

# Overview of the Hatch-Waxman Act and Its Impact on the Drug Development Process

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## I. INTRODUCTION

There is a paucity of legislative history on the Hatch-Waxman Act.<sup>1</sup> This article will try to provide a general overview of the legislative process and some insight into the Act's underlying assumptions, with the help of some graphics. With a bill as hard-fought as Hatch-Waxman, there was much written about it after the fact, but not a great deal of coherent legislative history. The article also provides a timetable to compare the drug discovery and development, patent protection, and generic competition processes that the Act affects.

Prior to 1962, drugs were approved for safety only. Senator Estes Kefauver (D-TN) tried for years to add an efficacy requirement, a concept that the research-based industry fully supported, but as often happens in Washington, there was a logical disconnect. The Thalidomide problem in infants — involving safety — resulted in the 1962 drug amendments<sup>2</sup> to the Federal Food, Drug, and Cosmetic Act,<sup>3</sup> which added a proof-of-efficacy requirement to new drug approval. Thus, new drugs must be proven safe and effective prior to the Food and Drug Administration's (FDA's) approval. Also, for drugs approved prior to 1962, generic versions could be approved with a "paper" new drug application (NDA). The paper NDA was based solely on published scientific or medical literature; a generic manufacturer could get its drug approved by showing that learned articles had been written about the chemical demonstrating that it was safe. After 1962, there was congressional testimony that there were 150 drugs that were off-patent, but for which there were no generics because generic companies simply would not spend the time and money doing the clinical trials to get to market, and that there were only fifteen "paper NDAs," for post-1962 generics.<sup>4</sup>

For those who ask whether Hatch-Waxman was a good deal or a bad deal for the research-based pharmaceutical industry, the most learned response is: It was not a good deal, unless one believed that FDA was going to go forward with its plans to implement abbreviated new drug applications (ANDAs) through regulation. If one thought that was going to happen — and FDA was working on it — then Hatch-Waxman probably was a good balance. If one did not think that would ever happen, Hatch-Waxman probably was not a good balance, at least at the time.

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<sup>1</sup> Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (codified at 15 U.S.C. §§ 68b-68c, 70b (1994); 21 U.S.C. §§ 301 note, 355, 360cc (1994); 28 U.S.C. § 2201 (1994); 35 U.S.C. §§ 156, 271, 282 (1994)).

<sup>2</sup> Pub. L. No. 87-781, 76 Stat. 780 (codified at 21 U.S.C. §§ 321, 331-32, 348, 351-53, 355, 357-60, 372, 374, 376, 381).

<sup>3</sup> Pub. L. No. 75-717, 52 Stat. 1040 (1938) (codified as amended 21 U.S.C. §§ 301 et seq.).

<sup>4</sup> H.R. REP. NO. 98-857, pt. 1 (1984); see also Gilston, *The Generic Patent Compromise*, MED. ADVERTISING NEWS, Apr. 30, 1984, at 16-17.

## II. DRAFTING THE HATCH-WAXMAN ACT

The plan for patent term restoration had its beginnings in President Carter's Administration. In 1978 President Carter launched a major domestic policy review on industrial innovation and that team recommended patent term restoration for pharmaceuticals and any other product that required regulatory review — to compensate for, or restore to the term of the patents, the time lost in regulatory review. President Reagan's Cabinet Council on Commerce and Trade also supported the proposal. Indeed, the Reagan Administration's first-term use of Cabinet Councils was a very orderly management and policymaking process. Then-Secretary of Commerce Malcolm Baldrige set up an intellectual property committee under the Cabinet Council on Commerce and Trade; chaired by the author, the committee was set at the Assistant Secretary level, including Bill Baxter of the Antitrust Division at the U.S. Department of Justice. The committee recommended, and the Cabinet Council supported, patent term restoration. That recommendation turned into a bill — S. 255 —<sup>5</sup> that passed the Senate and was referred to the House of Representatives. In the House, the bill's supporters put it on the suspension calendar, which requires a majority of two-thirds to suspend all the rules and enact the bill.<sup>6</sup> If a bill fails to get a two-thirds majority, then it must go back to the House Rules Committee and go through the regular committee process. S. 255 failed. Although it received a simple majority of the votes, it failed to pass the House by the necessary two-thirds majority on the suspension calendar. The vote, however, served as a wake-up call for generic drug manufacturers. Congressman Henry A. Waxman (D-CA), one of the most effective in the House of Representatives and then-Chairman of the Health Subcommittee, took on the issue. Suddenly, what had been a patent term restoration bill became a patent term restoration and drug price competition bill, and a whole new title was added that complicated the bill even further.

