



**Pharmaceutical Research and Manufacturers of America**

**WHITE PAPER**

**On**

**IMPLEMENTATION OF THE HATCH-WAXMAN ACT**

**BY THE U.S. FOOD AND DRUG ADMINISTRATION**

**Submitted To**

**DANIEL E. TROY, ESQ.,**

**CHIEF COUNSEL, FDA**

January 18, 2002

## TABLE OF CONTENTS

	<u>Page</u>
Introduction.....	1
I. Congress Enacted the Hatch-Waxman Act to Protect Incentives for Innovation While Reducing Study Requirements for Generic Drug Approvals.....	2
II. The Terms of the Hatch-Waxman Act Establish a Streamlined Framework for Generic Drug Approvals That Protects Innovator Patent and Data Rights.....	5
A. Orange Book Listing.....	6
B. Types of Abbreviated Applications .....	7
C. Timing of Use of Pioneer Data .....	8
D. Special Patent Litigation Provisions .....	9
1. Patent Certification Requirements .....	10
2. Notice and 45-day Period.....	12
3. 30-Month Stay .....	14
E. 180-day ANDA Exclusivity.....	14
III. FDA’s Implementation of the Hatch-Waxman Act has Departed From the Statutory Language and Legislative Intent by Favoring Generic Drug Interests at the Expense of the Protections for Innovation Promised by Congress.....	16
A. Erosion of Standards for Approval of ANDAs.....	19
1. The Sameness Requirement.....	21
a. Differences in Active Ingredients.....	21
b. Differences in Labeling .....	22
c. Differences in Dosage Forms .....	24
d. Use of Limited Confirmatory Studies .....	26
2. Bioequivalence.....	27
3. Other Standards.....	29
B. Citizen Petitions .....	31

**TABLE OF CONTENTS (continued)**

	<b><u>Page</u></b>
C. Section 505(b)(2) Applications.....	32
D. Patent Listing and Litigation.....	35
1. Listable Patents.....	35
a. Listing Patents That Do Not Cover the Approved Product.....	35
b. FDA’s Role in Reviewing Patents for Listing.....	38
c. Listing of “Late-Issued” Patents.....	39
2. The 30-Month Stay on ANDA Approvals.....	41
a. Certifications That Trigger the Stay.....	41
b. Termination of the 30-Month Stay.....	41
E. Exclusivity.....	43
1. 5-year Exclusivity.....	43
2. 3-Year Exclusivity for Supplemental NDAs.....	45
Conclusion.....	46

**THE HATCH-WAXMAN ACT EMBODIES AN AGREEMENT  
TO MAINTAIN INCENTIVES FOR PHARMACEUTICAL INNOVATION  
IN THE CONTEXT OF A SIMPLIFIED GENERIC APPROVAL PROCESS**

**Introduction**

The Drug Price Competition and Patent Term Restoration Act of 1984,<sup>1</sup> commonly known after its principal sponsors as the “Hatch-Waxman Act,” is the legislative foundation for both the generic drug approval process and the protection of pharmaceutical patent rights. It establishes a framework for both competition and innovation within the pharmaceutical industry. As such, the Act represents one of Congress’s most ambitious and complex pieces of public health legislation.

Congress did not enter this terrain lightly or quickly. Rather, the Hatch-Waxman Act represented the culmination of years of public policy thinking and legislative consideration. Congress, the Reagan Administration, and the research-based and generic drug industries entered into an agreement to streamline the approval requirements for generic drugs, but only as part of a package of substantive and procedural rights intended to safeguard pharmaceutical patents and maintain incentives for innovation.

The vast majority of generic drugs has been approved without controversy. Public attention has focused on a relatively small number of disputed patent infringement cases arising at the margin. The courts and FDA are addressing the unavoidable ambiguities and areas of uncertainty through individual decisions, guidance, and rulemaking, as should be expected in the implementation of any difficult and complicated law.

---

<sup>1</sup> Pub. L. No. 98-417, 98 Stat. 1585 (1984).

FDA's approach to the Hatch-Waxman Act, however, has been heavily tilted toward the interests of the generic drug industry. The agency must pay closer attention to the words of the statute and must heed the agreement embodied in it to maintain incentives for innovation. New medicines will only be there for the American public, and will only be available for copying, if the incentives are there for the research-based industry to find and develop them in the first place.

This paper has three parts. The first describes the legislative history leading up to enactment of the Hatch-Waxman Act. The second summarizes the principal features of the law. The third addresses those areas in which the agency has departed from the statute.

