From Hatch-Waxman to the Biologics Price Competition and Innovation Act: A Roadmap for Assuring Access to the Best New Medicines

or

Creating the Best Medicines for Patients, Making Medicines More Affordable, But Not Limiting Research to Medicines With the Best Patents

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Access to Medicines Depends on Creating Them: A Short Medical History of Two Great Americans

Arthur Ashe was infected with the HIV/AIDS virus during a routine surgical procedure. He was diagnosed in 1988 and died from AIDS in 1993. Another great American, Earvin Johnson, faced the same diagnosis in 1991. Thereafter, among other achievements, he was part of the U.S. Olympic basketball "Dream Team," winning a gold medal in 1992. Unlike Arthur Ashe, Magic Johnson had newly available choices in AIDS therapy—access to new medicines that were mere research ideas just a few short years before his diagnosis. Magic has been able to lead a full and active life after contracting HIV/AIDS.

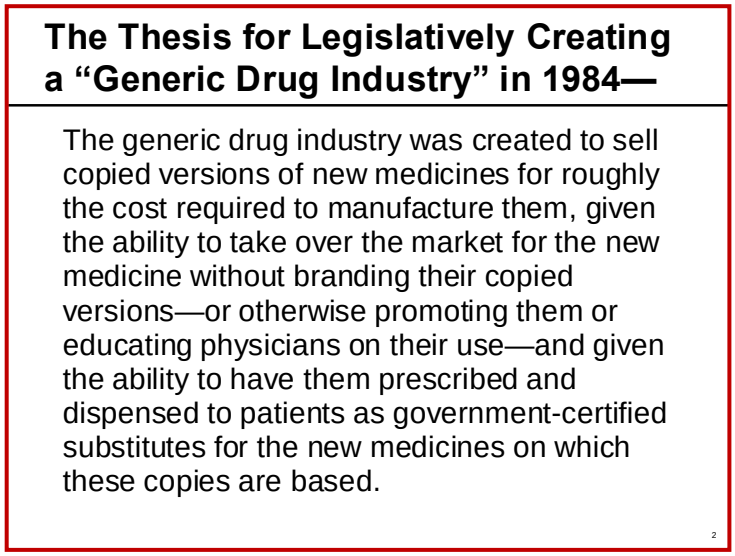
Arthur Ashe, like many Americans diagnosed with AIDS in 1988, would have paid any price for access to medicines effective to treat his illness. His plight was not unlike that of patients today diagnosed with Alzheimer's disease and many cancers. The medicines they need are simply unavailable at any price. As for cost and access to effective AIDS medicines, Magic Johnson's treatment regimen has not been inexpensive. His HIV/AIDS medicines still do not come cheap. Medicines effective against AIDS have cost Mr. Johnson, and other HIV/AIDS patients, many thousands of dollars each year.

The future of HIV/AIDS treatment will, of course, be quite different in two respects. First, the era of the empty AIDS medicine cabinet that gave way to AIDS patients taking a fistful of expensive pills every day to keep their disease in check has now given way to a choice that many HIV/AIDS patients have for controlling their disease—and having the prospect of a long and productive life—with a single pill-a-day therapeutic regimen. Second, we are about to embark on the era where AIDS medicines will come in the form of remarkably inexpensive drugs—copied versions sold by generic drug manufacturers. In the near future, one latte trip to Starbucks for many patients with AIDS will likely cost them more than a visit to the pharmacy to pick up their entire next-month's supply of their HIV/AIDS medicine.

Copied versions of amazing medicines being available at a nominal cost is the legacy of the Drug Price Competition and Patent Term Restoration Act of 1984. It has made a month's supply of many miracle medicines less costly than a Starbuck's Venti. *Will this inexpensive access to new and innovative medicines—indeed, by any measure, access at bargain-basement pricing—be sustained over the coming decades?* Sustaining that access depends upon creating new medicines in the first place, which turns on the intellectual property rules that permit investments in the research needed to create them, define when they can be freely copied, and, thus, trigger when they can be made available almost for free.

The Thesis for Creating a New Industry: The Drug Price Competition and Patent Term Restoration Act

The Drug Price Competition and Patent Term Restoration Act of 1984 is most commonly referred to as the Hatch-Waxman Act. The name comes from its status as a compromise forged by Senator Orrin G. Hatch (R-UT) and Representative Henry Waxman (D-CA). The Act created the modern generic drug industry, which is the source of most of the prescription drugs used in the United States today.



The thesis for creating this new industry was a simple one. The research-based biopharmaceutical industry is the consummate high-risk business, both in its efforts to create new medicines and in subsequent investments to get those innovations understood and used by physicians and their patients. There are no high-risk, low-reward businesses that can sustain themselves over the long term—investors expect returns on risky investments in R&D and marketing that are commensurate with those risks. New medicines are, out of necessity, expensive—priced to pay back the investments needed to create them and get them prescribed.

The modern generic drug industry was created to have the mirror-opposite risk profile. It was designed to exist without the need either to discover new medicines or the need to undertake the massive R&D effort thereafter required to get them approved by the U.S. Food and Drug Administration. In sum, the "product acquisition" cost for a generic drug manufacturer is less than a penny on the dollar of the comparable cost for a research-based biopharmaceutical company to bring a new medicine to market.

On the marketing side, the same 99% cost-discount structure applies. Their copied products are literally *generic* products; they are unbranded, copied versions of new medicines. Generic drug manufacturers not only do not need to brand their products, they do not need to educate physicians on their use, or otherwise promote them. The FDA regulatory regime provides that generic drugs are approved solely by demonstrating bioequivalence to the new medicine which they have copied.

Finally, their copied versions of new medicines are government certified as substitutes for the original version of the new medicine. In the business of prescribing and dispensing medicines to patients, they are freely substitutable and—today—typically freely substituted for the original version of the medicine.

As a result, virtually the only business risk faced by a generic drug manufacturer is the risk of failing to be among the lowest-cost manufacturers of the copied versions of a new medicine. In effect, the business model of the generic drug manufacturer today means that generic drugs can be profitably sold—and provide a profit for the generic drug manufacturer proportionate to the minimal risks of being in the generic drug business—at little more than the cost to manufacture those copies.

The Hatch-Waxman Act Created a Patent-Centric Mechanism for Timing for Generic Drug Entry

The creation by the Hatch-Waxman Act of the modern generic drug industry has no parallel in any other industry. Generic drug manufacturers and research-based biopharmaceutical companies theoretically share the market for a new medicine. In practice, the original version of a new medicine and the copied versions sold by generic drug manufacturers rarely compete with one another for prescriptions. Today, the market for the original version essentially implodes once competition among generic drug manufacturers drives the cost of the generic substitutes down to near the cost to manufacture them.

The reason for this again lies in the risk-cost dichotomy between originator and copier. The originator of a new medicine, pricing it at a cost of $5 per day of therapy, may struggle to pay back the investment in the research needed to create it. A generic manufacturer may be able to profitably sell a copied version of that same medicine for $5 per month. This differential means that at the moment this compelling price advantage for patients (and their health-care plans), appears in the marketplace, the market for the original version of a medicine effectively disappears. In effect, the market for a $1 billion block-buster medicine quickly becomes a market fully served by generic copies, with immediate savings for consumers that reflect this pricing difference.

The Original 1984 Mechanism for Limiting Generic Drug Entry—

The entry of generic drugs into the market was to await the expiration of those patents listed with the FDA that relate to a new medicine and would be infringed if the generic version were marketed. That said, generic drug manufacturers were given a mechanism for challenging either invalidity or infringement of any of the originator's FDA-listed patents in order to determine the actual timing for generic drug entry.

