights (such as patents or data exclusivity). First, it would reduce undue barriers to access that exclusionary rights erect over those innovations that would have been generated at lower levels of protection. Second, it would curb undue rent dissipation—that is, wastefully duplicative innovative activity—that exclusionary rights may incur for innovations that would have been incentivized by a lower level of protection.[28] Specific versions

[22] *See infra* text accompanying note 43.

[23] *See infra* text accompanying notes 157, 178-180.

[24] *See infra* Section I.B.

[25] *See infra* Sections II.A *and* III.B.

[26] For the indirect coordinating and incentive roles played by patents for the data information, *see infra* Section II.B.2 and C.

[27] For the negligible coordinating and secondary incentive roles played by patents for the compound information good, see *infra* Sections II.A.1-B.1.

[28] For discussion of these, *see infra* text accompanying notes 48-49, 51-5454. Note that these are the main tradeoffs *internal* to exclusionary-rights incentive systems. There also exists a separate set of tradeoffs in choosing between such systems and alternative,

of each of these concerns have been prominently voiced in the critical literature on pharma, the first under the heading of "evergreening" practices, and the second that of "me-too" drugs.[29] And in both cases, analysis of the distinct information goods and of how existing rules fail to align with their relevant features, immeasurably improves *both* our diagnosis of the precise causes and extent of the problems *and* our prospects for prescribing effectively tailored solutions.

In the case of evergreening and related practices such as "reverse-settlement agreements" (RSAs), this present analysis identifies the generative cause of such practices: the specific *industry structure* of pharma that stems from the regulatory treatment of the data information good.[30] This information-good analysis fills a gap in the literature by explaining why such practices are, indeed, pharma-specific. The Feature then specifies better ways of evaluating the extent of the social costs of such practices, anchored in the distinction between the compound and data information goods.[31] Finally, analysis anchored in the information goods also points the way to reforms that attack the problem at its root—the basic misalignment between patents and data information—as opposed to proposals that seek only to remedy surface ills with how patents currently operate.[32] And similarly for the duplication wastes incurred by me-too drugs: an analysis focused on the distinction between generating new compounds and new clinical data is better able to specify both the extent to which such drugs do incur such wastes and how to tailor remedies for effectively curbing them.[33]

The upshot of these analyses is two-fold. First, with respect to evergreening and RSAs, the present analysis provides a firmer basis than has so far existed for two far-reaching reforms in this area: (a) simply abolishing all "Orange-Book" linkage between patent enforcement and regulatory delays in approval of generics; and (b) categorically barring all RSAs as per-se anticompetitive under antitrust law.[34] Second, as far as these reforms go, they do not go far enough: the underlying source of the problems they seek to address lies in the present regulatory-innovation policy treatment of the data information good. This treatment fuels the gaming of drug patents, and all reforms that stay within the patent system will remain hostage to further gaming efforts.[35] To solve the problem at its root, we need to phase out patents and replace them with regulatory exclusivity that realigns incentives by focusing directly on the core innovation, data information.

In sum, an analysis of pharmaceutical innovation policy that trains its attention on the data information good lying at its heart leads to the following two-fold conclusion. First, the actual protection provided by patents over the key information goods in pharmaceuticals is partial, indirect, and—owing to a misalignment between what the patent system focuses on (the compound information good) and what sensible innovation policy would center (the data information good)—haphazard and highly costly. Second, this protection would be radically improved by replacing

nonexclusionary innovation policies. For discussion of these as a general matter, *see infra* text accompanying notes 47-5047 and, for how the present analysis may affect our evaluation of them in the case of pharmaceutical innovation policy, *see infra* Part IV.

[29] "Evergreening" refers to practices by patentees to prolong the exclusivity enjoyed by their drug products beyond the expiration of their original patents. *See infra* text accompanying notes 170-175. "Me-too" drugs refer to newly patented drugs that are similar to existing patented drugs, achieving the same mechanism of action with a different compound. *See infra* text accompanying notes 195-197.

[30] *See infra* text accompanying notes 176-180.

[31] *See infra* text accompanying notes 185-193.

[32] *See infra* text accompanying notes 194, 207-208208.

[33] *See infra* text accompanying notes 195-202.

[34] *See infra* Section III.B.1.

[35] *See infra* text accompanying notes 213213-218.

patents' exclusionary rights with those of a revised—streamlined and tailored—form of data exclusivity: streamlined to curb the gaming and administrative costs associated with misaligned patents, and better-tailored to realign the system's focus onto the incentives that matter, those pertaining to the costs, risks, and desirability of generating different types of clinical data on drugs.

Turning from pharmaceutical innovation policy to broader debates in patent theory, this same analysis also provides a distinct explanation for the consensus view that patents are especially important for pharmaceuticals. The special case for protection presented by pharma, this analysis reveals, is a *regulatory artifact* rather than, as is commonly thought, the result of any generalizable technological or economic features of the pharmaceutical industry. That is, this case stems from the gap between innovation and imitation costs with respect to the second, data information good, and not the first, compound information good.[36] Specifically, it is due to the combined effect of *two distinct regulatory features* with respect to data information: first, how regulatorily-mandated clinical trials massively drive up innovation costs; and second, how regulatorily-permitted piggy-backing on clinical data massively drive down imitation costs.[37] Absent this combination, there is little reason to believe that pharma would be very different—i.e., with respect to the compound information good—from other sectors in terms of the ability of first-mover advantages and secrecy to sustain a robust level of innovative activity.[38] None of this is to query the regime of regulatory requirements and permissions. Far from it. Rather, it is to underline that it is *this regime* that makes pharma special, putting it in need of special innovation policy support.

This point has crucial import for general debates in patent theory. In those debates, pharma has long cast a shadow over the standard view that the overall case for patents—across the economy as a whole—is uneasy,[39] and likely at its best for modest protection for small inventors

[36] The majority of explanations of what makes pharma special focus on different aspects of the technological or economic features of the compound information good that affect innovator risks and costs, imitator costs and speed, the comparative role of patents versus alternative forms of private appropriability, and/or the comparative access costs of patents. *See, e.g.,* Mansfield et. al, *supra* note 2 at 913 (emphasizing the role of patents in raising imitation costs for drug compounds); Levin et. al, *supra* note 2, at 811 (same); Cohen et. al, *supra* note 2, at 23 (emphasizing the comparative appropriability of patents on drug compounds); Eisenberg, *The Shifting Functional Balance* (2001), *supra* note 8, at 479 (same); Merges & Nelson, *supra* note 20, at 897-98 (emphasizing the high risks, and costs of innovation, and ease of imitation for compounds); *id.* at 880-83 (emphasizing the lower access costs of broad patents for drug compounds as "discrete" rather than "cumulative" innovations); Posner, *supra* note 1 (emphasizing the high risks, costs, and length of innovating and low costs and time of imitating drug compounds); William W. Fisher III, *Regulating Innovation*, 82 U. CHI. L. REV. ONLINE DIALOGUE 251, 253-254 (same). For partial exceptions that briefly mention the role of regulatory requirements alongside other factors in driving up innovator costs, but without emphasizing their centrality or attending to their equally significant role in driving down imitator ones, see Fisher, *supra* note 1, at 11; and BOLDRIN & LEVINE, *supra* note 5, at 212-13, 236-37. Finally, for fuller exceptions that do mention both roles of regulatory requirements, i.e., in driving up innovation costs and down imitation costs, see Dan L. Burk & Mark A. Lemley, *Policy Levers in Patent Law,* 89 VA. L. REV. 1575, 1616-17 (2003); JAFFE & LERNER, *supra* note 2, at 40; and BESSEN & MEURER, *supra* note 2, at 88. Note, however, that neither of this latter set of authors draws out the implications of the point for patent theory and policy, perhaps due to their not registering that these regulatory features pertain to a *second, and very distinct,* information good. As a result, the point has been largely overlooked in the subsequent literature. *See, e.g.*, Sachs, *supra* note 6, at 499, 506-07 (citing Burk and Lemley's analysis for the special pharma case for patents, but without drawing out the implications for that case of the centrality of regulatory requirements and of the distinction between the two information goods); Roin, *supra* note 8, at 510-11 (same).

[37] This hypothesis was first ventured in Syed, *supra* note 8, at 14 ("[T]he case for strong patent protection for pharmaceuticals may be largely based on the combination of regulatorily-mandated clinical trials for innovators and regulatorily-enabled piggybacking for imitators."). A substantiation of it will be offered in a follow-up article to the present. Talha Syed, Reorienting Patent Theory: The Special Case of Pharma as Regulatory Artifact (unpublished manuscript) (on file with the author).

[38] More precisely, there is little reason to believe that pharma would be appreciably different from other sectors in terms of the overall trade-off between the incentive benefits of patents (in terms of enabling added innovation over nonpatent forms of appropriability) and their access and duplication costs (in terms of restrictions on consumers and follow-on innovators and rent dissipation). Fully developing this point, and elaborating its implications for broader debates in patent theory and policy, is the task of a follow-up article. Syed, *supra* 3737.

[39] *See* the historical studies, empirical surveys, and theoretical-empirical syntheses cited *supra* note 2.

at the margins.[40] Pharma has long operated as the key exception to that general rule, one that, so long as it remained unexplained, gnawed away at confidence in the rule. Showing that this exception can be not only explained, but explained *away*, reinforces the broader conclusion—that for most sectors strong patents are likely not needed for robust innovation—which may now be retained in its original force, without qualification.

Integrating these distinct implications—for pharmaceutical innovation policy on the one hand, and general patent theory on the other—allows us to see that the conventional view of "the special case of pharma" (as the one sector in need of strong patents) is triply wrong. First, the innovation taking pride of place in judicial and scholarly attention—the compound information good—poses no special case for strong patent protection. Second, the innovation that *does* present a strong case for protection—the data information good—is both sidelined by the patent system and in any case ill-suited for patent protection. Consequently, the special case posed by pharma is not for *patents* but, rather, for an alternative innovation policy intervention. Finally, the basis of that special case for innovation policy support in pharmaceuticals is itself a regulatory artifact.

The rest of the Feature proceeds as follows. Part I lays the theoretical foundations, by setting out a framework for the analysis of innovation policy, clarifying why all innovations need to be conceived as information goods, identifying the two distinct (compound and data) information goods at issue in pharmaceutical innovation, and specifying their divergent technological and economic features as relevant to innovation policy in theory. Part II then turns to analyzing how the two information goods are presently treated by pharmaceutical innovation policy in practice. It begins with a sketch of the technological and institutional pipeline of pharmaceutical innovation, and the roles played by patents, FDA regulatory requirements, and data exclusivity therein. It then details the coordination and incentive functions that patents and data exclusivity do (or do not) play with respect to each of the two information goods along the innovation pipeline. For the compound information good which patents directly protect, this Part shows they play only a modest role. Meanwhile, for the data information good for which patents serve more significant functions, they do so only indirectly. Part III then evaluates how well this system—of indirect, and so misaligned—protection performs. It finds that for each of the two main tradeoffs raised by exclusionary incentives—access costs and rent dissipation—the system performs quite badly indeed. The undue access (and gaming) costs incurred by "evergreening" practices and the duplication wastes associated with "me-too" drugs are very high, and in each case they stem from the basic underlying misalignment between patents and data information. The most effective way to curb these costs, then, is not so much to seek to improve how drug patents work, but rather to attack the problem at its root: eliminating the basic misalignment by replacing

[40] *See* Robert P. Merges, *Uncertainty and the Standard of Patentability*, 7 HIGH TECH. L.J.1, 8-9 (1992) (arguing that even if the average innovator is not induced by patent protection, the proper focus of incentives is on "the inventor at the margin," and that "small firms may be more likely to be marginal inventors"); John M. Golden, *Biotechnology, Technology Policy, and Patentability: Natural Products and Invention in the American System*, 50 EMORY L.J. 101, 111, 177 (2001) (suggesting that biotechnology patents serve less to "spur" than to "enable" innovative activity, by facilitating technology licensing agreements between upstream small biotech firms and downstream big pharma); Ashish Arora & Robert P. Merges, *Specialized Supply Firms, Property Rights and Firm Boundaries*, 13 INDUS. & CORP. CHANGE 451, 471 (2004) (advancing a "markets for technology" rationale for patents, based on their role in facilitating a specialized division of labor between small inventive firms and large established ones); ASHISH ARORA, ANDREA FOSFURI & ALFONSO GAMBARDELLA, MARKETS FOR TECHNOLOGY: THE ECONOMICS OF INNOVATION AND CORPORATE STRATEGY 261-62 (2004) (same). BESSEN & MEURER, *supra* note 2, at 185 ("The good news is that small inventors receive positive incentives from the patent system; this might, in fact, be one of the strongest rationales for having a patent system. The economic impact of important inventions from small inventors depends, however, on the market for technology.").

pharma patents with a revised system of tailored regulatory exclusivity. Finally, Part IV briefly canvasses three issues meriting future investigation, which are broached by the present analysis but not pursued here: (1) how to determine the precise duration and scope of regulatory-exclusivity protection; (2) how to supplement such an improved system of regulatory-exclusivity incentives on the "supply" side with better pricing (signals) on the "demand" side; and (3) whether the role of nonexclusionary innovation policies should be expanded in this area.

I. PHARMA'S TWO INFORMATION GOODS

This Part lays the analytical foundations of the Feature's argument. The first Section sets out a theoretical framework for the analysis of innovation policy that serves three related purposes. First, it identifies the relevant parameters of costs and benefits of exclusionary incentive systems, such as patents and data exclusivity, which provide the touchstone for the subsequent analysis of how well the present system of pharmaceutical innovation policy is working. Second, it distills the contours of the existing consensus in the literature—that pharma poses an especially strong case for patent protection—against which the present argument is directed. Finally, it provides the basis for the claim that all innovations are best conceived, for purposes of innovation policy analysis, as intangible information goods. The next Section then follows through on the last point, by providing a reconceptualization of pharmaceutical innovations *as* information goods, which paves the way to seeing that at the heart of such innovation lie not one, but two key, information goods. The final section then fully develops the point that these two information goods are indeed very distinct, by specifying their divergence in the economic and technological features relevant to policy analysis.

A. Innovation Policy Analysis of Information Goods

Innovation policy analysis of pharmaceuticals begins with the recognition of the intangible character of innovations, as information goods.[41] Because they are intangible, once such goods are generated, it may be difficult to provide access to their benefits to some while excluding it for others.[42] This *nonexcludability*, in turn, may give rise to an appropriability problem: the inability to charge some or many for accessing the good may result in the innovator failing to recoup the (capitalized, risk-adjusted) costs of generating the innovation. To be sure, in many contexts a combination of secrecy and first-mover advantages (such as lead time, moving down the learning curve, establishing supply chains, brand-name loyalty, and fixed-cost barriers to entry) may suffice

[41] *See* Nancy Gallini & Suzanne Scotchmer, *Intellectual Property: When Is It the Best Incentive System?*, *in* 2 INNOVATION POLICY AND THE ECONOMY 51, 53 (Adam B. Jaffe, Josh Lerner, & Scott Stern eds., 2002) ("Competitive markets may not be conducive to innovation, for a reason that was well articulated by Arrow (1962). Inventions are *information* . . ."); Arrow, *supra* note 7, at 610 (analyzing innovation policy in terms of the "economic characteristics of information"); Benkler, *supra* note 7, at 81 (analyzing innovation policy in terms of "various strategies for organizing information production"); Varian, *supra* note 7, at 1 (analyzing innovation economics as centering on "information goods" as the "basic unit" of transactions).

[42] *See* RICHARD A. MUSGRAVE, A THEORY OF PUBLIC FINANCE 9-10 (1959) (developing the concept of nonexcludability in general); Benkler, *supra* note 7, at 2-3 n.4 and accompanying text (developing how nonexcludability applies to information goods); Varian, *supra* note 7, at 4-5 (same). Not all information goods are equally nonexcludable: method-of-making "process" innovations that are not easily discoverable from any end product are more excludable than "product" innovations that are easily reverse engineered, while method-of-using "process" innovations may be less excludable still. The degree of excludability affects the extent to which patents are either not necessary (where alternative forms of excludability are effective) or not sufficient (where the patent form of excludability is ineffective) as an innovation policy. *See* Amy Kapczynski & Talha Syed, *The Continuum of Excludability and the Limits of Patents*, 122 YALE L. J. 1900, 1908-10 (2013).

to sustain a robust level of innovative activity.[43] But in other contexts, the appropriability enabled by secrecy and first-mover advantages may not suffice in the face of high innovation costs, and a large enough gap may open up between typical innovation costs and risks and imitation costs and delay to warrant an innovation policy intervention into competitive markets to address the concern.

Patents aim to solve this appropriability problem by making innovations more excludable, so as to enable innovators to charge more for accessing the fruits of their innovative activity and thus potentially recover its costs. In other words, patents aim to bolster "incentives to innovate."[44] But this patent solution raises a distinct problem of its own, stemming from the second key feature of information goods: their *nonrivalry*. Goods are nonrival to the extent that consumption by one does not subtract from consumption by another, and information goods are among the most highly, indeed typically purely, nonrival.[45] As a result, once such goods are created it is wasteful to deny anyone access to them—more precisely, from an efficiency point of view, access should be given

[43] *See* Roberto Mazzoleni & Richard R. Nelson, *The Benefits and Costs of Strong Patent Protection: A Contribution to the Current Debate*, 27 RES. POL'Y 273, 276 (1998) ("In a wide range of 'high-tech' industries, firms rated a head start, establishment of effective productions sales and service facilities, and rapid movement down the learning curve, as much more effective than patents in enabling them to profit from the R&D. Pharmaceuticals . . . are exceptions . . ."); F.M. Scherer, *First Mover Advantages and Optimal Patent Protection* 1 (Harvard Kennedy Sch. Fac. Rsch., Working Paper No. RPP15-053, 2014) ("Empirical studies have shown repeatedly that on average, but with notable exceptions, patent protection is a relatively unimportant requisite for business firms' investment in research, development, and innovation . . . This paper seeks to advance the theory of patent protection by quantifying approximations to the 'first mover advantages' that sustain investment in invention and innovation without formal patent protection."); firm surveys cited *supra* note 2.

[44] "Incentives to innovate" include here both "incentives to invent" a new idea or prototype technology and "incentives to develop and commercialize" that idea or technology into a practically workable and marketable product or process. *See* Mazzoleni & Nelson, *supra* note 43, at 274-76 (distinguishing between incentives to "invent" versus "develop and commercialize" theories of patents). That innovation should be thought to include both aspects has been long understood in economics, and is usually attributed to Schumpeterian analysis. *See e.g.*, MACHLUP, *supra* note 2, at 9, 21, 23-24, 27-31, 55-56 (tracing the development of an invention/innovation distinction in economics and giving pride of place to Schumpeter); Burk & Lemley, *supra* note 36, at 1615 ("We follow Joseph Schumpeter in distinguishing between an act of invention, which creates a new product or process, and the broader act of innovation, which includes the work necessary to revise, develop, and bring that new product or process to commercial fruition."). That patents may serve to induce both, the first directly and the second *indirectly*, has a similarly long pedigree in legal analysis. *See, e.g.*, Giles S. Rich, *The Relation Between Patent Practices and Anti-Monopoly Laws*, 24 J. PAT. OFFICE SOC'Y 159, 177 (1942) (emphasizing the "inducement to . . . commercialize the invention" as "by far the greatest in practical importance," over that of the "inducement to invent"); Robert P. Merges, *Commercial Success and Patent Standards: Economic Perspectives on Innovation*, 76 CALIF. L. REV. 803, 806-09 (1988) (developing the invention/innovation distinction and noting that "the patent system rewards *innovation* only indirectly, through the granting of patents on *inventions*"). The relevance of this point for pharmaceutical innovation is taken up *infra* text accompanying note 108. With respect to post-inventive activity, there also exists a sub-theory of the "prospect" function of patents in coordinating such activity, which is taken up *infra* Section III.A.2. Finally, alongside "invent" and "innovate," the third canonical incentive function of patents is to "disclose." *See* MACHLUP, *supra* note 2, at 21 (listing incentives to invent, innovate, and disclose); Merges, *id.* at 809-10 (same); Rebecca S. Eisenberg, *Patents and the Progress of Science: Exclusive Rights and Experimental Use*, 56 U. CHI. L. REV. 1017, 1024 (1989) (same); CRAIG ALLEN NARD, THE LAW OF PATENTS 34-36 (2017) (same); Mazzoleni & Nelson, *supra* at 274-75 (listing "incentive to invent," "incentive to develop and commercialize," "incentive to disclose," and "prospect theory"); PETER S. MENELL, MARK. A. LEMLEY & ROBERT P. MERGES, 1 INTELLECTUAL PROPERTY IN THE NEW TECHNOLOGICAL AGE 167 (2018) (identifying "incentive to invest in creating, developing, and marketing" as "the central theory behind patent law," and "prospect theory" as an "alternative to classical incentive theory"); DONALD. S. CHISUM ET. AL, PRINCIPLES OF PATENT LAW 70 (2001) (listing "(1) incentive to invent; (2) incentive to disclose; (3) incentive to commercialize; and (4) incentive to design around"). Disclosure's relevance here is taken up *infra* text accompanying note 224.

[45] *See* Paul Samuelson, *The Pure Theory of Public Expenditure*, 36 REV. ECON. & STATS. 387, 387-89 (1954) (developing the concept of nonrivalry in general); Benkler, *supra* note 7, at 2-3 n.4 and accompanying text (developing how nonrivalry applies to information goods); Varian, *supra* note 7, at 4-5 (same). The radically distinct—indeed opposed—roles of nonrivalry versus nonexcludability in the policy analysis of information goods are juxtaposed in Oren Bracha & Talha Syed, *Beyond the Incentive-Access Paradigm? Product Differentiation and Copyright Revisited*, 92 TEX. L. REV. 1841, 1849-50 (2014); and Oren Bracha, *Give Us Back Our Tragedy: Nonrivalry in Intellectual Property Law and Policy*, 19 THEORETICAL INQ. L. 633, 643-45 (2018). For the slow, halting recognition of both features as distinct aspects of "public goods," and for the collaborative yet distinct roles of Richard Musgrave and Paul Samuelson in forging this analysis, see Maxime Desmarais-Tremblay, *Musgrave, Samuelson, and the Crystallization of the Standard Rationale for Public Goods*, 49 HIST. POL. ECON. 59 (2017). As Desmarais-Tremblay notes, the first textbook distillation of the standard view of public goods as integrating these two features may be found in RICHARD A. MUSGRAVE & PEGGY B. MUSGRAVE, PUBLIC FINANCE IN THEORY AND PRACTICE 54 (1973).

to anyone willing and able to pay the marginal costs of disseminating the information good.[46] Yet the entire point of patents is to enable their holders to charge a mark-up over that marginal cost, for the sake of recovering the sunk costs of generating the innovation in the first place.[47] And the effect of such supramarginal pricing will be to raise the costs of accessing the information good, both for (a) end consumers[48] and, (b) in contexts of cumulative innovation, follow-on innovators.[49]

Recognition of the access costs attendant upon patent incentives gives rise, in its turn, to two debates: one internal to patent theory, the other more external or comparative. The comparative debate pertains to whether alternative innovation policies, such as public funding or prizes, may better solve the appropriability problem posed by information goods than patents with their access costs. Specifically, it centers on whether there exist nonexclusionary ways of fostering innovation that may rival the decentralized information and incentive virtues of the market price signals that patents and related exclusionary mechanisms (such as trade secret protection) are able to harness.[50]

Meanwhile, the debate internal to patents focuses on how best to maximize their incentive benefits while minimizing their access costs—the familiar "incentive/access" tradeoff.[51] More precisely, comprehensive analysis of the tradeoffs seeks to ascertain when: (1) the incentive benefits of added patent protection, in terms of innovations that otherwise would have been generated later or not at all, (2) outweigh: (a) the administrative costs of granting, monitoring, and

[46] *See* Arrow, *supra* note 7, at 616-17; Benkler, *supra* note 7, at 3.

[47] *See* MACHLUP, *supra* note 2, at 58-59; Eisenberg, *supra* note 44, at 1025-26.

[48] Specifically, some consumers will pay more for the good than they would have under competitive conditions, while others will be priced out and forego access entirely (this latter referred to as "deadweight loss"). *See, e.g.*, William W. Fisher III, *Reconstructing the Fair Use Doctrine*, 101 HARV. L. REV. 1659, 1700-02 (1988) [hereinafter Fisher, *Reconstructing Fair Use*] (analyzing the twin price effects on consumers from IP rights). The extent of both effects will depend on the availability and costs of administering price discrimination. For debate on the merits and demerits of price discrimination in the context of intellectual property, see William W. Fisher III, *Property and Contract on the Internet*, 73 CHI.-KENT L. REV. 1203 (1998); Wendy J. Gordon, *Intellectual Property as Price Discrimination: Implications for Contract*, 73 CHI.-KENT L. REV. 1367 (1998); Julie E. Cohen, *Copyright and the Perfect Curve*, 53 VAND. L. REV. 1799 (2000); James Boyle, *Cruel, Mean, or Lavish? Economic Analysis, Price Discrimination and Digital Intellectual Property*, 53 VAND. L. REV. 2007 (2000); Yochai Benkler, *An Unhurried View of Private Ordering in Information Transactions*, 53 VAND. L. REV. 2063 (2000); Michael J. Meurer, *Copyright Law and Price Discrimination*, 23 CARDOZO L. REV. 55 (2001); William W. Fisher III, *When Should We Permit Differential Pricing of Information?*, 55 UCLA L. REV. 1 (2007); and Glynn S. Lunney Jr., *Copyright's Price Discrimination Panacea*, 21 HARV. J.L. & TECH. 387 (2008).