**I. Congress Enacted the Hatch-Waxman Act to Protect Incentives for Innovation While Reducing Study Requirements for Generic Drug Approvals.**

Regulatory implementation of any Act of Congress must start with the literal meaning of the statute. In the case of the Hatch-Waxman Act, a strict statutory reading is informed by a brief description of the regulatory context in which the law was enacted. This perspective can facilitate an understanding of how the law came into being and why its implementation has, in the main, been so successful.

The origins of the Hatch-Waxman Act lie in two different, and ultimately complementary, strands of public policy thinking. On the one hand, starting in the early years of the Reagan Administration, there was broad bipartisan recognition in the Executive Branch and the Congress that the patent life of some inventions – especially drugs – had been seriously eroded by increasing delays in the pre-market approval processes of the Federal government related to the dramatic increase in regulation that accompanied the modern welfare state. These delays had the direct effect of eroding the effective patent term for those products because patents were usually granted long before FDA approval for commercial marketing. Thus,

starting in 1980, Congress began to consider in earnest legislation that would have fully restored the patent term lost due to regulatory delay. In fact, a measure to achieve that goal passed the Senate but failed in the House. The bill finally passed only after it was combined with another policy change on generic drug approvals, which created the political consensus necessary to permit the bill to become law.

In parallel with the concern over the need for action to address patent restoration in order to maintain incentives for innovation, there was also a concern that the FDA's operating statute did not permit the agency to approve generic applications (those without their own supporting clinical evidence of safety and effectiveness) when a patent expired except in a few instances. This pressure for a generic drug approval process eventually met up with the patent term restoration bill. This concern about an allegedly incomplete generic approval process led some to believe that the then-existing requirement that generic manufacturers essentially duplicate the clinical trial work and data development of the brand-name company – even after patent expiration – denied too many Americans access to what was labeled as the “same” drug at a lower price. After several years of controversy about the nature and extent of the FDA regulatory delay period and discussion about how to best limit the risk of “free riding” by generic companies by narrowly limiting any generic drug approval to the “same” drug, the two policy concepts were merged, and the Hatch-Waxman Act was the result.

The underlying premise of the final statute was of a contractual nature. The law effectively takes the data developed at great cost by the research-based pharmaceutical industry and allows generic manufacturers to gain approvals based on those data rather than their own safety and effectiveness studies – thereby reversing decades of regulatory practice recognizing an

innovator's sole proprietary right to its data.<sup>2</sup> The law also allows generic manufacturers to infringe patents prior to expiration in the course of their development of abbreviated applications – similarly reversing an important judicial precedent that had confirmed the prohibited nature of this practice.<sup>3</sup>

In exchange, the government made three statutory promises to the research-based pharmaceutical industry. *First*, patent term restoration would make up for some of the period of government-imposed delay prior to FDA approval. *Second*, innovator companies would have a meaningful opportunity to vindicate their patent rights prior to FDA approval of potentially infringing generic products. *Third*, the circumstances in which generic companies could free-ride on innovator data would be carefully limited.

These provisions reflected Congress's intent that the law would ensure that innovation was sufficiently rewarded to justify the risks and investment capital expended by the research-based companies. The research-based industry responded with "reasonable, investment backed" actions that increased research and development spending as a percentage of sales from 11.4% in 1970 to an estimated 18.5% for 2000 (from approximately \$3-1/2 billion in 1985 to more than \$30 billion in 2001, or a total increase of almost 9 times in dollar terms). If the statutory protections for the research-based industry are not respected and applied as Congress wrote them and as it intended, then the purpose of the law would be in jeopardy, because copying would become more ascendant than innovation.

---

<sup>2</sup> See, e.g., 39 Fed. Reg. 44602, 44634 (Dec. 24, 1974).

<sup>3</sup> *Roche Products, Inc. v. Bolar Pharmaceutical Co.*, 733 F.2d 858 (Fed. Cir. 1984).

**II. The Terms of the Hatch-Waxman Act Establish a Streamlined Framework for Generic Drug Approvals That Protects Innovator Patent and Data Rights.**

The public health is served by minimizing delay, and a major cause of delay is regulatory uncertainty. Uncertainty in the clinical development requirements, the approval process, patent protection, data protection, the timing of generic competition, and the process of patent infringement dispute resolution can delay or, in some cases, cease new product innovation. Similarly, uncertainty in the patents that the pioneer intends to assert against a generic competitor, in the ability to resolve patent infringement disputes prior to FDA marketing approval, and in the criteria for awarding 180-day Abbreviated New Drug Application (“ANDA”) exclusivity can delay generic drug marketing.