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Given generic drug entry with this pricing advantage, there would be no rational investment thesis for investing to create the original version of a new medicine unless that entry—and the market takeover by generic versions of the medicine—was delayed long enough for the originator of the new medicine to have some prospect of earning back the investment made to create it in the first place. The Hatch-Waxman mechanism for timing generic entry was entirely "patent-centric." It tied the FDA approval of generic copies to the expiration of all of the relevant patents of the originator of the new medicine.

To make this patent-based mechanism workable—and, specifically, to inform generic drug manufacturers when they might be free of the originator's patents—all potentially relevant patents of the originator were required to be listed with the FDA as part of the originator's New Drug Application (NDA) for approval of the original version of the medicine. In order to sort out which patents were actually relevant to the generic copier's version of the medicine (and which were not), the Hatch-Waxman Act provided a mechanism for the generic copier to challenge whether or not an FDA-listed patent was in fact valid and would be infringed by the sale of the copied version, once approved.

Generic drug applications could be filed as soon as four years after the originator's NDA was approved, with up to a further 42-month delay period provided for completing any patent challenges in court.

Awarding a "Generic Drug Market Monopoly" as an Incentive to be First to Challenge Listed Patents

As noted earlier, the patent listings in the NDA of the originator of a new medicine are not optional; all potentially relevant patents of the originator must be listed in its NDA. These include patents actually owned by the originator itself, as well as patents that the originator of the new medicine has licensed from others. Patents that must be listed include those on the active ingredient in the new medicine, physical forms of the active ingredient, and formulations and medicinal uses for the new medicine.

As a result, many (perhaps most) patents listed in NDAs prove irrelevant to copiers. They are sufficiently narrow in scope that a copied version can—and often does—use some unpatented, alternative technology that will not infringe the listed patents. Other patents listed in the NDA may be broad enough to be infringed by a generic copy, but are so broad that their validity cannot be sustained. Either way, the majority of FDA-listed patents, when challenged, have historically failed to be sustained as relevant—both valid and infringed.

The Original 1984 Incentive for Challenging FDA-Listed Patents—

Generic companies were given an incentive to challenge the validity or the infringement of the FDA-listed patents. The incentive was to encourage prompt challenges of questionable patents. Successful challengers were given the right to be the exclusive generic drug entrant into the market for a 180-day period. This generic monopoly period was justified on the basis that, absent the successful challenge, there would have been no generic drug entry until a later patent expiration date.

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To address potential patent infringement issues, the Hatch-Waxman Act set out a mechanism intended to provide a *successful* patent challenger with a 180-day monopoly on the entire generic drug market. This 180-day "generic monopoly period" was to go to the *first* generic drug manufacturer to mount a successful challenge. One justification for providing this type of monopoly over the generic drug market was that such a patent challenge would require a litigation investment by the first mover that would benefit all other generic drug manufacturers. Success by first mover against one or more listed patents would mean that both the first mover and other generic companies following it would gain generic drug entry earlier than would be the case if there were no incentive for anyone to make the challenge.

Over the course of the last 25 years, all the premises that might have justified this "patent challenge" regime, and especially the award of a generic monopoly period, have disappeared. First, few challenges by any one generic manufacturer benefit any other. Second, there is no shortage of generic drug manufacturers willing to bring patent challenges without any prospect of gaining a generic monopoly period. Third, the award of the 180-day generic monopoly period virtually always delays, not hastens, the onset of generic drug competition.

Finally, the courts long ago rejected any "successful challenge" requirement in order for the generic monopoly period to apply. Indeed, generic drug manufacturers that have lost patent challenges have nonetheless managed to secure a generic monopoly over their competitors. Thus, this provision now survives notwithstanding that any possible rationale for continuing it has been turned on its head.

Patents, Patents and More Patents Have Become the Key Feature of Hatch-Waxman Operation

As the foregoing suggests, the manner in which the Hatch-Waxman Act operates today can be summarized in a single word: *patents*. Patent listings in the originator's NDA for a new medicine are the foundation for *patent linkage*—the tie of the approval of generic drug applications for the new medicine to the expiration of the last of the relevant listed patents. This patent linkage, in turn, produces a *patent centricity* in the process that the originator uses in deciding whether to invest in the new medicine in the first instance. Absent the prospect of effective and long-lived patent protection, the most an innovator might hope for is a 4- or 5-year moratorium period provided under Hatch-Waxman after the NDA approval date when generic drug applications cannot be filed. Further, a patent linkage system cannot operate without provoking *patent litigation* to determine which patents are relevant to any particular generic drug application and which are not. Finally, the potential for a 180-day generic monopoly period in those situations where one or more FDA-listed patents are challenged has meant that *patent settlements* between the holder of the 180-day generic monopoly opportunity and the originator have become commonplace—much to the chagrin of the Federal Trade Commission and the Department of Justice, both of which have argued that they are being used to delay the onset of competition that would otherwise take place among generic drug manufacturers. See "Pay-for-Delay Settlements in the Pharmaceutical Industry: How Congress Can Stop Anticompetitive Conduct, Protect Consumers' Wallets, and Help Pay for Health Care Reform (The $35 Billion Solution)," Jon Leibowitz, Chairman, Federal Trade Commission (June 23, 2009) at www.ftc.gov/speeches/leibowitz/090623payfordelayspeech.pdf.

The policy justification for patent centricity came in part from the second title of the Hatch-Waxman Act, namely its provisions on *patent term restoration*. By the end of the 1970's it had become clear that patent terms for pharmaceuticals were highly variable. While some medicines enjoyed patent lives of 15 years (or even longer), other medicines had significantly shorter effective patent lives. Prior to 1995, patent life under U.S. law was a 17-year period from the date the patent ultimately *issued* and, therefore, could start very close in time to the time the FDA approved the original version of a new medicine. In other situations, an early-to-issue patent would start to run out long before a new medicine was FDA-approved. Congress decided that medicines should be able to secure at least a 14-year patent life through the patent term restoration provisions and did so by enabling the originator of a new medicine to pick a single listed patent for which up to five years of restored patent life could raise the post-approval patent term to 14 years.

Key Features of the Hatch-Waxman Legislative Model Today—

1. *Patent Linkage*: Patent expiration dates determine generic drug approval timing.
2. *Patent Centricity*: Absent patent protection, generic drug entry takes place rapidly (5-year moratorium period on seeking generic drug approval).
3. *Patent Litigation*: Most generic drug approvals are determined today only after patent litigation is brought.
4. *Patent Settlements*: Most common outcome of H-W litigation is settlement.

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Patent term restoration and patent linkage meant that Congress afforded only a nominal 4- or 5-year period after FDA approval of a new medicine before generic drug approval could be sought.

Patent Centricity Means Patent Perversity: How Patient Interests and the Public Interest Are Ill-Served

During the first decade of the Hatch-Waxman Act—and even for much of the second decade—the profound problems that would emerge from patent centricity—and absence of meaningful "moratorium" periods on the filing of generic drug applications—were not widely appreciated. For many medicines, late-to-issue patents meant 14+ years of protection even without patent term restoration. For many others, patent term restoration secured a 14-year effective patent life.

The Uruguay Round Agreements Act of 1994 then changed the rules of the patent game for new medicines quite dramatically. It changed the fundamental measuring stick for patent terms. For patents sought after 1995, a new 20-year patent begins to run on the date the patent is initially sought, not when the patent ultimately issues. Patent life runs down such that today patents sought early in the process of developing a new medicine have minimal patent life remaining by the time of FDA approval of the medicine. The nominal 20-year patent term can dwindle down to 5 years or less of effective patent life for a new medicine.

