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Should a Prize System for Pharmaceuticals Require Patent Protection for Eligibility?*

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Abstract: In an earlier iteration of the Health Impact Fund proposal, Aidan Hollis and Thomas Pogge argued that only those pharmaceutical innovations that are covered by patent protection should be eligible for receiving payments. This, however, would fail to take advantage of a distinct benefit held out by rewards as compared to patents in the context of pharmaceuticals: rewards can provide incentives for a broader range of valuable developmental activities than what would qualify as "innovative" under the patent system's proxies. Moreover, recognizing why and how this is so can produce a salutary shift in our understanding of the reasons for providing patent protection (or some alternative innovation policy) for pharmaceuticals. This short paper discusses why the patent requirement should be dispensed with and responds to some common concerns with such a position.

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In an earlier iteration of the Health Impact Fund (HIF) proposed by Aidan Hollis and Thomas Pogge, it was suggested that only those pharmaceutical innovations that are covered by patent protection should be eligible for receiving payments.[1] That approach, however, would fail to take advantage of a distinct benefit held out by rewards as compared to patents in the context of pharmaceuticals: rewards can provide incentives for a broader range of valuable developmental activities than what would qualify as "innovative" under the patent system's proxies. Moreover, recognizing why and how this is so can produce a salutary shift in our understanding of the reasons for providing patent protection (or some alternative innovation policy) for pharmaceuticals. This note briefly discusses why the patent requirement should be dispensed with and responds to some common concerns with such a position. While this note addresses the HIF specifically, the observations may also apply to other systems of prizes similar to the HIF.

The HIF presents a welcome opportunity to sharpen our understanding of what should count as socially valuable "innovation" or developmental activity in pharmaceuticals and, in particular, to delink that to some extent from what is deemed to qualify as new, useful, non-obvious, etc. under the patent system. The HIF aims to induce or enable the development of high health-impact medicines and their distribution at the lowest feasible cost and price. In light of these purposes, any pharmaceutical product that requires regulatory approval based on a "new drug application" (NDA) should qualify as an "innovation" that is then eligible to be assessed according to its added health benefits in order to receive a stream of reward payments.[2] The vagaries of patent protection—e.g., is the innovation eligible for product or only method-of-use protection? has it been previously disclosed or anticipated by compounds in the prior art? does it involve a genuinely non-obvious technical advance?—are less germane than (a) whether the product is sufficiently distinct from currently available treatments such that the FDA or similar regulatory agencies will require it to undergo (expensive and somewhat risky) testing for safety and efficacy in humans before general public use;[3] and (b) whether, once it passes that threshold,

[1] Aidan Hollis & Thomas Pogge, *The Health Impact Fund: Making New Medicines Accessible for All* 14, 24, fn. 2 (2008).

[2] This means, in the U.S., approval by the Food and Drug Administration (FDA) based on the submission of full safety and efficacy data on the product, pursuant to either of the two types of "new drug applications" ("505(b)(1)" and "505(b)(2)" applications). The contrast is with "abbreviated new drug applications" (ANDAs) for generics, based upon a demonstration of bioequivalence with an already-approved product ("505(j)"). See Federal Food, Drug and Cosmetic Act §§505(b)(1), (b)(2) & (j), codified at 21 U.S.C. §§ 355(b)(1), (b)(2) & (j). Although this note refers specifically to U.S. patent law and FDA regulation, its general ideas also apply to other countries that have similar regulatory authorities and laws.

[3] See the bibliographical note for references developing aspects of this point.

it provides an appreciable advance in health benefits over the existing armory of approved treatments.