The Hatch-Waxman Act includes mechanisms to address these delays and uncertainties for both pioneer and generic manufacturers. These mechanisms include a requirement that the pioneer list all composition and method of use patents for which a claim of infringement can be asserted against a generic copy, a definition of the types of and approval requirements for abbreviated applications, a defined period restricting the use of the pioneer’s proprietary safety and efficacy data, specialized litigation procedures to facilitate the resolution of patent disputes prior to generic drug marketing and, finally, criteria for 180-day generic drug exclusivity. These mechanisms simultaneously protect incentives for innovation and facilitate generic drug availability.<sup>4</sup>

---

<sup>4</sup> The Hatch-Waxman Act also includes provisions for partial patent term restoration. In order for a patent to be eligible for an extension, the patent cannot have been extended previously, the application for extension must be completed, the product covered by the patent must have been subject to regulatory review, and the regulatory approval must relate to the first such marketing or use of the product. Accordingly, a patent holder would not receive a second extension for another drug covered by a previously extended patent even if the drugs had separate review periods and associated development costs. The patent holder is entitled to restoration of one-half (continued...)

**A. Orange Book Listing**

An applicant who submits a New Drug Application (“NDA”) under section 505(b) of the Federal Food, Drug, and Cosmetic Act (“FDCA”) must submit information on each patent that “claims the drug or a method of using the drug . . . and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale” of the drug product.<sup>5</sup>

According to FDA’s regulations, patents that may be listed include drug substance (ingredient) patents, drug product (formulation and composition) patents, and method of use patents. Process patents are not covered by this section and information on process patents may not be submitted to FDA. For patents that claim a drug substance or a drug product, the applicant can submit information only on those patents that claim a drug product that is the subject of a pending or approved application or that claim a drug substance that is a component of such a product. For patents that claim a method of use, the applicant can submit information only on those patents that claim indications or other conditions of use of a drug substance or drug product in a pending or approved application.<sup>6</sup>

An NDA applicant must submit the following information for each patent:

- (i) patent number and the date on which the patent will expire;
- (ii) type of patent, *i.e.*, drug, drug product, or method of use;
- (iii) name of the patent owner; and

---

of the time required for safety and effectiveness testing, plus the entire period of time for FDA review of the NDA. The patent term restoration may not exceed five years, and the life of a patent remaining after the NDA is approved may not exceed 14 years. Under these provisions, the patent is restored only to the extent that it covers the approved product.

<sup>5</sup> FDCA § 505(b)(1); 21 U.S.C. § 355(b)(1).

<sup>6</sup> 21 C.F.R. § 314.53(b).

- (iv) the name of an agent (representative) of the patent owner or applicant (for foreign applicants).

FDA publishes the submitted patent information in its official publication, *Approved Drug Products With Therapeutic Equivalence Evaluations* (the “Orange Book”).

Upon approval of the application, FDA will publish in the Orange Book the patent number and expiration date of each patent that is submitted to FDA by an applicant. For each use patent, FDA will also publish the approved indications or other conditions of use covered by a patent.<sup>7</sup>

If any person disputes the accuracy or relevance of patent information submitted to the agency and published by FDA in the Orange Book, that person must first notify the agency in writing stating the grounds for disagreement. The agency will request the NDA holder to confirm the correctness of the patent information or omission of patent information. Unless the NDA holder withdraws or amends its patent information in response to FDA’s request, the agency will not change the patent information in the Orange Book. An ANDA (or a 505(b)(2) application) submitted for a listed drug must – despite any disagreement as to the correctness of the patent information – contain an appropriate certification for each listed patent.<sup>8</sup>

The purpose of the Orange Book listings is to provide clear notice to potential generic developers of the patents (other than process patents) that cover the product and may reasonably be asserted by the innovator against the generic drug manufacturer.

#### **B. Types of Abbreviated Applications**

The Hatch-Waxman Act establishes two types of abbreviated applications. First, the Hatch-Waxman Act establishes the ANDA that permits generic drug manufacturers to rely

---

<sup>7</sup> 59 Fed. Reg. 50338, 50363 (1994).