Key Drawback of "Patent Centricity" in the Hatch-Waxman Model Today—

Patent Perversity: Patents, especially in the post-URAA environment, are often perverse in the manner in which they protect new medicines from FDA approval of generic copies. Patent terms may run down or even run out before a new medicine can gain FDA approval, making it impossible for the new medicine to earn back in revenues the cost of the R&D needed to create it. Medicines most meriting an adequate protection period will typically enjoy the shortest patent lives.

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Unfortunately, the most relevant patents (often the *only* relevant patents) on any new medicine are those protecting the active ingredient. The active ingredient is the only feature that a generic manufacturer must copy exactly. Patents on the active ingredient, however, must be sought the earliest in the course of the R&D efforts to bring a new medicine to market.

How "Patent Perversity" Operates: Best Medicines, Worst Protection

The longest R&D path exists for medicines of greatest potential importance to patients because they require the longest, most difficult and most complicated studies for FDA approval for marketing:

- Medicines where no existing therapy currently exists.
- Medicines with novel mechanisms of action.
- Medicines for chronic diseases rather than acute conditions.
- Medicines for prevention rather than treatment of disease.
- Medicines otherwise needing extra persistence by the originator—after an initial failure.

The more difficult the R&D efforts, the longer they take, the shorter the prospective patent life.

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This relationship creates a profound perversity. Effective patent life is now the shortest where the path to getting FDA approval for a new medicine is the lengthiest. This means that entirely novel therapies, chronic disease treatments, preventative medicines, and medicines with untested mechanisms—in brief, the potentially most valuable contributions to human health—face the perverse prospect of the shortest effective patent protection in the post-URAA era. This perversity leaves innovators with the prospect that the most important new medicine will be left with the least in patent protection.

Patent Perversity, Part II: The 180-Day Generic Monopoly Period Awarded on Later-Expiring Patents

As perverse in its actual operation as providing the shortest periods of effective patent protection for many of the most innovative, important and challenging new medicines is the Hatch-Waxman provision providing the 180-day generic monopoly periods. As noted above, this provision has mostly done just the opposite of what it was intended to accomplish—by delaying rather than hastening generic drug entry. What made this provision operate with such perversity?

Most of the FDA-listed patents, as noted above, relate to technology that need not be copied by a generic drug manufacturer. Put simply, many patents can be "designed around" by finding some alternative physical form for the active ingredient or different medicinal formulation (a different set of ingredients used to make the pill) that is not patented. Such secondary patents are typically sought later in the drug development process, which in the post-URAA world, means they will expire later than the primary patents relating to the active ingredient in the new medicine.

More Perversity Today: The 180-Day Generic Monopoly Period—

The 180-day generic drug monopoly period, rather than accelerating generic drug entry, typically operates to *delay*, not *accelerate* it. Most Hatch-Waxman patent litigation involves one or more secondary patents that can be readily designed around and no generic will likely infringe. Without any monopoly period at all, generic companies would enter the market sooner, as each establishes non-infringement of relevant FDA-listed patents.

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Thus, most Hatch-Waxman patent challenges today are contests involving these types of later-expiring, secondary patents. These are patents where, if one generic drug manufacturer is entitled to the 180-day generic monopoly period shutting out other generic competition, it becomes a monopoly reward for nothing more than establishing non-infringement of the secondary patent, not removing the patent as an obstacle to others. This means that every other generic must challenge the same patent and demonstrate its copied version does not infringe. Instead of benefiting other generic drug companies, the generic monopoly period operates as a disincentive to generic competitors forced to face the same patent.

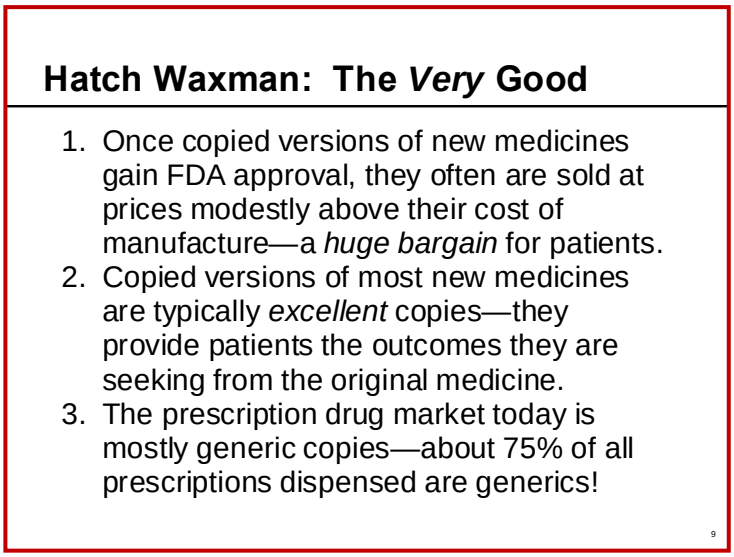
This situation, of course, compounds the other major flaw with this monopoly period: *it cannot come to an end until it begins*. This flaw is the genesis of much of the criticism of the 180-day generic monopoly period by the FTC. While the FTC labels patent settlements between the originators and the copiers of a new medicine as "pay for delay" arrangements, many are simply "delay for certainty" settlements in which the generic monopoly holder is able to secure a fixed, future date for the start of its generic monopoly period (and the originator of the new medicine, therefore, has a fixed date for the end of its patent exclusivity period). The problem comes when the *date certain* extends beyond the date when patents relevant to *other generic drug manufacturers' generic copies* have expired. Then, every generic competitor that should be on the market sooner must wait for the "agreed" 180-day period to start.

Today, the 180-day generic monopoly period, even though extensively reworked and reformed in 2003, remains beyond any hope of salvage as a mechanism to accelerate generic drug entry.

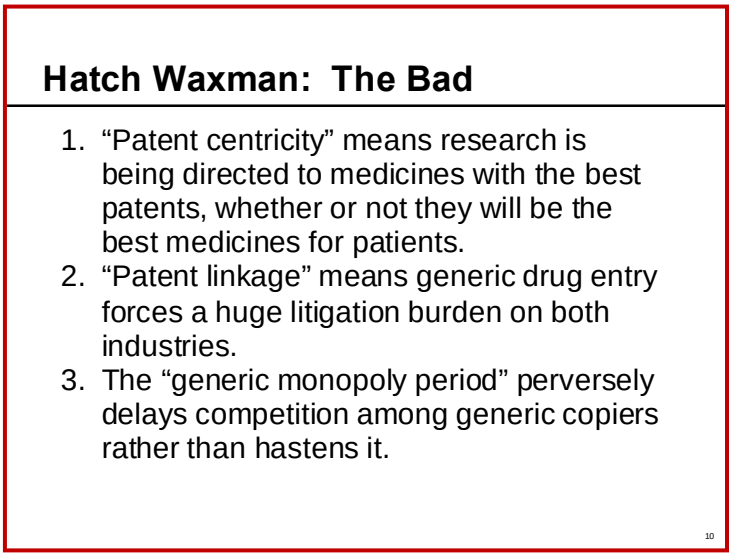
After 25 Years of Hatch-Waxman Operation, the Good is Very Good and the "Bad" Needs Addressing

Any effort at tallying an overall scorecard on the Hatch-Waxman law would have the upsides far outweighing any downsides. To draw the same accolade over the next 25 years, however, will depend on addressing the concerning aspects of Hatch-Waxman, particularly its demonstrable perversities.

The good from Hatch-Waxman is, without serious dispute, *very good*. The goal of creating a viable generic drug industry was realized. Today, copied versions of new medicines are a huge bargain for patients—often available at a cost modestly above their cost of manufacture. Their excellent value is matched by their quality; they are reliably used by millions of Americans—approximately 75% prescriptions that are dispensed in the United States are for a generic copy of a medicine, not the original, branded version. See http://www.gphaonline.org/media/press-releases/2010/statement-gpha-president-and-ceo-kathleen-jaeger-response-remarks-fda-comm.