Finally, Public Law 98-417 (the Hatch-Waxman Act) was enacted in 1984. There have been several other developments in Hatch-Waxman's history, although these are not nearly as significant as the bill's enactment. First, animal drugs were added with the 1988 Generic Animal Drug and Patent Term Extension Act,<sup>7</sup> where generic animal drugs were added to the mix with an identical statutory template. The Uruguay Round Agreements Act<sup>8</sup> provided for what was called the "Delta Period." That Act provided that any drug with a patent in effect on June 8, 1995, or any patent application pending at that time would get the term of twenty years from the time of filing or seventeen years from the time of grant, whichever was longer. The difference between those two dates was referred to as the "Delta Period." In effect, the Act created a compulsory licensing provision during the delta period. If someone had invested significant amounts of money to get ready to come on the market during the Delta Period, the owner of the patent could not get an injunction, but would be entitled to receive only "equitable remuneration." The "equitable remuneration" term came out of the actual negotiations for the Agreement on Trade-Related Aspects of Intellectual Property Rights.<sup>9</sup> The issue was immediately raised: During this Delta Period, could

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<sup>5</sup> S. 255, 98th Cong., 2d Sess. (1984).

<sup>6</sup> CHARLES W. JOHNSON, *HOW OUR LAWS ARE MADE*, S. DOC. NO. 105-14, at 20 et seq. (1997).

<sup>7</sup> Pub. L. No. 100-670, 102 Stat. 3971 (1988) (codified at 21 U.S.C. §§ 301 note, 360b, 360b notes, 321, 353; 28 U.S.C. § 2201; 35 U.S.C. §§ 156, 271).

<sup>8</sup> Pub. L. No. 103-465, 108 Stat. 4809 (1994) (codified at 19 U.S.C. §§ 2252 et seq. (1994)).

<sup>9</sup> Agreement on Trade-Related Aspects of Intellectual Property Rights, Apr. 15, 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, LEGAL INSTRUMENTS — RESULTS OF THE URUGUAY ROUND vol. 31; 33 I.L.M. 81 (1994).

an ANDA be approved to permit a generic to come to the market? The issue was determined authoritatively in 1995 — and the answer was “no” — by the U.S. Court of Appeals for the Federal Circuit in *Bristol-Myers Squibb v. Royce*.<sup>10</sup> The court held that, during the Delta Period, a generic drug company could not bring a drug to market under the ANDA route. A generic company could bring a drug to market if it did all the clinical trials, but if it did not do the trials and wanted to go the ANDA route, the drug could not come on the market during the Delta Period.<sup>11</sup> Senators David Pryor (D-AR) and John Chafee (R-RI) tried to change that ruling through legislation, and it became a major issue. The research-based industry sought a resolution in which anybody could come onto the market during the Delta Period, but if one wanted to use the Hatch-Waxman shortcut, one had to use the whole Hatch-Waxman process. It is no longer a major issue but to several companies it was a significant financial development.

Another key development was the case of *Merck v. Kessler*,<sup>12</sup> the defendant parties of which were David Kessler, then-Commissioner of Food and Drugs, and Bruce Lehman, Commissioner of Patents and Trademarks. This case involved the issue of whether a patent holder can take twenty years from time of filing or seventeen years from time of grant, whichever is longer, and add it to the Hatch-Waxman extension. Originally, the U.S. Patent and Trademark Office (PTO) decided that patent holders could not; they could add the Hatch-Waxman extension to the seventeen-year period from time of grant, and not to the additional Delta Period. The Court of Appeals for the Federal Circuit reversed that PTO determination, although it did sustain it for the patents on five drugs that were still in force *only* because of Hatch-Waxman. The court ruled that, because the patents had not expired only by reason of Hatch-Waxman extensions, they did not get the benefit of the Delta Period.