<sup>8</sup> 21 C.F.R. § 314.53(f).

on the data of the pioneer drug manufacturer to demonstrate the safety and effectiveness of an identical “generic” drug. Because of the fundamental presumption of sameness, an ANDA applicant is required to conduct studies only to show that the generic drug is bioequivalent to the pioneer drug. Second, the Hatch-Waxman Act establishes an additional abbreviated application under section 505(b)(2) of the FDCA. Section 505(b)(2) codifies the FDA practice of permitting a new drug applicant to demonstrate safety and effectiveness of a product in part through the use of publicly available studies. In addition to the publicly available studies, the 505(b)(2) applicant conducts one or more of its own studies to demonstrate safety and effectiveness of the product.

**C. Timing of Use of Pioneer Data**

The Hatch-Waxman Act limits the exclusivity for the data demonstrating safety and efficacy for certain pioneer drugs to specified time periods. For a drug which constitutes a new chemical entity (“NCE”), FDA cannot *accept* an ANDA for a generic version of the drug until five years after the date of approval of the pioneer submission.<sup>9</sup> However, a generic drug manufacturer may submit an ANDA as early as forty-eight months after the approval of the pioneer NDA for an NCE, but only if the application includes a Paragraph IV Certification.<sup>10</sup> If a drug is not an NCE (*i.e.*, if the drug is a new use or formulation of a previously approved NCE that has required additional studies to demonstrate its safety and effectiveness), then an ANDA for a generic version of the drug cannot be *approved* by FDA until three years after the date of

---

<sup>9</sup> FDCA § 505(j)(5)(D)(ii); 21 U.S.C. § 355(j)(5)(D)(ii). The 3-year and 5-year data exclusivity provisions apply equally to ANDAs and applications submitted under Section 505(b)(2) of the FDCA.

<sup>10</sup> See discussion below, II.D.1., and FDCA §§ 505(j)(2)(A)(vii)(IV) & 505(J)(5)(D)(ii); 21 U.S.C. §§ 355(j)(2)(A)(vii)(IV) & 355(j)(5)(D)(ii).

approval of the pioneer submission.<sup>11</sup> These all represent limitations on the innovator's intellectual property because prior to the Hatch-Waxman Act, the proprietary safety and efficacy data could not be used by an unauthorized third party at any time.

The difference between the prohibition on FDA *accepting* an ANDA for an NCE and the prohibition on FDA *approving* an ANDA for a non-NCE has a significant practical consequence. This difference permits FDA to accept an ANDA for a non-NCE submission prior to the expiration of the data exclusivity period. Accordingly, FDA can make the approval of the application effective on the date the exclusivity period expires. In contrast, an ANDA for an NCE cannot be accepted until the exclusivity period expires. Any approval to market the drug would not be effective until FDA had the opportunity to review the ANDA and, in most cases, until the listed patent had expired or until all relevant patent issues had been resolved. This review process takes several months, and during the review period, the pioneer drug would not face generic competition.

The purpose of the data exclusivity periods is to assure that some basic guaranteed period of exclusivity is available, in addition to the often-disputed protection afforded by patents, in order to encourage innovators to develop pioneering drug discoveries.

**D. Special Patent Litigation Provisions**

Congress recognized that patent infringement disputes should be resolved prior to FDA product approval. Final and orderly resolution of patent disputes before product approval benefits both the pioneer and the generic manufacturers. Pioneer manufacturers want to be protected against an infringing product entering the market because that circumstance could

---

<sup>11</sup> FDCA § 505(j)(5)(D)(iii); 21 U.S.C. § 355(j)(5)(D)(iii).

result in destruction of market share and the price structure without the availability of meaningful compensation by the potential generic competitor. Similarly, generic manufacturers want to be protected from a judgment of infringement or an additional finding of intentional infringement after they market the generic product. Accordingly, the special patent litigation provisions of the Hatch-Waxman Act benefit both pioneer and generic manufacturers.

**1. Patent Certification Requirements**

The need for patent certifications arises from the legislative intent: (1) to permit the marketing of generic copies of pioneer products immediately upon the expiration of any relevant patents; (2) to encourage generic challenges of innovator patents, while prohibiting FDA's approval of any abbreviated application whose marketing would infringe a valid patent covering the pioneer product; and (3) to provide an effective remedy to patent holders whose patents are alleged to be invalid or not infringed by the generic product.

Accordingly, section 505(j)(2)(A)(vii) of the FDCA provides that an ANDA must include:

“a certification . . . with respect to each patent which claims the listed drug . . . or which claims a use for such listed drug for which the applicant is seeking approval . . .

- (I) that such patent information has not been filed
- (II) that such patent has expired,
- (III) of the date on which such patent will expire, or
- (IV) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted; . . .”