What does this "good" mean for the originators working on the next generation of new medicines? Future innovations in medicines will need to be truly remarkable medicines—addressing unmet medical needs in meaningful ways—if they are to successfully compete with very low cost generic copies of earlier-generation medicines.



Facing competition from these low-cost, copied versions has profound implications. First, it means that originators need to develop the *best* new medicines for patients, irrespective of whether they have the best patent protection. Patent centricity will become a more concerning issue. Second, originators need to undertake increasingly risky research, which means the additive risks posed by patent linkage (namely, that an apparently valid patent vital to the ability to invest in developing a new medicine will fail to survive a generic challenge) will become more difficult to bear. In brief, a patent-centric system with its built-in perversity and unavoidable uncertainties simply undermines the ability to make the investments in the research needed to produce the new best medicines.

Ending Patent Centricity and Its Perversity: Affording Data Package Protection from Generic Copying

There is a viable alternative to patent centricity—and patent linkage, patent litigation, allegedly collusive patent settlements, and a generic monopoly period—to define the interface between the research-based biopharmaceutical companies and generic drug manufacturers. It is based on a data package protection period (DPPP) that imposes limits on the FDA approval of copied versions of new medicines.

Substituting such a data-based interface for a patent-linked one is entirely consistent with the original thesis for the creation of the modern generic drug industry: affording it the ability to sell drugs at little more than the cost to manufacture them, by stripping away the typical business risks. The problem with patent centricity and the resultant patent litigation is that the uncertainties and risks relating to patents and the timing of generic drug entry have become confounding factors for the low-risk generic business model.

A Better Way: How Can the *Very Good* Be Kept and the Bad Not?

A "better way" would provide for generic (and other follow-on copied) versions of new medicines to come to market with—

- No patent centricity.
- No patent linkage.
- No patent perversity.
- No generic monopoly period.
- No collusive patent litigation settlements.
- *No uncertainty over generic approval date*.

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The patent risks and uncertainties in a patent-linked, patent-centric system are, of course, faced equally by both originators and copiers, with both benefiting if those risks can be mitigated or even eliminated.

A Better Way: Data Package Protection from Follow-On Copies

"Patent linkage" is removed from the law and the rule that FDA approval must await expiration of all relevant FDA-listed patents is eliminated. In its place, *a fixed period of data package protection from FDA approval of generic or other follow-on copies* is instituted, sufficiently long to permit the originator of a new medicine to recover the investment in the research needed to discover and develop the new medicine through FDA approval.

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At the heart of a data-centric regime is setting out a fixed date when copied versions of a new medicine can be approved by the FDA by relying on the data package of the originator of the new medicine. This type of data package protection period or DPPP need only be sufficiently long to afford the originator of a new medicine the prospect of earning back from sales of the new medicine enough to recover the investment in the research needed to discover and develop the medicine.

An interface based entirely upon a sufficient DPPP, devoid of patent linkage, can be as simple in actual operation as the Hatch-Waxman patent-centric system is complex. The only significant challenge in creating the DPPP architecture lies in determining the length for the protection period itself—a sufficient period for the originator of the new medicine to have the prospect of earning back the investment required to discover and develop it through FDA approval in the first place.

What Is (And Isn't) a "Data Package Protection Period" and What Is (And Isn't) The Right Length?

A data package protection period or DPPP is the period in which the FDA will not approve a copied version of a new medicine that is the subject of the data package protection *unless* the copied version is supported by its own independently developed, fully complete data package, containing pre-clinical data and clinical data establishing the safety and effectiveness of the copied version. The protection period is a period in which the FDA will rely only on the data actually obtained by the person seeking FDA approval of the copied version to determine whether the copied version can be approved for marketing.

The protection period, therefore, is a period that runs from the initial approval for the original version of the new medicine and, as such, runs *concurrently* with any patent protection that might exist. However, unlike effective patent protection—where a court might enjoin the marketing of any and all copied versions of the new medicine until the patent expires—a DPPP does not create marketplace exclusivity. Anyone independently creating its own data package from studies that it has sponsored can gain FDA approval of a copied version of any new medicine.

What Is (and Isn't) a Data Package Protection Period from a Follow-On?

1. Runs from the date of FDA approval of the original version of the new medicine; runs concurrently with—and is not additive to—any available/remaining patent protection.
2. Does not provide any form of exclusivity—any competitor is free to seek and obtain FDA approval based upon an *independently created* data package.
3. During the protection period, the sole effect of the protection is the *independent creation* requirement to gain FDA approval for a copied version of a new medicine.

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Since the DPPP merely determines when the FDA is able to, in effect, rely on the data package filed by the originator of the new medicine to determine whether copied versions of that medicine might be approved for marketing without the need to independently recreate the data establishing safety and effectiveness, the question of what period is the right period for a DPPP is potentially complicated only in a political sense. In economic terms, the right DPPP should be relatively straightforward to determine, *if the objective is to assure that the DPPP is adequate for the originator of the new medicine to be able to earn back in profits from sales revenues the investment needed to create the new medicine in the first place*. By this measure, a 15-20 year DPPP is appropriate, given a 14+ year period is fully consistent with the Hatch-Waxman Act's obvious intention to create a 14-year floor on patent life for new medicines.

What Is (and Isn't) the Right Length for Data Package Protection?

1. ***Not Too Long***. Protection beyond 20 years is largely meaningless to the objective of recovering investment in R&D.
2. ***Not too Short***. Any period less that 15-20 years after original FDA approval is insufficient to recover R&D investment and pursue optimal level of post-approval research to define the best and most complete uses for the new medicine.
3. ***Just Right***. 14+ years, roughly the same 14-year patent term "floor" contemplated in 1984 under the Hatch-Waxman Act.

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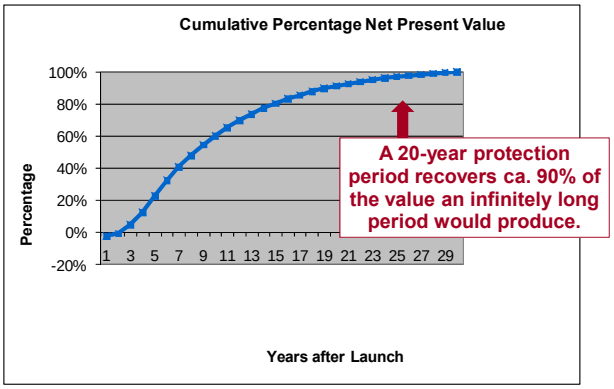
The Mathematics of a Data Package Protection Period: The Long and the Short of It

The mathematics of avoiding a DPPP that is either too long or too short are fairly straightforward. First, the determinant is the ability to pay back the investment in the research needed to create the original version of a new medicine in the first place. The best way to look at such a "payback period" is by looking at future revenues and profits in terms of their "net present value" or NPV. The net present value is determined by discounting profits that come in the future using a discount rate that reflects the return that an investor would want from assuming the risk inherent in the investments being made.

By this NPV measure, it is self-evident that a DPPP need not be infinitely long. Using any set of reasonable assumptions concerning the market for a new medicine, the profits that might be earned once it gets to market and the appropriate discount rate that should apply, protection beyond 20 years does very little to generate incremental NPV sufficient to assure the original research investment gets paid back. At 20 years, roughly 90% of the NPV is recovered that could be recovered based upon a DPPP of infinite length.