[49] Specifically, some follow-on innovators will incur transaction costs and royalty fees of licensing, while others may fail to secure a license or simply steer clear of that zone of research. For general analysis of the effects of IP rights in cumulative-innovation contexts, see Merges & Nelson, *supra* note 20; Suzanne Scotchmer, *Standing on the Shoulders of Giants: Cumulative Research and Patent Law*, 5 J. ECON. PERSPS. 29 (1991); and Mark Lemley, *The Economics of Improvement in Intellectual Property Law*, 75 TEX. L. REV. 989 (1997). For debate on the prospects of licensing as an effective solution see, in addition to the foregoing, Robert P. Merges, *Intellectual Property Rights and Bargaining Breakdown: The Case of Blocking Patents*, 62 TENN. L. REV. 75 (1994); Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCI. 698 (1998); Gallini & Scotchmer, *supra* note 41, at 68-69; John P. Walsh et al., *Effects of Research Tool Patents and Licensing on Biomedical Innovation, in* PATENTS IN THE KNOWLEDGE-BASED ECONOMY 285 (Wesley Cohen & Stephen A. Merrill eds., 2003); Fiona Murray & Scott Stern, *Do Formal Intellectual Property Rights Hinder the Free Flow of Scientific Knowledge: An Empirical Test of the Anti-Commons Hypothesis* (Nat'l Bureau of Econ. Rsch., Working Paper No. 11465, 2005); Rebecca S. Eisenberg, *Anticommons, Transaction Costs, and Patent Aggregators*, *in* RESEARCH HANDBOOK ON THE ECONOMICS OF INTELLECTUAL PROPERTY LAW 27 (Ben Depoorter & Peter S. Menell eds., 2019).

[50] For the key works framing the modern debate between public funding, patents, and prizes in these terms, see Arrow, *supra* note 7, which emphasizes the nonexclusionary benefits of public funding of information goods, given their nonrivalry; Harold Demsetz, *Information and Efficiency: Another Viewpoint*, 12 J.L. & ECON. 1 (1969), which replies to Arrow by pointing to the allocative virtues of exclusionary rights, given their harnessing of market price signals; and Brian W. Wright, *The Economics of Invention Incentives: Patents, Prizes, and Research Contracts*, 73 AM. ECON. REV. 691 (1983), which suggests that prizes may provide a nonexclusionary way of tracking market signals..

[51] *See, e.g.,* William M. Landes & Richard A. Posner, *An Economic Analysis of Copyright Law,* 18 J. LEG. STUD. 325, 326 (1989) ("Striking the correct balance between access and incentives is the central problem of copyright law."); Glynn S. Lunney, Jr., *Reexamining Copyright's Incentives-Access Paradigm*, 49 VAND. L. REV. 483, 485-86 (1996) (documenting the "enduring and widespread" reliance by "Congress, courts, and commentators . . . on [the] incentives-access balance in defining some of copyright's most basic parameters").

enforcing patent rights;[52] (b) the access costs of such rights;[53] (c) rent dissipation, or waste from duplicative innovative activity;[54] and (d) global distortions, or diversion of resources away from other sectors with higher social value but lower private returns.[55]

In sum, then, innovation policy analysis centers on three key questions.[56] First, to what extent is *any* innovation policy intervention in competitive markets merited, as opposed to simply relying on secrecy and first-mover advantages to suffice?[57] Second, where the administrative costs and risks of an intervention are deemed necessary, should that intervention take the form of patents or some alternative innovation policy?[58] Third, where patents are the instrument of choice, how should their rights be shaped so as to properly weigh their benefits and costs across innovations?[59] And for all three questions, the inquiry may be pursued at either an aggregate or a more fine-grained level, i.e., for the economy as a whole or contextualized to specific industries or sectors.[60]

[52] *See* BESSEN & MEURER, *supra* note 2, at 14-19, 130-38.

[53] Access costs refer to unnecessary barriers to consumers and follow-on innovators over those innovations that anyway would have been induced at lower levels of protection. For incentive/access frameworks that focus on these parameters, see WILLIAM NORDHAUS, INVENTION, GROWTH, AND WELFARE: A THEORETICAL TREATMENT OF TECHNOLOGICAL CHANGE 70-90 (1969); Fisher, *Reconstructing Fair Use*, *supra* note 48, at 1700-18; Landes & Posner, *supra* note 51, at 326-44. For some leading works exploring tradeoffs between different aspects of these parameters for patents, *see generally* NORDHAUS, *supra*; F.M. Scherer, *Nordhaus' Theory of Optimal Patent Life: A Geometric Reinterpretation*, 62 AM. ECON. REV. 422 (1972); Richard Gilbert & Carl Shapiro, *Optimal Patent Protection and Breadth*, 21 RAND J. ECON. 106 (1990); Paul Klemperer, *How Broad Should the Scope of Patent Protection Be?*, 21 RAND J. ECON. 113 (1990); BESSEN & MEURER, *supra* note 2.

[54] Rent dissipation refers to duplication wastes from any overlapping innovative activity lured by the excess returns ("rents") held out by the stronger levels of protection accorded to some innovations than was needed to recover their generation costs. For incentive/access frameworks that fold in this further set of incentive effects, see MACHLUP, *supra* note 2 at 62-73; Louis Kaplow, *The Patent-Antitrust Intersection: A Reappraisal*, 97 HARV. L. REV. 1813, 1823-29 (1984); Bracha and Syed, *supra* note 45, at 1848-59. For brief recognition of wastes from patent races, see NORDHAUS, *supra* note 53, at 17, 19-21. For some leading works exploring different facets of rent dissipation analysis and their implications for patent rights, see generally Yoram Barzel, *Optimal Timing of Innovations,* 50 REV. ECON. & STAT. 348 (1968); Edmund Kitch, *The Nature and Function of the Patent System*, 20 J.L. & ECON. 265 (1977); Donald G. McFetridge & Douglas A. Smith, *Patents, Prospects and Economic Surplus: A Comment*, 23 J. L. & ECON. 197 (1980); Donald G. McFetridge & Mohammed Rafiquzzaman, *The Scope and Duration of the Patent Right and the Nature of Research Rivalry*, 8 RES. L. & ECON 91 (1986); Merges & Nelson, *supra* note 20; Mark F. Grady & Jay I. Alexander, *Patent Law and Rent Dissipation*, 78 VA. L. REV. 305 (1992); Robert P. Merges, *Rent Control in the Patent District: Observations on the Grady-Alexander Thesis*, 78 VA. L. REV. 359 (1992); and John Duffy, *Rethinking the Prospect Theory of Patent Rights*, 71 U. CHI. L. REV. 439 (2004). For a synthesis of the economic literature on innovation races, see DENNIS W. CARLTON & JEFFREY W. PERLOFF, MODERN INDUSTRIAL ORGANIZATION 539-54, 560-66 (2005 4th ed.).

[55] For incentive/access frameworks that fold in this final set of incentive effects, see MACHLUP, *supra* note 2, at 62-65; and Oren Bracha & Talha Syed, *Beyond Efficiency: Consequence-Sensitive Theories of Copyright*, 29 BERKELEY TECH. L.J. 229, 237-44 (2014). For some leading works exploring diversionary distortions from IP rents, see Arnold Plant, *The Economic Theory Concerning Patents for Inventions*, 1 ECONOMICA 30, 38-43, 45-46 (1934); Lunney Jr., *supra* note 51, at 492-98; and Lunney Jr., *supra* note 48, at 425-33. *See also* Kapczynski & Syed, *supra* note 42, at 1942-50 (discussing patents' potential to distort incentives).

[56] *Cf.* Gallini & Scotchmer, *supra* note 41, at 52 ("For all […] technologies, the same questions arise: Are there natural market forces that protect inventors so that formal protections or other incentives are not necessary? If not, is intellectual property the best incentive system, or would the technology more appropriately be developed by a public sponsor and offered freely in the public domain? How should intellectual property be designed so as to minimize deadweight loss due to monopoly pricing without undermining incentives to innovate?").

[57] *See* sources cited *supra* notes 2, 4343.

[58] *See* sources cited *supra* notes 5050.

[59] *See* sources cited *supra* notes 5151-5555.

[60] For contextualization of the first inquiry, see Bhaven N. Sampat, *A Survey of Empirical Evidence on Patents and Innovation*, 19-21 (Nat'l Bureau of Econ. Research, Working Paper No. 2538, 2018) (arguing that field-specific empirical studies provide a basis for moving past general indeterminacy regarding the case for patent interventions in competitive markets). For the second and third, see generally Fisher III, *supra* note 1, (arguing for contextualized, sectoral analysis of both comparative innovation policies and internal-to-IP concerns). For the third, see Merges & Nelson, *supra* note 2020, at 880-84 (contextualizing analysis of patent scope within different industries); and Burk & Lemley, *supra* note 3636, at 1615 (arguing that to advance patent debates, we must shift from aggregate to field-specific application of different theories).

Each of these questions remains hotly contested in the literature, both with respect to the economy as whole and for many specific sectors. However, in the case of pharmaceuticals, a strong consensus has settled on all three fronts: First, that some innovation policy intervention *is* needed, over and above first-mover advantages and secrecy.[61] Second, that the comparative case for patents versus alternative policies is quite strong here.[62] And, finally, that the shape of the rights conferred upon pharmaceuticals should be relatively strong in terms of scope, duration, and remedies.[63]

The analysis that follows aims to revisit that consensus along all three dimensions. Presently, however, what bears emphasis is that its starting point will be simply to follow through, in the specific context of drugs, on the point that all innovations are, indeed, information goods. Doing so in a systematic way opens up a new picture of pharmaceutical innovation and the role that patents and alternative polices do, can, and should play in sustaining this innovation.

B. Two Information Goods in Pharma

Innovation in pharmaceuticals consists of not one but two key sets of information goods. Behind this claim lies, of course, a prior, more basic point: namely, that the resources at issue in pharmaceuticals are indeed, for innovation policy purposes, best conceived as information goods. The basis for this was set out in the previous Section: it is the *intangible* character of innovations that (1) renders them potentially nonexcludable enough as to perhaps give rise to an appropriability problem requiring some innovation policy intervention; and (2) renders them so highly nonrival as to pose problems with the patent solution. Absent these two features of innovations—i.e., absent their intangibility as *information goods*—none of the distinctive questions that innovations pose for policy analysis gets off the ground. To fail to conceive of innovations in solely intangible terms, as information goods, is to fail to get in proper focus the apt object of the relevant policy analysis.

For many this point may seem straightforward enough.[64] But for others, there may exist two lingering sources of skepticism toward the claim that are worth addressing at the outset. First, whatever the underlying purpose or spirit of patent law, the letter of many of its key texts—both statutory material and judicial opinions—contain *physicalist* formulations of the subject matter of patent rights, namely that patents obtain in some "thing" itself rather than *knowledge of* something. In previous work I have argued that these are terminological slips that, while sometimes harmless,

[61] *See* sources cited *supra* notes 1-5 and 36.

[62] This statement needs qualification in two respects. First, many recent prize proposals are motivated by the improved performance these hold out over patents for pharmaceuticals in the international context of incentives for neglected diseases and access in developing countries. *See* HOLLIS & POGGE, *supra* note 50, 83-95; Fisher & Syed, *supra* note 50, 181-90. These issues are not germane to the present analysis, which focuses on the domestic performance of patents for drugs. Second, there exist some important exceptions to the general consensus, which argue for public funding or prizes to replace patents for drugs in the domestic U.S. setting. *See* Baker, *supra* note 50, at 2-4; Hollis, *supra* note 50, at 1; Love & Hubbard, *supra* note 50, at 1520. The present analysis pursues a different course than the analyses and proposals of these authors, and in particular its arguments for phasing out drug patents do not depend on any increased role for public funding or prize alternatives.

[63] *See, e.g.*, Burk & Lemley, *supra* note 36, at 1615-17 (concluding that the pharmaceutical industry presents the best case for "[s]trong patent rights"); Epstein & Kuhlik, *supra* note 3, at 56 (stating that the case for "strong" patent protection "take[s] on special urgency in connection with pharmaceutical products").

[64] And they are invited to skip the next four paragraphs and turn directly to the specific conceptualizations offered of the information goods at issue in pharmaceutical innovation.

also often enable conceptual errors that hobble sound analysis of patent doctrine or policy.[65] And in that work I also proposed a prophylactic remedy against such errors: whenever confronted with a physicalist formulation of the object of patent rights, as obtaining in some "product" or "process" itself, we should always insert the phrase "knowledge of" before the relevant article.[66] This helps to install a properly *dephysicalized* conception of the subject matter of patents, as always and only obtaining in *knowledge of* the structure or property of some "thing" (for "product" patent claims) or *knowledge of* some way of making or doing something (for "process" patent claims).[67] It is "knowledge" of a particular sort—namely, of an applied, technological sort—that is the specific "information good" relevant to analysis of patent law and policy, the one apt for its protections.[68]

Against this dephysicalization claim and its "knowledge of" prophylactic, however, some may lodge a second, less terminological and more substantive objection, by suggesting that certain features of how patent law actually functions push against the claim of dephysicalization. On this view, such features indicate that in fact patents do not obtain merely in knowledge of some product or process, but, rather, in the product or process "itself." Four such features, in particular, may be pressed in service of this view, and in each case there is a straightforward-enough reply.

A first is the doctrine that not all knowledge "disclosed" in the patent is protected, but only that specifically marked out in the patent "claims."[69] However, while only use of that knowledge set out in the claims is infringing, it remains the case that it is use of *knowledge* that is infringing. That a patent may contain some knowledge that is free for all to use does not affect the point that some other knowledge is what the patent restricts the use of.[70] Second, a requirement that was once imposed on patent claims (but presently is not) was that they must take an *embodied* form, as being tied to some "machine or transformation" to be eligible for protection.[71] But even if we wished to impose (as we currently do not) a requirement that the knowledge in patent claims must take an embodied form to be protected, it would remain the case that it was embodied *knowledge*.[72] A third

[65] *See* Talha Syed, *Reconstructing Patent Eligibility*, 70 AM. U. L. REV. 1937, 1942-45, 1956-57, 1978-80, 2005-10 (2021) (documenting recurring physicalist terms in statutory and judicial construal of patented inventions and their hobbling effects in the analysis of eligible subject matter).

[66] *Id.* at 1942-45.

[67] *See id.* at 1956-58, 1977-80 (dephysicalizing statutory and judicial subject matter categories); *id.* at 2003-20, 2027-36 (reconstructing, post-dephysicalization, more plausible rationales for statutory and judicial subject-matter bars).

[68] For elaboration on these delimitations on the sort of knowledge that is aptly seen to be eligible for protection by the patent system—"applied" rather than "basic" knowledge, and of a "material" or technological, rather than "social" or cultural, sort—see *id.* at 1980-2040. In a nutshell, patents obtain in "spaces of knowledge" and, in particular, "spaces of functional knowledge," where "functional" is a stand-in for "applied knowledge of a technological or material sort." By way of contrast, it may help to specify the distinct information goods at issue in copyright, which pertains not to any *content* (of knowledge) at all but, rather, to *forms*. Specifically, copyright obtains in "forms of expression" and, in particular, "forms of creative expression," where "creative" is a stand-in for (a) expressions of facts, functions, or ideas that exhibit a degree of aesthetic judgement as to selection, description, or arrangement, or (b) expressions *simpliciter*, meaning expressions without any necessary underlying factual, functional, or ideational content, such as expressions of imagination, personality, or mood. And just as with patents' "spaces of knowledge," so with copyright's "forms of expression": these are *intangible* "information goods" from the point of view of innovation policy and, thus, must be conceptualized in thoroughly *dephysicalized* ways for purposes of legal analysis. And again, this is not changed by the fact that the expressive forms in copyright must be tangibly fixed (just as a similar requirement in patents that their spaces of knowledge must be embodied would not change the point that patents would still pertain to, now embodied, knowledge).

[69] *See* 35 U.S.C. § 112(a), (b) (2018).

[70] As I have put the point previously: "while patents do not cover *all* uses of *disclosed* knowledge—but only *some* uses of *claimed* knowledge—nevertheless what they cover does remain use of *knowledge*." Syed, *supra* note 65 at 1955.

[71] Such a "machine or transformation" requirement for "process" claims was once adopted by the Federal Circuit but subsequently rejected as a strict requirement by the Supreme Court in Bilski v. Kappos, 561 U.S. 593, 604 (2010).

[72] Syed, *supra* note 65 at 1951-54.

feature is that patents cover the *practice* of knowledge, not merely its contemplation.[73] But that patents only cover the practice of knowledge does not change the point that they cover the practice of *knowledge*.[74] Finally, we may require that to be found infringing, a practice of knowledge must be "physical" or externally manifested in the world, and not merely involve mental processes.[75] Yet even if we wished to delimit as infringing only those practices of knowledge that are physically embodied or externally manifest in the world (as we may have good reason to), it remains the case that it is the embodied or otherwise externally manifested practice of *knowledge* that is infringing.[76]

What each of these objections betrays is what we may call the lingering spell of *physicalism* in our understanding of the subject matter of patent law, namely the misconception that patents protect some concretely tangible product or process.[77] And the reasons for dwelling on, at the risk of belaboring, the need to cast out this spell and dephysicalize our conception of the innovations at issue in innovation policy and patent law, as "information goods" and "knowledge," are two-fold. A first is to show that even the core innovation standardly taken to lie at the heart of pharmaceutical innovation—a new drug "product"—must be conceived in a fully dephysicalized way, in terms of not the product *itself*, but rather *knowledge of* the product. How this works for the different types of patent claims typically filed in relation to drug product and process innovations is taken up next. The salient point here is that all these innovations are usefully grouped under a single umbrella category: "compound information goods." And this realization then paves the way for another: innovation in pharmaceuticals also involves a *second* information good, knowledge of the safety and efficacy of a drug for human use, as shown by clinical trials. It is the radically distinct character of this "data information good," and its centrality to the theory and practice of pharmaceutical innovation policy, that form the spine of the present argument. And here the salient point is that one possible reason why this second information good has tended to be missed as a distinct innovation in pharma is because *all* innovations in pharma—as in patents more generally—have tended not to be seen as information goods or "knowledge," owing to a lingering physicalism.

The innovations typically seen to lie at the core of pharmaceuticals—new or improved drug products or processes—are helpfully broken down into five main sub-categories of patent claims: (1) New or improved *chemical or biological compounds*, including both: (a) parent claims on a new *active pharmaceutical ingredient* (API); and (b) secondary claims on various *chemical forms* taken by the API (e.g., isomers, salts, crystals, polymorphs, metabolites). (2) New or improved *pharmaceutical formulations* of such compounds (e.g., modes of administration such as capsules, gels, patches, or inhalers; or dosage forms such as extended release or extra strength). (3) New or improved *methods of using* such compounds (e.g., for different conditions). (4) New or improved

[73] *Id.* at 1955.
[74] *Id.* at 1955.
[75] *See id.* at 2023-24.
[76] *Id.* at 2023-24. As discussed therein, the reasons for delimiting infringing conduct to external manifestations lie in privacy concerns.
[77] What accounts for the spell of physicalism in our understanding of patents' subject matter? I have previously ventured that it stems from three features of the knowledge that patents protect, namely that it tends to be: (1) "applied" rather than "basic"—or oriented toward intervening in the world rather than merely understanding it; (2) "technological" rather than "social"—or oriented toward interventions in nature and the body rather than society or culture; and (3) "practiced" rather than merely contemplated. Consequently, even though patents, as a form of innovation policy, always and only protect information goods or "knowledge," the fact that the specific knowledge patents aptly cover is applied knowledge of a technological sort, and only when that is put into practice, tends to pull away from the abstract, even ethereal notion of "information goods" and toward more earthly, concrete notions, which then tend to get falsely physicalized. *Id.* at 2041.

methods of making such compounds.[78] Each of these main types of drug innovations needs to be conceived in fully dephysicalized ways. They need to be understood, that is, as involving not the generation of a new "product" or "process" per se, but rather the generation of new *knowledge of* a product or process. More precisely, for each of the first three "product" innovations—of a new API, or a new or improved chemical or pharmaceutical formulation thereof—their statutory "composition of matter"[79] claims should be construed as *knowledge of the structure* of a compound or formulation.[80] And similarly for the latter two innovations, of a new method of using or making a compound: their statutory "process"[81] claims should be construed as *knowledge of a way of using or making* a compound.[82] To construe the claims in any other way, as going to some physical thing or process rather than knowledge of a thing or process, risks failing to keep our analysis of patent law in touch with its underlying purposes of securing protection over information goods.[83]

To internalize fully that drug product and process innovations consist in generation of *new knowledge* with respect to compounds and methods also paves the way to recognizing the existence of a second, discrete set of innovations in pharmaceuticals: the generation of new (knowledge of) clinical data on the safety and efficacy of such products and processes for humans. And this second set of information goods, as discussed next, is *very distinct* from the first, differing radically in those technological and economic features relevant from an innovation-policy point of view.

C. Two Distinct Information Goods in Pharma

To appreciate the distinct existence and character of data information goods from those of compound ones, consider examples of each of the two main types of pharmaceutical innovation. The first is a "new molecular entity" (NME): a compound for which the active pharmaceutical ingredient (API) has not been previously approved for any uses by the FDA.[84] The second is an

[78] *See* OFF. OF TECH. ASSESSMENT, OTA-H-522, PHARMACEUTICAL R&D: COSTS, RISKS, AND REWARDS 290 (1993) ("For most newly discovered pharmaceutical chemical entities, a patent applicant can make four types of claims: A *compound claim* covers the chemical entity per se, including any and all formulations and uses of the chemical entity. A *composition claim* covers a chemical entity for use as a pharmaceutical. . . . A *method-of-use claim* covers the use of a chemical compound or composition in a specified way. . . . A *process claim,* or *method of manufacture claim*, covers the way in which the compound or composition is produced."); JOHN R. THOMAS, PHARMACEUTICAL PATENT LAW 40-45 (2020 4th ed.) (breaking out compound claims into a parent API claim and subsidiary claims over various distinct chemical forms that the API might take). This breakdown of different types of drug innovations for purposes of patent claims closely overlaps with, but is not identical to, the FDA's breakdown of different types of drug products for purposes of its regulatory review processes and data exclusivities. *See infra* notes 84-85 and accompanying text.

[79] 35 U.S.C. § 101 (2018) (providing that a "new and useful […] composition of matter, or any new and useful improvement thereof" is eligible for patent protection).

[80] More precisely, the knowledge must be of not only the structure but also at least one property of the compound, given the combined effect of patent eligibility and utility doctrines, as discussed in Syed, *supra* note 50, at 2038. But we may abstract from that refinement here, while we return to it below at *infra* note 128136136136.

[81] 35 U.S.C. § 101 (2018) (providing that a "new and useful process . . . or any new and useful improvement thereof" is eligible for patent protection).

[82] For a full elaboration of how the Patent Act's four categories of subject matter—"process, machine, manufacture, or composition of matter," laid out in 35 U.S.C. § 101—should be construed as dephysicalized knowledge goods, see Syed, *supra* note 50, at 1956-58, 2036-37.

[83] The farther they depart from their underlying rationales, the more we risk patent doctrines—ranging from eligibility, novelty, and nonobviousness, to analysis of claim scope and infringement—becoming increasingly under- or over-inclusive. For under- and over-inclusiveness in the case of eligibility doctrine, see Syed, *supra* note 50, at 1979-80, 2007-08. The case of other doctrines is the subject of work in progress: Talha Syed, Dephysicalizing Patent Law (<full date>) (unpublished manuscript) (on file with the author).

[84] NMEs so defined are referred to as "type 1" products by the FDA in its classification scheme for new drug-product approvals. OFF. OF PHARMACEUTICAL QUALITY, U.S. FOOD & DRUG ADMIN., MAPP 5018.2, MANUAL OF POLICIES AND PROCEDURES: NDA CLASSIFICATION CODES 2-3 (2022), https://www.fda.gov/media/94381/download [https://perma.cc/T2R7-ZMT2]. Such products typically

"incrementally modified drug product" (IMP): a specific chemical form, pharmaceutical formulation, combination product, or new use of one or more compounds whose API has been previously approved by the FDA, but not in this variant.[85] NMEs and IMPs are commonly taken to be the two main categories of drug innovations.[86] Not only do they adhere to the FDA's division of its new drug product approvals, but they also track the distinction, commonly drawn in the literature on drug patents and products, between pioneer and improvement products: the former being "primary" products with parent-patent claims and the latter being "secondary" products with subsidiary-patent claims.[87] In both areas, what shapes the distinct contours of these innovation types is the respective intensity of the R&D processes that generate their compound and data information goods. And that of course is of direct concern from an innovation-policy point of view.

For each of these main types of drug innovation, consider the following examples. In both cases, suppose we have an early-stage candidate drug that shows some initial promise for treating an important condition. In one case, it is a new molecular entity (NME) in embryo: an antiviral for treating hepatitis C that is an analog (i.e., a human-modified version) of a naturally occurring nucleoside, with the modification having the therapeutic property of interfering with viral DNA replication.[88] In the other, it is an incrementally modified formulation of an existing drug (IMP): a new once-a-week dosage form of an osteoporosis drug that may considerably reduce its side effects (of severe stomach irritation and toxicity) and thereby result in far greater patient compliance (by reducing the number of times you have to fast for eight hours before taking the pill).[89]

In each case, two questions need to be answered in the course of developing the relevant drug innovation. First, what specific chemical variant of the compound or formulation is promising enough to work with and make various modifications and refinements to, in devising a treatment? Second, will the refined version of the drug prove safe and effective for human use, as validated by clinical trials?[90] And the answers to these two questions will involve, it is the present point to establish, the generation of *two very distinct* innovations or information goods.