To see why this is so, it is useful briefly to step back and identify three broad stages or types of innovative or developmental activity in the case of drugs:[4]

> (1) the "applied research" stage of "drug discovery," where basic biomedical research is translated, through the processes of "search, synthesis and screening," into technical knowledge of molecular targets and mechanisms of actions that are linked to specific diseases and the development of chemical or biological materials with potentially high pharmacological activity;
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> (2) the "development" stage of pre-clinical testing, where high-activity and low-toxicity variants of compounds are identified and refined through computer simulations, animal models and "wet lab" *in vitro* testing, with the results forming the basis of an IND application ("investigational new drug") to obtain FDA permission for clinical trials; and
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> (3) testing (and perhaps further refinement of) compounds in clinical trials for safety and efficacy in human patients (submitted to obtain NDA-based FDA approval).

Each of these stages involves the expenditure of considerable R&D funds for the sake of generating valuable intangible outputs, which may be highly nonexcludable without government assistance. In particular, even when R&D that is concentrated at the later stages of testing (which are less risky but remain expensive) does not involve very "technically innovative" activity, it may nonetheless be valuable developmental activity, generating information on safety and efficacy that is indispensable for wide public use of medicines. And where some combination of patent, trade-secret and FDA exclusivity protection is unavailable or ineffective, such information risks being undersupplied on the market. This would seem especially to apply to new uses (for which patent rights, even when available, may provide little effective protection),

[4] "Innovative" or "developmental" activity refers here to any activity that produces an intangible good that may go underprovided in a pure market system, because its nonexcludable properties enable competitors to use it in a manner that undercuts the ability of the developer to privately appropriate enough of its social value to recover the R&D costs involved in generating it.

but extends more generally to any work done on known chemical or biological materials to arrive at beneficial therapeutic effects or information thereon that passes muster under FDA-mandated clinical testing, whether or not the work or results from testing qualify under patentability standards.

Specifically, we can identify at least the following distinct types of valuable developmental activities that are at risk of being undersupplied as result of an exclusive reliance on meeting the criteria of patentability:

> (1) New uses: researching and testing for newly-approved uses or "indications" for compounds on which product patent protection is either held by another or expired or not available, so that at most all that is available is a method-of-use process patent.[5] Such a patent provides, roughly, a right to exclude others from using the drug in a certain way or for certain purposes. It is, however, notoriously difficult to effectively enforce such an exclusion right when it is not accompanied by the rights to exclude others from making or selling the product itself (i.e., for any other purposes). As a result, if the compound has been previously approved for another use, the holder of the product patent and/or original FDA data exclusivity period (which effectively runs between 6.5 and 7.5 years) on that compound will likely also be able to sell it, *de facto*, for the follow-on use, notwithstanding both the method patent and the three-year data exclusivity for the new use.[6] (If the product patent and original FDA data exclusivity period have expired, then generic producers may also join in.) Where the compound has not been previously approved for any other use, then the new-use developer is in a better position, now enjoying the longer period of data exclusivity of 6.5 to 7.5 years—although in these cases

[5] Note that the problem is exacerbated when the use itself is known or obvious but has not undergone FDA-mandated testing.

[6] We may also observe an additional point, stemming from the fact that the developer of the new use will also have to negotiate a license from the holder of the original product patent before it can begin sales: Often such deals between pioneers and improvers involve cross-licenses, since they present a case of "blocking patents" whereby not only is the improver prevented from selling its improvement without the pioneer's permission but the pioneer is also prevented from using the improved version of the original without the improver's permission. However, in situations such as ours the original patentee's incentive to obtain a license for the new use is significantly diluted since it can sell its product for both the original non-infringing use and the new use without significant fear of liability for infringing the new-use developer's method patent. This, consequently, reduces the bargaining power of the follow-on innovator and, perhaps, the chances that a deal will be struck or, if it is, the chances that it will be one on terms that do not unduly chill potential future follow-on innovators.

it may also be that the costs and risks of development were significantly higher than for developing a follow-on use.[7]

(2) First-time uses of "non-novel" compounds: this refers to the last case just mentioned, where the new use is the first-approved use of a compound, which compound may be barred from patentability on grounds of non-novelty or may have its patent expired or about to expire (i.e., the compound was inadvertently or otherwise disclosed by the developer or known by others, but no FDA approved use has yet been developed). The key point here is that, in the absence of preclinical development and clinical demonstration of safety and efficacy for a previous indication, the risk-adjusted cost of development and testing for this use *may* exceed what is profitably recoverable through 6.5 to 7.5 years of data exclusivity.