### III. A LOOK AT HATCH-WAXMAN

Title I of the Act contains the drug price competition part, specifically authorizing ANDAs and specifically prohibiting FDA from doing more than asking for bioavailability studies. In that regard, it is a unique piece of legislation because it actually ties the hands of a regulatory agency — in the area of public health — by providing specifically that FDA can require only bioavailability studies for ANDAs.<sup>13</sup> There is a five-year data exclusivity for new molecular entities (NMEs). The Act provides for a period of exclusivity such that once an NME is approved, a generic version cannot be approved for five years. That generally is referred to as “data exclusivity.” The Act also calls for a three-year data exclusivity period for supplements requiring clinical trials. One of four certifications must be made when someone files an ANDA: 1) that the drug has not been patented; 2) that the patent has already expired; 3) the date on which the patent will expire, and that the generic drug will not go on the market until that date passes; and 4) that the patent is not infringed or is invalid. Those certifications are now referred to as the paragraphs I, II, III, and IV certifications.

A major issue during the pendency of the Hatch-Waxman legislation involved paragraph IV certifications. If a generic company said the patent was invalid or not

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<sup>10</sup> 69 F.3d 1130 (Fed. Cir. 1995). Also, the *Bristol-Myers* opinion provides a good summary of the key provisions of the Hatch-Waxman Act.

<sup>11</sup> *Id.* at 1137.

<sup>12</sup> 80 F.3d 1543 (Fed. Cir. 1996).

<sup>13</sup> H.R. REP. NO. 98-857, pt. 1, at 72 (1984).

infringed, how long would FDA be required to wait before approving the generics for marketing? For much of the debate, that period was eighteen months, however, through the work of the research industry, that time period was changed to thirty months. Thus, there is a thirty-month litigation, or cooling-off period such that once a generic determines that the patent is invalid or not infringed, it has to notify the patent owner, who has forty-five days in which to file an infringement action and then another thirty months of exclusivity before an ANDA can be approved (unless there is a final appellate decision earlier, which is highly unusual).

The patent term restoration part of the Act generally appears in title 35 of the *United States Code*. These are very long, very complicated provisions. For the patent term restoration period, a pioneer receives an extension term equal to one-half of the time of the investigational new drug (IND) period — running from the time in which a pioneer can begin human clinical trials — plus the NDA period — the period during the NDA review.<sup>14</sup> The maximum extension is five years and the total market exclusivity time cannot exceed fourteen years. The length of the exclusivity periods are strictly arbitrary legislative numbers pulled out of the air. Pipeline drugs — drug applications pending at the time the Act was passed — received two years or less of exclusivity on the assumption that if they were in a pipeline already, they would be approved in a year or two, so there was no need to give them more. Some pipeline drugs, however, have taken eight years for approval.

Finally, there is a provision that the pioneer must exercise due diligence in order to achieve patent term restoration, or a period of lack of diligence will be subtracted from the equation; that provision has never been used. The famous case of *Roche Products v. Bolar Pharmaceuticals*<sup>15</sup> was reversed specifically in section 271(e)(1) of title 35 of the *United States Code*. The result is that the day after the patent expires, generics are being served and dispensed to patients. Thus, the day after the patent is ineffective or expired, generic competition comes onto the shelves in the pharmacies ready to be dispensed to patients.

Another patent issue is constructive infringement. A constructive infringement is a fictional infringement, which in effect states that filing an ANDA and informing FDA under paragraph IV that the patent is either invalid or not infringed amounts to a patent infringement in and of itself.<sup>16</sup> Then all the other provisions of title 35 and title 28 of the *United States Code* come to bear, and a patent holder can file a regular infringement action against the generic company in a federal district court. The Act specifies that each patent can be extended only once, but the extended patent does cover subsequently approved uses for the period of the extension.