Not Too Long: More Than 20 Years Produces Small Incremental Value—



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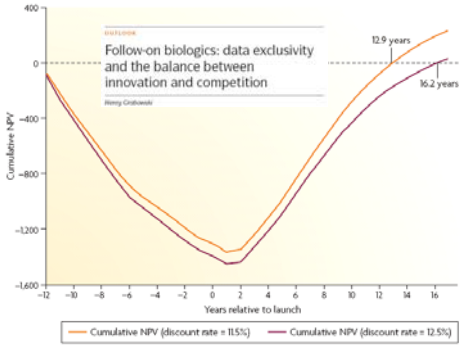
By the same measure that more than 20 years would be too long (or at least of modest significance to paying back the investment in research), much less than 15 years is too short. See Henry Grabowski, Nature Reviews, Vol. 7 (pp. 479-488) at http://www.nature.com/nrd/journal/v7/n6/pdf/nrd2532.pdf.

Not Too Short: "Breakeven Time" on R&D Investment is 13-16 Years

"The figure shows the cash-flow patterns for the mean product in this portfolio analysis from the initiation of research and development (R&D) to payback. When the net present values (NPV) of inflow just equals outflows, this is the break-even point at which a firm recovers its R&D investment and earns a risk-adjusted rate of return. The breakeven time is 12.9 years for a discount rate of 11.5%, and 16.2 years for a 12.5% discount rate."



Henry Grabowski, Nature Reviews Drug Discovery, Vol. 7 (June 2008) pp. 479-488.

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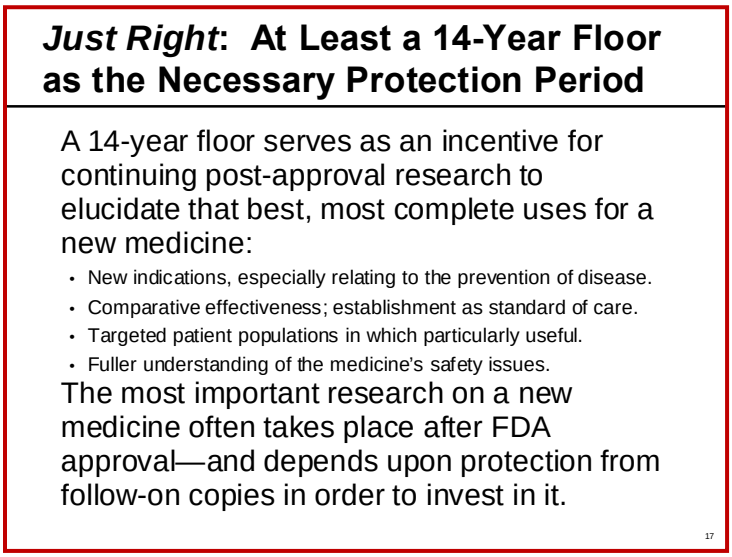
The Grabowski work uses a pair of discount rates to calculate possible "breakeven" scenarios. The conclusion from his work is straightforward: a payback period that is short of 13 to 16 years would not be sufficient. While the Grabowski work was done on new biologic medicines, its fundamental methodology applies to new medicines of all types—and increasingly so as the costs and risks of bringing new medicines successfully to market have steadily accelerated.

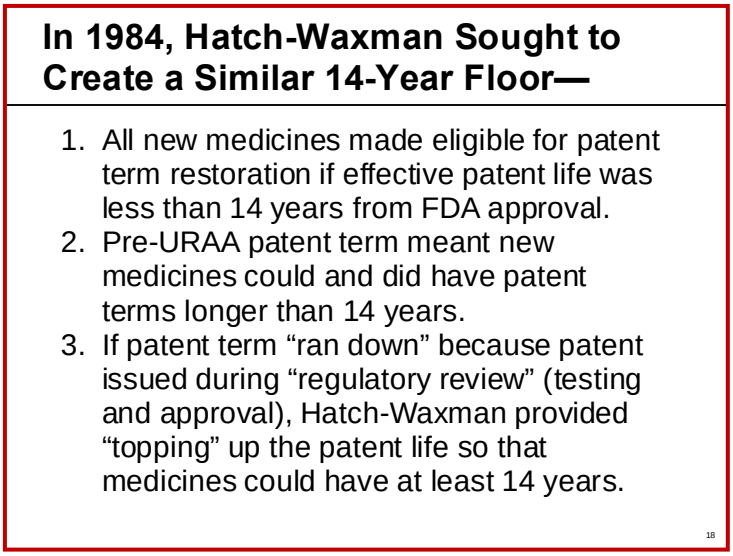
If more than 20 years is too long and anything less than 13-16 years is too short, what is just right?

A Period of 14+ Years of Data Package Protection is Just Right and Rightly Justified

Once FDA approval for generic copies of new medicines is delinked from patent protection, the period of data package protection solely determines generic drug approval timing and, thus, whether the investment in research needed to create a new medicine can be earned back. This makes a period of at least 14 years, i.e., towards the low side of the 13- to 16-year sweet spot determined by Grabowski, the appropriate protection period. Two other considerations, however, point to this same 14+ year period.

First, much of the most important research on every new medicine takes place not before, but *after*, the FDA has approved the medicine for use. This is the research into new indications for use, uses to prevent and not just treat a disease, patient populations where the medicine may be especially effective and useful (or carry particular risks and liabilities) and safety issues that arise and need to be fully understood. For this research to be sustained—and for the fullest and best uses of the medicine to be understood and for physicians to be fully educated on the use of the medicine by the time generic copies arrive on the market—it is critical that incentives exist to continue this type of post-approval research during the decade after the medicine reaches the market.





Without a 14+ year DPPP, there is no way in which the originator is positioned to continue investments in research during the decade after the medicine first reaches the market. If inexpensive generic copies come to market too soon, investment needed to create and disseminate the information needed to put the medicine to its fullest uses will never have been made.

Second, the Hatch-Waxman Act's clear intention was that patent protection for new medicines would be "topped off" to this same 14+-year period proposed for data package protection. In 1984, Congress clearly believed, and intended, that Hatch-Waxman would apply to medicines with shorter patent lives than 14 years, such that they would be given the opportunity for a full 14 years of patent life following FDA approval.

The Perversity of a Long R&D Path Producing a Short Effective Patent Life Cannot Be Easily Fixed

Since patent term restoration for new medicines was enacted in 1984, hundreds of Hatch-Waxman patent extensions have issued. Patent perversity has meant only about one-third to 40% could be extended to 14 years from the date of FDA approval of the medicine on which the extension was based.

Patent Term Restoration Was Not Successful at Achieving 14+ years—

1. Between one-third and 40% of all new medicines approved since 1984 had a patent "topped up" to 14 years.
2. Many of the remaining new medicines did not otherwise have other patent protection of 14 years or longer.
3. Even worse, many of the medicines most deserving of at least 14 years of protection got shortest effective patent life.
4. Worse yet, some new medicines secured no effective patent protection at all.

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For many of the medicines failing to get to the 14-year mark, patent perversity could not be surmounted. Medicines that were the most innovative therapies, represented the most risk-laden research, and were the most challenging and otherwise difficult to see through to FDA approval were simply shortchanged. They consumed far too much patent term before gaining FDA approval to be able to get restoration back to a 14-year patent life, even with an extension for the full five-year period permitted under the Hatch-Waxman Act. For other medicines, patent perversity was simply the lack of any relevant patents to extend at the time of FDA approval—thereby opening the medicine to copying after the end of a brief "moratorium" period.

Such perversity is inherent in part because demonstrating the safety and effectiveness of a medicine under the Food, Drug and Cosmetic Act does not necessarily qualify the medicine as novel, useful and non-obvious under the Patent Act. In some cases, even the most innovative medicines simply fail to qualify for any effective patent protection whatsoever.