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undergo the most onerous form of clinical safety and efficacy investigations and are eligible for a data-exclusivity period ranging between 5-7.5 years, as discussed *infra* note 144. The term "active pharmaceutical ingredient" (API) (or "active ingredient" for short), that is embedded within this definition of an NME, is the one most widely used by most commentators. *See, e.g.*, OFF. OF TECH. ASSESSMENT, *supra* note 78 at 4-5 78; JOHN R. THOMAS, PHARMACEUTICAL PATENT LAW 38-43 (2005). It was also, until recently, the term deployed by the FDA itself, but the FDA has recently substituted the narrower term "active moiety" for these purposes, with API now used in a broader sense to also encompass some new chemical forms that fall under the incrementally modified drug product (IMP) category of drug products. *See* CONG. RSCH. SERV., R46110, DEFINING ACTIVE INGREDIENT: THE U.S. FOOD AND DRUG ADMINISTRATION'S LEGAL INTERPRETATION OF REGULATORY EXCLUSIVITIES 4 (2023), https://crsreports.congress.gov/product/pdf/R/R46110 [https://perma.cc/9GMU-C8R3]. Given the wide currency of the API term, the present analysis will retain it, while using it in the stricter, narrow sense of what the FDA now refers to as an "active moiety," so as to be limited to NMEs and not extend to certain IMPs.

[85] IMPs so defined are referred to as types 2-6 and type 10 products by the FDA in its classification scheme for new drug-product approvals. OFF. OF PHARMACEUTICAL QUALITY, *id.* at 3-7. Such products also undergo original clinical safety and efficacy investigations, but typically of a less onerous form than NMEs, and are eligible for a data-exclusivity period of 3 years, as discussed *infra* note 127.

[86] *See, e.g.*, NAT'L INST. FOR HEALTH CARE MGMT., CHANGING PATTERNS OF PHARMACEUTICAL INNOVATION 5-6 (2002) (identifying three types of chemical innovation: NMEs, IMDs, and "other drugs"); CONG. BUDGET OFF., RESEARCH AND DEVELOPMENT IN THE PHARMACEUTICAL INDUSTRY 1-2, 14-17. (2006) (differentiating between IMPs and "innovative drugs").

[87] *See* references cited *supra* note 78; and *infra* Section III.A.1 (discussing the role in "evergreening" of parent patents on primary products and subsidiary patents on secondary products)

[88] This example is drawn from *Bristol-Myers Squibb v. Teva*, 752 F.3d 967, 969-70 (Fed. Cir. 2014).

[89] This example is drawn from *Merck v. Teva*, 395 F.3d 1362, 1366-67 (Fed. Cir. 2005).

[90] There are also, of course, a series of more "upstream" questions, the answer to which may inform the development of the drug. These include: what kinds of biophysical processes of degeneration and regeneration are associated with this condition? What are especially promising "molecular targets" in the body to attack for treating the condition? What "mechanisms of action" are most effective in attacking

The point may be easiest to see in the case of the IMP drug product, the new formulation of a once-a-week osteoporosis drug. Suppose that both the idea of a new dosage form that leads to better compliance *and* the specific formulation that may be best were relatively easy to discover.[91] Suppose, in other words, that the generation of the compound information good was quite straightforward. Nevertheless, before the drug product is ready for human use—that is, before the drug innovation is complete—we need to verify that this specific dosage form is indeed safe and effective in humans, by passing it through mandated clinical testing. And this holds even more strongly in our NME case, where the required clinical testing is likely to be rather more intensive. In both cases, that is, we need to generate a distinct second innovation, the data information good.

It may be objected that to call this data information an "innovation" is somehow strange. And not because innovations need to be tangible or embodied—the present objection is based less on lingering physicalism than a sense that to qualify as an "innovation," an information good must have special features. In particular, its generation should involve a risky undertaking "in the dark" that may not pan out: an exploration of various options facing uncertain prospects, all of which may ultimately result in failure.[92] And to sharpen the objection, suppose that at the start of clinical testing, the prospects of success for the IMP formulation were high, say fifty or perhaps even eighty or ninety percent. The point remains that to eliminate the residual risk that the drug will not prove safe and effective is both costly and socially valuable. And it is *this*, from an economic point of view, that constitutes an "innovation" or policy-relevant "information good": namely, a socially valuable information good that is costly to generate.[93] And here the socially valuable information is the elimination of the residual risk—that is, the attaining of the knowledge that the drug is, indeed, to our satisfaction safe and effective enough for human use.

A final objection: accepting that the data information good does qualify as an "innovation" despite being purely intangible and often low risk in its generation, is it really a *distinct* innovation from the compound information good? Aren't the two information goods so closely related as not to merit separating out the latter as distinct from the former? To be sure, the two goods *are* closely related: the generation of the data information good depends on the existence of a prior compound information good, while the compound information good's social value depends on the generation of the data information good. But it would be a mistake to conclude from this that the goods are closely *similar*. In fact they are very distinct, sharply diverging in their *technological* and *economic* features as relevant to innovation policy analysis. And, despite being closely related, they are also not necessarily *correlated* in the social desirability of their generation.

The generation of new knowledge of a compound, and new knowledge of its safety and efficacy, have dramatically different risk/cost profiles. As elaborated in the following Section's review of the biopharmaceutical pipeline, investment in drug development obeys a "step function":

such targets? While our focus here is on the "downstream" questions, we return to how they relate to the more upstream ones in Section II.A, *infra*.

[91] This was the case in the real-world facts from which this is example is drawn, where both the idea and the specific formulation ratio were suggested in a trade publication by someone other than the patentee. *Merck*, 395 F.3d at 1368 (noting a description from *Update: Bisphosphonate, Lunar News*, Apr. 1996, at 31; *Update: Bisphosphonate, Lunar News*, July 1996, at 23).

[92] For the role of something like this view in shaping patent doctrine, *see infra* text accompanying notes 105-106.

[93] Such that, once generated, its costs of generation may not be recoverable owing to high nonexcludablility—so as to perhaps justify a policy intervention—while it remains highly (typically, purely) nonrival, so that exclusionary policy interventions come with a downside.

early steps in the space of an uncertain innovation-possibility frontier come with high risk of error, and hence warrant relatively low costs per step, while later steps warrant greater expenditures as the risk or uncertainties begin to be winnowed out.[94] Specifically in the case of drug development, generating the compound information good involves exploration of a *highly* uncertain possibility space: only about one in 1,000 candidate compounds makes it through the drug-discovery phases of "search, synthesis, and screening" and preclinical testing to enter clinical trials,[95] so as to warrant relatively low expenditures per step. In contrast, generating the data information good is a comparatively low-risk, high-cost endeavor. By the time we arrive at clinical testing, most of the risks have been winnowed out, and roughly one in five to ten drugs that enter trials successfully make their way to FDA approval.[96] At the same time, and correspondingly, the costs of phase 1, 2, and 3 trials massively outstrip those of each step of preclinical drug discovery.

This stark divergence in their risk/cost bears two crucial implications for the apt innovation policy treatment of these two information goods. The first goes to the difference in the *economic* significance of the two goods, in terms of their respective contributions to the industry's R&D costs and so its need for innovation policy support. The driver of the industry's innovation economics is not the compound, but the data information good—that is, the generation of clinical trial results. To be clear, the *overall* cost of drug development remains an ongoing topic of fierce controversy.[97] A 2021 meta-review of 22 individual studies spanning four decades found that estimates continue to range wildly, from a low of $161 million to a high of $4.54 billion.[98] What is *not* controversial, however, is that clinical-trial expenditures comprise the lion's share of the costs: between 60% and 70% according to industry-sponsored studies,[99] and even higher for some

[94] *See infra* text accompanying notes 131-134.

[95] *See* references and discussion *infra* note 129.

[96] *See* references and discussion *infra* note 129.

[97] *See* Steve Morgan, Paul Grootendorst, Joel Lexchin, Colleen Cunningham & Devon Greyson, *The Cost of Drug Development: A Systematic Review*, 100 HEALTH POL'Y 4, 4 (2011) ("Despite three decades of research in this area, no published estimate of the cost of developing a drug can be considered a gold standard.") Key sources of controversy include: (a) whether the data are industry-supplied or audited; (b) whether the drug projects are self-selected by firms or aggregated; (c) what are the right estimates of failed projects; (d) for what time periods are investments tied up without seeing a return; and (e) what capitalization rates to apply (i.e., the apt risk-adjusted time discounts). For sharply varying assessments on these scores, resulting in sharply varying overall estimates, compare DiMasi et. al, *Price of Innovation*, *supra* note 17, at 151 (2003) (estimating the total average pre-approval cost of developing a new drug at between $403 and $802 million in 2000 dollars); and DiMasi et. al, *Innovation in the Pharmaceutical Industry*, *supra* note 17, at 20 (estimating the total average pre-approval cost of developing a new drug at between $1.4 and $2.6 billion in 2013 dollars); with Donald W. Light & Rebecca Warburton, *Demythologizing the High Costs of Pharmaceutical Research*, 6 BIOSOCIETIES 34, 36-43, 46 (2011) (critiquing the DiMasi et al. method and estimating the mean and net corporate R&D costs for new-drug development to be between $43.4 and 80.3 million, depending on the calculation method); Donald W. Light & Joel R. Lexchin, *Pharmaceutical Research and Development: What Do We Get for All That Money?* 345 BRIT. J. MED.art. e4348, at 2 (2012) (arguing that the "hidden business model for pharmaceutical research, sales, and profits" depends not on massive investment but instead "turning out scores of minor variations, some of which become market blockbusters"); JAMIE LOVE, CONSUMER PROJ. ON TECH., EVIDENCE REGARDING RESEARCH AND DEVELOPMENT INVESTMENTS IN INNOVATIVE AND NON-INNOVATIVE MEDICINES 1-14 (2003), http://www.cptech.org/ip/health/rnd/evidenceregardingrnd.pdf [https://perma.cc/A6XF-SYW7] (expressing skepticism about the methods used and conclusions drawn by DiMasi et al., and summarizing alternatives); and James Love, *The 2016 Tufts Estimates of the Risk Adjusted Out-of-Pocket Costs to Develop a New Drug*, KNOWLEDGE ECOLOGY INT'L (April 12, 2016), https://www.keionline.org/23054 [https://perma.cc/J4MZ-7MQ9] (critiquing DiMasi et al.'s methods and lack of transparency). *See generally* CONG. WATCH, PUB. CITIZEN, R&D MYTHS: THE CASE AGAINST THE DRUG INDUSTRY'S R&D "SCARE CARD" 1-7 (2001) (criticizing a pervasive drug-industry claim that developing a new drug costs $500 million).

[98] In 2019 U.S. dollars. *See* Michael Schlander, Karla Hernandez-Villafuerte, Chih-Yuan Cheng, Jorge Mestre-Ferrandiz & Michael Baumann, *How Much Does It Cost to Research and Develop a New Drug? A Systematic Review and Assessment*, 39 PHARMACOECONOMICS 1243, 1243 (2021).

[99] DiMasi et. al, *Price of Innovation*, *supra* note 17, at 166 (70%); DiMasi et. al, *Innovation in the Pharmaceutical Industry*, *supra* note 17, at 25 (57.1% to 69.2%). It bears noting that even these estimates understate the full contribution of clinical trials to industry R&D costs: since the figures are for capitalized costs rather than out-of-pocket cash outlays, the share estimated to be taken by preclinical R&D costs includes the time such expenditures are tied up without seeing a return, which is significantly increased by the length of clinical trials.

others.[100] Indeed, the same meta-study found that over half (13) of the 22 studies reviewed did not even consider preclinical drug-discovery expenditures—those generating the compound information good—significant enough to factor in as a part of total costs.[101]

A second set of implications derives from the fact that, in addition to their very distinct economic significance for pharmaceutical innovation, the compound and data information goods also strongly diverge in the *technological* features of the innovation processes generating them. Preclinical drug discovery, with its higher risks and lower costs, is well-suited for a decentralized search, with "many minds" given free rein to explore various different avenues, even at the risk of a fair bit of overlapping, duplicative activity.[102] Clinical trials, on the other hand, with their lower risks and high costs, are better suited for coordinated development, to curb duplicative efforts that would be highly wasteful at this stage.[103]

Integrating these distinct economic and technological aspects of the two innovations leads us to the following pair of policy insights. First, from an *incentive* point of view, it is the data, not the compound, information good that should be at the center of pharmaceutical innovation policy. Yet the patent system *entirely sidelines* this good, providing no direct protection over it, as we will see. Meanwhile, what patents directly protect—the compound information—likely poses no special incentive case for patent protection. Not only is its share of overall industry innovation costs relatively minor but—what is really the relevant focus for innovation policy analysis—the differential between its average innovation costs and imitation costs and speed (i.e., the time and costs involved in reverse engineering and getting ready to manufacture a new or improved drug product or process) is likely no greater than in many other sectors where a combination of first-mover advantages and secrecy suffice to ensure a relatively robust level of innovative activity.[104]

Second, from a *coordinating* point of view, patents serve no useful function with respect to the compound information good. The research phase leading to this innovation is suitable for competitive, decentralized search owing to its comparatively high risks and low costs. On the other hand, while data information does need a strong coordinating mechanism, patents, if they are to serve it, can only play that role indirectly, given their sidelining of this good. Patent doctrines all focus on the results of preclinical research, not clinical testing. And it is not just that patents *presently* ignore the results of clinical trials, so as to provide no direct protection over clinical data. It would also be highly implausible to try to reconfigure the patent system to provide such protection, given the technological profile of this innovation: inquiries into its desirability and feasibility are simply not ones that the patent system is well-suited to carry out, as discussed next.

[100] Schlander et. al, *supra* note 98, at 1250 (citing Cristopher P. Adams & Van V. Brantner, *Estimating the Cost of New Drug Development" Is It Really 802 Million Dollars?*, 25 HEALTH AFF. 420, 422 (2006))

[101] Schlander et. al, *supra* note 98, at 1246.

[102] *See* Merges & Nelson, *supra* note 20, at 874; Lemley, *supra* note 47, at 1059.

[103] *See* Kitch, *supra* note 52, at 265; McFetridge & Smith, *supra* note 52, at 197; Grady & Alexander, *supra* note 52 at 305; William Fisher, *Theories of Intellectual Property,* in NEW ESSAYS IN THE LEGAL AND POLITICAL THEORY OF PROPERTY 168 (Stephen R. Munzer ed., 2001),

[104] As discussed *supra* note 38, the full elaboration of this claim is the task of a follow-up article. For present purposes, even if we suppose the compound information good does need an innovation policy intervention to secure adequate protection, regulatory exclusivity over the data information good will suffice to protect it, as a new compound information good has no commercial value without the new data information good. The converse, however, is not true.

This takes us to a crucial third difference between these innovations, which is that very distinct *institutional tools* are needed for assessing them, given their distinct character as outputs. The preclinical research that generates knowledge of a new drug product or process is, again, marked by a high degree of risk, even uncertainty.[105] As such, it results in a paradigm of the type of "innovation" recognized by the patent system, which requires not only the "novelty" but also the "nonobviousness" of an invention. The latter requires, if not quite a "flash of genius," typically more than a trial-and-error elimination of finite possibilities.[106] By contrast, clinical development involves precisely the latter sort of activity: testing and refining a drug candidate's toxicity and therapeutic properties to ensure it is safe and effective for humans, a determination that is successful in roughly one out of five to ten trials.[107] Indeed, it may be precisely this comparatively "low risk" feature of clinical testing that, along with physicalist misconceptions, has led to the knowledge it generates not being appreciated as a distinct information good or "innovation."

The same technological features of clinical data—that tend to get it sidelined by the patent system and overlooked as an "innovation" by observers—also point to the infeasibility of trying to revise the patent system to extend patent protection over it.[108] Any system of innovation policy requires mechanisms in place to assess the desirability and validity of innovations submitted for its support. The patent system's main mechanisms are its doctrines of nonobviousness and utility, as applied to innovations after they have been generated and then submitted to the patent system for protection. To try to apply these to the generation of clinical data on safety and efficacy would be untenable, for two reasons. First, the determination of the desirability of a new clinical trial has little to do with patent inquiries into "nonobviousness"—with their focus on "uncertainty" rather than mere trial-and-error elimination of "risks." Instead, it has more to do with precisely what sorts of likely risks are worth reducing or eliminating through costly trial-and-error testing. Second, the validity of such tests—that is, their reliability and generalizability across patient populations—can hardly be assessed by the patent system and its tools, such as patent examiners and courts applying the "utility" doctrine. In both respects, the FDA is the better institutional system, not only for the substance but also the timing of these determinations—that is, for deciding which potential trials are merited and which actual ones successful.[109] Similarly, the FDA system is also better placed to determine the apt reward or incentive for carrying out such innovative activity, in the form of

[105] By "risk" is meant a state where probabilities of different possible outcomes are known, while "uncertainty" denotes a state where not even the probabilities of all the possible outcomes are known. *See* FRANK KNIGHT, RISK, UNCERTAINTY AND PROFIT 224-25 (1921).

[106] A leading pharmaceutical case in this regard is *Pfizer v. Apotex*, 480 F.3d 1348, 1363 (Fed. Cir. 2007) (holding a chemical salt formulation of a drug as "obvious" since it was one of a finite number of 53 possible variants that were identified in a prior art article as options to explore). *See generally* Rebecca Eisenberg, *Pharma's Nonobvious Problem*, 12 LEWIS & CLARK L. REV. 375 (2008) (discussing how many drug patents are invalid for obviousness). The "flash of creative genius" language is from a 1942 Supreme Court decision, which was legislatively overruled by the 1952 Patent Act's codification of the nonobviousness requirement. *See* Cuno Engineering Corp v. Automatic Devices, 314 U.S. 84, 91 (1941); 35 U.S.C. § 103 ("Patentability shall not be negated by the manner in which the invention was made."); Graham v. John Deere, 383 U.S. 1, 15 (1966) ("It also seems apparent that Congress intended by the last sentence of § 103 to abolish the test it believed this Court announced in the controversial phrase 'flash of creative genius,' used in *Cuno* . . . ."). There has since been continued controversy regarding how "qualitative" (or "synergistic") versus "quantitative" or ("trial-and-error") a view to take of the "ingenuity" needed to satisfy non-obviousness. *See* KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 406-07, 413-19 (2007) (reviewing the post-*Graham* history of competing views and tests of the Supreme Court, the Court of Appeals of the Federal Circuit, and its predecessor the Court of Customs and Patent Appeals).

[107] *See infra* note 130.

[108] Similarly, they point to the untenability of relying on patent protection over the compound information good, as an "invention," to "indirectly" provide apt incentives for generation of the data information good, as an "innovation," as a sub-literature on patent theory has suggested may often take place. See *supra* note 44.

[109] Regarding timing, the FDA can also, to anticipate an issue taken up below, replicate the coordinating function of patents, since alongside greenlighting one firm's clinical trials, it can also redlight any other firm's duplicative trials. *See infra* II.B and III.B.(2).

data-exclusivity protection. While the form that protection should take merits significant revisions in light of the present system's misalignments, as discussed in Part III below, it remains the case that the two information goods vary sharply in the determination of their *social desirability*.[110]

II. PRESENT INNOVATION POLICY FOR THE TWO INFORMATION GOODS

This Part turns to how existing pharmaceutical innovation policy treats the compound and data information goods in practice. It begins with an overview of the pipeline of biopharmaceutical innovation: its key technological phases, institutional actors, and the basic roles played by patents, FDA regulatory requirements, and data exclusivity therein. It then dives more deeply into precisely how patents and data exclusivity operate here: Section II.B analyzes the coordination functions that patents do (and do not) serve for each of the two information goods, while Section II.C does the same for the incentive functions of patents and data exclusivity.

A. The Biopharmaceutical Pipeline

Biopharmaceutical innovation[111] in the United States takes place in what is often called a "triple helix" institutional setting, in which government, universities, and private industry all play a significant role.[112] This Section briefly sketches the roles of each sector along the main stages of drug development: basic and applied research, translational research shading into drug discovery, preclinical testing, and clinical trials.[113] Both these stages and the roles of the respective sectors, it should be noted, have increasingly tended to overlap as transformations in molecular biology, biotechnology, genomics, and combinatorial chemistry continue to reorient drug development away from "trial-and-error" strategies and toward "rational drug design" models that rely on greater understanding of human physiology and the actions of chemical and biological materials.[114]

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[110] This crucial point tends to be overlooked by those who treat patent and data-exclusivity protection as functional equivalents. *See, e.g.,* Maxwell R. Morgan, *Regulation of Innovation under Follow-on Biologics Legislation: FDA Exclusivity as an Efficient Incentive Mechanism*, XI COLUM. SCI. & TECH. L. REV. 93 (2010) (treating data exclusivity as a functional substitute for patent protection without attending to the differences in the respective information goods they cover, and their implications for shaping sound innovation policy); Yaniv Heled, *Patents v. Statutory Exclusivities in Biological Pharmaceuticals—Do We Really Need Both*, 18 MICH. TELECOMM. & TECH. L. REV. 419, 424 (2012) (same).

[111] The term *bio*pharmaceutical innovation reflects the impact of transformations in molecular biology, biotechnology, and cognate fields on how drug development is carried out today, as discussed below.

[112] *See* Henry Etzkowitz & Loet Leydesdorff, *The Dynamics of Innovation: From National Systems and "Mode 2" to a Triple Helix of University-Industry-Government Relations*, 29 RSCH. POL'Y. 109, 111-12 (2000); Golden, *supra* note 40, at 132.

[113] The following Section synthesizes accounts provided in the following sources: OFF. OF TECH. ASSESSMENT, *supra* note 78 at 3-6; RICK NG, DRUGS: FROM DISCOVERY TO APPROVAL 3-5, 43-72 (2004); Jürgen Drews, *Drug Discovery: A Historical Perspective*, 287 SCI. 1960 (2000); Gary P. Pisano, *Pharmaceutical Biotechnology*, *in* TECHNOLOGICAL INNOVATION AND ECONOMIC PERFORMANCE 347 (Benn Steil, David G. Victor & Richard R. Nelson eds., 2002); CONG. BUDGET OFF., *supra* note 86; *Biopharmaceutical Research & Development: The Process Behind New Medicines*, PHARM. RSCH. & MFRS. OF AM. (2015), https://www.phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/P-R/rd_brochure.pdf [https://perma.cc/XP7M-ZZXZ] (hereinafter "PhRMA").

[114] *See* ALFONSO GAMBARDELLA, SCIENCE AND INNOVATION: THE US PHARMACEUTICAL INDUSTRY DURING THE 1980S, at xiii (1995) ("[T]he 1980s attested a clear shift from largely empirical industrial research processes (based on trial and error of many compounds) to a more rational search for innovation, based on effective use of scientific knowledge and computerized research technologies."); Pisano, *supra* note 113, at 354-55 ("*Rational drug design* is an approach that emerged during the 1980s that sought to 'design' drugs based on detailed knowledge of the biochemical pathways of diseases."); Arti K. Rai, *The Information Revolution Reaches Pharmaceuticals: Balancing Innovation Incentives, Cost, and Access in the Post-Genomics Era*, 2001 U. ILL. L. REV. 173, 174-75 ("In this new era . . . researchers should be able to develop drugs in a faster, more streamlined fashion, through computerized analysis of the genes, proteins, and biochemical pathways that cause particular diseases."); NG, *supra* note 113, at 44 ("There are two main approaches to discovering small molecule drugs: the irrational approach, or the most recent structured rational approach.")

Basic and applied research: The process begins with creation or refinement of fundamental knowledge concerning mechanisms of disease and biochemical processes. Most of this activity is undertaken in universities and government labs, but an increasing portion is done in university-industry partnerships—that is, in faculty-led biotech labs clustered in research parks around campuses.[115] Research at the more "basic" end focuses on mechanisms of disease and regeneration in the body, while the more "applied" end focuses on specific "targets" or receptors for diseases and "mechanisms of action" or pathways to attack such targets.[116] A sharp basic/applied distinction would in any case be overdrawn here, as much of this activity takes place in "Pasteur's Quadrant" of dual-purpose or "use-inspired basic research."[117] The "basic" outputs of this research likely are (and should be) ineligible for patent protection due to subject-matter bars on knowledge of "laws" or "products" of nature. Outputs toward the more "applied" end—or lying in Pasteur's Quadrant—*may* qualify if their claims are strictly delimited to applications.[118]

Translational Research/Drug Discovery: Next, based and applied research needs to be "translated" into the concrete specifics of preventing, diagnosing, or treating particular diseases. Much of this activity still takes place in universities, but an increasing share is done by small biotech and genomics firms, led by former faculty and involving university-based scientists. Large pharmaceutical firms may also enter at the later "drug discovery" phase of this stage. This involves the three sub-steps of "search, synthesis, and screening": (a) searching for molecular targets for a specific disease; (b) synthesizing potentially active chemical or biological compounds; and (c) screening the compounds against the targets for pharmacological activity.[119] Patents are likely available for a subset of the biotech "research tools" created in this phase, although much depends on the vagaries of the above-mentioned subject-matter bars,[120] and their timing and scope may also be affected by the practical utility and regulatory research exemptions discussed below.[121]

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[115] In 2018, the share of basic research carried out by public-sector institutions of government labs, universities, and non-profits was 71%, and the share of university-based research funded by the federal government came to 53%, with most of the rest coming from state and local governments, nonprofits, and in-house, and private-sector funding comprising 6%. *Science & Engineering Indicators*, NAT'L SCI. FOUND. (Jan. 15, 2020), https://ncses.nsf.gov/pubs/nsb20201/u-s-r-d-performance-and-funding [https://perma.cc/L3ZL-ULW2].

[116] In 2018, while the majority (62%) of academic R&D was classified as "basic," a sizeable share of 38% went to "applied research" and "development." *Academic Research and Development*, NAT'L SCI. FOUND. (Jan. 2020), https://ncses.nsf.gov/pubs/nsb20202 [https://perma.cc/728G-QMGS].

[117] *See* DONALD E. STOKES, PASTEUR'S QUADRANT: BASIC SCIENCE AND TECHNOLOGICAL INNOVATION 6, 80 (1997).