A number of assumptions were made in enacting Hatch-Waxman. One major assumption underlying the Hatch-Waxman Act was that duplicates of pioneer drugs would be the same as the innovator's drug. FDA still uses the plus-or-minus-twenty-percent test to determine blood serum bioavailability (i.e., the amount of active ingredient in the blood over a period of time has to come within plus-or-minus twenty percent of that which is observed when the innovator's drug is ingested). Twenty percent is a fairly good margin, and many medical professionals believe that for drugs that have a wide index of tolerance, twenty percent is not important at all; in such instances, twice as much or half as much of the active ingredient in a generic product will still work. For drugs where there is a very narrow therapeutic band, for example, where a patient gets antiseizure medication, plus-or-minus twenty percent may not be

<sup>14</sup> 35 U.S.C. § 156.

<sup>15</sup> 733 F.2d 858 (Fed. Cir. 1984).

<sup>16</sup> See 35 U.S.C. § 271(e)(2).

appropriate. This is true particularly if a drug is at that higher end of bioavailability and a patient is titrated on the higher end (plus twenty percent) and then a second generic is dispensed where the active ingredient was at the lower end (minus twenty percent); mathematically, that is a fifty percent swing and may not be safe or effective. It is a curious thing that FDA has not altered its regulatory approach to this situation. With the advances in modern pharmaceuticals, those standards could be tightened. Although such tightening might not be to the advantage of the brand name companies, it could be to the advantage of patients.

A second assumption was that bioequivalence data was an effective surrogate for safety and efficacy — that products approved pursuant to ANDAs would meet the same regulatory requirements as pioneers. That was a good assumption, but there was always a feeling on the part of the research-based industry that, in FDA's view, pioneers wore the "black hats" and generics wore the "white hats," and review and approval were slightly relaxed. In fact, Joseph Stetler co-authored a book about the "generic scandal," when procedures got very relaxed during that period of time.<sup>17</sup> ANDA applicants need not meet additional requirements, but there remains a specific provision that bioavailability is the only test FDA can require.

Another assumption was that pipeline drugs would be approved shortly after the Act's enactment, and that two-year extensions were adequate. In one famous case, the drug was not approved for eight years.<sup>18</sup> Two key assumptions were that five years of extension and fourteen years of market exclusivity were sufficient to stimulate research and development — again, numbers pulled out of the air. The reasoning used in determining the patent term restoration part of the Act was, "If a mousetrap gets seventeen years of protection, why not a new life-saving drug?" If a mousetrap gets seventeen years or twenty years from time of filing, why would a brand-name research-based drug be limited only to fourteen years?

Another assumption underlying Hatch-Waxman was that development of generic products prior to patent expiration would have minimal effects on pioneer products. In practice, however, many generics have impacted pioneer sales quickly. Three months after Naprosene<sup>®</sup> went off-patent, its manufacturer, Syntax, lost seventy-five percent of its market to the generic product.

Another assumption was that it was not necessary to increase incentives for pioneers to develop second uses for patented products. There appears to be little basis for this assumption, and the Act actually removes incentives for finding new uses for patented drugs. In fact, there are many cases where it is a good idea to be able to extend the same patent for a new NME or a new use of an approved NME.

#### IV. POTENTIAL HATCH-WAXMAN REVISIONS

There are several key potential revisions that were identified in the Boston Consulting Group study in 1996.<sup>19</sup> Two of the Hatch-Waxman revisions mentioned include a one-for-one extension, and a change from the one-half of IND period to a full IND. Medical reviewers change as people come through FDA, and each reviewer makes a new contribution to the approval process. The reviewers ask questions regarding drugs that are brand new, perhaps, or have new pharmacological activity, but

<sup>17</sup> C. JOSEPH STETLER & WILLIAM C. CRAY, *PATIENTS IN PERIL? THE STUNNING GENERIC DRUG SCANDAL* (1991).

<sup>18</sup> Gerald J. Mossinghoff, *Independent Patent Review for "Pipeline" Drugs Would Advance Intellectual Property Rights*, 13 *LEGAL BACKGROUNDER* (Washington Legal Found. Aug. 7, 1998).