(3) First-time uses of "obvious" compounds: this is similar to the previous, but now extending to compounds or formulations thereof that, while not strictly identical to those disclosed in the prior art, are nonetheless deemed to be insufficiently technically innovative in light of that art and present technical knowledge. As techniques for "rational drug discovery" and design advance, this category may expand.

(4) Generation of new safety and efficacy data on already-approved drugs: Such data faces the classic information paradox—to communicate its value requires disclosing its content, but such disclosure makes it unnecessary for the recipient to purchase it, and disclosure to one means, in principle, disclosure to the world. And reliance on patents as a solution is insufficient in two respects: much of this information may be disqualified for protection on grounds of being "abstract ideas" or "laws of nature" and, in any case, there is really no effective way to enforce the exclusion right once it has been released. And while a patentee may nevertheless internalize enough of the benefit—through increased

[7] Note that the absence of product patent protection also leaves open the option of a second firm entering before the expiry of FDA exclusivity period, by generating and submitting its own clinical trial data on either the same or an alternate use. However, even where the first developer's returns are high enough to make such duplicative clinical trials profitable for a second entrant, the second firm would have a difficult time, in the absence of regulatory approval for another use, of showing a "substantial non-infringing use" (although the option of off-label uses keeps the possibility open).

sales—of positive studies to generate and disclose them, it is unlikely that any private-sector actor has sufficient incentives to uncover negative information.[8]

Note that it is *not* being advocated that we should remedy these gaps by extending exclusion rights over such information goods. As mentioned, such an approach may be quite ineffective for some of these cases. And in any case, a better response for many might be to expand the role for publicly funded downstream activity (given the lower uncertainty and high potential for conflicts of interest attending much of this activity). The point here, rather, is that *some* form of innovation policy—be it exclusion rights, prizes, or direct funding—is necessary whenever the costs/risks of generating an information good are high enough that alternative ways of appropriating its benefits will not suffice to privately cost-justify its generation in the face of corrosive competition. And a prize system like the HIF presents an opportunity to fill in some of that gap. At the very least, products resulting from the first three activities should be eligible. More intriguing—but also more challenging—would be the possibility of fashioning the HIF's criteria for added health benefits in such a way that it can reward the independent generation of further safety and efficacy information on already-approved products. However, going down that road may open up more difficulties than it is worth, and in this regard it may be that more suitable alternatives would be a greater role for publicly-funded testing, more stringent requirements by publishing journals for full disclosure of all private data and/or increases in the testing mandated by regulatory agencies post-regulatory-approval.

To put it another way, the main point being advanced here is that not only should patent protection not be understood as a *sufficient* criterion for registration in the HIF, but also that it should not be seen as a *necessary* criterion. Many observers of the patent system would agree that obtaining a patent over a product or process does not guarantee that the product or process represents either a "genuine" technical advance or, even if so, one that is socially valuable.[9] The

[8] There are a number of reasons why competitor firms may be insufficiently incented: suspicion over their motives may cast doubt on the credibility of the information; there may be not be a strong link between a decrease in sales of a rival's product due to negative information and an increase in their own; and to the extent that there is such a link, it may to that extent be more likely that negative evaluations will also affect its own product, perhaps being common to a whole class of rivals that share the same mechanism of action (e.g., negative evaluations of Vioxx spilling over to other Cox-2 inhibitors).

[9] In the specific context of pharmaceuticals, critics point out that patents are sometimes granted over incremental modifications or "line extensions" of patented parent compounds that represent little or no "inventive step" or are relatively "obvious" to one skilled in the field (the so-called "evergreening" problem). In another vein, patents are commonly granted over drugs that, although structurally distinct enough to represent a genuine technical leap, are

additional point here is that not only may the patent system encompass many innovations of dubious value within its net, but there may also be significant gaps in that net, with highly valuable development activity slipping through the mesh.