Nearly identical certifications for “paper NDAs” can be found in section 505(b)(2)(A) of the FDCA. The Special Litigation Provisions apply equally to ANDA and to applications filed under Section 505(b)(2) of the FDCA, unless otherwise noted.

The certification requirements determine the date on which approval of an ANDA can be made effective and, therefore, the date on which commercial marketing may begin. If the applicant makes either the first or second certification, approval can be made effective immediately. Under the third certification, approval of the application can be made effective on the date the patent expires. If, however, the applicant challenges the innovator’s patent and makes the fourth certification (the Paragraph IV Certification) the applicant is required to give notice to the holder of the patent alleged to be invalid or not infringed.

Approval of an ANDA containing the fourth certification may become effective immediately only if the patent owner has not initiated a patent infringement suit within 45 days of receiving notice of the certification.<sup>12</sup> When a patent owner initiates a patent infringement action, FDA automatically stays approval of the ANDA.<sup>13</sup> The stay remains in force until the earliest of four dates: (1) if the court decides that the patent is invalid or not infringed, the date of the court’s decision; (2) if the court decides that the patent has been infringed, the date that the patent expires; (3) the date that is thirty months from the patent owner’s receipt of notice of the filing of the Paragraph IV Certification; or (4) following patent expiration, upon the filing of an amended Paragraph III Certification.<sup>14</sup> For an ANDA containing a Paragraph IV Certification that is filed during the one-year period beginning 48 months after approval of the pioneer’s

---

<sup>12</sup> FDCA §§ 505(j)(4)(B)(iii) & 505(c)(3)(C); 21 U.S.C. §§ 355(j)(4)(B)(iii) & 355(c)(3)(C).

<sup>13</sup> *Id.*

<sup>14</sup> *Id.*

NDA, the initiation of a patent infringement suit by the patent holder in response to such a challenge would result in FDA approval of the generic application at a point in time up to 7-1/2 years after NDA approval for the NCE. This period is equal to 5 years of market exclusivity, plus a 30-month stay of approval of the generic application (to allow for court review of the patent) running from the end of the 5 year period instead of from the patent owner's receipt of notice.

## **2. Notice and 45-day Period**

In order to permit a patent holder to challenge the allegation that the listed patent is invalid or not infringed, the patent holder must be able to bring a patent infringement action against the generic applicant. Without a provision expressly making it an act of infringement to file an ANDA containing a Paragraph IV Certification, the patent infringement exemption provided by 35 U.S.C. § 271(e)(1) would prevent a finding of infringement in such an action. Accordingly, 35 U.S.C. § 271(e)(2) provides:

“[i]t shall be an act of infringement to submit –

(A) an [ANDA] for a drug claimed in a patent or the use of which is claimed in a patent, . . .

if the purpose of such submission is to obtain approval . . . to engage in the commercial manufacture, use, or sale of a drug . . . product claimed in a patent or the use of which is claimed in a patent before the expiration of such patent.”

Through this provision, the Hatch-Waxman Act provides an exception to the exemption from patent infringement provided by 35 U.S.C. §271(e)(1).

Sections 505(j)(2)(B)(i) and 505(b)(3) of the FDCA require the sponsor of an ANDA that contains a Paragraph IV Certification to notify the patent owner. This notice requirement is necessary so that the patent owner can exercise the right to challenge the Paragraph IV Certification, as described below.

The notice must state that an application has been filed seeking approval to engage in the commercial manufacture, use, or sale of the drug before the expiration of the patent, and must set forth a detailed statement of the factual and legal basis for the applicant's opinion that the patent is not valid or will not be infringed.

Within 45 days of receiving notice of the filing of an ANDA for a generic version of the pioneer product that contains a Paragraph IV Certification, the patent holder may initiate a patent infringement action. Prior to the expiration of this 45-day period, no declaratory judgment action regarding the patent may be initiated by the generic applicant.

As discussed above, the act of infringement occurs when the generic drug manufacturer submits an ANDA containing a Paragraph IV Certification for a drug claimed in a patent for the purpose of gaining FDA approval to engage in the commercial manufacture, use or sale of the patented drug before the expiration of the patent.<sup>15</sup> For this act of infringement, the court may: (1) order that the approval date of the generic manufacturer's ANDA must be no earlier than the expiration of the pioneer patent; (2) order that an injunction be granted against the infringer preventing the commercial manufacture, use, or sale of an approved drug; or (3) order that monetary relief be awarded against the generic drug manufacturer "only if there has been commercial manufacture, use or sale of an approved drug."<sup>16</sup> These are the only forms of relief available to the patent holder in these cases, aside from the possibility of winning attorneys fees.<sup>17</sup>

---

<sup>15</sup> 35 U.S.C. § 271(e)(2).