Post-URAA, a 14-Year Patent "Floor" Became a 14-Year "Ceiling"—

1. The most significant patents on a new medicine—the protection for the active ingredient—are sought early in the 12-15 year period needed to get FDA approval.
2. Patent term restoration only permits 5 years of patent life to be added back—and only for a single patent on the medicine.
3. Since the 20-year patent term begins to run as soon as a patent is first sought, the 1984 "floor" is now actually a "ceiling."

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Moreover, the intended "floor" on patent life envisioned by Congress in 1984 has now become a "ceiling" rather than a "floor." As noted earlier, the running down of the patent clock on a new medicine now begins the day a patent is sought. A typical new medicine can take 12-15 years of non-stop investigations before gaining initial FDA approval for marketing. Only a few years of this post-URAA, 20-year patent term may remain when a medicine receives FDA approval. Thus, perversely, the merit of a medicine is often unrelated (or inversely correlates) to its patent life and a medicine of great therapeutic merit may merit no relevant patent protection whatsoever. The patent law dictates this perversity and its irremediable character.

Persistent Patent Perversity Makes 14+ Years of Data Package Protection a Compelling Alternative

Given a choice between developing the best new medicines and new medicines with the best patent protection, there is a full alignment of interests among patients, their physicians, providers of their healthcare plans, and the creators of those medicines in the biopharmaceutical industry. The common desire is to make the best new medicines, not focus research on medicines with the best patents.

One compelling solution to the problems of patent uncertainty and patent perversity is simple: afford new medicines 14+ years of data package protection running concurrently with any available patent protection. Such a DPPP would provide greater patent agnosticism in selecting new medicines to develop. It would mean that the best uses of the medicine could be pursued after FDA approval through extended post-approval research.

Why 14+ Years of Data Package Protection Is a Compelling Solution—

- Levels the playing field—only about 40% of new medicines achieve 14+ years of patent term—the others are among the most deserving of it.
- The highest and best uses of the medicine can be fully developed before copied versions come to market—affords the innovator approximately 10 years to continue post approval research.
- Affords innovators the minimum time needed to reinvest the revenues of today's new medicines to produce tomorrow's "wonder drugs."

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It would also better assure that the most deserving medicines—those that would most consume effective patent life because of the extended path to FDA approval—would enjoy protection from FDA approval of copied versions for a period long enough to have the prospect of earning back the investment in the research needed to create them.

Why 14+ Years of Data Package Protection Is a Compelling Solution—

- Shortest period that avoids the need for patent linkage and would obviate most patent challenges—only secondary patents will remain.
- Provides a certain and fixed date for approval of copied versions of a new medicine.
- Affords follow-on copiers fewer risks and greater certainty—focus on being the best copiers, not copiers with the best patent litigators.
- Assures that innovators can develop the best medicines, not medicines with the best patents.

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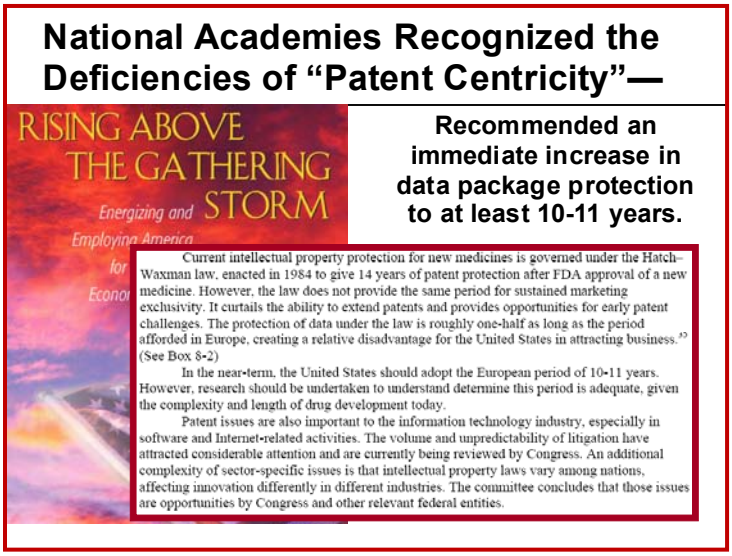
Finally, providing 14+ years of data package protection in the post-URAA world means that effective patent protection will expire simultaneously with or prior to effective patent production, given patent term restoration post-URAA. This obviates both the need and desirability of continuing patent linkage. Jettisoning it provides for a fixed date for generic drug entry, free from uncertainties over patents, as soon as the 14+ year protection period from FDA approval of generic copies comes to an end.

Generic drug manufacturers could focus on being the best copiers of new medicines, not the best of patent litigators. In a similar vein, innovators could focus on doing what they do best, devising the best in new medicines, rather than marshalling often futile efforts to secure relevant, long-lived patents.

The National Academies Recommended a Data-Package Focus for Protecting All New Medicines

In 2007, the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine jointly published a 2007 report, "Rising Above the Gathering Storm: Energizing and Employing America for a Brighter Economic Future," (http://cart.nap.edu/cart/deliver.cgi?record_id=11463), in which the deficiencies of patent centricity were laid out in case-study form.

The National Academies concluded that a serious effort was needed to determine how best to balance available patent protection for new medicines with data package protection. It laid out the case for a more data-focused regime. Pending completion of a study to determine a fully adequate protection period, the National Academies recommended that Congress should move ahead immediately with at least a 10-11 period of data package protection to provide at least some parity with the European data package protection regime that currently affords up to an eleven-year protection from the approval of generic copies of all new medicines:



> "The demands for data on a molecule's safety and efficacy are increasing. The generation of the necessary data requires time and money. It is to patient's benefit for as much time as appropriate to be devoted to the development of the data, but spending the time lessens the return on the developer's investment because it encroaches on the patent term. Bringing a new medicine to patients requires a sequence of major breakthroughs, which in the current system must be accomplished well before the life of a patent runs out. Often, the clock does run out, and the innovator must start over with a new molecule simply to get time 'back on the clock.' As a result, there is an ever-growing 'graveyard' currently comprising more than 10 million compounds. There is no incentive to exhume these compounds in the absence of substantial data-package exclusivity, because patents will be either unavailable or of such narrow coverage that they would be easy to avoid in developing a related drug.
>
> "In addition, there is little incentive to pursue new indications for old molecules without appropriate data-package protection. … If there is no compound patent and one of the indications is unpatentable, the generic medicine may be approved only for the unpatented indication. The innovator's entire market could then be eroded because physicians have the latitude to prescribe the generic compound for any indications, including patented ones. Every reasonable effort should be made to encourage the development of new indications for known compounds because of the greater level of knowledge about safety for already-marketed compounds than for brand-new ones." (See pp. 191-192.)

Data Package Protection Enacted for Biologic Medicines Provides a Model for Hatch-Waxman Reform

In the current Congress (and in the preceding 110th Congress), legislation was introduced to create a follow-on (generic-type) pathway for the FDA approval of copied versions of new biologic medicines. Biologic medicines are more chemically complex than the traditional "small molecule" drugs that are subject to the Hatch-Waxman Act's provisions for FDA approval of generic copies. The most important biologic medicines today are made in living cells modified using recombinant DNA technology.

After considering a number of competing legislative proposals, Congress passed the Biologics Price Competition and Innovation Act in March of this year with a 12- to 12.5-year protection period.

Healthcare Bill (H.R. 3590), Title VII, Follow-On Biologics (Biosimilars)—

"Balancing innovation and consumer interests."

TITLE VII—IMPROVING ACCESS TO INNOVATIVE MEDICAL THERAPIES

Subtitle A—Biologics Price Competition and Innovation

SEC. 7001. SHORT TITLE.

(a) IN GENERAL.—This subtitle may be cited as the "Biologics Price Competition and Innovation Act of 2009".