To summarize, there are two related but distinct benefits of dispensing with the patent requirement for eligibility to receive payments under the HIF. First, and most tangibly, it will broaden the range of valuable pharmaceutical development activity that may be enabled or incented.

Second, and more subtly, it may catalyze clearer analysis and discussion in public policy debate regarding the precise justification and limits of patent protection in the one sector widely recognized to present the clearest case for strong protection, pharmaceuticals. It is not yet widely appreciated the extent to which the case for strong patent protection in pharmaceuticals is less the result of inherent technical-economic features of drug "innovation" than of special regulatory features pertaining to drug safety and quality: namely, the combination of mandated safety and efficacy testing for new products (increasing manifold the costs of drug development) and abbreviated approval for generics (decreasing manifold the costs of imitative entry). This is not to say that without this regulatory regime patents would be no more necessary for pharmaceuticals than in other sectors—although that is an issue meriting further examination. Nor that these regulatory aspects are a "problem." Rather, simply that the special role of patents in this context is not easily generalizable.

There may also seem to be a third benefit, which is that removing the patent requirement might lead to a reduction in the costs associated with obtaining and enforcing patents on pharmaceuticals. However, this is unlikely to be significant, and understanding the reasons why sheds some light on how the system would work.

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nevertheless functionally similar enough to available treatments that their added social value, in terms of increased health benefits, is modest (so-called "me-too drugs"). (This is not to say that all or even most such "me-too drugs" are not socially cost-justified; rather, simply that, under the patent system, the potential for cannibalizing a current entrant's patentee's rents opens up a troubling gap between the social and private value of such drugs.) And, of course, a leading motivation behind the HIF is that the social value of a drug as measured by health-market-based patent revenues may significantly diverge from a more normatively defensible measure. Such a measure would ideally correct for a number of troubling features of that market: primarily, its reflection of aggregate effective preferences, meaning those that are backed by ability to pay (the "neglected diseases" problem) and which are summed along a single-scale (the "orphan drugs" problem), but also its asymmetric-information-, agency-incentives/conflicts-of-interest- and insurance-based insensitivity to accurate, effectively cost-constrained quality assessments.

First, take the case where the innovation is eligible for patent protection. How would or should the HIF affect a registrant's patent rights? A drug patentee's entitlements are usefully divided into four main sets: (1) exclusion rights against pre-commercial or pre-regulatory-approval generic replicative activity; (2) exclusion rights against commercial or post-regulatory-approval generic replicative activity; (3) exclusion rights against pre-commercial or pre-regulatory-approval rival innovator activity; and (4) exclusion rights against commercial or post-regulatory-approval rival innovator activity. We needn't fully address here the complicated question of which, if any, of these rights should be contractually waived or modified upon reception of a stream of payments from the HIF. It suffices to assume that, regarding set (4), the registrant would retain, if not control rights over follow-on commercial activity, then at least an entitlement to some share of the pecuniary benefits accruing to follow-on products.[10] And, further, that that entitlement would most likely be contingent upon a finding by the patent system that the follow-on product does infringe the pioneer under patent law (or upon the follow-on innovator's assent under threat of lawsuit), rather than upon an independent determination by the HIF administrators. Consequently, even where innovators choose to register their products with the HIF, they have a significant interest in also obtaining patent protection wherever available.

What about cases where the HIF-eligible innovations likely would not qualify for patent protection? Here, the approach being advocated would, again, have the benefit of providing incentives for their generation notwithstanding the unavailability of patents. However, in general there would not be any additional benefit of saving patent transaction costs. This is because the innovator's decision of whether or not to apply for a patent would be relatively independent of the eligibility for registration with the HIF, being based on its assessment of the costs and likelihood of success in obtaining a patent versus the likely benefits of receiving one (primarily a function of the expected returns from follow-on activity down the road). The one possible exception is that in some close cases, the absence of a patent-eligibility requirement may result in the registrant foregoing patent prosecution and saving on costs that it might otherwise have fruitlessly incurred.