[118] For a distillation of how subject-matter doctrine currently operates with respect to biotech outputs at the basic/applied interface, including a discussion of its ambiguities and suggestions for how to resolve them in the manner suggested in the text, see Syed, *supra* note 65, at 2003-27. The leading Supreme Court cases on the doctrine as relevant to the biotechnology sector are *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. 66 (2012), and *Ass'n for Molecular Pathology v. Myriad Genetics, Inc*., 569 U.S. 576 (2013).

[119] For excellent descriptions of the "search, synthesis, and screening" phases, including the roles of advances in biotech in reorienting their character and improving their chances of success, see Pisano, *supra* note 113, at 354-56; and Rai, *supra* note 114, at 189-92.

[120] *See* Syed, *supra* note 65, at 2003-27.

[121] *See infra* Section III.B.1. The function of such biotech patents—whether on research tools or embryonic drug candidates—is sometimes thought to be less to provide incentives-to-innovate than to facilitate licensing, and thereby sustain a "markets-for-technology" division of labor between smaller, entrepreneurial biotech firms and larger, incumbent pharma ones, in which the former generate "inventions" in embryo before passing the baton to the latter for subsequent "developmental" work. *See* Golden, *supra* note 40, at 110-11, 144; Arora & Merges, *supra* note 40, at 32-33; ARORA, *supra* note 40, at X. On this view, incumbent firms may be driven to innovate less by the "pull" of patent returns than the "push" of the drive for competitive advantage over rivals, with the benefits of innovative activity being privately appropriable by first-mover advantages and secrecy or downstream patents. And these benefits may suffice to recoup not only the late-stage developmental activity but also the royalties paid for the early-stage inventive activity by their upstream partners. Thus the role of the upstream patents would be less to *incentivize* the early-stage invention than to facilitate its licensing to later-stage developers, by solving Arrow's "information paradox" in contracting over information goods: the prospective buyer of the good may not be able assess its value until "he has the information, but then he has in effect acquired it without cost." Arrow, *supra* note 7, at 615. *See also* Mazzoleni and Nelson, *supra* note 43, at 1035, 1040-41. The extent to which patents are necessary to prevent such leakage has always been uncertain,

Preclinical testing: Drug discovery shades into preclinical testing, where leading-candidate compounds undergo further evaluation for pharmacological activity and toxicity in wet labs, animal models, and computer simulations.[122] At this stage, public-sector activity tends to dwindle and private firms, both small biotech and big pharma, play the predominant role. If a candidate compound makes it through this stage, the firm will typically file both for a patent,[123] and, to get the green light for clinical trials, an investigational new drug application (IND) with the FDA.

Clinical trials: If the IND passes muster, the compound proceeds to clinical trials on human subjects. These consist of three to four "phases."[124] Phase one involves testing for toxicity and safe dosage ranges, as well as early evidence on effectiveness and side effects, usually on a group of less than one hundred healthy volunteers.[125] If the results are promising enough, controlled phase two tests are carried out on a small number of people (typically between fifty to two hundred) who actually suffer from the disease the drug aims to treat. Phase-two tests reveal the effectiveness of the compound and short-term side effects and risks. Finally, in phase three, much larger controlled and uncontrolled trials of the drug's safety, effectiveness, and optimal dosage are undertaken in hospitals and outpatient settings, usually involving thousands of patients. If an entity successfully navigates phase three, a new drug application (NDA) is submitted to the FDA.[126] If it is approved, the drug is ready for market entry and also typically eligible for a form of "data exclusivity" on the results of its clinical trials—that is, a period of time during which no other firm may rely on its

given the availability of trade-secret protection combined with non-disclosure agreements, and subsequent work has cast some doubt on this rationale. *See* Michael J. Burstein, *Exchanging Information Without Intellectual Property*, 91 TEX. L. REV. 227, 232-34 (2012). For present purposes, we may set aside this issue, since the reforms proposed *infra* Section III.B.2 retain patent protection for midstream biotech outputs, be it over research tools or drug candidates themselves.

[122] For the role of advances in biotech-related fields in enhancing preclinical testing through computer models, to add to the traditional toolkit of *in vitro* (test tube) and *in vivo* (animal model) tests, see NG, *supra* note 12, at 16, 43-66; and Victor Gilsing & Bart Nooteboom, *Exploration and Exploitation in Innovation Systems: The case of Pharmaceutical Biotechnology,* 35 RSCH. POL'Y 1, 10-11 (2006).

[123] The timing of drug patent applications is affected by two doctrines. First, the utility requirement as applied to chemical compounds requires of applicants information on the drug's properties that is typically only available around this stage. *See infra* Section III.B.1. Second, if applicants delay much past this stage, they risk running afoul of the "public use" bar. *See* 35 U.S.C. § 102(a)(1) (2018); JOHN R. THOMAS, PHARMACEUTICAL PATENT LAW 123-28 (2d ed. 2010).

[124] *See The Drug Development Process: Step 3: Clinic Research*, FDA (Jan. 4, 2018), https://www.fda.gov/patients/drug-development-process/step-3-clinical-research#Clinical_Research_Phase_Studies [https://perma.cc/5B95-3ZYU].

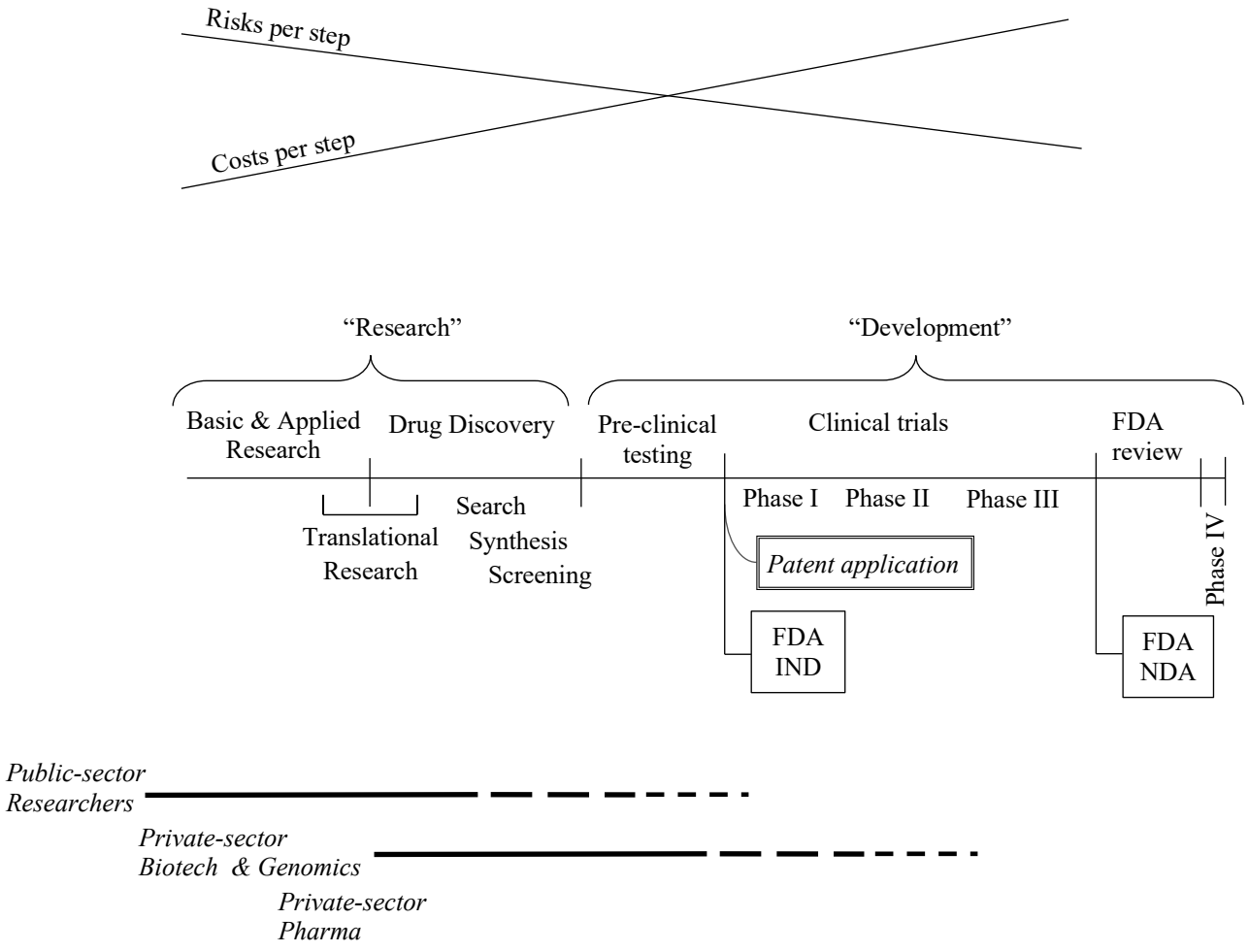
[125] *Id.*

[126] There are three main types of NDAs: (1) 505(b)(1) applications, for those reporting full investigations of a candidate drug's safety and efficacy based on wholly original or authorized clinical studies; (2) 505(b)(2) applications, for those reporting full investigations of a candidate drug's safety and efficacy, but now based at least in part on outside studies for which authorization has not been obtained; and (3) 505(j) applications that duplicate previously reported, outside, safety and efficacy findings, and must show "bioequivalence" between their variant of the product and the original drug whose data they are relying on. *See* 21 U.S.C. §§ 355(b)(1), 355(b)(2), 355(j) (2018). The main type of originator NDA is 505(b)(1), applicable to both NMEs and IMP drugs. 505(j) applications are abbreviated new drug applications (ANDAs), made available starting in 1984 to allow generic firms to piggyback on originator clinical data after a period of data exclusivity has expired. 505(b)(2) applications, also referred to as "paper ANDAs," were the only quasi-generic variant available prior to 1984, and their relevance has faded, although they have not been fully eclipsed. *See* U.S. FOOD & DRUG ADMIN., DETERMINING WHETHER TO SUBMIT AN ANDA OR A 505(B)(2) APPLICATION: GUIDANCE FOR INDUSTRY (2019), https://www.fda.gov/media/124848/download [https://perma.cc/TV2C-W2QA]; Beth Goldstein, *Overview of the 505(b)(2) Regulatory Pathway for New Drug Applications*, CTR. FOR DRUG EVALUATION (2021), https://www.fda.gov/media/156350/download [https://perma.cc/7V6K-V47X]. Finally, there is a further subdivision within 505(j) ANDAs. The first category includes those where the generic drug not only has the same active ingredient, but also the same route of administration, dosage form, and strength as the reference drug, for which only a showing of bioequivalence is needed. *See* 21 U.S.C. §§ 355(j)(2)(A)(iii), 355(j)(2)(C). The second encompasses those where the generic drug, while having the same active ingredient, varies in its route of administration, dosage form, or strength from the reference drug, in which case it will have to file a further "suitability petition" with the FDA, and the Agency may (or may not) require further safety and efficacy tests or a modified label for the drug vis-à-vis the reference drug. *Id.*

data for abbreviated approval.[127] Finally, postclinical and postmarketing phase-four testing may be done to investigate undetected side effects, especially in population samples that were not adequately represented in the clinical phases, including children, the elderly, and pregnant women. This phase is sometimes required by the FDA and sometimes undertaken by the firm on its own.[128]

Figure 1 summarizes these stages and actors. Not counting early-stage basic research, the entire process, from initial identification of promising active compounds through FDA approval, typically takes between ten and fourteen years.[129]

Figure 1: Biopharmaceutical innovation



[127] The main types of data exclusivity relevant here are: (1) for NMEs, between 5-7.5 years; and (2) for IMPs, three years. There also exist other types of exclusivity for "orphan drugs," phase four pediatric trials, and a distinct regime for biologic drugs. For details and refinements, see *infra* text accompanying notes 144-147. These exclusivities are limited to firms filing originator NDAs, principally 505(b)(1) applications, but also (more partially) for those filing 505(b)(2) applications. Generic firms—that is, those filing ANDAs—are not eligible for data exclusivity, but as discussed below, a "first filer" of a "paragraph IV" ANDA (ones involving a patent challenge) is eligible for a six-month "generic bounty" during which time it is the sole ANDA-based firm on the market. *See infra* text accompanying note 158.

[128] And where undertaken, the drug typically qualifies for another six months of data exclusivity: 21 U.S.C. §§ 355a(b).

[129] *See New Drug Development and Review Process*, FDA (July 31, 2023), https://www.fda.gov/drugs/cder-small-business-industry-assistance-sbia/new-drug-development-and-review-process [https://perma.cc/567U-LCCB].

Three aspects of this process bear emphasis. First, while highly uncertain at the start, and in a sense risky throughout, the uncertainties of drug development successively decrease as we move down the pipeline. Roughly only one in a thousand compounds initially chosen for screening and preclinical testing make it through to clinical trials, while about one in five to ten of those selected for clinical testing receive FDA approval.[130] Second, while research becomes less risky as we move down the pipeline, it also becomes more costly per unit of activity. This interaction between risks and costs in biopharmaceuticals comports well with the general insights developed in the economic literature on innovation.[131] As that literature discloses, the investment curve for R&D does not involve one sweeping decision, but rather a series of sequentially related decisions, in a kind of step function: while each subsequent decision requires a higher rate of investment, it also increases the information available for later decisions.[132] With each step, the uncertainties winnow out.[133] Finally, the respective roles of public- and private-sector actors also shift as we

[130] *See* NG, *supra* note 113 at 4 ("of 5000 compunds that show initial promise, five will go into human clinical trials, and only one will become an approved drug."); *and* PhRMA, *supra* note 113 at 8 ("After starting with thousands of candidate compounds, preclinical testing is used to identify one or more lead compounds that will go on to be studied in clinical trials.") and 1 ("the likelihood that a drug entering clinical testing will eventually be approved [] is estimated to be less than 12%."). Three points about these estimates bear noting. First, the figures for success rates prior to clinical trials vary considerably, depending on how early in the process of drug development one starts to identify the number of candidates being chosen, be it the "screening" phase of drug discovery or that of preclinical "testing." *See* NG., *id.* ("Typically, tens of thousands of compounds are screened and tested, and only a handful make it into the market as drug products."); PhRMA, *id.* at 1 ("of the thousands and sometimes millions of compounds that may be screened and assessed early in the R&D process, only a few of which will ultimately receive approval."); Shingo Yagamuchi, Masayuki Kaneko, and Mamoru Narukawa, *Approval success rates of drug candidates based on target, action, modality, application, and their combinations*, 14 CLIN. TRANSL. SCI. 1113, 1114 (2020) ("The drug research and development process . . . is associated with an extremely low success rate, ~1 in 20,000-30,000."); Attila A. Seyhan, *Lost in translation: the valley of death across preclinical and clinical divide—identification of problems and overcoming obstacles*, 4:18 TRANSL. MED. COMM. 1, 4 (2019) ("for every drug that gains FDA approval, more than 1000 were developed but failed."). Second, the figures for success rates in clinical trials vary considerably less (understandably given their more determinate starting point), with most ranging between 10-20%. *See* NG, *id.* (giving a 20% figure); PhRMA, *id.* ("less than 12%"); Yagamuchi et. al, *id.* ("10%-20%"); Seyhan, *id.* (giving a 10-20% range). *See also* J.A. DiMasi, L. Feldman, A. Seckler, & A. Wilson, *Trends in Risks Associated with New Drug Development: Success Rates for Investigational Drugs*, 87 CLIN. PHARMOC'GY & THERAP. 272 (updating historical estimates of "approval rates averaging approximately one in five" from the 1970s to the mid-1990s with an estimate of 19% for the 1993-2009 period); and Chi Heem Wong & Kien Wei Siah, *Estimation of Clinical Trial Success Rates and Related Parameters*, 20 BIOSTATISTICS 273, 277 (2019) (suggesting that a 10-14% success rate is more accurate than the 20% range of earlier studies). Finally, whatever the variance in particular estimates given for preclinical and clinical success rates, studies tend to converge in finding an overall "funneling" effect across these, whereby the uncertainties or risks reduce over time to result in successively lower rates of failure. *See* Steven M. Paull, Daniel S. Mytelka, Christopher T. Dunwiddie, Charles C. Persinger, Bernard H. Munos, Stacy R. Lindborg, & Aaron L. Schacht, *How to improve R&D productivity: the pharmaceutical industry's grand challenge*, 9 NATURE REVIEWS DRUG DISCOVERY 203, 206 (2010); Richard C. Mohs & Nigel H. Greig, *Drug discovery and development: Role of basic biological research*, 3 ALZHEIMER'S & DEMENTIA: TRANSL. RES. & CLIN. INTERV'NS 651, 656 (2017); Tohru Takebe, Ryoka Imai, & Shunsuke Ono, *The Current Status of Drug Discovery and Development as Originated in United States Academia: The Influence of Industrial and Academic Collaboration on Drug Discovery and Development,* 11 CLIN. TRANSL. SCI. 597, 599 (2018). The main possible exception to this generalization—a possible uptick in risk that may take place during the translational phase of research, referred to as the "valley of death"—is discussed *infra* note 133.

[131] *See* NORDHAUS, *supra* note 12, at 36, 70; F. M. SCHERER, INNOVATION AND GROWTH: SCHUMPETERIAN PERSPECTIVES 165 (1984).

[132] *See* NORDHAUS, *supra* note 12. at 36, 70; OFF. TECH. ASSESSMENT, *supra* note 12, at 279 ("R&D projects are in reality *sequential* investments that buy opportunities for further R&D along the way. . . . Therefore, early R&D projects are riskier than later projects and have a higher [opportunity] cost of capital. . . . [T]he investment in early R&D can be viewed as an investment in information that allows the firm to reduce the uncertainty of its later investments.").

[133] A possible exception here is a potential spike in risk during the translational phase between basic/applied research and preclinical and clinical testing, referred to as "the valley of death." *See* Arti K. Rai, Jerome H. Reichman, Paul F. Uhlir & Colin Crossman, *Pathways Across the Valley of Death: Novel Intellectual Property Strategies for Accelerated Drug Discovery*, 8 YALE J. HEALTH POL'Y, L. & ETHICS 53, 58 (2008); Seyhan, *supra* note 130 at 4. Its import here is to reinforce the present argument in both its prescriptive aspects—namely, that research activity prior to clinical trials is comparatively high-risk and merits a many-minded decentralized search—and its descriptive aspects, namely that existing patent rules largely comport with this analysis, by only calling off the patent race near the end of preclinical testing, and allowing follow-on innovative activity a "freedom-to-operate" zone prior to clinical trials. *See infra* Section II.B.

move down the pipeline. Public-sector activity is concentrated at the earlier stages of upstream research activity—with its farther-off and more diffuse, uncertain payoffs[134]—and then gradually tapers off. Private-sector firms pick up the baton at the midstream phases, with their expenditures most heavily concentrated at the lower-risk, higher-cost downstream development phases.

B. Coordinating Innovative Activity

We now turn to examining more closely how patents and data exclusivity presently operate with respect to their twin functions of incentivizing and coordinating drug development. When undertaken with a refined understanding that there are two distinct information goods lying at its heart, such a reexamination reveals some surprising features of how patents work.

(1) Patents' Absence at the Preclinical Stage

First, with respect to research at the preclinical drug discovery phase, the policy prescribed by innovation analysis in theory turns out to be surprisingly close to the one put in place by patent law in practice. In theory, again, the comparatively high uncertainty and lower costs of each step of this phase of innovation counsels a decentralized exploration of the possibility frontier, with the benefits from "many minds" trying out different options tending to be greater than the costs of duplication from overlapping successes or failures.[135] And patent law, through a pair of sector-specific doctrines primarily applicable only to pharma, provides roughly as much in practice. Decentralized exploration in this phase proceeds relatively unencumbered by drug patents, both (a) for pioneering or new compounds, owing to a sector-specific "practical utility" doctrine that pushes the patenting of these further downstream;[136] and (b) for improvement or follow-on compounds, owing to a sector-specific "regulatory research" exemption that keeps this phase of research largely a freedom-to-operate zone for follow-on innovators.[137] With this pair of sector-

[134] For discussion of the far-off time horizons, high uncertainty, and large spillover effects of upstream research, all of which militate against adequate private-sector investments, and provide strong rationales for public investment, see Syed, *supra* note 6550, at 1987-88.

[135] *See* Merges & Nelson, *supra* note 20, at 873-74 (developing the point that in zones of highly uncertain technological exploration, "[t]he only way to find out what works and what does not is to let a variety of minds try."); *see also* F.A. Hayek, *The Use of Knowledge in Society*, 35 AMER. ECON. REV. 519, 519-20 (1945) (explaining that in a "rational economic order . . . knowledge . . . never exists in concentrated or integrated form, but solely as the dispersed bits of incomplete and frequently contradictory knowledge which all the separate individuals possess"). *See generally* CASS SUNSTEIN, INFOTOPIA: HOW MANY MINDS PRODUCE KNOWLEDGE (2009) (describing the benefits and costs of information aggregation).

[136] *See* Brenner v. Manson, 383 U.S. 519, 528-530, 535-36 (1966); *In re* '318 Patent Infringement Litigation, 583 F.3d 1317, 1325, 1329 (Fed. Cir. 2009). By contrast, for almost all other sectors, the utility doctrine operates simply as a "low bar" requirement of showing the bare operability of the claimed invention, that is, that it works for some "use," without any further requirement that the "use" itself be of relatively downstream character. *See* CRAIG NARD, THE LAW OF PATENTS 234 (4th ed. 2017) ("The utility requirement . . . looks to whether the claimed invention simply works . . . ."); ROBERT P. MERGES & JOHN F. DUFFY, PATENT LAW AND POLICY 193 (7th ed. 2017) (stating that for the "vast majority" of cases "the test for utility sets the bar at a very low level" of "bare operability"). The only other sector where the doctrine has similar "downstream" bite is one adjacent to pharma, biotechnology, and the reasons it does dovetails with the present analysis of the divergence between preclinical and clinical information goods and the special innovation policy problems they pose, namely that in biotech, too, there are concerns that patents do not reach too far upstream into zones more suitable for decentralized, many-minded searches. *See* Utility Examination Guidelines, 66. Fed. Reg. 1092 (USPTO Jan. 5, 2001); *In re* Fisher, 421 F.3d 1365 (2005); *see also* NARD, *supra*, at 236-40 ("Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field."); MERGES & DUFFY, *id;* at 209-45.

[137] *See* Merck KGaA v. Integra Lifesciences, 545 U.S. 193 (2005). The statutory "regulatory review" exemption to patents at issue in *Merck* was traditionally thought to be limited in its purview to allowing generic firms to use a patented drug in the course of preparing their ANDA application, so as to be ready for market entry upon patent expiration—something passed as part of the Hatch-Waxman Act's

specific doctrines, patent law has in effect carved out for pharmaceuticals something available nowhere else: a freedom-to-operate zone for many minds during a phase of research, that, while practically-oriented, remains upstream and comparatively high-risk and low-cost.[138] This both reflects and finds its rationale in the fact that innovation in pharma is bifurcated into two distinct information goods, corresponding to distinct stages of innovative activity. The innovative activity generating the compound information good does not require patents' coordinating function.

(2) Patents' Coordinating Role at the Clinical Stage

Next, when we turn to the development stage of clinically testing promising compounds, here too the policy prescribed by theory closely resembles that put in place in practice. Again, in theory the lower risks yet much higher costs of each step of this stage counsel a shift from decentralized to coordinated activity, with the costs from duplication now tending to be greater than those from error. And this is largely what we find in practice, as it is typically when a firm has promising-enough preclinical results on a compound to file an Investigational New Drug (IND) application with the FDA—for purposes of starting clinical trials on humans—that it will also qualify for patent protection on the compound, with the practical utility doctrine calling off the race so as to coordinate further developmental activity in the hands of a single patentee.[139]

C. Incentivizing Innovative Activity

(1) Patents' Commercial Role at the Market-Entry Stage

Upon FDA approval of a drug product's NDA for purposes of market entry, the main value of its patents kick in, enabling the firm to exclude others from making, using, or selling the compound, leaving it to be the only one free to commercially exploit it.[140] There are two special features of drug patents to flag here, going to aspects of patent protection available only to pharma.

compromise between innovator and imitator firms, to overrule a Federal Circuit decision to the contrary. *See infra* note 160 and accompanying text. The Court's decision in *Merck* expanded its purview to cover the use of patented inventions by rival innovator firms as well, so long as such use was "reasonably related" to generating data relevant to submitting any application to the FDA, i.e., an NDA as well, not just an ANDA. *Merck*, 545 U.S. at 206-08; *see also* Classen Immunotherapies, Inc. v. Biogen IDEC, 659 F.3d 1057, 1071 (Fed. Cir. 2011) (recounting the impact of the Hatch-Waxman Act and "reasonably related" standard); Momenta Pharma., Inc. v. Teva Pharma, USA Inc., 809 F.3d 610, 618-19 (Fed. Cir. 2015) (evaluating the "reasonably related" standard and "the broad contours of the exemption"); Classen Immunotherapies, Inc. v. Elan Pharms., Inc., 786 F.3d 892, 894-95 (Fed. Cir. 2015) (finding that clinical data satisfied the "reasonably related" standard when submitted to the FDA along with a citizen petition and sNDA). For almost no other sector does such a research exemption exist, after the common law "experimental use" doctrine was gutted by the Federal Circuit. *See* Madey v. Duke Univ., 307 F.3d 1351, 1362 (2003), *cert. denied*, 539 U.S. 958 (2003) (any common law "experimental use" exemption is limited to "very narrow and strictly limited" contexts of mere experimentation "solely for amusement, to satisfy idle curiosity, or for strictly philosophical inquiry," and does not extend to research of any organized institution, even of a non-commercial or non-profit sort). Yet the statutory regulatory-research exemption *does* extend beyond pharma to any other sector also subject to FDA regulatory requirements, such as medical devices. *See* Eli Lilly & Co. v. Medtronic, Inc., 496 U.S. 661, 678 (1990); Edwards Lifesciences Corp. v. Meril Life Sciences Pvt., 96 F.4th 1347, 1351 (Fed. Cir. Mar. 25, 2024). Given that such regulatory requirements result in a similar bifurcation of preclinical and clinical information goods, this reinforces the present point that the special innovation policy problems posed by pharma are largely a regulatory artifact. For further discussion of medical devices in this connection, see *infra* note 142.