<sup>19</sup> THE BOSTON CONSULTING GROUP, *SUSTAINING INNOVATION IN U.S. PHARMACEUTICALS, INTELLECTUAL PROPERTY PROTECTION & THE ROLE OF PATENTS* (Jan. 1996).

nobody ever goes back and “unasks” the old questions. FDA reform legislation<sup>20</sup> was enacted because of the concern that overall drug development time was getting longer and longer. FDA has done a remarkably good job in cutting back the time for NDA review, but human clinical trials take a long time to conduct before that review; indeed, clinical trial testing time actually is getting longer.

Removing the two-year limit for pipeline drugs and the arbitrary five- and fourteen-year limitations is another proposal put forward. The revision also would permit multiple extensions of the same patent and then change the five-year data exclusivity to ten years in accordance with international standards, such as those in Europe and Japan. Why should foreign patent holders have ten-year data exclusivity while U.S. patent holders only have five?

### V. NEW MEDICINES TIMETABLE

The new medicines timetable, above, illustrates pioneer drug development, patent activity, and generic competition activity. It illustrates a textbook case, as there probably is no drug in existence that follows this timetable exactly. The timetable does, however, permit a realistic basis on which the afternoon interactive workshop discussion is focused. It shows drug discovery in the early stages and the major milestones — when the drug IND is approved, when the drug enters human clinical trials, and so forth. The timeline tracks the progress from Phases I, II, and III through the acceptance of the NDA at FDA. A lot of time and thought go into the preparation of an NDA (although the review time is decreasing) before it is approved. The timeline also provides a general idea of when resources are committed on the generic side and the steps that need to be taken before there is an expiration of the patent, and the generic can be marketed.

Discovery is a continuing process, not a single point in time. Preclinical testing, i.e., laboratory and animal testing, occurs later. Sometime during that preclinical testing, but well in advance of the IND filing, the U.S. patent application is filed. Foreign patent applications must be filed within one year if the patent holder is under the Paris Convention<sup>21</sup> and a slightly longer period under the Patent Cooperation Treaty,<sup>22</sup> which most of the industry uses.

At some point the IND is approved by FDA — either it is approved pro-actively or a thirty-day period goes by without a hold. Then begins the very expensive Phase I, II, and III studies following the IND approval. At some point, FDA accepts an NDA (although in practice companies do some negotiating and discussing with FDA before they file the NDA). From IND approval through FDA acceptance is what is referred to as the IND period. Patent holders receive a restoration of one-half of the IND period. FDA then reviews the NDA in about fifteen or sixteen months. When the agency approves the drug, it may then be marketed.

The U.S. patent, however, has been issued long before clinical trials begin. When the Hatch-Waxman formula operates, the twenty-year patent term is measured from the time of filing the drug application, so the twenty-year period is extended. Postmarket testing (Phase IV) is a continuous thing, so it has been left open-ended. The extension will fall exactly within the five-year limitation and the time from drug approval (roughly sixteen years) to the time the patent expires (twenty-eight years), still falling within the fourteen-year cap of the Hatch-Waxman Act.