Note a crucial implication here. For those innovations that are uncovered by patent protection but are otherwise still eligible for payments from the HIF, the absence of patent protection makes unavailable reliance on the patent system to help resolve follow-on disputes.

[10] Irrespective of whether the developer of the follow-on product selects the prize route.

Although that likely will mean that the registrant of an unpatented product will get no share of any follow-on innovators' rewards, such a result is still better than not even being eligible for rewards for the original product in the first place.

I now take up some common concerns or objections to dispensing with a patent requirement for HIF eligibility.

Wouldn't this flood the HIF with applications for registering products of dubious innovative value? In other words, doesn't the patent requirement provide a valuable screening or filter mechanism?

What is being proposed here is not to eliminate all filters, but rather to replace patents with NDA-based regulatory as the appropriate screening mechanism. Obtaining such approval is in fact a greater financial and administrative hurdle than obtaining patent rights, and thus it should suffice to ensure that the HIF is only charged with reviewing serious applicants. With respect to "dubious innovative value," remember that what is of value here is the development and introduction of products passing FDA muster that will improve upon the health benefits provided by currently approved medicines. And for that, the HIF does well to rely on the FDA's review of the product's safety and efficacy as compared to baseline treatments as the starting point for its own more sophisticated, longer-term assessments. Of course, a question that remains unanswered using this filter is whether the applicant seeking to register an innovative product or use with the HIF is the party properly credited with developing the product under review. That issue is taken up next.

A second screen inherent in the HIF is that the registrant is ultimately only paid on the basis of assessed health impacts—if those impacts are small, the payment will be proportionally small. If the registrant is required to pay the average cost of health impact assessment as an annual fee for participating in the system, the gains from registering a product of little value in terms of improving health could be negative.

Wouldn't foregoing a patent requirement mire the HIF in all sorts of priority and/or ownership disputes?

No. There would be no additional complications raised by dropping the requirement of patentability, as indicated by reflecting on how the HIF likely would handle the main types of situations that might arise.

Consider first two cases where the non-patented innovation is alleged to infringe another party's patent. In one situation, the innovation of the party alleging infringement is not itself registered with the HIF. Remember that the HIF does not affect any non-registrant's patent rights. Thus, if another party alleges that a registered innovation is infringing its patent, then it has full recourse to the courts, which may grant it monetary damages (possibly paid out of the registrant's stream of HIF payments) and perhaps injunctive relief (in which case the product will cease to be sold or manufactured in affected jurisdictions pending negotiated settlement with the patentee).

Roughly the same would likely occur if the patent alleged to be infringed covers a product that is registered under the system. Most likely, the HIF would, as in the previous case, defer to the patent system's determinations and respond accordingly, as described above (regarding resolution of follow-on disputes). Of course, it might be decided that the HIF should make its own infringement/sequential-innovation determinations (and require registrants to defer to these), but then it would be that decision, rather than the one to drop a patent eligibility requirement, that would involve the system in settling ownership disputes.

Now consider a third scenario, where two parties are competing to obtain FDA approval over a non-patented innovation. Here, the HIF can, in settling priority, defer to the FDA process (who gets marketing approval first) just as it would defer to the patent system's determinations of first to file or invent.[11]

Wouldn't this lead to "privatization" of what is already in the public domain?

Recall that the HIF does not grant any exclusion/control rights or exclusive-use privileges with respect to technologies. Rather, it provides exclusive pecuniary remuneration to registrants.

[11] Note that the HIF does not have to so defer. That is, it could be fashioned so as to confer discretion upon the reward authority in certain cases to override the patent system's determinations of who is the first "inventor" and to choose the loser of a patent interference dispute as its recipient. This would then give the loser a bargaining chip (potential reward stream) with which to force a settlement with the patent winner. And similarly with FDA approval and the question of who is the first "developer." As discussed below, although in general it would seem wise to limit such discretion, there are some cases for which the HIF may wish to preserve it.