[138] As discussed *supra* notes 136 and 137, one each of the two discrete aspects of the upstream research carve-outs are also applicable to the pharma-adjacent sectors of, respectively, biotech and medical devices, for reasons that reinforce the present analysis since they dovetail with the reasons why they are available in pharma. The two carve-outs in tandem are applicable only to pharma.

[139] *See* Nelson v. Bowler 626 F.2d 853, 856 (C.C.P.A. 1980); Cross v Iizuka, 753 F.2d 1040, 1046-47 (Fed. Cir. 1985); In re Brana, 51 F.3d 1560, 1569 (Fed. Circ. 1995); MANUEL OF PATENT EXAMINING PROCEDURE 2107.03 (USPTO 2023), https://mpep.uspto.gov/RDMS/MPEP/current#/current/d0e200058.html [https://perma.cc/3XP9-TCG5]

[140] *See* 35 U.S.C. § 271(a) (2018).

The first concerns the length of patent protection. While the general patent term in the United States is twenty years from the date of filing the original application,[141] drug patents have special "patent term restoration" provisions. Passed as part of the 1984 Hatch-Waxman Act, these provide for extensions to patents on drugs that undergo a period of regulatory review prior to market entry—that is, for drugs that have some part of their patent life tied up in a precommercial waiting period, prior to commercial drug sales. Section 156 of the Patent Act provides that for drugs undergoing clinical trials, patent terms may be extended by (a) tacking on a clinical-term extension of one-half of the time spent in clinical trials, up to a five-year cap; (b) to result in a total patent term of no more than fourteen years post-clinical trials.[142]

A second specific feature of drug patents is how their protection is "linked" to an entirely separate system, that of FDA regulatory approval. This "Orange Book" FDA regulatory linkage applies only to patents and not to data exclusivity periods. Still, data exclusivity periods form another part of the overall compromise between the innovator and generic sectors of the industry in the 1984 Hatch-Waxman Act, and it is as part of that compromise that the patent linkage is best understood. And so we first briefly detail data exclusivity protection, before turning to the overall compromise put in place by Hatch Waxman and the place of Orange Book linkage therein.

(2) Data Exclusivity

Upon its approval of a drug product's NDA, the FDA will also typically grant that product a period of "data exclusivity." During this period, no other firm is permitted to rely on its original data for purposes of gaining approval for its own product.[143]

Data exclusivities vary in two central dimensions: duration and scope. As to duration, NMEs receive roughly 7.5 years of exclusivity or more, depending on how long the FDA's ANDA approval process takes for the first generic applicant. IMPs receive a strict three-year period.[144] By

[141] 35 U.S.C. § 154(a)(2) (2018).

[142] *Id.* §§ 156(c), (g)(6)(A) (2018). More precisely, the provision provides that any inventions— not only "drug products"—subject to regulatory review are eligible for these patent term extensions or restorations. The main other category of inventions so subject to FDA regulatory processes are "medical devices" and, similarly to the "regulatory review exemption" discussed *supra* text accompanying note 137, their eligibility for this doctrine renders its characterization as "pharma-specific" not quite accurate. But as also discussed there, the reasons why medical devices are eligible for similar treatment goes precisely to the underlying point that is the heart of the present analysis, namely that what makes pharma special, from an innovation policy point of view, is the regulatory aspects of its data information good. That another sector *may* be similarly special, for similar reasons, is beyond the scope of the present analysis. (I say "may" because to determine whether the medical devices sector is really similar would require assessing the gap between the costs of generation and replication of its data information good, and the centrality of that to the industry's economics). The present point is that to speak of "pharma-specific" patent treatment is to signal the way in which the existing patent system already (albeit partly implicitly and certainly inchoately) registers the regulatorily-specific features of this sector.

[143] *See supra* text accompanying note 127.

[144] The difference between these lies in the statutory language governing them: for NMEs, the statute stipulates that the FDA may not *accept* an ANDA application until the expiration of five years from the approval of the NDA of the originator, while for IMPs, it provides that the FDA may not *approve* an ANDA application until the expiration of three years from the approval of the originator's NDA. *See* 21 U.S.C. §§ 355(j)(5)(F)(ii)-(iii) (2018). Since the approval time for an ANDA ranges roughly between thirty and forty months, the resulting effective exclusivity for NMEs is between roughly 7.5 to 8.33 years. *See Generic Drugs Program Activities Report—FY 2024 Monthly Performance,* FDA (Dec. 5, 2024), https://www.fda.gov/drugs/abbreviated-new-drug-application-anda/generic-drugs-program-activities-report-fy-2024-monthly-performance (reporting quarterly mean ANDA approval times yielding annual averages of 33.94 months in 2022, 34.17 months in 2023, and 41.42 months in 2024). In the case of "paragraph-IV" ANDAs (i.e., those challenging patents on the drug—see *infra* note 158), the five-year delay in acceptance for NMEs is shortened to four. But even here, where the patentee timely files

contrast, new biologic drugs receive twelve years of exclusivity.[145] As to scope, NMEs and IMPs are identical: the FDA may not allow any other firm to rely on the protected data in their own (abbreviated) NDA. This differs from the broader scope accorded "orphan drugs," whose data exclusivity is not only longer (seven years) but also forbids the Agency from accepting even originally-generated data on the same drug by a rival firm during the exclusivity period—this broader protection is typically referred to as "market exclusivity" rather than merely "data exclusivity."[146] Finally, a third distinct dimension of exclusivity is whether it is extendable: both for NMEs and IMPs (and biologics), there is a six-month extendable option for pediatric testing.[147]

Our concern here, as throughout, is with chemical drugs, bracketing biologics.[148] Further, our focus here will be on the NME and IMP exclusivities (without attending to orphan drugs).[149]

(3) The Orange Book System

The present system of combined innovation-regulatory policy for pharmaceuticals consists of four distinct but interlocking regimes of institutional rules:

(1) Patent protection, as administered by the Patent and Trademark Office (PTO) and the courts;
(2) Regulatory requirements and permissions, as administered by the FDA;
(3) Data exclusivity rights, as administered by the FDA; and,
(4) At the direct intersection of the previous three, the FDA's "Orange Book" system.

The Orange Book "lists" two things: (a) generic equivalents for approved brand-name drugs, as guidance for pharmacies where state "automatic substitution" laws exist;[150] *and* (b)

an infringement suit in response to the paragraph-IV challenge, this triggers a further automatic thirty-month stay in the FDA's approval of the ANDA, and in the case of NMEs that delay is to be extended until the expiry of 7.5 years from the date of approval of the originator's NDA. *See* 21 U.S.C. § 355(j)(5)(F)(ii).

[145] Biologics Price Competition and Innovation Act, Pub. L. No. 111-148, § 7002(k)(7)(A), 124 Stat. 804, 807 (2010) (codified as amended at 42 U.S.C. § 262 and 35 U.S.C. § 271(e) (2018)). The exclusivity protection is set out at 42 U.S.C. § 262(k)(7)(A)—(B).

[146] Orphan Drug Act, Pub. L. No. 97-414, § 1, 96 Stat. 2049, 2049 (1983) (codified as amended at 21 U.S.C. §§ 360aa—360ff-1 (2018)). The exclusivity protection is set out at 21 U.S.C. § 360cc(a) (2018). Note that a more precise term for this form of exclusivity is arguably "product exclusivity," to signal that it is the product itself, rather than only the firm's clinical data on it, that is being protected against competition. This would more precisely indicate the midway scope that this affords, with the term "market exclusivity" better reserved for the broadest possible protection, against not only competition by the same product, but even by a different product in the same "market"—i.e., in the same therapeutic class, meaning a product that treats the same condition using the same mechanism of action, but with a different compound. While this form of very broad protection is not provided for any type of drug by the FDA, it is a possible option to bear in mind in our regulatory-exclusivity toolkit, as we seek to design an improved regulatory-exclusivity regime.

[147] For chemical drugs, *see* 21 U.S.C. §§ 355a(b)—(c). For biologics, *see* 42 U.S.C. § 262(m)(2)—(3).

[148] Our scope is restricted to chemical drugs for reasons of length. Biologic drugs differ in key respects along the central dimensions relevant to the present analysis, in ways that would need special attention: (1) the scope and strength of their patent rights; (2) the availability and cost of abbreviated regulatory approval for "generic" variants of the drugs (called "biosimilars" to denote their difference from chemical counterparts in terms of close replication of originator products); (3) the length of their data exclusivity periods; and (4) the way that patent rights and regulatory permissions for abbreviated approval are statutorily linked. It should be noted that these differences do not undermine so much as reinforce the central claims of the present analysis, namely that: (1) it is the gap between the costs of generation and replication of the data information good that is central to the innovation economics and policy of pharmaceuticals; and (2) that phasing out patent protection, including the biologic "patent dance" version of Orange-Book linkage, would significantly curb access and gaming costs, while retaining apt innovation incentives. These matters are taken up in a follow-up article to the present: *see* Syed, *supra* note 38.

[149] Orphan drugs raise a host of their own very specific and important concerns that merit a separate analysis.

[150] A key feature of the FDA regulatory system for generics is not just the grant of ANDA-based approval for bioequivalent versions of already-approved brand-name drugs, but also the listing of these generics as "therapeutically equivalent" in the FDA's "Orange Book."

existing patents over such drugs. It is this last feature that accounts for much of the inordinate complexity of the system.

To get a proper handle on the system's present complexity, it is helpful to proceed in stages. Table 1 first summarizes how the three core systems—patent protection, regulatory requirements and permissions, and data exclusivity—relate to one another. The FDA system of regulatory requirements was first put in place in 1938 with the introduction of required "safety" testing for drugs prior to market entry.[151] In 1962, "efficacy" testing was added.[152] In 1984, an "abbreviated" regulatory approval pathway for generics was added, permitting firms to piggyback on innovator data (an "abbreviated" NDA or "ANDA") rather than have to generate their own data ("NDA") or rely on a mix of published studies and supplemental trials ("paper NDA").[153] That same Act, Hatch Waxman, then also provided for data-exclusivity protection to delay generic reliance on data for periods varying according to whether the newly approved innovator drug was an NME or IMP.

Table 1: Patents, Regulatory Requirements and Permissions, and Data Exclusivity

Drug Product	Patent Law	FDA Regulatory Requirements	FDA Data Exclusivity
NME	Parent patents	Stringent safety and efficacy testing	about 7.5 years
IMP	Secondary patents	Lighter safety and efficacy testing	exactly 3 years
Generic	N/A[154]	ANDA piggybacking and bioequivalence	N/A[155]

Next, we must inject into this scheme the FDA's Orange Book system. This system—the subject of ongoing controversy and reforms—was also created by Hatch Waxman. And to get a proper handle on it, it helps first to have the full structure of that statutory scheme in view. Hatch Waxman was a watershed compromise between generic and innovator sides of the pharmaceutical industry, and the structure it put in place set in motion most of the dynamics taken up in Part III.[156] The foundation of the Act was the understanding that it is socially wasteful to require generic firms to replicate the clinical data of an innovator drug, when they seek to sell a bioequivalent version. Consequently, we should allow them to "piggyback" on the innovator's clinical data—to result in

See U.S. DEPT. HEATH & HUM. SERVS., APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS vii (2024). The effect of that classification is to trigger "automatic substitution" laws where states have passed them, which either permit or require pharmacists to substitute a generic for a brand-name drug when filling out a doctor's prescription for a patient (unless the doctor or patient expressly stipulates otherwise). *See* U.S. FOOD & DRUG ADMIN., ORANGE BOOK PREFACE https://www.fda.gov/drugs/development-approval-process-drugs/orange-book-preface

[151] Federal Food, Drug, and Cosmetic Act, Pub. L. No. 75-717, § 201(p)(1), 52 Stat. 1040, 1041-42 (1938).

[152] Drug Amendments of 1962, Pub. L. No. 87-781, § 105(f), 76 Stat. 780, 786 (1962).

[153] Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (codified as amended at 15 U.S.C. §§ 68b-68c, 70b (1994); 21 U.S.C. §§ 301 note, 355, 360cc (1994); 28 U.S.C. § 2201 (1994); 35 U.S.C. §§ 156, 271, 282 (1999)).

[154] Strictly speaking, generic firms may well engage in innovative (manufacturing) activity that results in outputs that might garner "process" or "method" patents. But we can abstract from that here, for two reasons: (1) first, such patents play virtually no role in any of the innovation policy questions taken up below; and (2) relatedly, such patents would remain untouched by the reform proposed below, as that reform requires firms to waive their drug patents in return for data exclusivity protection: since generic firms would not be eligible for the latter, they would not have to give up the former.

[155] *But see* the 180-day "generic bounty" granted to the first patent-challenging generic entrant, detailed *infra* note 158.

[156] *See* Gerald J. Mossinghoff, *Overview of the Hatch-Waxman Act and Its Impact on the Drug Development Process*, 54 FOOD & DRUG L. J. 187, 187-91 (1999). The article is part of a 25-year anniversary symposium on Hatch Waxman in the *Food and Drug Law Journal*, with its theme being precisely that of its watershed compromise: "Striking the Right Balance Between Innovation and Drug Price Competition: Understanding the Hatch-Waxman Act."

enormous social savings.[157] At the same time, however, it was understood that such savings should not come at the cost of unduly eating into innovators' returns, and thus their incentives to innovate. The resulting compromise consists of an interlocking system of essentially eight components, four that facilitate generic entry and four that offset it by strengthening innovator exclusivity (Table 2).

Table 2: The Structure of the Hatch-Waxman Compromise

(A) Facilitating Generic Entry	(B) Strengthening Innovator Exclusivity
(1) Piggybacking on innovator clinical data	(1) Innovator data exclusivity (~7.5 years NME; 3 years IMP)
(2) Regulatory-review exemption to patent rights	(2) Patent term extensions of up to 5 years
(3) Orange Book listing of therapeutic equivalence	(3) Orange Book listing of patents on drugs
(4) 180-day exclusivity for 1st "para-IV" entrant[158]	(4) 30-month stay for ANDAs challenging patents[159]

The first two rows are relatively straightforward. In return for massively lowering the costs of imitative entry through ANDA trials, the Act protects innovator returns with data exclusivity. And, to facilitate generic firms being ready for market at the date of patent expiration, the Act provides a regulatory-review exemption from patent rights—overruling the Federal Circuit's *Bolar* decision that disallowed use of a patented drug by a generic firm for purposes of preparing its ANDA application.[160] On the other side, the Act extends the duration of the patent rights themselves, through the system of patent-term adjustments detailed above.[161]

It is the next two rows that merit careful attention here:

(3) Orange Book listing of therapeutic equivalence	(3) Orange Book listing of patents on drugs
(4) 6-month exclusivity for 1st "paragraph IV" entrant	(4) 30-month stay for ANDAs challenging patents

Three of these features raise troubling questions. Only the Orange Book's listing of therapeutically-equivalent generic drugs to guide pharmacies has a straightforward rationale. Each of the other three are perplexing—"doctrine in search of justification,"[162] if there ever was.

Take first the "generic bounty": a six-month exclusivity period where the firm is the sole competitor to the patentee. A statutory incentive, in other words, to challenge granted patents. This in effect treats the challenge of granted patents as a "public good," one requiring special incentive to undertake or provide, lest others "free ride" on one's efforts. A statutory admission, it would seem, that many of the industry's drug patents are "weak."[163]

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[157] The savings come in two distinct forms: (1) removing the duplicative wastes involved in running clinical trials on a product already validated as safe and effective; and (2) increasing the price competition resulting from the entry of generic rivals having lower average total costs, owing to such savings. The form that piggybacking takes is the ANDA application, as described *supra* note 126.

[158] The Hatch-Waxman Act not only *enables* generic piggybacking on innovator trial data but it also *encourages* generic challenges to innovator patents, by giving a "generic bounty" in the form of a 180-day exclusivity period to the first generic firm that enters not by waiting for patent expiration but by successfully challenging patents still in force, as either invalid or not infringed, by filing a so-called "paragraph-IV ANDA." *See* 21 U.S.C. §§ 355(j)(2)(A)(vii)(IV), 355(j)(5)(B)(iv)-(v).

[159] When a generic firm files a paragraph-IV ANDA, the Act provides for an automatic 30-month stay in the FDA's approval of the ANDA should the patentee, upon notice of the paragraph-IV challenge, timely file an infringement claim. 21 U.S.C. § 355(j)(5)(B)(iii).

[160] *See* 35 U.S.C. § 271(e)(1); Roche Prods. Inc. v. Bolar Pharm. Co., 733 F.2d 858, 858 (Fed. Cir. 1984).

[161] *See supra* text accompanying note 142.

[162] Robert G. Bone, *A New Look at Trade Secret Law: Doctrine in Search of Justification*, 86 CALIF. L. REV. 241 (1998).

[163] Indeed, it is in the legislative history of the Act where the term "evergreening" first arises in the patent literature. *See* THE PATENT TERM RESTORATION ACT OF 1981—S. 255: HEARING BEFORE THE S. COMM. ON THE JUDICIARY 97TH CONG. 122, 132, 140 (1981);

Yet right alongside this incentive or admission comes a check: the grant of an automatic extension of 2.5 years (thirty months) in the approval of an ANDA should the patentee accept the challenge and file a lawsuit. Quite apart from the generic bounty's puzzle, this feature raises a distinct troubling question of its own: what justifies intertwining two seemingly entirely separate systems—patent protection over the compound information good and regulatory approval for the data information good—in this way? Why shouldn't they simply be delinked, so that even if a patentee takes up the generic challenge, the generic firm can continue to proceed on its merry way with the FDA regulatory process, getting its bioequivalent drug ready for market entry, and leaving the patent barriers and risks to such entry entirely outside the FDA's purview?[164]

Finally, a third troubling feature is the way Orange-Book listing of patents invites abuse or gaming, such as listing of multiple patents on the same NDA-approved product, to enjoy multiple automatic thirty-month stays—that is, *de facto* 2.5-year extensions on the product's data exclusivity. To be sure, some of the troubling abuses have been curbed by subsequent legislative reform, such as the ending in 2003 of the practice of granting multiple stays, so as to limit each product to a single thirty-month delay.[165] Yet others may remain.[166] And in any case, the central puzzles remain to be addressed: (1) Why provide a statutory incentive to challenge granted drug patents? (2) And even supposing that is a good idea, why should the patent processes for handling infringement claims be intertwined with those of the FDA for conferring regulatory approval?

The Orange Book system has come in for much scrutiny, playing a starring role in concerns raised over two related industry practices that have been strongly criticized: "evergreening" practices in general and, what are a specific sub-variant of these, "reverse settlement agreements." We turn to these next as part of a general assessment of the potentially high costs incurred by the present system in place, in terms of barriers to access, duplication wastes, and gaming. But it is important to note at the outset that while the Orange Book system certainly merits critical scrutiny, it itself is a surface effect, and not the underlying cause, of the system's deeper misalignments.

III. REVISING PHARMA INNOVATION POLICY

PATENT TERM EXTENSION AND PHARMACEUTICAL INNOVATION: HEARING BEFORE THE SUBCOMM. ON INVESTIGATIONS AND OVERSIGHT OF THE COMM. ON SCI. AND TECH., 97TH CONG. 132, 177-78 (1982).

[164] Note that this is a separate matter from another, more justified, intersection, which is that the statute also provides that where a patentee does not file an infringement suit, a generic filer of an ANDA may proceed to "obtain patent certainty"—i.e., to avoid at-risk market entry—by seeking a declaratory judgment of invalidity or non-infringement. 21 U.S.C. § 355(j)(5)(C).

[165] *See* Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, § 1101, 117 Stat. 2066 (codified as amended at 21 U.S.C. § 355(j)(5)).

[166] The principal controversies—subject of subsequent legislative amendments, agency interpretations by both the FDA and FTC, and judicial decisions—center on the extent to which (1) a first-filer of a paragraph IV application should be able to reach a settlement agreement with the patentee (i.e., not pursue their patent challenge to completion) and still enjoy the six-month exclusivity upon the date of entry stipulated in the agreement; and (2) thereby not only retain the challenger bounty while striking a deal with the patentee, but also, by "parking" their ANDA until the stipulated time of entry, cause a "bottleneck" of subsequent generic firms, whose later-filed ANDAs the FDA will have to sit on. For the legislative revisions to what counts as a "forfeiture" of the bounty, and reviews of the ensuing controversies in agency and judicial interpretations of these, see 21 U.S.C. § 355(j)(5)(D); U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY—180-DAY EXCLUSIVITY: QUESTIONS AND ANSWERS 14-26 (Jan. 2017), https://www.fda.gov/media/102650/download [https://perma.cc/C69G-LD2X]; ROBIN FELDMAN & EVAN FRONDORF, DRUG WARS: HOW BIG PHARMA RAISES PRICES AND KEEPS GENERICS OFF THE MARKET 38-40 (2017).

Part II disclosed two key aspects of how the present system of pharmaceutical-innovation policy works in relation to its two central information goods. First, of the two primary functions that patents serve in pharmaceutical innovation—coordinating innovation races and incentivizing innovative activity—they do so only indirectly, with respect to an information good, data, that they do not directly protect.[167] Meanwhile, for the compound information good that patents do directly cover, they play little to no coordinating role and a secondary incentive one.[168] A sounder innovation policy would change both aspects. First, it would replace the primary, yet indirect, role played by patents over data information with a form of regulatory exclusivity that directly attends to the distinctive features of this innovation. Second, it would phase out the direct but secondary role played by patents over compound information.

The point of these reforms is, fundamentally, to better align our system of innovation policy with the underlying innovations they seek to incentivize. Only by directly attending to the relevant features of the information goods that they govern, can our innovation policy rules squarely face the various tradeoffs facing any innovation system. In particular, such reforms would significantly improve the performance of our innovation policy for drugs along the two central tradeoffs facing incentive systems that use exclusionary rights (such as patents or data exclusivity): (1) the undue barriers to access such rights erect for innovations that could have been generated at lower levels of protection; and (2) the undue duplication costs rent that such rights may incur with respect to those innovations that would have been incentivized by a lower level of protection.[169]

Each of these concerns have been prominently aired in the critical literature, the first under the heading of "evergreening" practices, and the second under the heading of "me-too" drugs. And in both cases, it is possible vastly to improve both our diagnosis of the causes and extent of the problems and our ability to propose effective solutions by focusing our analysis on the centrality of the data information good to pharmaceutical innovation and the misalignment of existing rules with respect to that information good.

A. Problems: Undue Access Costs and Rent Dissipation

(1) Access Costs: Evergreening and Reverse-Settlement Agreements (RSAs)

We turn first to "evergreening." The concerns associated with this practice in pharma have generated a massive literature in recent years, spawning over three hundred scholarly articles on the topic.[170] While the term has been used to cover a bewildering array of different practices,[171] at its core we may take "evergreening" to refer to efforts by drug companies to prolong the effective period of exclusivity enjoyed by a drug beyond the formal expiration of its core patents on the compound. Such efforts come in two principal forms: (1) efforts to obtain and defend "secondary

[167] *See supra* Sections II.B.(2) and II.C.(2).

[168] *See supra* Sections II.B.(1) and II.C.(1).

[169] *See supra* text accompanying notes 53-54.

[170] Erika Lietzan, *The "Evergreening" Metaphor in Intellectual Property Scholarship*, 53 AKRON L. REV. 805, 808 (2019) (reviewing a "scholarly literature" of "342 articles in legal, medical and scientific, and economic journals" that address "'evergreening'")

[171] For criticism of how the term is often used vaguely, even inconsistently, in the literature, see *id.* For an incisive effort at clarifying the different possible meanings of the concept, see Uri Y. Hacohen, *Evergreening at Risk*, 33 HARV. J. L. & TECH. 479, 484-91 (2020). The following builds on Lietzan and Hacohen'a analyses to offer a clear and consistent conceptualization of the notion and associated practices.

patents" on a drug that expire at a later date than that of the primary or core patents that originally covered it; (2) efforts to obtain and defend patents on new "secondary products" that can effectively compete with generics of the original.[172] The extent to which such practices can be successful and why they should be troubling remain contested issues.[173] The core concern however

[172] There are key sub-variants within each of these: (1) *Single-product lifetime extensions* may be pursued either by: (a) "Submarine patents," whereby secondary patents are filed at the same time as the parent ones, but then "lie low" during the application process, only to resurface at a later date, to enjoy a later expiration. This practice was effectively undermined when the U.S. switched from a patent term starting at the date of issue to one starting at the date of filing. (b) "Secondary patents" on the same primary product that, while not representing a significant technological advance (and hence subject to being ruled "obvious"), can enjoy some significant measure of protection on account of infirmities in the processes of granting, challenging, and invalidating patents—such as those involved in Orange-Book listing and thirty-month automatic stays, *see supra* text accompanying notes 158-159, 165, and RSAs, *see infra* text accompanying notes 182-183. (2) *Multiple-product life cycle extensions* may be pursued either by: (a) "Secondary products" that, while obtaining both their own patents *as well as* NDA-based IMP drug approval, nevertheless hold out either a modest or even trivial advance over the primary product, one that, again, escapes (for a time at least) the filters of the patent system. The question this case raises is: if the IMP is not a genuine advance over the parent product, then why, after expiration of the parent's patents, does a generic variant of the parent not provide effective price competition with the (not so) "new and improved" variant? One set of answers lie in infirmities in the price signals of the healthcare market, owing to the presence of insurance, formulary managers (who may be "captured"), and provider incentives (which may be price-insensitive and excessively cautious or risk-averse in not wanting to choose the "latest" drug over a generic of the older one). Another set goes to the other sub-variant here: (b) "Product hopping," whereby the patentee switches out the parent for the improvement product some time before the expiration of the parent's patent—thus at a time where there is no generic competition for either—so as to make patients, providers, and payers accustomed to the "new and improved" variant as to make it "sticky" to switch "back" to the (generic version) of the "original" when it goes off patent. As these sub-variants of this latter category show, the problems with multiple-product extensions only lie partly with the patent system; the other part lies with the way price signals are muffled in the healthcare market.