<sup>16</sup> 35 U.S.C. § 271(e)(4).

<sup>17</sup> 35 U.S.C. §§ 271(e)(2) and (4), and 35 U.S.C. § 285.

**3. 30-Month Stay**

If the patent holder initiates a patent infringement action in response to a Paragraph IV Certification within the 45-day period described above, FDA cannot approve the ANDA for 30 months, unless the action is resolved in favor of the generic applicant before that time or if the patent expires before that time.<sup>18</sup> If the action is resolved in favor of the patent holder, then the court will issue an injunction preventing the approval of the generic application from being effective before the expiration of the valid and infringed listed patent.<sup>19</sup>

The purpose of the Special Litigation Provisions is to allow the orderly and timely resolution of patent infringement conflicts between the pioneer and generic challenger prior to FDA approval of the generic. This avoids the intractable situation that would occur if a generic manufacturer ultimately loses a patent suit after marketing its version of a pioneer drug prior to resolution of the patent conflict. As recognized by Congress when drafting the law, such a situation would destroy market share and pricing structure for the pioneer product and create crippling damage claims for the generic manufacturer.

**E. 180-Day ANDA Exclusivity**

The first follow-on (generic) product approved through an ANDA containing a Paragraph IV Certification receives 180 days of market exclusivity during which no subsequent ANDA for the same product can be approved. The purpose of the 180-Day ANDA exclusivity is to reward a generic drug manufacturer for the expense and effort involved in challenging a listed patent of the pioneer company.

---

<sup>18</sup> See FDCA §§ 505(c)(3)(C) & (j)(iv)(B)(3); 21 U.S.C. § 355(c)(3)(C) & (j)(iv)(B)(3).

<sup>19</sup> 35 U.S.C. § 271(e)(4).

According to FDA's original regulations:

“If an abbreviated new drug application contains a certification that a relevant patent is invalid, unenforceable, or will not be infringed and the application is for a generic copy of the same listed drug for which one or more substantially complete abbreviated new drug applications were previously submitted containing a certification that the same patent was invalid, unenforceable, or would not be infringed and the applicant submitting the first application has successfully defended against a suit for patent infringement brought within 45 days of the patent owner's receipt of notice submitted under [21 C.F.R.] § 314.95, approval of the subsequent abbreviated new drug application will be made effective no sooner than 180 days from whichever of the following dates is earlier:

- (i) The date the applicant submitting the first application first commences commercial marketing of its drug product; or
- (ii) The date of a decision of the court holding the relevant patent invalid, unenforceable, or not infringed.”<sup>20</sup>

As discussed further below, this regulation (and its successful defense requirement) has been withdrawn, and the 180-Day ANDA exclusivity is the subject of pending rulemaking.<sup>21</sup>

\* \* \*

As described in the above summary, the Hatch-Waxman Act is composed of many complex provisions that achieve a balance between encouraging innovation and providing competition through generic copies. These provisions are constructed in a highly interrelated, even contractual manner so that seemingly simple modifications to one of the provisions may upset the statutory promises contained within the four corners of the Hatch-Waxman Act in extraordinary and unintended ways.

---

<sup>20</sup> 21 C.F.R. § 314.107(c)(1).

<sup>21</sup> The 180-day exclusivity provision does not apply to applications filed under Section 505(b)(2). 505(b)(2) products are not the same as, and do not follow-on from, innovator products; they are not “generic,” and so also there can be no subsequent generic copies, hence no role for 180-day relative exclusivity.

**III. FDA's Implementation of the Hatch-Waxman Act has Departed From the Statutory Language and Legislative Intent by Favoring Generic Drug Interests at the Expense of the Protections for Innovation Promised by Congress.**

The Hatch-Waxman Act has been an overwhelming success for the generic drug industry. The generic industry has flourished since the Hatch-Waxman Act eliminated the barriers to entry and made it much easier, far less costly, and quicker for low-cost generic drug manufacturers to get their copies of innovator medicines to market following patent expiration.

- Since 1984, the generic industry's share of the prescription-drug market has jumped from less than 20 percent to almost 50 percent.
- Before 1984, it took three to five years for a generic copy to enter the market after the expiration of an innovator's patent. Today, generic copies typically come to market as soon as the patent on an innovator product expires, and in most cases, sales of pioneer medicines drop as much as 75 percent within weeks after a generic copy enters the market.
- Prior to 1984, only 35 percent of top-selling innovator medicines had generic competition after their patents expired. Today, virtually all innovator medicines expect to face generic competition.