(b) SENSE OF THE SENATE.—It is the sense of the Senate that a biosimilars pathway balancing innovation and consumer interests should be established.

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Under this new regulatory pathway, the FDA can approve highly similar ("biosimilar") copies of new biologic medicines by relying on the data package of the originator of the new medicine. Access to this new pathway and the ability to effectively rely on the originator's data package exists in the new law *without any patent linkage.* The new data package protection period forms the sole constraint on the FDA's ability to approve the follow-on versions of new biologic medicines.

Congress described this new DPPP regime as "balancing innovation and consumer interests." In creating the new follow-on biologic approval pathway, Congress considered—and rejected proposals that would have created much shorter data package protection periods.

Healthcare Bill (H.R. 3590), Title VII, 12-Year Base Protection Period—

12-year base period extended to 12.5 years based on pediatric studies

"(7) EXCLUSIVITY FOR REFERENCE PRODUCT.—

"(A) EFFECTIVE DATE OF BIOSIMILAR APPLICATION APPROVAL.—Approval of an application under this subsection may not be made effective by the Secretary until the date that is 12 years after the date on which the reference product was first licensed under subsection (a).

"(A) the periods for such biological product referred to in subsection (k)(7) are deemed to be 4 years and 6 months rather than 4 years and 12 years and 6 months rather than 12 years;

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One proposal from the 110th Congress would have provided no patent linkage and zero years of data package protection, with its sponsor in this Congress eventually upping that number to 5 years of data package protection. (See H.R. 1427, 111th Congress.) On the other side of the DPPP equation, H.R. 1528 was introduced by Representatives Eshoo, Inslee and Barton calling for an optimal 14-year DPPP.

By any measure, the Act's elimination of patent linkage in favor of more adequate data package protection is a model for making reforms to the Hatch-Waxman Act to address its growing perversities.

"Small Molecule" Medicines Should Not be Left with a Perverse, Patent-Centric Protection Regime

The Biologics Competition and Innovation Act recognized the maturity of the era of rDNA-produced medicines, launched over 25 years ago when Eli Lilly and Company, in partnership with Genentech, gained FDA approval for Humulin, recombinant human insulin, the first such rDNA medicine. See http://www.fda.gov/AboutFDA/WhatWeDo/History/ProductRegulation/SelectionsFromFDLIUpdateSeriesonFDAHistory/ucm081964.htm).

Key Features of Biosimilars Law on Protection Periods—

1. New biologic medicines subject to follow-on copied versions being FDA approved based upon originator's data package.
2. Originator entitled to both patent term restoration of up to 14 years and data package protection of up to 12.5 years.
3. No patent linkage—FDA approval is made independently of any patent protection.
4. Limits significantly "patent centricity."
5. But, falls short of being *just right*—at least 14 years of data package protection.

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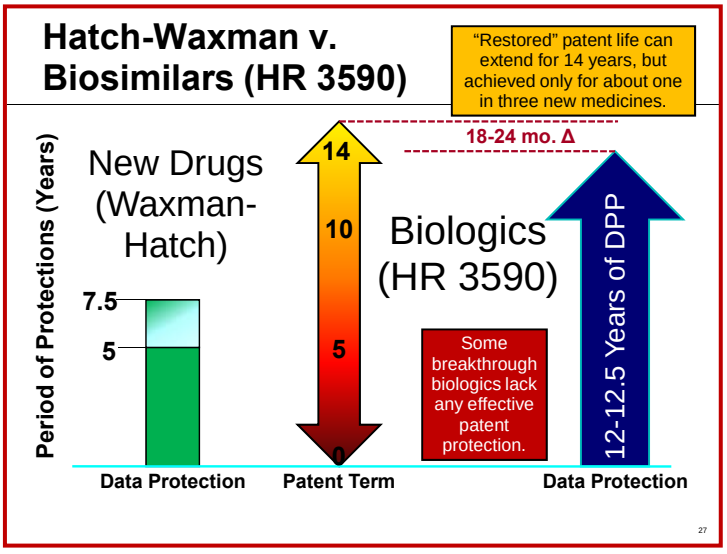
Since the FDA approval of Humulin, biologic medicines have become a progressively larger share of the research pipelines of the research-based biopharmaceutical industry. Even though the Biologics Act falls short of a 14+ year protection period for new biologic medicines, the new law's predictable and certain protection period from follow-on copies represents a striking improvement over the Hatch-Waxman regime's 4- or 5-year "moratorium" periods during which a generic drug application cannot be filed seeking FDA approval for a copied version of a new "small molecule" medicine.

The new law has now created a significant disparity between protections against generic drug entry and those that now apply to biosimilar medicines. This disparity has the potential to skew research towards these "large molecule" medicines, which are typically injected or infused into the patient. Now at greater risk is research aimed at bringing more "small molecule" medicines through the R&D pipelines of biopharmaceutical companies, medicines commonly available in pill form.



Such a skewing would be neither rational nor desirable—given that patients, physicians and the providers of their healthcare plans all have a vested interest in biopharmaceutical companies focusing on the best in new medicines, not just medicines that hold the prospect of garnering the most secure IP protection from being freely copied. It is imperative, therefore, that the new model for new biologic medicines be given a careful vetting as a model for "small molecule" medicines, hopefully addressing the gap between a full 14+ year protection period and the 12-year DPPP in the Biologics Act.

The Brief for Data Package Protection for 14+ Years Running Concurrently with Patent Protection

The opponents of providing an adequate period of data package protection often assert that this protection should not be granted in *addition* to available patent protection, failing to note that the two types of protection are not in any sense additive because the respective protections run concurrently.

No one—at least no one with a sense of fair play—seriously disputes that data package protection is warranted where patent protection is unavailable or the length of the research and development process has eaten up all of a medicine's meaningful patent protection. In such situations—and in other situations of deficient patent protection—data package protection is not only fair, but the only way in which anyone would rationally invest in the research needed to create a new, promising, but patent-deficient medicine.

Why Use Concurrent Data Package Protection to Supplement Patents—

- Required R&D can consume most (all) patent life.
- Limitations on patent term restoration can operate to prevent adequate protection for the key patents.
- Effective patent protection can be unavailable because patentability requirements cannot be met.
- The validity of an issued patent often may not be sustained once challenged in court.
- The patented technology may be avoided in a copied version; patents can be successfully circumvented.

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When strong, effective and long-lived patent protection does exist, then affording concurrent data package protection is of no economic consequence. Strong and long-lived patent protection provides *exclusivity*—it invokes the power of the courts to enjoin all competition, whether from a generic or follow-on approval pathway or from someone by recreating the entire FDA data package.

Why Adequate "Data Protection" and Patent Protection Should Co-Exist—

- Inverse relationship between the best medicines and a patent life long enough to justify investment in them.
- Absence of any necessary correlation between the best medicines and strong patents protecting them.
- Effective patent life cannot be assessed short of patent litigation to test validity and infringement.
- Primacy of patent protection produces the need for patent challenge and patent linkage regimes.
- Fullest and best uses of a new medicine may never be defined because of variability/brevity of patent life.