Examples of these kinds of patent practices abound in the literature. A prominent example of "submarine patents" in the legislative history of Hatch-Waxman was the case of Valium, where continuation applications allowed a patent with a priority date of 1959 to be issued in 1968, and hence expire only in 1985. *See* Hon. Albert Gore, Jr., *An Unwarranted Patent Stretch*, 128 CONG. REC. E3771 (1982). Notorious examples of trivial "secondary patents" are the case of metabolites of a drug, such as Claritin, that are produced automatically as a chemical byproduct of the drug's ingestion into the body. *See* Schering Corp. v. Geneva Pharm., 348 F.3d 992 (Fed. Cir. 2003). For illustrative examples of modest "secondary patents" on specific chemical or pharmaceutical formulations of the same drug, *see* Eisenberg, *The Role of the FDA, supra* note 8 at 354; C. Scott Hemphill & Bhaven N. Sampat, *When Do Generics Challenge Drug Patents?*, 8 J. EMPIRICAL LEGAL STUD. 613, 615, 621 (2011); Amy Kapczynski, Chan Park & Bhaven Sampat, *Polymorph and Prodrugs and Salts (Oh My!): An Empirical Analysis of "Secondary" Pharmaceutical Patents*, 7 PLOS ONLINE 12 (Dec. 5, 2012); Tahir Amin & Aaron S. Kesselheim, *Secondary Patenting of Branded Pharmaceuticals: A Case Study of How Patents on Two HIV Drugs Could Be Extended for Decades*, 31 HEATLH AFF. 2286 (2012); Lisa Larrimore Ouellette, Note, *How Many Patents Does It Take To Make a Drug? Follow-on Pharmaceutical Patents and University Licensing*, 17 MICH. TELECOMM. & TECH. L. REV. 299, 315-16 (2010). For illustrative examples of patents on modest "secondary product" patents on "new and improved" variants of a pioneer drug product—ranging from new dosage forms (e.g., from tablet to capsule), or strengths (e.g., extended release), or methods of delivery (e.g., pill to patch) or combinations, to distinct chemical variants (such as a single-enantiomer of a racemic mixture, as Nexium is to Prilosec)—*see* Hempill & Sampat, *supra,* at 619-24; Kapcyznski et. al, *supra,* at 1-8; Lietzan, *supra,* at 841-45. For illustrative examples of "product hopping" *see* Michael A. Carrier, *A Real-World Analysis of Pharmaceutical Settlements: The Missing Dimension of Product Hopping*, 62 FLA. L. REV. 1009, 1022-30 (2010); Michael A. Carrier & Steve D. Shadowen, *Product Hopping: A New Framework*, 92 NOTRE DAME L. REV. 167, 192-200 (2016); Robin Feldman & Evan Frondorf, *Drug Wars: A New Generation of Generic Pharmaceutical Delay,* 53 HARV. J. LEG. 499, 516-24 (2016). For an illustrative study of the various infirmities in the health-care market that facilitate product hopping, see Frederico J. Piñeiro, *A case study of AstraZeneca's omeprazole/esomeprazole chiral switch strategy*, 11 GENERICS & BIOSIMILARS INITIATIVE J. 57, 57-64 (2022).

[173] Thus, regarding the extent to which such practices can be effective or successful, critics of the evergreening concern may argue as follows against each of the four variants canvassed *id.*: (1)(a) the concern over "submarine" patents is no longer a live one as the U.S. now has a date-of-filing patent term; (b) the concern over "secondary patents" should be effectively remedied by proper patent enforcement; (2)(a) the concern with "secondary products" is, first, only partly a patent problem and that, again, should be redressed by proper patent enforcement and, second, the other part is either not much of a concern (as it merely reflects consumer preferences) or, if so, requires reform outside the patent system, to address infirmities in the healthcare market; and (b) similarly for "product hopping." *See* Jonathan J. Darrow, *Debunking the "Evergreening" Patents Myth,* 131 HARV. L. REC., December 8, 2010, at 6; Dorothy Du, Novartis AG v. Union of India: *"Evergreening," TRIPS, and "Enhanced Efficacy" Under Section 3(d)*, 21 J. INTELL. PROP. L. 223 (2014); Emily Michiko Morris, *Much Ado About the TPP's Effect on Pharmaceuticals*, 20 SMU SCI. & TECH. L. REV. 135 (2017); Christopher M. Holman, *In Defense of Secondary Pharmaceutical Patents*, 50 IND. L. REV. 759 (2017); Lietzan, *supra* note 163; Israel Agranat & Hili Marom, *In Defense of Secondary Pharmaceutical Patents in Drug Discovery and Development*, 11 ACS. MED. CHEM. LETT. 91 (2020); McKenzie E. List, *The Hollow Rhetoric of Evergreening*, 61 JURIMETRICS J. 495 (2021). To each of the last three, however, there are effective replies: the problem with both "secondary patents" and "secondary products" is precisely that the patent system is not in good working order, and evergreening-type practices of Orange-Book linkage and RSAs exacerbate the difficulties; and this also partly addresses the patent-aspect of "product hopping," while the healthcare market infirmities aspects of this and "secondary product" concerns are, to be sure, outside the proper province of patent or even general innovation policy, that is no reason for infirmities in the latter to reinforce the former. More generally,

is that, when successful, such practices might provide an unduly long buffer for parent or improvement drug products against effective generic price competition, to price some out of access and price hike others.[174]

The judgement that protection of a parent drug against generic competition beyond the formal expiry of its core patents is "unduly long" rests on either one of two premises: (1) First, that a drug's core patents reflect the amount of "innovation" it embodies, and thus the protection afforded by these patents tracks the amount of "incentive" such innovation merits, with any more eating too far into the "access" side of the tradeoff. (2) Alternatively, even if the added protection afforded by secondary patents or products confers incentives for innovating the primary product that are valuable net of their access costs, such incentives are being obtained in very indirect ways, incurring extra administrative costs (of obtaining and defending secondary patents) and distortions to innovative activity (by skewing incentives toward developing indirectly valuable secondary products, that derive much of their value parasitically from the primary product). These latter sets of administrative and distortionary costs may be referred to as the costs of "gaming" the system.

The judgment that protection of an improvement drug product against generic competition is "unduly strong" rests on either one of two different premises: (1) First, where the protection is against generic variants of its parent drug, the concern is with infirmities in the healthcare market that muffle the effectiveness of price signals (including health insurance, formulary managers, and healthcare providers' incentives). (2) Second, where the protection is against generic variants of its own "new and improved" secondary product, then the concern is that the "improvement" represented by this variant is not as great as that reflected in the amount of patent protection it is conferred, owing to infirmities in the processes of granting, enforcing, and invalidating patents. And, to anticipate the discussion that follows, more fundamentally the concern is that even a well-functioning patent system is simply unable to provide the properly calibrated incentives, since its focus is on the "innovativeness" or not of compound information good, while the more significant question of innovation policy here is the social desirability of the data information.[175]

Clarifying how evergreening works, however, raises its own puzzle: why is the practice so heavily concentrated in, even specific to, pharma? The basic incentive to try to extend the effective protection from competition that one's product enjoys, beyond the formal life of its core patents, would seem to be present more generally, existing in all sectors that enjoy robust patent protection. Yet the literature on evergreening has focused its attention exclusively on pharma, but without adducing a satisfactory explanation for why it is this sector, more than others, that engages in the

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the fundamental reply is that secondary patents and products do not represent genuine innovations in proportion to the increased prices they incur, and this merits redress by directly curbing skewed innovation incentives. What the critics of evergreening concerns point to, thus, is the need for better ways both to assess and to curb the incentive skews properly—and it is precisely these tasks that, as argued in the rest of this section, the present analysis enables us to do, being anchored in the centrality of the data information good and its regulatory treatment in explaining, evaluating, and addressing the sources, extent, and ills of evergreening.

[174] These two distinct ways that higher prices affect access—namely, pricing some out of access and charging others higher prices for such access—tend to be treated differently in the literatures of IP and antitrust: the former being a "deadweight loss" or "inefficiency" and the latter merely a "surplus transfer" or "distributive" effect. *See, e.g.,* Fisher, *supra* note 48 at 1701-02 (distinguishing between the deadweight-loss and surplus-transfer effects from IP-enabled raised prices); RICHARD POSNER, ECONOMIC ANALYSIS OF LAW 256 (3rd Ed. 1986) ("the transfer of wealth from consumers to producers brought about by increasing the price from the competitive to the monopoly level [is] a wash [for] … the economic conception of welfare.") The present analysis makes no such sharp distinction.

[175] *See infra* text accompanying notes 188-191.

practice.[176] That explanation lies in the *specific industry structure* of pharma, namely a sharp bifurcation into innovator/imitator profiles of its firms and products, with patented products made and sold as "brand name" ones by firms in one sector of the industry, and fully imitative ones made and sold as "generics" by firms in another sector.[177] With this sharp bifurcation comes a sharp—indeed massive—differential in the prices of the competing brand-name and generic products, with the latter being 75-85% cheaper than the former on average.[178] It is this steep drop in price—operating upon a base of product sales in the millions to hundreds of millions per year[179]—that the generic-form of competition threatens in pharma that provides its firms the massive extra fuel, on top of the basic incentive shared by all patentees, to extend effective patent life on their products. What explains this steep price differential, in turn, is the gap between innovator and imitator costs with respect to clinical data: ever since the passage in 1984 of the Hatch-Waxman Act, generic firms have been allowed to regulatorily "piggyback" on the data originally generated by the brand-name firm. Indeed, the effect of Hatch Waxman has been not just to lower entry costs for specific generic firms but to have made such entry widely feasible enough as to create a *generic industry*.[180]

What explains the pharma-specific character of intensive evergreening, then, is precisely the centrality of data information to pharmaceutical innovation: the gap between its generation and replication costs explains not only the steep price differential between particular brand-name and

[176] As discussed *supra* note 163, the term "evergreening" was introduced in the patent literature in the drug context. For the exclusive concentration on pharma in the evergreening literature, see Lietzan, *supra* note 170 at 807-810 (reviewing the literature and its pharma-specific focus). For partial but unsatisfactory explanations for why the practice is especially prominent and concerning in the case of drugs, see S. Sean Tu & Charles Duan, *Pharmaceutical Patent Two-Step: The Adverse Advent of* Amarin v. Hikma *Type Litigation*, 12 NYU J. INTELL. PROP. & ENT. L. 1, 1, 4 (2022) (focusing on Orange-Book enabled practices); Jeffrey Wu & Claire Wan-Chiung Cheng, *Into the Woods: A Biologic Patent Thicket Analysis*, 19 CHI.-KENT J. INTELL. PROP. 93, 98, 153-163 (2020) (suggesting that evergreening is more intensive for biologics than for chemical drugs, and explaining it by their higher sunk costs and greater technological complexities).

[177] The rise of "authorized generics"—subsidiaries of brand-name firms that make and sell imitative variants of the firms' products upon expiration of their patents—does not alter so much as reinforce the present point.

[178] *See* Seema Ledan, *Discussing Brand Versus Generic Medications*, 45 U.S. PHARMACIST, June 2020, at 25 ("Generics range from 80% to 85% lower in cost when compared with their brand product."); CONG. BUDGET OFFICE, EFFECTS OF USING GENERIC DRUGS ON MEDICARE'S PRESCRIPTION DRUG SPENDING 8-9 (Sept. 2010), https://www.cbo.gov/sites/default/files/111th-congress-2009-2010/reports/09-15-prescriptiondrugs.pdf [https://perma.cc/X3JA-7DG5] ("On average, the retail price of a generic drug is 75 percent lower than the retail price of a brand-name drug."). Note these are the *average* price differentials, with variations depending on: (1) how many brand-name entrants there are; (2) how many generic entrants there are; (3) whether there is an "authorized generic"; and (4) whether the brand-name firm chooses to "stay and fight" for the generic tier of the market or, rather, *increase* its price by going after the residual brand-name echelon at the top. *See* CONG.L BUDGET OFFICE, HOW INCREASED COMPETITION FROM GENERIC DRUGS HAS AFFECTED PRICES AND RETURNS IN THE PHARMACEUTICAL INDUSTRY 14-35 (July 1998), https://www.cbo.gov/sites/default/files/105th-congress-1997-1998/reports/pharm.pdf [https://perma.cc/4983-EGCQ]; U.S. FOOD & DRUG ADMIN., GENERIC COMPETITION AND DRUG PRICES: NEW EVIDENCE LINKING GREATER GENERIC COMPETITION AND LOWER GENERIC DRUG PRICES (Dec. 2019), https://www.fda.gov/media/133509/download?attachment [https://perma.cc/WE9E-XBQ4]; U.S. GOV'T. ACCOUNTABILITY OFFICE, GAO-18-40, DRUG INDUSTRY PROFITS, RESEARCH AND DEVELOPMENT SPENDING, AND MERGER AND ACQUISITION DEALS 47-49 (2017), https://www.gao.gov/assets/gao-18-40.pdf [https://perma.cc/E4WK-S38R].

[179] One study of 361 out of 558 new therapeutic agents introduced in the period between 1995 to 2014 found mean sales to come to a little over $1 billion per year (i.e., mean total sales of $15.2 billion over a mean average of 13.2 years on the market). Olivier J. Wouters, Aaron S. Kesselheim, Jouni Kuha & Jeroen Luyten, *Sales Revenues for New Therapeutic Agents Approved by the United States Food and Drug Administration From 1995 to 2014* 27 VALUE HEALTH 1373, 1373 (2024). Another estimate of "the average peak sales" for each new drug product introduced by the top 20 firms by R&D between 2013 to 2023 ranged from $362 million to $555 million per year. *Unleash AI's Potential: Measuring the Return from Pharmaceutical Innovation*, DELOITTE 6 (April 2024), https://www2.deloitte.com/content/dam/Deloitte/us/Documents/life-sciences-health-care/us-rd-roi-14th-edition.pdf [https://perma.cc/67T9-76P8].

[180] *See* Mossinghoff, *supra* note 156 at 194 ("The robust generic drug industry owes its very existence to the Act . . . ."); *What is Hatch Waxman?,* PHARM. MFRS. OF AM. 1 (June 2018) https://www.phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/D-F/Fact-Sheet_What-is-Hatch-Waxman_June-2018.pdf [https://perma.cc/K3U4-CRGQ] ("The Hatch-Waxman Act established the legal and economic foundation for today's generic pharmaceutical industry).

generic products that provides individual firms the special fuel to engage in evergreening, but also the generalized industry structure that has made the practice pervasive in this sector in its wake.

This explanation of the underlying causes of evergreening practices allows us, in turn, to better understand both the character and extent of the problems they raise—and, ultimately, to fashion more effective solutions for their redress. The point is best illustrated by considering a key aspect of evergreening that has garnered a sizeable critical literature of its own over the past two decades: "reverse settlement agreements" (RSAs) between brand-name plaintiffs and generic defendants involved in patent litigation.[181] In typical litigation settlements, it is the defendant who pays the plaintiff some amount to drop the lawsuit, so as to avoid higher prospective damages should they be found liable for infringement. In RSAs, by contrast, it is the reverse (thus the moniker): the plaintiff patentee pays the defendant(s) to drop the suit. This raises the specter that the plaintiffs are "buying off" a challenge to their (potentially weak) patents—that they are, in the words of the other moniker common for such agreements, "paying for delay" of generic entry.[182]

As with evergreening more generally, there remains debate on the extent to which RSAs should trouble us. Critics of the agreements charge that they are a way for pharma firms to insulate "weak" patents—that is, secondary patents on a parent product or primary patents on a secondary product—from effective challenge. Defenders point to various possible benefits, ranging from reduced costs of litigation or uncertainty, to firming up necessary patent incentives.[183] What has been missing from the literature, however, is a satisfactory explanation for the one feature of such agreements all are agreed on: that they are specific to pharma patent litigation.[184] And that missing explanation is supplied, again, by the fact that the key distinguishing innovation in pharma is the data information good and how it is regulatorily handled: *this* is what explains the price gap fueling patentees in this sector (alone) to seek to ward off (generic) competition with such intensity.

Explaining what drives pharma-specific RSAs (and evergreening in general) equips us to better assess their costs. In 2010, the Federal Trade Commission estimated the costs of RSAs to be $3.5 billion annually in raised prices for American consumers.[185] A more recent study suggests this that is a significant underestimate, and offers instead a figure of $6.2 billion annually for the

[181] *See, e.g.,* Einer Elhauge & Alex Krueger, *Solving the Patent Settlement Puzzle*, 91 TEX. L. REV. 283, 284-85 (2012); Traci Aoki, *The Problem of Reverse Payments in the Pharmaceutical Industry Following* Actavis, 67 HASTINGS L. J. 259, 362-64 (2015); Erik Hovenkamp, *Antitrust Law and Patent Settlement Design*, 32 HARV. J.L. & TECH. 417, 434 (2019); Eric Hovenkamp & Jorge Lemus, *Antitrust Limits on Patent Settlements: A New Approach* 70 J. INDUS. ECON. 257, 258 (2022).

[182] *See, e.g.,* C. Scott Hemphill, *Paying for Delay: Pharmaceutical Patent Settlement as a Regulatory Design Problem* 81 NYU L. REV. 1553, 1573-77 (2006); Aaron Edlin, C. Scott Hemphill, Herbert J. Hovenkamp & Carl Shapiro, *Activating* Actavis, 28 ANTITRUST 16, 16-21 (2013); Robin Feldman, *The Price Tag of "Pay-for-Delay,"* 23 COLUM. SCI. & TECH. L. REV. 1, 2-5 (2021); CONG. RSCH. SERV., R46679, *The Role of Patents and Regulatory Exclusivities in Drug Pricing* 56-59 (2024).

[183] For critics, see, for example, references cited in notes 181-182. For defenders, see, for example, Note, FTC v. Actavis, Inc., 127 HARV. L. REV. 358, 367 (2013); FTC v. Actavis, 570 U.S. 136, 160-77 (2013) (Roberts, C.J., dissenting); Daniel A. Crane, *Ease over Accuracy in Assessing Patent Settlements*, 88 MINN. L. REV. 698, 699-702 (2004).

[184] For examples of incomplete partial explanations of why RSAs are specific to pharma, see Hemphill, *supra* 182 at 1560-61, 1579-86, tying the prevalence of RSAs in pharma to the specifics of the Hatch-Waxman Act's first-filer generic "bounty" provisions, but not addressing the fact that RSAs often extend beyond the first-filer eligible for the bounty, FTC v. Actavis, Inc., 570 U.S. 136, 154-56 (2013) (same); Elhauge & Krueger, *supra* note 181, at 285-93 (attributing RSAs to when patents confer "market power" on their holder, but not addressing the fact that patents ubiquitously confer some measure of market power on their holders, as they must to serve their incentive function).

[185] FED. TRADE COMM'N, PAY-FOR-DELAY: HOW DRUG COMPANY PAY-OFFS COST CONSUMERS BILLIONS 2 (Jan. 2010), https://www.ftc.gov/sites/default/files/documents/reports/pay-delay-how-drug-company-pay-offs-cost-consumers-billions-federal-trade-commission-staff-study/100112payfordelayrpt.pdf [https://perma.cc/3SKW-VUVD].

period of 2006 to 2017.[186] While highly suggestive, as estimates of the overall "access costs" of RSAs these figures face two gaps. First, to fully account for the access costs on consumers, we need to consider the effects of higher prices not only on those paying more (which these studies look at), but also on those priced out (which they do not). Second, any consideration of the access costs of IP rights due to higher prices must also, to be complete, consider any possible "incentive benefits" of such prices, in terms of new innovations lured by the prospects of higher returns. To be sure, the entire thrust of the criticisms of evergreening practices is that they erect barriers to access not justified by any corresponding incentive benefit. But the basis of that criticism must lie in an assessment that the secondary patents and products involved in evergreening represent trivial or nonexistent innovations, or at best modest ones that are disproportionate to their formal patent protection.[187] And to make *that* assessment, we need some metric of the *innovativeness* of the products apart from their formal patent protection.

The main metric deployed in the literature is to attempt to assess the innovativeness of the patents at issue in evergreening cases in light of their ultimate validity and scope as determined by litigation—by looking, in effect, at the win/loss rates of the patents at issue in generic challenges. This approach faces two difficulties. The first, and less serious, is well recognized in the literature: selection bias, whereby those patents that are litigated to trial may well be the ones that patentees had higher confidence would ultimately hold up, an effect that—as the literature discloses—may increase over time as settlement rates go up (partly in response to greater opportunities for them).[188] Thus, while earlier studies (in 2002 and 2006) found that generic challengers won almost three-quarters of such cases,[189] later studies (in 2010 and 2014) found the ratio had dropped to under half.[190] And this trend has been confirmed by the author: a review carried out for the purposes of

[186] Feldman, *supra* note 182, at 5. The author also states that an upper-bound estimate of "the cost could be as high as $37 billion per year—ten times higher than the FTC's estimate." *Id. See also* Robin Feldman, *May Your Drug Price Be Evergreen*, 5 J. L. & BIOSCIS. 590, 596 (2018) (presenting an expansive study of evergreening in the drug-development market); FELDMAN & FRONDORF, *supra* note 166 (analyzing the benefits and pitfalls of the Hatch-Waxman Act).

[187] More precisely, as discussed *supra* text following note 174, the basis of that assessment must be (1) that the direct innovations embodied in such secondary patents and products are disproportionate to their formal patent protection, and (2) that any *indirect* incentives they provide for innovations embodied in the original parent patents and products is purchased at too high a price, in terms of the gaming costs involved.

[188] C. Scott Hemphill & Mark Lemley, *Earning Exclusivity: Generic Drug Incentives and the Hatch-Waxman Act*, 77 ANTITRUST L.J. 947, 979 (2011) ("The patent owner win rate is substantially higher than in the previous decade, when brand-name firms won only 27% of cases that went to judgment. The drop in generic win rate is likely traceable to two changes we think occurred in challenge and settlement practice. The first is an increase in settlements in weak-patent cases after the FDA's earned-exclusivity rule was rejected, a fact which further strengthens our view that those settlements are problematic. The second is an increase in the filing of weak generic claims, motivated in part by the prospect of a future settlement payoff.") (citing *Generic Drug Entry Prior to Patent Expiration: An FTC Study*, FED. TRADE COMM'N vi (July 2002), https://www.ftc.gov/sites/default/files/documents/reports/generic-drug-entry-prior-patent-expiration-ftc-study/genericdrugstudy_0.pdf [https://perma.cc/TB33-BBYR].

[189] *See Generic Drug Entry Prior to Patent Expiration: An FTC Study*, FED. TRADE COMM'N vi (July 2002), https://www.ftc.gov/sites/default/files/documents/reports/generic-drug-entry-prior-patent-expiration-ftc-study/genericdrugstudy_0.pdf [https://perma.cc/TB33-BBYR] (finding that generics win 73% "of the cases in which a court has resolved the patent dispute"); Paul M. Janicke & LiLan Ren, *Who Wins Patent Infringement Cases?* 34 AIPLA Q.J. 1, 5 (2005) (finding that approximately 75% of cases were won by the infringer).

[190] *See* Adam Green & D. Dewey Steadman, *Pharmaceuticals: Analyzing Litigation Success Rates*, RBC 1 (Jan. 15, 2010), https://amlawdaily.typepad.com/pharmareport.pdf [https://perma.cc/3SFX-2EPZ] (finding that generics won 48% of cases against patent holders); Ruben Jacobo-Rubio, John L. Turner & Jonathan W. Williams, *The Distribution of Surplus in the US Pharmaceutical Industry: Evidence from Paragraph iv Patent-Litigation Decisions*, 63 J.L. & Econ 203, 221-22 (2020) (finding generics won about 43% of paragraph (iv) ANDA infringement cases at the trial court level); *cf. 2014 Patent Litigation Study: As Case Volume Leaps, Damages Continue General Decline*, PWC 21 (2014), available at http://www.pwc.com/en_US/us/forensic-services/publications/assets/2014-patent-litigation-study.pdf [https://perma.cc/SN2Q-LPG9] ("Since 2006, ANDA litigation success rates have ranged from a low of 22% to a high of 83%. However, the sample size in the earlier years was low, possibly explaining the wide swings in success rates. Because the majority of ANDA litigations continue to end in settlement, the adjudicated case sample size remains modest.")

this Article shows that of all 109 drug patent cases involving generics litigated to judgment in the period from 2013 to 2022, the generic challenger won only 45, or just under 40% (39.4%).[191]

The second, and more serious, difficulty facing this approach is that the innovativeness of the *patents* at issue in such cases is a highly imperfect metric of the innovativeness of the *products*. And this is because the core "innovation"—or information good—embodied in such products is fully sidelined by the patent system's inquiries: the data information good. It is this information good that, again, is the driver of the industry's economics and the apt focus of its innovation policy rules. And whether or not a patent is merited on the preclinical results for any drug is a highly imperfect indicator of whether—or, more precisely, *how much*—clinical testing is required. This last wrinkle goes to a further difficulty with using patents as our measure of innovativeness: the on/off inquiry of whether a patent is valid or not is too blunt an instrument when the more apt inquiry is determining the *degree* of innovativeness its covered product embodies.