Whether or not the registered technologies are subject to property rights is the purview of patent law (as well as trade secrets and data exclusivity). Whatever coverage is provided by these, no further propertization results from registration with the HIF or eligibility for payments from the HIF. And, perhaps more to the point, simply because some innovation or information cannot or does not enjoy patent protection does not mean that it is therefore already publicly available in valuable form. The approach advocated here is premised on the assumption that without some prize (or alternative innovation policy), some potentially valuable pre-approval innovations may lie fallow and some valuable but costly-to-generate safety and efficacy information may not be generated. And the contemplated remedy does not entail any added proprietary control-rights.

Should firms be rewarded with payments from the HIF merely for manufacturing and distributing drugs for which the underlying technology, not being eligible for patent protection, is thus in a sense already in the public domain?

In those cases where firms are given rewards based on products that were, for some reason or other, not deemed eligible for patent protection, then the reward is primarily for undertaking valuable, and expensive, clinical trials to secure the knowledge that a product is safe and effective for public use. Satisfying this is a key component of socially valuable activity in the case of pharmaceuticals. Of course, by itself it is insufficient—the product must also provide gains in health impact over available treatments. But that is already taken care of by the HIF's reward formula (which will also, recall, reward registrants for finding cost-effective ways of achieving widespread delivery and proper use and administration of the drug).

One of the possible concerns which may arise here is that new uses are often discovered by doctors in the normal course of their practice/research and then implemented off-label.[12] The registrant may have made an investment in undertaking clinical trial to provide evidence in support of new labeling. If successful, in expectation of rewards from the HIF, the registrant could engage in promotional activities to increase the sales of the product for the new indication. Such an investment may result in a fuller realization of the value of the off-label discovery by ensuring the appropriate level of use given improved information on risk and efficacy, but it may be difficult to determine the real health impact created by generating clinical data and engaging

[12] I thank Aidan Hollis for emphasizing the significance of this point.

in on-label promotional activity (both of which are costly and result in non-excludable intangible outputs).

One approach that could be used to assess health impact of the new use would be to determine the increase in sales of the product in the (now on-label) use. A complication, however, is that the counterfactual comparison is with the amount of use that would have arisen had the new use remained unapproved and unpromoted. Off-label uses, if they are really effective, may grow even without promotion or regulatory approval, and so determining what the counterfactual should be might be exceedingly difficult. The limitation of the reward period for new uses to only five years in the HIF will help to mitigate, but not eliminate, this difficulty.

Should the HIF have discretion as to whether to allow a proposed product or new use to be registered?

Whenever feasible, it is desirable to err on the side of reducing discretion—both out of actual concerns about mismanagement and abuse by administrators[13] and, perhaps more significantly, because a major handicap facing any prize system is the perception that it is much more vulnerable to such concerns than the seemingly less "regulatory" patent system of the Patent and Trademark Office and the courts. And specifically in this context, any discretion should occur not at the point of determining eligibility but rather in determining the best methods for measuring the health impact of a given treatment.

There are three main situations where it might seem reasonable to leave open the possibility of rendering ineligible a product that has obtained FDA approval, or at least reducing the prize amount for it from what the standard formula of incremental value in health-impact would yield:

(1) Despite obtaining a patent or safety-and-efficacy-based approval, the product is deemed an insufficient advance over existing, available treatments. Here, however, the straightforward application of the HIF's health-impact approach should suffice.

[13] The effects of which would be to increase the uncertainty of potential registrants or innovators regarding the prospects of a reward, which in turn might lead them to require higher rewards before opting, in some cases, for the HIF over patents or, in others, even to attempt to develop the product where it is of a type that would yield substantial returns under the HIF but not patents.