Since 1984, the research-based pharmaceutical industry has responded as well in its own spheres of endeavor, by continuing to increase its investment in research and development and to develop new, more advanced, and more effective medicines.

- The industry's investment in pharmaceutical R&D has jumped from approximately \$3-1/2 billion in 1984 to more than \$30 billion this year.
- During the 1990s, the industry developed 370 new life-saving, cost-effective medicines – up from 239 in the previous decade.

- The research-based pharmaceutical industry now has more than 1,000 new medicines in development – either in human clinical trials or at FDA awaiting approval. These include more than 400 for cancer; more than 200 to meet the special needs of children; more than 100 each for heart disease and stroke, AIDS, and mental illness; 26 for Alzheimer’s disease; 25 for diabetes; 19 for arthritis; 16 for Parkinson’s disease, and 14 for osteoporosis.

Accordingly, the Hatch-Waxman compromise is benefiting the public health both by promoting generic competition and by preserving and providing incentives for pioneer product innovation. As a result, consumers are receiving the benefits of early access to low-cost generic copies and the benefits of an expanding stream of new, more precise, and more sophisticated medicines.

Despite the benefits to all parties under the Hatch-Waxman Act, there have also been substantial changes in the marketplace that affect incentives for innovation. *First*, there is earlier and more vigorous competition in new products within particular therapeutic categories among innovators than there was in 1984. Now, a pioneer product must anticipate competition from comparable competitive products of other pioneer companies much earlier than the expiration of the patent term. This innovator-innovator competition reduces the period during which a company can recover the costs of research and development for the approved products as well as for product failures. *Second*, the cost of developing a drug has climbed on average to more than \$800 million. This increased cost in combination with a shorter expected time in which to recover the costs substantially complicates the incentives for innovation. Moreover, pressures on the ability to recover research costs through sales decrease the funding available to invest in the next generation of products. *Finally*, the incentives for innovation are further

diminished when innovator companies must undertake longer, larger and more complicated clinical trials to demonstrate safety and efficacy. This trend is expected to continue as the industry pursues more complex diseases with subtle endpoints that are possible to target through our greater understanding of genetics and disease processes.

The context in which the Hatch-Waxman Act exists has changed since 1984, and the balance has shifted away from the innovation of new cures and treatments and towards the marketing of copies of already approved drugs. In addition, however, the research-based industry is concerned that FDA's actions in implementing the Hatch-Waxman Act are exacerbating the shift away from innovation that has occurred in recent years. Correcting this imbalance does not require amending the Act but simply a return by FDA to the fundamentals of statutory construction and application.

The principal role of FDA in implementing the Hatch-Waxman Act is in the operation of the procedures to permit generic drug entry.<sup>22</sup> However, as described above, these procedures also contain important provisions for protecting incentives for pioneer product innovation. The fair implementation of the Hatch-Waxman Act benefits the public health, protects the balance between product innovation and generic marketing, and maintains the legislative compact among competing interests established by Congress.

The research-based pharmaceutical industry is particularly concerned about FDA's policy positions regarding:

- (1) standards for approval of ANDAs;

---

<sup>22</sup> Although FDA has a role in the implementation of the patent term restoration provisions of the Hatch-Waxman Act, its role is limited to providing input on the product that was subject to regulatory review, whether the approval is the first such marketing or use of the product, and the characterization of the approved product.

- (2) use of citizen petitions;
- (3) section 505(b)(2) applications;
- (4) patent listing and litigation; and
- (5) market exclusivity protections.

Because of deference owed to administrative agencies under the *Chevron* doctrine,<sup>23</sup> and because many FDA issues have a scientific or technical aspect, the courts have frequently upheld FDA's implementation of Hatch-Waxman. A review of FDA's actions, however, reveals how FDA has increasingly departed from the statutory language and exercised its administrative discretion to an undue extent in favor of generic drugs and against innovator rights.