For both these reasons, to better assess the extent to which secondary products involve relatively small degrees of innovativeness—and hence the pernicious effects of undue access and gaming costs associated with evergreening—we need shift the focus of our analysis from the compound information good and its patent protection, to the data information good and its data exclusivity protection. Doing so allows us to zero in on the two core questions: (1) First, to what extent do new drug products approved in the U.S. consist of secondary rather than primary products—meaning products modifying active ingredients already on the market versus those introducing new active ingredients? (2) Second, to what extent do such secondary products hold out significant as opposed to modest or even trivial advances or improvements over existing treatments? The first question allows us to distinguish between those new drug products involving a high versus modest degree of clinical testing—and accordingly meriting strong versus modest data exclusivity protection. The second allows us to distinguish *within* the latter group—of secondary products involving modest testing—between those holding out a significant therapeutic advance, and hence meriting significant data-protection incentives, and those not.

Table 3 distills the results of a review conducted by the author of all new drug approvals by the FDA from 1990 to 2023 (with the exception of the years 2005-2007, for which refined data is not available), as broken down first into "Primary products" or "new molecular entities" (NMEs) and "Secondary products" or "incrementally modified products" (IMPs). Each category is then further sub-divided into drug products rated "priority" by the agency (representing "significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions when compared to standard applications"[192]) and those rated "standard."

Table 3: Breakdown of New Drug Approvals, 1990-2004, 2008-2023[193]

	Drug Product Type	

[191] Author's database of Westlaw searches of all ANDA-based patent litigation from 2013 to 2022, available upon request.

[192] U.S. FOOD & DRUG ADMIN., MAPP 6020.3 REV. 2, REVIEW DESIGNATION POLICY: PRIORITY (P) AND STANDARD (S) 2 (2013).

[193] Author's review of FDA drug approvals database, available on request. For the original FDA databases, see *Drug Approvals and Databases→Compilation of CDER New Molecular Entity (NME) Drug and New Biologic Approvals* U.S. FOOD & DRUG ADMIN. (Apr. 22, 2024) https://www.fda.gov/drugs/drug-approvals-and-databases/compilation-cder-new-molecular-entity-nme-drug-and-new-biologic-approvals; and *Drug Approvals and Databases→NDA and BLA Calendar Year Approvals* U.S. FOOD & DRUG ADMIN (Mar. 15, 2024) *https://www.fda.gov/drugs/nda-and-bla-approvals/nda-and-bla-calendar-year-approvals*.

Drug Rating	NMEs	IMPs	Totals
Priority	433 (49% of NMEs)	287 (14% of IMPs)	720 (25% of all approvals)
Standard	452 (51% of NMEs)	1700 (86% of IMPs)	2152 (75% of all approvals)
Totals	885 (31% of all new approvals)	1987 (69% of all new approvals)	**2872**

A focus on the second column of IMPs or secondary products reveals two crucial points (we turn to the first column of NMEs or primary products below, when discussing me-too drugs). First, of the 2,872 new drugs approved in this period, 1,987 or 69% were IMPs or secondary products. Once we realize that the relevant focus is not on patent protection for the compound information good but data exclusivity on the data information good, then we already have in hand the main tools needed for curbing excessive protection over such secondary products: patents over them should be phased out and replaced with a revised form of data exclusivity. This data exclusivity structure can and should make a crucial distinction unavailable within the patent system, between stronger protection for NMEs—with their more onerous clinical testing requirements—and weaker protection for IMPs, with their lighter requirements. Indeed, the present system already draws this distinction, conferring upon NMEs 5-7.5 years of exclusivity and IMPs only three years. To be sure, these precise figures may need adjustment once data exclusivity becomes the central or sole source of protection. But the basic point remains: data exclusivity, by focusing on the right information good, provides more supple tools for tailoring innovation incentives. And this extends to a second point: a further distinction should be drawn, *within* IMPs, between those holding out truly significant advances—here, 14% of such products—and those bearing more modest or even negligible ones (86%).

That almost 70% of the industry's output consists of secondary products, of which 86% are considered not to hold out significant advances, are strong indications that evergreening *is* a serious problem—meaning that the incentive benefits of secondary products and patents do not justify the exorbitant access and gaming costs involved in their pursuit. And the most effective and well-tailored means for addressing this problem is simply to remove the role of patents—and their concomitant misaligned focus and invitation to gaming—and replace them with a revised form of data exclusivity that retains incentives for improvement innovations while adjusting and curtailing them appropriately.[194]

In sum, when it comes to evergreening and its potential for undue access and gaming costs, an analysis focused on the data information good lying at the center of the system allows us finally to go to the roots of the problem. It points to the underlying cause of this pharma-specific practice, enables us to better assess its extent, and directs us to more effective—farther-reaching and better-tailored—solutions. Removing patents attacks the generative source of troubling practices, while revising data exclusivity uses the institutional tools best fitted to handle the relevant concerns.

(2) Duplication Costs: Me-Too Drugs

[194] The alternative would be to retain patents, and their generative sources of the problem—lying in the basic misalignment between what patents focus on and what is central to innovation policy here—and deal only with surface manifestations through partial reforms such as attempts to improve the processes of granting or challenging patents, reducing abuses of the Orange-Book system, or restricting the availability of RSAs. For discussion of these partial reforms, most of which are apt but none of which go far enough, see Section III.B.

The same points apply when we turn to a second crucial concern: that of "me-too" drugs.[195] This concern is one familiar from the general literature on innovation races and patents: At any given level of robust patent protection, the incentives held out will, for some subset of innovations, not merely equal or just exceed the (risk-adjusted, capitalized) costs of generating the innovation, but rather exceed such costs significantly, holding out the lure of "rents" beyond normal profits.[196] Such rents will tend to draw multiple participants into the relevant innovative activity, resulting in a potentially high degree of overlapping activity, with firms duplicating each other's successes and failures. The manifestation of this in pharma are "me-too" drugs: patented, brand-name drugs clustered in the same "therapeutic class," or drugs operating through the same mechanism of action (such as selective serotonin reuptake inhibition) to achieve the same effect or "indication" (such as treatment of depression), with each drug using a distinct(ly patented) compound for doing so.[197]

In both general innovation theory and pharmaceutical policy, the trick is to assess when such overlapping activity is beneficial—or at least not unduly pernicious—and when it is wasteful. In theory, the answer lies in drawing two sets of distinctions: (1) The first is between (a) "race-to-invent" activity in which many participants are seeking to be the first to reach the prize and its promise of rents; and (b) "invent-around" activity, in which some are seeking to "cannibalize" the rents of existing winners by developing their own, non-infringing but also patent-protected, variant of a good. The former we may plausibly view as tending to be beneficial: "many minds" may better explore a highly uncertain possibility frontier, even with some duplicative activity.[198] The latter less so: while each new entrant *may* provide some added benefit over existing variants, there exists in such cases a basic misalignment between the social value of the new entrant (its net added benefit) and its private value (its share of total rents).[199] (2) Second, *within* "racing" activity, a distinction should be drawn between: (a) zones of highly risky or uncertain stages of research, where the benefits of many-minded exploration are greatest; and (b) later, less risky stages, where the costs of duplication loom larger.

In light of these considerations, analysis of the distinct character of data and compound information goods—in terms of their risk and cost profiles—as well as of the distinct tools of data exclusivity protection, puts us in much better stead to pinpoint and address the problem of rent dissipation in pharma than would a focus on the compound information good and patents. This is for two reasons. First, once we realize that the most costly, yet lower-risk, stage of research is clinical trials, it is clear that this is where we most wish to reduce duplicative "racing" activity.

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[195] *See generally* Aidan Hollis, *Me-Too Drugs: Is There a Problem*? (2004), https://www.researchgate.net/profile/Aidan-Hollis/publication/228919661_Me-too_drugs_Is_there_a_problem/links/596578234585157fcc5e3ead/Me-too-drugs-Is-there-a-problem.pdf [https://perma.cc/7KEK-FLJ4] (critiquing me-too drugs); Joseph A. DiMasi & Cherie Paquette, *The Economics of Follow-On Drug Research and Development: Trends in Entry Rates and the Timing of Development – The Authors' Reply*, 23 PHARMACOECONOMICS 1193 (2005) (defending me-too drugs against Hollis's criticisms); Jeffrey K. Aronson & A. Richard Green, *Me-Too Pharmaceutical Products: History, Definitions, Examples, and Relevance to Drug Shortages and Essential Medicines Lists,* 86 BRIT. J. CLINICAL PHARMACOLOGY 2114 (2020) (defending me-too drugs); Laura Fegraus & Murray Ross, *Sovaldi, Harvoni, and Why It's Different This Time*, HEALTH AFFS. (November 21, 2014), https://www.healthaffairs.org/do/10.1377/hblog20141121.042908/full [https://perma.cc/L5CH-3TKX] (critiquing me-too drugs); OFF. OF TECH. ASSESSMENT, *supra* note 78 at 7, 29-30 (canvassing both sides).

[196] *See* Edmund W. Kitch, *The Nature and Function of the Patent System*, 20 J.L. & ECON. 265, 266 (1977); Donald G. McFetridge & Douglas A. Smith, *Patents, Prospects, and Economic Surplus: A Comment*, 23 J.L. & ECON 197, 198 (1980); Mark F. Grady & Jay I. Alexander, *Patent Law and Rent Dissipation*, 78 VA. L. REV. 305, 317 (1992); William W. Fisher III, *Theories of Intellectual Property,* in NEW ESSAYS IN THE LEGAL AND POLITICAL THEORY OF PROPERTY 168, <pincite> (Stephen Munzer, ed., 2001).

[197] *See* CBO 1998, *supra* note 178, at 19-20; NIHCM, *supra* note 86, at 17-18.

[198] *See* Merges & Nelson, *supra* note 20, at 873-74.

[199] For the implications of this point for institutional design of tailored data exclusivity, see *infra* note 219.

But while patents may be able to call off the race for clinical development of any one candidate drug, they are relatively hamstrung to do so *between* drugs—i.e., to curb costly invent-round trials. Data exclusivity, on the other hand, is precisely oriented toward incenting (or not) this stage of innovative activity. Similarly, and second, FDA data exclusivity is also well-suited to attend to the distinction between salutary race-to-invent and pernicious invent-around activity: those NMEs embodying priority treatments warrant stronger incentive than those rated standard.[200]

With these distinctions in hand, a review of the pharmaceutical industry's output discloses the following diagnosis of the extent of the problem and prescriptions for addressing its ills. Just over half of all the industry's primary products or NMEs since 1990—452 out of 885 or 51%—and fully three-quarters of its products as a whole were rated standard rather than priority at the time of their FDA review.[201] While this metric is only a rough proxy of "me-too" drugs,[202] it remains a better one than any other we have—and of a problem that we have every reason of both theory and evidence to believe is a serious one not to be ignored. And the right solution is two-fold. First, race-to-invent should be allowed to proceed unhampered at the compound information stage, but curbed at the data information stage. Second, invent-around activity should be curbed at both stages, by drawing a distinction within NMEs parallel to that drawn above for IMPs: standard or me-too NMEs should not receive the same protection as truly priority or pioneering ones.

B. Reforms: Cleaning Up Versus Phasing Out Patents

The foregoing diagnosis of what explains evergreening and me-too drugs *and* how to assess the extent of the undue access and gaming, or duplication costs that they respectively incur comes with its own prescription. Given that the generative source of the problems lies in the misalignment between what drug patents focus on and the main pharmaceutical innovation requiring adequate incentives—the data information good—so the solution lies in properly realigning the system, by phasing out patents and replacing them with a well-tailored system of regulatory exclusivity.

Before outlining the contours of that reform, however, it is worthwhile to point to two more modest reforms suggested by the present analysis, both going not to phasing out patents but, rather, "cleaning up" the patent system in its handling of drugs. Regarding both Orange Book linkage and RSAs, the present analysis offers a stronger basis than presently exists in the literature for simply abolishing both. At the same time, it points to the limits of even such far-reaching improvements to drug patents, also in contrast to the prevailing literature where reform proposals tend to stay cabined within improving the patent system's performance. In other words, the present analysis

[200] By contrast, patents would be relatively blunt instruments in any effort to draw such a distinction even when it comes to the first, compound information good: it would be an uphill climb indeed to stretch the patent "doctrine of equivalence" to the point that it would cover an entirely structurally distinct compound simply because it operates on a therapeutically similar "mechanism of action" as a prior patented one. Such judgments regarding functional similarity in therapeutic contexts are, however, precisely the province of the FDA when it reviews the NDA of a new drug (at the start of which review process is when it assigns its "priority" versus "standard" rating). Extending that province to tailoring data exclusivity periods, post-NDA approval, is a small enough institutional step.

[201] *See supra* Table 3. Again, the years 2005-2007 are excepted owing to the unavailability of refined data.

[202] There are two distinct reasons why FDA ratings are only rough (yet still serviceable) proxies for the concerns raised by me-too drugs. First, the ratings are made at the time of a drug's NDA submission, and thus prior to market entry, while a drug's benefits may only be fully revealed after market entry, in terms of refined safety, efficacy, and convenience effects on a more heterogenous patient population than those studied in clinical trials. Second, even drugs closely similar to existing entrants may involve socially valuable innovative activity in their generation, when that activity is incurred in a "race to invent" rather than "invent around" activity. For the implications of the latter point for institutional design of tailored data exclusivity, *see infra* note 219.

both goes farther than existing rationales for why and how to reform to drug patents, but also shows why even the farthest such reforms do not go far enough—we need, instead, to phase patents out.

(1) Cleaning up Patents: Orange Book Delinkage and RSAs as Per Se Anticompetitive

We turn first to the system of Orange Book linkage, which provides that a generic challenge to any patents on a drug is linked to a delay in the FDA regulatory process of approving its ANDA. Consider again the question raised above: what justifies intertwining these two distinct systems—patent protection on the compound information and regulatory approval for the data information—in this way?[203] Why shouldn't the generic firm be free to pursue its regulatory approval process independently of the patent litigation one, so that once the parent data exclusivity has expired on a product, it can enter the market at its own risk with respect to the patent? Why should the FDA's decision-making processes be entangled with those of dispute resolution in the patent system? To ask the question would seem to answer it: there simply is no good reason. No plausible rationale exists for such unnecessary entangling of what are two entirely separate processes.

But while there is no plausible justification for linkage, there is a very plausible *explanation* for it. From a drug innovator's perspective, the more important protection is that provided on the data, not the compound, information good. What good is the (often weak) patent once the (more apt) data exclusivity period has expired, so that a defendant is now free to replicate the crucial information good, and then take their chances vis-à-vis protection over the compound? This will appreciably lower imitator's costs and result in a high degree of price competition. Consequently, it is greatly to the innovator's benefit that any challenge to its patents be linked to a delay in the approval of an ANDA based on its data. And this explanation issues its own prescription: given that innovators *are* right to intuit that the data information good is the central pivot of the system, we need to focus our attention directly on it, and better calibrate its protection to weigh incentives against access. While fully delinking that protection from the vagaries of patents on the compound information good, as being simply beside the point.

Along with abolishing any Orange-Book linkage, we should also rule out all RSAs. Once we understand precisely why RSAs are specific to pharmaceutical patent litigation, we also have our reason for ruling them out as a matter of antitrust law. Not merely on a case-by-case analysis of their anticompetitive features, requiring the challenger to such agreements to engage in fact-intensive, costly, and highly uncertain "rule of reason" analysis.[204] Nor even merely as

[203] *See supra* note 164 and accompanying text. As clarified there, another form of intersection does have plausible justification and is not being challenged here, namely the statutory provision empowering a generic filer of an ANDA to seek a declaratory judgment that the brand-name drug's patents are either invalid or non-infringed, so as to enable the generic to seek to avoid at-risk market entry.

[204] As is the current legal standard: *see* FTC v. Actavis, 570 U.S. 136 (2013). Under this standard, currently in some disarray, either (1) the plaintiff must first make out a plausible anticompetitive theory regarding the conduct, after which the burden shifts to the defendant to advance a plausible procompetitive justification, after which the parties take turns adducing evidence in support of their theories, and then the defendant must show their conduct is the "least restrictive alternative" for realizing the procompetitive benefits, upon a successful showing of which the court must then "balance" the competing considerations; or (2) the plaintiff must first make out a full anticompetitive case, both theory and evidence, only after which burden shifts to the plaintiff to make out their full procompetitive case, both theory and evidence, upon which showing the burden shifts back to the plaintiff to show that a "substantially less restrictive alternative" was available to the defendant for pursuing their procompetitive purposes. For the first variant of rule-of-reason analysis, *see* California Dental Ass'n v. FTC, 526 U.S. 756 (1999); for the second, *see* Ohio v. American Express Co., 585 U.S. 529, 541 (2018). For an account of the uncertainty regarding which of these standards, or some mix of both, currently does or should prevail among the several circuits, see Mark A. Lemley & Michael A. Carrier, *Rule of Reason? The Role of Balancing in Antitrust Law* (Rutgers L. Sch. Rsch. Paper, July 15, 2024), available at SSRN: https://ssrn.com/abstract=4896529 [https://perma.cc/HFG2-6JZ2].

"presumptively anticompetitive," such that the challenger is relieved of their initial burden of showing a case-specific anticompetitive harm unless the defendant can first offer up a plausible justification.[205] Rather, RSAs should be ruled out as *per se* anticompetitive—i.e., categorically barred without any need for a fresh, case-specific anticompetitive theory by the challenger nor any allowance for a case-specific procompetitive justification by the defendant.[206] They should be treated as simply generically anticompetitive, on par with price-fixing, output-restriction, and market-division agreements.[207] So that the *only* way a defendant can save such an agreement is by arguing that it satisfies *not* a general procompetitive justification, but one narrow exception: it is reasonably ancillary to a "productive joint venture."[208] But that is simply inapplicable to settlement agreements, the purported procompetitive virtues of which (reducing litigation costs and risks) are unrelated to a limited-purpose integration between competitors (i.e., a productive joint venture).[209]

What is the basis in antitrust law for such a categorical bar? Once we understand what is really going on in RSAs—namely, that the plaintiff patentee is indeed "paying for delay" of a generic defendant, who would otherwise be a direct product competitor threatening a steep price drop—we can see RSAs for what they are: "market divisions," only here not geographically or by consumer segment but by time. RSAs are simply a way for plaintiff patentees to buy some more time without competitive entry, and such a "temporal" market division is as clear such a division as any other. By contrast, in most other patent litigation contexts, the technology at issue may not even cover a distinct product market (think of patent disputes between Samsung and Apple over components of smartphones),[210] and even if it does, rarely will the defendants threaten the price drop of a purely imitative ("generic") competitor in pharma. This is why plaintiffs in other cases do not have the same incentive to offer "pay for delay" reverse settlements. Recognizing the *sui generis* character of pharma-specific RSAs—the effect, again, of the regulatory treatment of the data information good[211]—provides the basis, then, for a categorical bar that closes the various loopholes patentees and generics continue to use in avoiding antitrust invalidation.[212]

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[205] As was argued by the FTC before the Court in *Actavis*. FTC v. Actavis, *id.* at570 U.S. at 159--160. *C.f.* C. Scott Hemphill, *An Aggregate Approach to Antitrust: Using New Data and Rulemaking to Preserve Drug Competition*, 109 COLUM. L. REV. 609, 668-70 (2009).

[206] *See, e.g.,* United States v. Topco Assocs., Inc., 405 U.S. 596, 607 (1972) ("[C]ertain business relationships are *per se* violations of the Act without regard to a consideration of their reasonableness.").

[207] *See* United States v. Trenton Potteries, 273 U.S. 392, 396-97 (1927) (holding that price-fixing is per-se illegal); NCAA v. Bd. of Regents of Univ. of Okla., 468 U.S. 85, 100 (1984) (stating that output restrictions are typically per-se anticompetitive); Palmer v. BRG of Ga, Inc., 498 U.S. 46-49 (1990) (holding that market divisions are per-se anticompetitive).

[208] *See* Broad. Music, Inc. v. Columbia Broad. Sys., 441 U.S. 1, 19 (1979) (holding that while general procompetitive defenses against price-fixing are not permitted, arrangements "reasonably necessary to effectuate" a productive collaboration are); Arizona v. Maricopa Cnty. Med. Soc'y, 457 U.S. 332, 355-56 (1982) (holding that, unlike in *BMI*, the impugned arrangement here was not a "necessary consequence" of realizing the productive aims of the defendants' collaboration); EINER ELHAUGE, UNITED STATES ANTITRUST LAW AND ECONOMICS 56-57, 71-75, 84-85, 88-89 (4th ed. 2022) (setting out the "productive joint venture" rationale as the best explanation for existing Supreme Court precedents for when an exception to per-se treatment of a horizontal agreement is or is not allowed).

[209] And where such agreements contain features that reach beyond litigation savings and into aspects of productive collaborations—as many may, especially in a post-*Actavis* world, as discussed below—nevertheless they should not qualify for the exemption from *per se* condemnation because the delay in generic entry, be it procured by cash or some other in-kind benefit, will remain a market division unrelated to the productive collaborative aspects of any such agreement. *See infra* note 212.

[210] For further discussion of this point, *see infra* note 234.

[211] *See supra* text accompanying notes 177-180 and 184.

[212] Thus, while the Court in *Actavis* declined to hold RSAs as per se or even presumptively anticompetitive but instead subject to the rule of reason, many commentators have urged that the Court's guidance on how to structure the inquiry, and especially its emphasis that large and unexplained cash payments would render an agreement highly suspect, should be used by lower courts to provide more stringent scrutiny of such agreements. *See* Edlin et al., *Activating* Actavis, *supra* note 182, at 21; Michael A. Carrier, *Payment After* Actavis, 100

As thoroughgoing as these reforms may seem, they are not thoroughgoing enough. Because they do not go to the underlying, generative, root cause of the problem. While Orange Book linkage and the legality of RSAs provide extra *opportunities* to pursue evergreening gaming practices, removing them would still leave untouched the underlying *motive*—namely, the extra fuel given to holders of drug patents to protect themselves from the especially fierce drop in price associated with the loss of the patent and entry of *generic* competition. This competition enjoys much lower costs owing to regulatory piggybacking on the innovator's data information good. To tackle the problem at its root requires attending to the specific innovation policy needs of that information good. And that requires ignoring the distraction of patents and their gaming in terms of linkages, litigation, settlements, etc., all of which center on the wrong (compound) information good.

To seek to redress the problems of evergreening by improving the patent system is simply to play a game of whack-a-mole: once one symptom of the underlying cause is addressed—say listing of multiple patents to get multiple automatic stays[213]—whack!—another symptom comes to the fore, say filing of frivolous patents on metabolite byproducts.[214] Whack! At which point taking center stage may be nonfrivolous but still modest or even trivial patents on secondary formulations[215]—whack!—or perhaps those on secondary products.[216] Whack! Next, exacerbating the gaming of patent acquisition we get the gaming of patent enforcement, via RSAs involve large cash payments to delay entry[217]—whack!—which may then give way to RSAs masking the payments for delay with various in-kind side deals, ranging from withholding competition by subsidiaries to licensing unrelated products of the defendant to conferring perks in foreign markets to dropping unrelated claims over less lucrative drugs.[218] Whack! Whack! Whack! Whack!

No matter how many of these symptoms are addressed, others will continue to crop up unless and until we tackle the underlying source of the ills: namely, that patents in pharma work differently than elsewhere because innovation in pharma works differently, owing to the centrality of its distinct second, data, information good and this good's regulatory treatment. It is the gap between the regulatorily-mandated high costs of innovation and regulatorily-permitted low costs of imitation that opens up the price gap between patentees and generic competition that fuels the

IOWA L. REV. 7, 47-49 (2014); Robin Feldman, *Ending Patent Exceptionalism and Structuring the Rule of Reason: The Supreme Court Opens the Door for Both*, 1 MINN. J.L. SCI. & TECH. 61, 72-76 (2014); *cf.* Elhauge & Kruger, *supra* note 181, at 297-311 (setting out, in advance of *Actavis*, a structured rule-of-reason analysis focusing on the size of cash payments in relation to projected litigation savings). And some, citing FTC analysis showing that the incidence of agreements centering on cash payments significantly decreased post-*Actavis*, have thought that troubling "[p]ay-for-delay settlements may now be uncommon." HICKEY & WARD, *supra* note 182, at 58. But as others have pointed out, that agreements may no longer center on cash payments but rather confer various other "in-kind" benefits—ranging from the plaintiff patentee withholding entry by its authorized generic enter during the defendant generic's 180-day exclusivity period, to agreeing to license other, unrelated products of the defendant, to giving the defendant licensing perks in foreign markets, to settling unrelated claims in suits over less lucrative drugs—does not mean that such agreements are not troubling, only that the "payments" for delay may now take the form of various "side-deal" perks. *See* FELDMAN & FRONDORF, DRUG WARS, *supra* note 166, at 49-65. What the present analysis indicates is that all such side deals—whatever their independent procompetitive virtues—simply fail to justify a delay of entry, as that delay is a market division and as such per se barred, absent a showing that it is reasonably necessary to effectuate a productive collaboration. None of the side deals or "productive collaborations" disclosed in the case law as discussed by Feldman and Frondorf bear any such relation to the delay of entry. *Id.*

[213] *See supra* text accompanying note 165.

[214] *See supra* note 172.

[215] *See id.*

[216] *See id.*

[217] *See supra* text accompanying note 182.

[218] *See supra* note 212.

gaming of patents in pharmaceuticals. Thus, any reforms to how drug patents work—even those as far-reaching as abolishing the linkage of patent enforcement with the regulatory process and categorically barring RSAs—will, by remaining internal to the patent system, still be vulnerable to further gaming efforts within it. The only way out of this quagmire is to phase out patents and their distractions and focus directly on the issues of innovation policy posed by the central information good in pharma, the generation of clinical data.

In other words, we need to weigh the access benefits of generic entry against its possible costs of dampening incentives, for the generation of the *data information good*. And this requires properly tailoring such incentives in the first place, providing stronger ones where they are needed and curbing them where they are not. The only effective way of doing so is directly to attend to the features of the information good giving rise to the incentive concern: clinical data. And the right tool for the job is to tailor the protection that directly attaches to that good: data exclusivity.