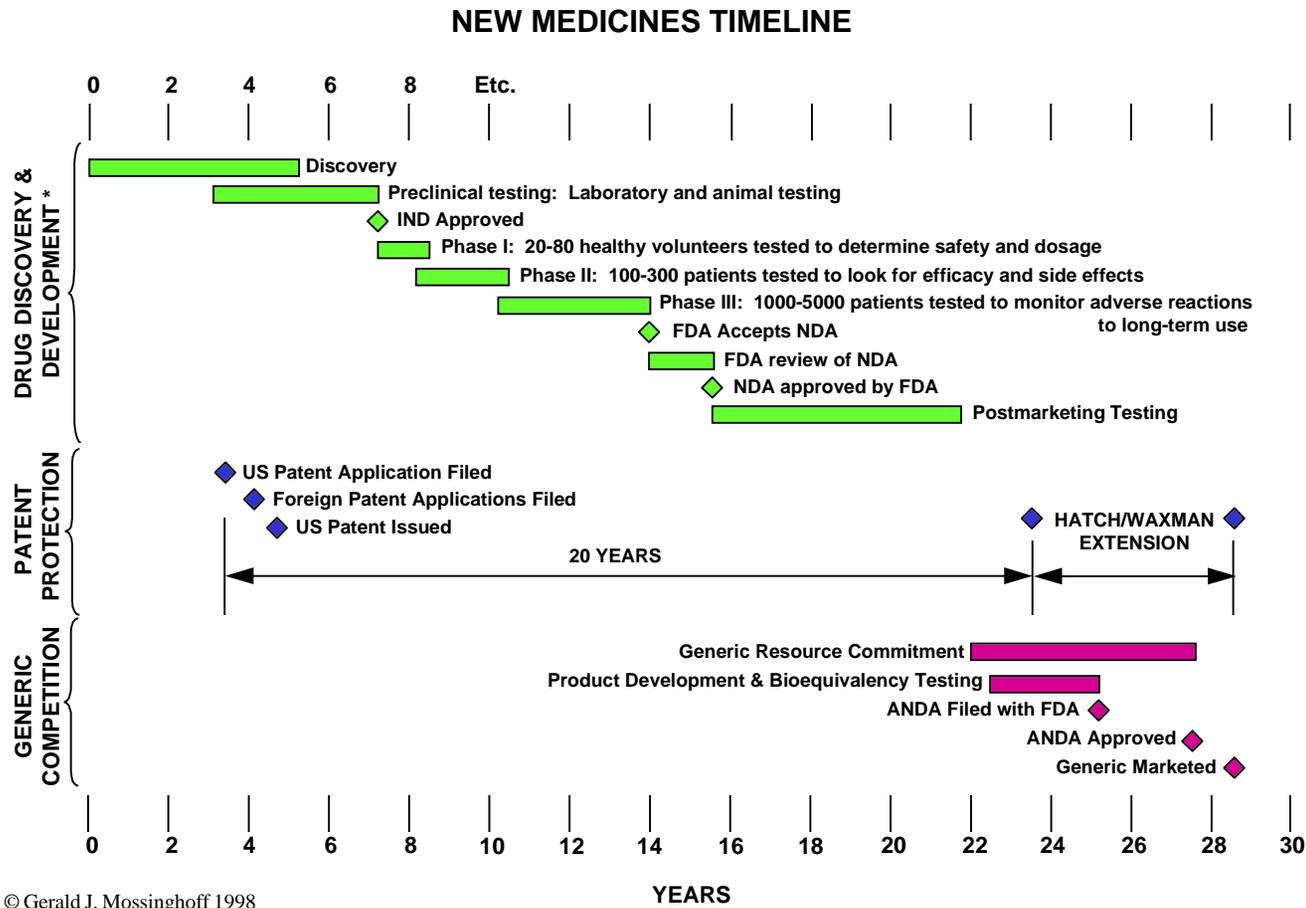
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<sup>20</sup> Food and Drug Administration Modernization Act, Pub. L. No. 105-115, 111 Stat. 2296 (1997).

<sup>21</sup> Reprinted in SELECTED INTELLECTUAL PROPERTY & UNFAIR COMPETITION STATUTES, REGULATIONS & TREATIES 805 (Roger E. Schecter ed. 1997).

<sup>22</sup> *Id.* at 700.

This timeline is an idealized view of the development process regarding the time frames and the regulatory procedures. At some point prior to the expiration of the original patent, however, generic resources are committed. A key issue in the area is product bioequivalency testing under paragraph III. The chart is not big enough to accommodate a paragraph IV certification with a litigation timeline, so this timeline uses a paragraph III ANDA filing. The ANDA is approved in the timetable in over two years. Generic marketing occurs on the day that the patent expires after having been extended.



## VI. CONCLUSION

The Hatch-Waxman Act is significant to the U.S. healthcare system in many important respects. The robust generic drug industry owes its very existence to the Act, and patent term extensions or restorations are very important to the research-based pharmaceutical industry. But many of the assumptions made fifteen years ago when this Act was passed — which provided the bases for the arbitrary time limits established in the Act — have proven to be invalid, as pointed out in the Boston Consulting Group study.<sup>23</sup> Thus, it is time to revisit the Hatch-Waxman Act with a view to increase the patent incentives for the creation of new life-saving medicines.

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<sup>23</sup> See *supra* note 19.