(2) The case seems to be an unusual one where the costs of innovation or development are quite low compared to the social value, and thus a reward determined as some ratio of social value might overcompensate the registrant. Here, we *may* wish to carve out distinct categories where we think there is a systematic tendency for different private-cost to social-value ratios to obtain (e.g., new molecular entities versus new uses)—although that is a complex issue meriting careful consideration.[14] If, however, we do take that road, then having done so we should stick with the general categories rather than make further case-specific adjustments—to allay concerns about predictability and vulnerability to discretionary abuses. (The current HIF proposal for a five, rather than ten, year reward period for new uses of already approved compounds is an example of such a predetermined, general category.)

(3) The HIF suspects that the applicant is not properly credited with the innovation/development, despite obtaining the patent rights or first NDA-based approval. As suggested in footnote 11, there are situations in which it may be desirable for the HIF to have discretion to "overrule" the PTO/FDA priority decisions. A particularly problematic case that may arise here is in the situation in which: a product has been in use for some time; an off-label use arises from experience; and a firm conducts clinical trials to demonstrate the efficacy of the product in the new use. While such a clinical trial may indeed be valuable, it is also possible that off-label use has provided such strong evidence of the effectiveness of the product in that use that the trial is almost certain to end positively.

[14] Terry Fisher and I are currently in the process of exploring this issue and hope to circulate soon a draft discussion of it.

BIBLIOGRAPHICAL NOTE

The basic argument linking the need for patent protection of pharmaceuticals to regulatory requirements of safety and efficacy is advanced in Rebecca Eisenberg, *Lecture: Patents, Product Exclusivity, and Information Dissemination: How Law Directs Biopharmaceutical Research and Development*, 72 Fordham L. Rev. 477 (2003-2004). It has since been reiterated and developed by Valerie Junod, *Drug Marketing Exclusivity Under United States and European Union Law*, 59 Food & Drug L. J. 479 (2004); Rebecca Eisenberg, *The Problem of New Uses*, 5 Yale J. Health Pol'y. L. & Ethics 717 (2005); Rebecca Eisenberg, *The Role of the FDA in Innovation Policy*, 13 Mich. Telecomm. & Tech. L. Rev. 345 (2007); and Ben Roin, *Unpatentable Drugs and the Standards of Patentability*, Texas L. Rev. (2009).

These and other writers have also drawn out a number of significant implications of this point. Eisenberg 2003-2004 and 2005 developed the important implication of there being a potential for gaps between patent protection and the costs and risks of generating regulatory safety and efficacy data, focusing on the problem of follow-on uses of already-marketed products but also mentioning the cases of generating of new safety and efficacy information on such products and of first-time uses for products facing patent expiration. Junod 2004 similarly discusses, briefly, the case of new uses and suggests that the legislative purpose behind FDA exclusivity periods was to encourage "the development and testing of unpatentable pharmaceuticals." Others pointing out the disconnect between regulatory requirements of safety and efficacy and patent requirements for technical innovativeness under the non-obviousness standard include Mark Lemley & Dan Burk, *Patent Policy Levers*, Va. L. Rev. (2003), John Barton, *Non-obviousness*, 43 Idea 475 (2003); and Stuart Benjamin & Arti Rai, *Who's Afraid of the APA? What the Patent System Can Learn from Administrative Law*, 95 Geo. L. R. 269 (2007). Roin 2009 extends (and documents) the argument to the case of novelty and statutory-bar requirements and generalizes the argument from non-obviousness beyond the case of new drug-discovery/design technologies.

Finally, in *The Shifting Functional Balance of Patent and Drug Regulation*, Health Aff., Sept.-Oct. (2001), Eisenberg drew attention to the fact that FDA exclusivity periods can serve as

rough functional substitutes for patent protection, a point elaborated in Eisenberg 2003-2004, Junod 2004, Eisenberg 2005, Eisenberg 2007 and Roin 2009.

The foregoing writers have not advanced the further point that the 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. That conjecture, and its implications for patent theory and policy in general, are currently being explored by the author.