(2) Phasing Out Patents with Revised Regulatory Exclusivity

The central aspects of the reform being proposed here have already been specified above. The first is to replace drug patent protection with a revised system of "regulatory exclusivity" that is able to attend to the distinctive features of the central innovation in the system, data information. Next, to address the undue access and gaming costs associated with evergreening-type practices, we need to tailor the system's protection by providing priority IMPs with stronger data exclusivity and standard IMPs with weaker, unlike the case at present where all IMPs get three years. Finally, to address the undue duplication wastes associated with me-too drugs, we also need to distinguish between priority NMEs that get stronger data exclusivity[219] and standard NMEs that get weaker, unlike the case at present where all get between five and 7.5 years.

We now turn to three crucial refinements of the proposal. First, by what procedure should we "replace" or "phase out" patent protection for drugs? The preferable mechanism is to have firms "waive" their patents in order to receive data exclusivity upon getting NDA approval for their drug product and being ready for market entry. At that point, drug developers will be confronted with a choice: patents or data exclusivity? Unlike the present system where both are available, innovators will have to choose their preferred form of protection. The premise of the present proposal, supported by the foregoing analysis, is that innovators will realize that a properly tailored form of direct protection over the data information good is preferable to the indirect, and thus hazardous and often "weak," protection afforded by patents. This choice will be made easier when patents are stripped, as they still need to be, of the gaming opportunities afforded by Orange Book linkage and RSAs. In addition, the unavailability otherwise of tailored data exclusivity will be an important stick to go along with the carrot of offering such tightened protection.

[219] An important refinement here is that the stronger form of data exclusivity should not be limited only to "priority" treatments if it turns out upon closer examination that the FDA rates even 2nd- or 3rd-entrants into a therapeutic class as no longer bearing "significant" therapeutic potential and hence meriting a "standard" rating. Since 2nd- or 3rd-entrants—indeed, any number of entrants within a certain time period of the first (likely about two years)—are likely "close finishers" in a "race to invent" rather than more distant "invent-around" cannibalizers, they are engaged in valuable innovative activity for which incentives need to be retained. Consequently, the right calibration here would be that "priority-plus" entrants get stronger NME data exclusivity, where "priority-plus" includes close finishers.

But why not simply legislatively abolish patent protection for drugs? Two reasons counsel against this route. First, from a procedural point of view, it would likely run afoul of the United States' obligations under the TRIPS Agreement, Article 27.1 of which prohibits "discrimination" against specific "fields of technology."[220] Second, from an administrative point of view, patent protection—both in general and for drugs—likely provides a valuable institutional "safety valve": a check against any alternative innovation policy, by providing innovators with a choice. So long as such protection is not unduly strong or flawed—as it, alas, clearly is at present—a modest form of protection for "inventors at the margin" likely makes good sense,[221] even for pharma.

A second question: if drug patents are not abolished but replaced by waiver, does this not mean we must retain them into the indefinite future, and so are not really "phasing" them out? In particular, why require firms to still go through the motions—and all the costs—of obtaining a patent only to waive it prior to commercial exploitation? Can we not simply have data exclusivity available to innovators *in lieu of* patents? Yes. There is no reason why a firm obtaining NDA approval on a drug should cease to become eligible for the data exclusivity protection merely because, rather than obtain and waive, they simply chose not to file for a patent in the first place.

But to enable firms to forego patent protection requires an important further refinement in the system of "regulatory exclusivity": on top of "data exclusivity" at the end of the clinical trials-NDA process, we should add a form of "testing exclusivity" at the starting IND stage. Why? First, to assure innovators engaging in costly clinical trial development that a later entrant with the same or highly similar product will not beat them to the punch—this being, in effect, the main valuable "coordinating" function that patents perform presently[222] Second, and relatedly, from a social point of view, duplicative clinical trials would be highly wasteful. Thus, fully to phase out patents we need to replace their "coordinating" function with a form of FDA-granted "testing exclusivity."

This raises a third issue. As the foregoing refinement makes clear, "regulatory exclusivity" here means more than merely "data exclusivity": it is "data exclusivity" plus "testing exclusivity." But this raises another question: should it also perhaps be *less* than "data exclusivity"? Presently, when FDA data exclusivity expires, other firms are able to rely on the originator data for purposes of ANDA submissions to the FDA, but they cannot actually "see" or *use* the originator data in any other way.[223] That is, even after "data exclusivity" has expired, the firm still retains full "data

[220] Agreement on Trade-Related Aspects of Intellectual Property Rights, art 27.1, Apr. 15, 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, 33 I.L.M. 1125 (providing that "patents shall be available for any inventions, whether products or processes, in all fields of technology" and that "patents shall be available and patent rights enjoyable without discrimination as to . . . the field of technology."). While subsections (2) and (3) of Article 27 carve out some exceptions to this requirement, none of these apply here. Article 27.2 allows an exemption from patent protection for those inventions "the commercial exploitation of which" may be necessary to curb in order "to protect *ordre public* or morality." This does not apply, since under the proposed regime drugs (and the inventions they embody) would continue to be commercially sold. Article 27.3 allows carveouts for "diagnostic, therapeutic and surgical methods for the treatment of humans or animals." Application of this to drugs would require stretching the notion of "therapeutic . . . methods" past the point of breaking: drugs are not "methods" within the technical meaning of that term in this context, which applies to "process" claims pertaining methods-of-doing something, i.e., "functional" claims, rather than the process claims at issue in drugs, those going to methods-of-making or -using a product. And even if we wished to include some or all of the latter within its ambit, it would remain that the majority of relevant patents here are "product" not process ones.

[221] *See supra* references cited in note 40.

[222] *See supra* Section II.B.2.

[223] *See* Eisenberg, *The Role of the FDA*, *supra* note 8, at 380-81 (detailing that this is the current position taken by innovator firms and the FDA, while also indicating why "the statutory language invoked in support of this position is ambiguous").

secrecy."[224] Is that sensible? No. The benefits of data transparency are massive: both for improving cumulative innovation by allowing others to build on a firm's clinical results, learning from both its successes and failures,[225] and for improving the quality of clinical testing in the first place, by opening up the firm's results for more effective peer review as a form of "quality control" in a context where conflicts of interest afflicting (firm-sponsored) researchers are rife.[226] The present proposal, then, joins the chorus of scholars calling for greater clinical "data transparency."[227]

A final point: the attentive reader may have noticed that one aspect of the reform proposal not elaborated here is what the actual duration and scope of the requisite data exclusivity periods should be—be it for priority or standard drug products, and NMEs or IMPs—once patent protection is phased out. The present analysis has simply used the existing system as the baseline to illustrate *the kind* of tailoring or finer-grained calibrations called for by an analysis of the causes and extent of evergreening and me-too drugs and their access, gaming, and duplication costs. A fuller analysis to determine the precise duration and scope of data exclusivity periods is beyond the present scope, although the approach deployed here is, I believe, the right method for answering that question. This is briefly discussed next, in the final Part.

IV. FUTURE DIRECTIONS

This Part briefly canvases three further questions for pharmaceutical innovation policy that are raised by the present analysis but lie beyond its scope. The first was just flagged: how to go about determining the precise scope and duration of data-exclusivity periods that will serve as the sole incentive mechanism for drug innovation once patents are phased out? A second is whether we should be concerned that data exclusivity, like patent rights, remains an exclusionary incentive mechanism, and as such still erects barriers to access over the information goods it incentivizes. This question may in turn be broken into two further ones. First, should we not supplement these "supply side" reforms, to improving pharmaceutical innovation policy's *incentives*, with "demand side" reforms, that might further improve such policy's *access* performance? In particular, might not some reforms to pharmaceutical *pricing*—even with patents replaced by data exclusivity—be

[224] This parallels a concern in patent law: firms are often able to enjoy both patents *and* secrecy, in parallel, over the same information good, such that (1) once the patent form of proprietary protection ends, (2) they still retain a distinct second, if thinner, layer of protection. The parallel question here is whether there should be both (1) data exclusivity; and (2) then residual "data secrecy," such that the data always remains "proprietary." And the answer being proposed here is: "no." The firms' clinical data is a highly socially valuable information good, with its generation regulatorily mandated and its replication regulatorily prohibited and then after a time regulatorily permitted. To this we should add a fourth: after the right amount of time, both data exclusivity *and* data secrecy should expire. There is no reason to allow the firm to continue to "own" such an intensively regulated, socially valuable, information good. The parallel debate over whether the patent system should alter by requiring more forceful "disclosures"—so that, in effect, secrecy evaporates upon the patent filing—is hotly contested. *See* Colleen V. Chien, *Contextualizing Patent Disclosure*, 69 VAND. L. REV. 1849, 1854-66 (2016) (reviewing the history of the doctrine and the debate on its actual and desirable contours). The position being taken here with respect to "data secrecy" is analogous to the one adopted by Lisa Larrimore Ouellette in the case of secrecy when it comes up against patents: while "disclosure" is unlikely to be a persuasive *justification* for conferring patents, once a patent system is up and running, disclosure remains a persuasive (if secondary) *function* for the system to pursue. *See* Lisa Larrimore Ouellette*, Do Patents Disclose Useful Information?*, 25 HARV. J. L. & TECH. 545, 554-61, 587-601 (2012). Here, that means that in return for data exclusivity, firms should be required to give up data secrecy. Firms wishing to retain data secrecy should be denied data exclusivity.

[225] *See* Eisenberg, *The Role of the FDA*, *supra* note 8, at 382-84; Morgan, *supra* note 110, at 116.

[226] *See* Tracy R. Lewis, Jerome H. Reichman, & Anthony D. So, *The Case for Public Funding and Public Oversight of Clinical Trials*, 4 ECONOMISTS' VOICE 1 (2007); Morgan, *supra* note 105, at 116.

[227] Eisenberg, *The Role of the FDA, supra note* 8, at 381-84; Lewis et. al, *supra* note 219.; Morgan*, supra* note 105; Trudo Lemmens & Candice Telfer, *Access to Data and the Right to Health: The Human Rights Case for Clinical Trials Transparency,* 31 AMER. J. L. & MED. 62 (2012); Christopher J. Morten & Amy Kapczynski, *The Big Data Regulator, Rebooted: Why and How the FDA Can and Should Disclose Confidential Data on Prescription Drugs and Vaccines*, 109 CAL. L. REV. 493 (2021).

merited, as an "access" supplement to the improved "incentive" side of data exclusivity? Finally, what about non-exclusionary incentives, or alternative innovation policies such as public funding or prizes? Should an expanded role for one or more variant of these be contemplated?

A. Setting the Scope and Duration of Regulatory Exclusivity

We take up first the question of how to set the right level of data exclusivity protection. The analytic approach taken to that issue here eschews two common alternatives in the literature on exclusionary incentives, in favor a third. One prominent approach is to try and set "optimal" levels of protection, by seeking to determine the overall level of exclusionary rights at which the added incentive "bang" is no longer worth the added access and duplication "bucks." But if there is one conclusion to be drawn from the theoretical, empirical, and historical literature on patent theory and innovation economics, it is that to try to determine the optimal balance between the incentive, access, and rent dissipation parameters is a heroic, most likely hopeless, undertaking.[228]

In the wake of its demise, the most favored alternative to "optimal" incentives has been "average" incentives: namely, to try to determine what level of incentives would sustain the average innovation in a given sector, in light of present gaps between average innovation and imitation costs. This was the approach used in the legislative debate around the right level of data exclusivity to accord biologics to accompany the statutory creation of their abbreviated pathway—i.e., the biologics version of Hatch Waxman, the 2009 Biologics Price Competition and Innovation Act. Industry-sponsored economists proposed an average of 12-14 years data exclusivity; industry-skeptical economists urged the five formally granted to chemical NMEs; and the FTC was unable to decide between them.[229] The legislation ultimately passed was closer to the industry's advocates than its critics: a twelve-year period that is extendable by six months with pediatric testing.[230] The trouble with both estimates, quite apart from any empirical flaws, is simply that any "average" approach is hostage to a deep status quo bias: the average innovation currently generated in a sector is one generated under *existing* innovation policy rules. To take that existing average as a yardstick is to assume that existing rules are more-or-less optimal. But, as we have seen with evergreening and me-too drugs, we have good reason to believe that the existing rules are far from optimal. To seek simply to mimic their performance is to harbor an indefensibly (or at least undefended) complacent position with respect to how (well or badly) the present system is already working.

Rather than seek to fashion either first-best "optimal" rules or status-quo "average" ones, a better third approach, also present in the literature but less well-developed, is to *start from where we are and seek to improve*. Two key sub-variants here are as follows. First, we might try to "do

[228] For two leading demonstrations of the inordinate theoretical and empirical complexities involved, not to mention the problem that a solution today may not be valid tomorrow in light of dynamically changing conditions, *see* Kaplow, *supra* note 54, at 1888 (concluding that a properly fulsome analysis of the relevant tradeoffs reveals that "any careful attempt to resolve" the issues "will be far more complex than has been previously realized"); *and* Fisher, *supra* note 48, at 1795 (concluding that a properly fulsome analysis of the relevant tradeoffs should contribute to "an appreciation of just how encompassing and complex a serious effort to maximize allocative efficiency must be").

[229] *See* Henry Grabowski, *Follow-on Biologics: Data Exclusivity and the Balance Between Innovation and Competition,* 7 NATURE: DRUG DISCOVERY 479 (2008); Laurence J. Kotlikoff, *Stimulating Innovation in the Biologics Industry: A Balanced Approach to Marketing Exclusivity* (2008); Henry Grabowski, *Data Exclusivity Periods for Biologics: Updating Prior Analyses and Responding to Critiques*, (Duke U. Dept. Econ. Working. Paper No. 2008-10 (2008)); FED. TRADE COMM'N, EMERGING HEALTH CARE ISSUES: FOLLOW-ON BIOLOGIC DRUG COMPETITION (2009).

[230] *See supra* notes 145-146 and accompanying text.

no harm": that is, we determine what level of overall incentives the system is currently providing and then, without either lowering or raising that aggregate level, simply seek to tweak or fine-tune how to supply it, conferring the same level of incentives with a lower set of access costs. We seek, that is, to improve upon the present system's "incentive/loss" ratio.[231] Hopefully, the drawback of this approach is clear: while certainly an improvement upon the "average" approach, it too harbors an indefensibly status quo bias, simply assuming that the overall level of incentives being provided cannot be improved upon or, at least, should not be tampered with.[232] A better alternative, then, to "do no harm" is, rather, to try to "do better." How? By identifying especially salient drawbacks of the present system and trying to improve upon those. As is hopefully clear, this is the approach taken by the present analysis: the undue access, gaming, and duplication costs of the present system are highly salient, and measures to assess their extent and redress their sources readily available. We should continue to work along these lines to calibrate the apt overall scope and duration of a new system of regulatory exclusivity that is to replace the present forms of misaligned protection.

B. Improving Drug Pricing

Should a system of exclusionary incentives for pharmaceuticals on the supply side—whether it be via patents or data exclusivity—be supplemented by reforms to pharmaceutical pricing on the demand side? Likely, yes. And this for two very distinct, even if similarly important, reasons. A first is simply "access." With any system of exclusionary incentives, the resulting innovations will come with a price premium—over and above the marginal costs of producing and distributing the embodied unit of the innovation—that will have the effects of pricing some persons out and price hikes for others. There is no way around it: that is simply how exclusionary incentives over information goods work.[233] And suppressing for the moment the third issue of whether we should therefore pursue an expanded role for non-exclusionary innovation policies, is there a way we can do better with exclusionary ones by reforms to pricing to improve access?

In answering that question, it is good to attend to a second, perhaps equally important, concern, going to the interaction between demand-side infirmities in healthcare and supply-side incentives based on exclusionary rights. In healthcare urgent needs are served, and often paid for by insurance. Healthcare is also informationally asymmetrical—producers and doctors often know far more about innovations than users or patients. Incentivizing the generation of healthcare goods with marginal price mark-ups is to inject a high dose of potential demand distortion into an already noisy system. The holder of an exclusionary right has a time-limited motive to massively increase

[231] For this approach in the patent context, *see* Kaplow, *supra* note 54, at 1821-45. For copyright, *see* Fisher, *supra* note 48, at 1700-44.

[232] To be sure, both of the main developers of this approach offer plausible, if different, reasons for advocating it. Louis Kaplow's argument is tethered to administrability concerns with alternatives. Kaplow, *supra* note 54, at 1833-34. Terry Fisher's argument, on the other hand, supplements this sort of economic analysis with pursuit of a "richer sense" of normative concerns than is typical of economists—specifically, pursuit of those adjustments beyond improving its incentive/loss ratio that are counseled by a vision of a "just and attractive society" in general and, in particular, one that aims to increase both the diverse stock of expressive works generated under copyright and the opportunities for active, meaningful engagement with such works as opposed to simply passive consumption of them. Fisher, *supra* note 48, at 1697, 1744-1746. The present point is to urge that we should try to "do better" even when our concerns remained cabined within standard economic ones, and even when attending to administrability considerations.

[233] *See* Bracha & Syed, *supra* note 45, at 1852-54 (establishing the point that to confer IP rights to provide incentives without incurring a price mark-up is "as conceivable as a perpetual motion machine").

sales, while demand-side "price signals" are often highly malleable to such efforts, be they of aggressive promotion or, simply, hiked prices.[234]

For health goods such as drugs, then, to use exclusionary incentives requires supplementing them with some form of social valuation of their worth, over and above market price signals. It requires, that is, some form of *embedded pricing:* prices embedded within some social judgment of the value or variable value-range of the good, with (price) ceilings and (subsidy) floors both to hold in check expansionary pressures on the one side and address access concerns on the other.

C. Expanding the Role of Nonexclusionary Innovation Policies?

We turn now to the suppressed third question: might we not also wish to pursue, alongside exclusionary incentives—even of an improved form of data exclusivity—an expanded role for alternative, nonexclusionary innovation policies? The present analysis's contributions to that question are modest, but not negligible. First, the analysis of the relation between high risks and a strong public role in biopharmaceutical pipeline suggests there is merit to experimenting with an expanded role further down the pipeline, to its low-risk, high-cost end. To consider, in other words, an expanded public role in preclinical testing and the carrying out of clinical trials.[235]

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[234] This point brings together two insights, one from the legal literature on how patents work for drugs, the other from the economic literature on advertising and related promotional activities. In the legal literature, it has often been observed that while a one-to-one mapping between patents and a product may be rare (consider the case of a car or smartphone, embodying many distinct technological inputs, which may each enjoy their own patent protection, often held by different firms), drugs are an instance where patents do tend to map onto discrete products (even if a given drug product may enjoy protection from multiple, overlapping, patents. *See supra* note 87). *See* Robert P. Merges, *Intellectual Property Rights and the New Institutional Economics*, 53 VAND. L. REV. 1857, 1859 (2000) ("Often . . . there is no simple 'one-to-one' mapping of products and property rights."); Eisenberg, *supra* note 8, at 479 ("Patents on drugs seem to operate the way legal scholars and economists imagine patents are supposed to work, by giving their owners monopoly power in product markets. This is not so in every industry . . ."); Burk & Lemley, *supra* note 36, at 1590 ("The effective scope of patents . . . varies tremendously by industry. This variance results from the relationship between a patent and a product. In some industries, such as chemistry and pharmaceuticals, a single patent normally covers a single product. Much conventional wisdom in the patent system is built on the unstated assumption of such a one-to-one correspondence . . . Such a correspondence is the exception rather than the rule, however."); *id.* at 1617 ("As a general rule, the scope of patents in the pharmaceutical industry tends to be coextensive with the products actually sold. Patents do not merely cover small components that must be integrated into a marketable product."); Mark A. Lemley, Lisa Larrimore Ouellette, & Rachel E. Sachs, *The Medicare Innovation Subsidy*, 95 N.Y.U. L. REV. 75, 77, n.8 (2020) ("In practice, patents rarely map neatly onto monopoly markets . . . But they are more likely to do so in pharmaceuticals than elsewhere.") (internal citations omitted). Consequently, the pricing power conferred by drug patents pertains to a direct markup on a consumer product. To this point we may add another, drawn from the economic literature on promotional activities, where the "Dorfman-Steiner" theorem holds that promotional expenditures are a function of two factors: (1) the elasticity of demand to such expenditures, meaning the extent to which such expenditures increase the volume of sales; and (2) the supramarginal price mark-up enjoyed by the firm on each sale. *See* Robert Dorfman & Peter O. Steiner, *Optimal Advertising and Optimal Quality* 44 AMER. ECON. REV. 826 (1954). Integrating the two points, we see that whenever patents map onto an end consumer product, the supramarginal pricing power they confer translates directly into a time-limited hyper-incentive to engage in promotion to pump up the volume of sales. Further, in the case of drugs, not only is the second of the two Dorfman-Steiner factors especially in play, so is the first: owing to the various infirmities in the "market" for healthcare mentioned above—i.e., insurance-induced price insensitivities, information asymmetries, and principal-agent problems—the demand for drugs is especially elastic or malleable to promotional efforts.

[235] To do so would be to follow through on two key insights disclosed in the recent literature on the "developmental" or "innovative" state, namely that: (1) first, contrary to common perception, many important innovations in high-tech sectors of the economy can be traced to activity undertaken in a dynamic "public sector" of publicly-funded research by government, university, and private contractors; (2) second, that while much of this public support has taken the form of "socialized risks, privatized profits"—whereby the riskier parts of innovation are carried out in the public sector, after which the fruits are passed on to private firms for profitable commercial development—that division of labor is neither necessary nor always socially desirable. *See* Fred Block, *Swimming Against the Current: The Rise of a Hidden Developmental State in the United States*, 36 POL. & SOC'Y 169 (2008); FRED L. BLOCK & MATTHEW R. KELLER, STATE OF INNOVATION: THE U.S. GOVERNMENT'S ROLE IN TECHNOLOGY DEVELOPMENT (2011); Mariana Mazzucato, *The Innovative State*, FOR. AFF. (Dec. 15, 2014) https://www.foreignaffairs.com/articles/americas/2014-12-15/innovative-state [https://perma.cc/7KNS-GMWG]; MARIANA MAZZUCATO, THE ENTREPRENEURIAL STATE: DEBUNKING PUBLIC VS PRIVATE SECTOR MYTHS (2015).

Second—and finally—one further point disclosed by the present analysis is that not only is the case for some policy intervention in pharmaceuticals a regulatory artifact, but *the central innovation in pharmaceuticals is itself a regulatory artifact*. That is, while the data information good's creation is *incentivized* by a mix of patents and data exclusivity, the actual *creation* itself is not the result of market demand (upon which the patents or data exclusivity operate) but, rather, regulatory demand (or command). In other words, it is the result of *regulating* innovation rather than incentivizing it.[236] And the specific form this regulatory demand takes repays close attention: unlike much regulation today, it is not simply a response to a market failure to be efficient, nor does its institutional form attempt to mimic the market (the way that, say, pollution taxes or cap-and-trade do). No, the way this regulation—that is, the requirement that drugs show their clinically validated safety and efficacy before being marketable—works is neither by substituting for, nor by mimicking, but rather by *embedding* the market: constraining market incentives within a matrix of public judgments of the social value of the affected interests that are distinct from standard ones of efficiency or distribution.[237] This institutional form differs sharply from the prevailing options in the innovation policy toolbox, in ways holding promise for post-neoliberal innovation policy.[238]

CONCLUSION

Wisely shaping innovation policy for pharmaceuticals requires registering that at its core, pharmaceutical innovation consists of two distinct information goods: new knowledge of candidate drugs and new knowledge of their safety and efficacy for use in humans, as validated by clinical trials. These distinct compound and data information goods differ sharply in their *technological* and *economic* features, as well as in their *social desirability*, as these pertain to innovation policy analysis. Only by attending to the distinction between these goods and their relevant features can we properly understand how patents and data exclusivity do, can, and should work in this sector.

Doing so allows us to see that, first, the driver of the industry's economics, and apt focal point of its innovation policy rules, is not the compound but data information good. The latter is what poses the special case for an innovation policy intervention in this area. Second, the form that such innovation policy takes cannot be patents. Patents neither provide effective protection for the data information good at present, nor can they be reformed to offer such protection. Patents *do not* directly protect the data information good because the distinctive technological features of this good—its low-risk, yet high-cost profile—make it ill-suited for existing patent doctrines. And patents *cannot* effectively protect this good because assessments of its desirability and validity are ones that patent institutions are simply ill-equipped to make. Most fundamentally, patents *should not* be used as our innovation policy of choice in this area, because a superior policy instrument—

[236] *See* Amy Kapcyznski & Ian Ayres, *Innovation Sticks: The Limited Case for Penalizing Failures to Innovate*, 82 U. CHI. L. REV. 1781 (2016); William W. Fisher III, *Regulating Innovation*, 82 U. CHI. L. REV. ONLINE 251 (2016).

[237] Explicating the normative and institutional components of this argument—namely, that the concerns being addressed by imposing safety and efficacy requirements on drugs before they are marketable are not best understood in terms of either efficiency or distribution as these are conceived in welfare economics, and that the institutional form by which these concerns are being pursued is distinct from the standard options in the regulatory policy literature, of either market-replacing ("regulatory command") or market-mimicking ("incentive-based regulation") tools—is the task of a work in progress. Talha Syed, *Embedding Innovation* (unpublished manuscript) (on file with author).

[238] For neoliberalism as an ideology of market fundamentalism that helps sustain increasing economic inequality, *see* Talha Syed, *Legal Realism and CLS from an LPE Perspective* 18-19 (2024) (unpublished manuscript) (on file with author).

regulatory exclusivity—is available, one that can be properly tailored to tackle effectively the undue access, gaming, and duplication costs incurred by evergreening practices and me-too drugs.