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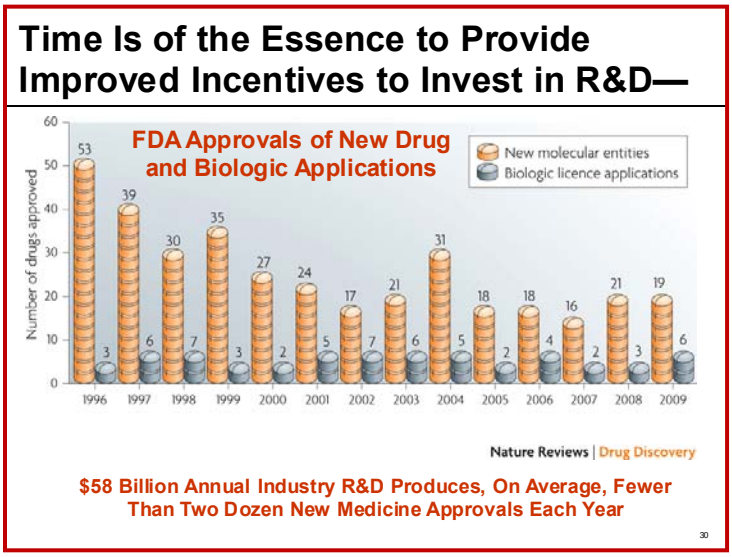
The case for data package protection of 14+ years is compelling because there is *no situation* where it is ever unjustified. When there is no patent deficiency, the DPPP cannot be unfair because it is at worst superfluous; when there is a patent deficiency, DPPP is not simply a manifestly fair and entirely justified protection, but a necessary incentive to any rational investment in the research needed to create the new medicine.

Unfortunately, patent-centered protection in the context of the high-risk research investments needed to create new medicines is unacceptably unpredictable and ultimately perverse. This unpredictability and perversity is what makes data package protection from the FDA's approval of follow-on or generic copies of new medicines so rational, so fair, and so compelling.

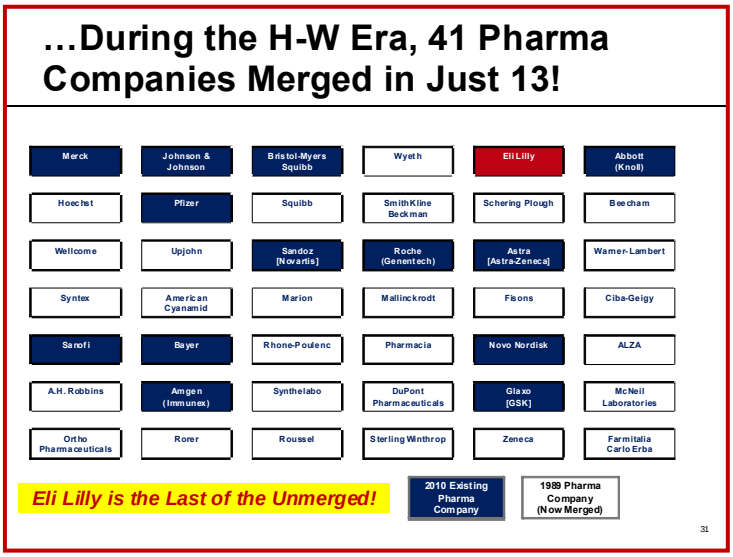
The Time for Hatch-Waxman Reform from a Patent-Centric to Data Package-Centric Regime is Now!

The research-based biopharmaceutical industry has changed in fundamental ways during the Hatch-Waxman era. It has increased spending on research and development dramatically over the past quarter century. As an industry, it now approaches a 20% reinvestment of sales revenues into the creation of new medicines. As noted earlier, it no longer owns most of the prescription drug market; the medicines that it sells account only for about three of every ten prescriptions dispensed to patients.

Another sobering statistic is the relative dearth of new medicines coming to market—and able to pay back the investment in R&D needed to bring them to market. Today, only about 3 of every 10 FDA-approved medicines are able to do so—7 of 10 do not. Getting a new medicine to market has never been more difficult. The number of "small molecule" and biologic medicines coming to market each year remains at about two dozen—for an industry that is now spending nearly $60 billion each year on R&D.



Sustaining success in a high-risk industry by placing huge R&D bets to create an entirely new generation of medicines—and to show advantages over inexpensive generic copies of earlier generations of medicines—is a daunting challenge. The magnitude of this challenge can perhaps be best understood by reflecting on the number of research-based biopharmaceutical companies that have ceased to exist over the last twenty years—41 companies active in the research-based business in 1989 have now merged down to 13 that remained in existence as of the end of 2009.

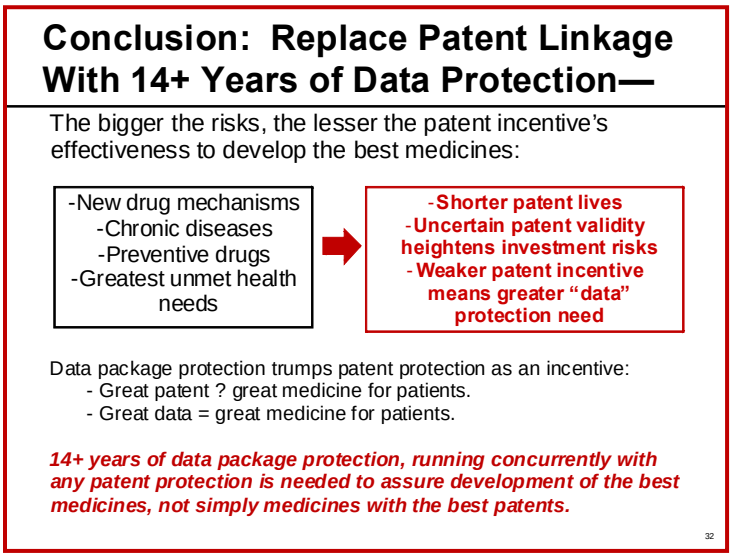


For what today remains of the biopharmaceutical industry in the era of generic and other follow-on competitors able to sell copied versions of new medicines remarkably inexpensively, Congress must assure more predictable and sustaining IP protection regimes. Effective, secure and adequate protection from low-cost copiers provides the ability to make the investment needed to create the next generation of new medicines. Without it, the United States runs the risk that what remains of the research-based industry might fail to sustain itself.

Conclusions: Getting to the Best New Medicines, Not Medicines That Happen to Have the Best Patents

The Hatch-Waxman Act was an experiment that has today met or exceeded all of its expectations, at least as they related to the creation of a new generic drug industry able to reliably supply low-cost, high-quality copied versions of new medicines to the marketplace. Its 75% and growing market share of the U.S. prescription drug market suggests that nothing more needs doing to further secure its role as a major contributor to the health of the American public.

The story for the research-based industry is, however, more mixed. Over the Hatch-Waxman era, its new medicines have revolutionized the treatment of many diseases. It has been able to increase its R&D investments. At the same time, consolidation has reduced the ranks of the innovators dramatically. Its declining share of the prescription medicines business, coupled with the relentlessness of low-cost generic competition from earlier-generation innovations of the research-based industry, makes its future less assured.



For the research-based industry to have a reasonable opportunity to innovate its way to a successful future, it is critical that it be able to focus the talents of its researchers on the best ideas for new medicines, with the assurance that, if those ideas are successfully brought through the research process to the market, fair and predictable protection from low-cost generic and other low-cost, follow-on competition will exist for a period sufficient to create a reasonable prospect of paying back the investment in the research needed to get those medicines to market.

By providing 14+ years of data package protection, running concurrently with any available patent protection, Congress can achieve a "win-win-win" outcome.

The research-based biopharmaceutical industry will be able to bring the best new medicines to market. Patients and their physicians will have access to the best new choices in therapy—with the best and most complete uses of those medicines fully elaborated through continuing, post-approval research. Finally, when inexpensive copied versions of those new medicines take over the market from the original version of the medicine, the market will be a fully developed one in which the best and most complete uses of those medicines will be well understood by physicians, so that the best and fullest use can be made of the copied versions and their value completely realized.

If there are lingering questions about whether or not congressional action to further secure a next generation of innovation in new medicines is really needed, it is worth remembering Arthur Ashe—and those today who wait, often desperately, for access to those medicines not yet available at any price.