**A. Erosion of Standards for Approval of ANDAs**

In contrast to the statutory provisions applicable to innovator drugs – which allow for broad FDA discretion in developing standards to determine whether a drug is safe and effective – Hatch-Waxman sets forth most of the standards for approval of ANDAs as an objective checklist.<sup>24</sup> The statute requires FDA to approve a generic drug if it (1) is the same as a reference drug in terms of indication(s), active ingredient(s), route of administration, dosage form, and strength,<sup>25</sup> and (2) is bioequivalent to that reference drug.<sup>26</sup> Apart from those requirements, the only other statutory requirements are that the inactive ingredients in the proposed product cannot be unsafe,<sup>27</sup> the manufacturer must meet good manufacturing practices

---

<sup>23</sup> See *Chevron U.S.A., Inc. v. Natural Resources Defense Council*, 467 U.S. 837 (1984).

<sup>24</sup> See FDCA § 505(j)(2)(A); 21 U.S.C. § 355(j)(2)(A).

<sup>25</sup> FDCA § 505(j)(4)(D); 21 U.S.C. § 355(j)(4)(D).

<sup>26</sup> FDCA § 505(j)(4)(F); 21 U.S.C. § 355(j)(4)(F).

<sup>27</sup> FDCA § 505(j)(4)(H); 21 U.S.C. § 355(j)(4)(H).

(GMP) requirements,<sup>28</sup> and the ANDA must not contain false statements of material fact.<sup>29</sup> The limitation on FDA's discretion in setting standards for ANDAs is emphasized by the provision – presumably added at the behest of the generic industry – that expressly prohibits FDA from requiring any information from ANDA applicants beyond the items specifically required in the Hatch-Waxman Act.<sup>30</sup>

Despite the clear statutory structure designed to allow FDA to approve only those generic drugs that are *the same as*, and bioequivalent to, previously approved drugs, FDA has sought opportunities to put forth misinterpretations of the statute to expand the class of drugs eligible for approval through the ANDA process. For example, instead of requiring a generic drug to be the same as the reference drug in all respects required by the statute, FDA allows for differences that are viewed, in the exercise of Agency discretion, as medically acceptable. In addition, instead of adhering to the statutory definition of bioequivalence, FDA devises new methods of assessing whether, in its view, a generic drug will have the same clinical effect as its reference drug. While FDA is no doubt sincere in its conclusions that the deviations it permits are medically justifiable, the agency is not implementing the legal rules intended and enacted by Congress. This also undercuts the assurances given by successive Commissioners to the American people that they can take for granted that generics are identical to, and hence (FDA would also urge) interchangeable with, the innovator reference drug.

---

<sup>28</sup> FDCA § 505(j)(4)(A); 21 U.S.C. § 355(j)(4)(A).

<sup>29</sup> FDCA § 505(j)(4)(K); 21 U.S.C. § 355(j)(4)(K).

<sup>30</sup> See FDCA § 505(j)(2)(A); 21 U.S.C. § 355(j)(2)(A) (sentence following clause (viii)).

**1. The Sameness Requirement**

**a. Differences in Active Ingredients**

The Hatch-Waxman Act requires a generic drug to have the “same” active ingredient(s) as its reference product.<sup>31</sup> Sameness is critical to the statutory scheme, because sameness assures that the clinical studies pertaining to the reference innovator drug are applicable to the proposed generic product. The FDA regulations provide that “same” in this context means “identical.”<sup>32</sup> Despite this apparent clarity, FDA deviates from the terms of the statute and its own regulations in a legally unsustainable manner to approve generic products that, although plainly not identical to the reference product as required, are viewed by FDA as close enough.

Contrary to the recommendation of its own chemistry reviewer, FDA approved a generic version of Pergonal<sup>®</sup> (menotropins), a complex, naturally derived product, despite a difference between the chemical composition of the proteins in the generic version and those in the innovator product. FDA justified the approval by interpreting the statutory sameness requirement as allowing differences that the agency estimated were not “clinically significant.”<sup>33</sup> In FDA’s view, the relevant question is “how much variation should be permitted.”<sup>34</sup> This interpretation converted the statutory requirement for sameness into a judgmental standard based

---

<sup>31</sup> FDCA § 505(j)(2)(A)(ii); 21 U.S.C. § 355(j)(2)(A)(ii). Changes in active ingredients are permitted through the suitability petition process, but only for substitutions in a combination product, such as using acetaminophen in the generic version of a combination product in which the innovator uses aspirin.

<sup>32</sup> 21 C.F.R. § 314.92(a)(1).

<sup>33</sup> See *Serono Laboratories, Inc. v. Shalala*, 158 F.3d 1313, 1317-18 (D.C. Cir. 1998).

<sup>34</sup> See *id.* at 1318.

on the expected clinical effects of differences, rather than an objective standard based on identical chemical composition.

Similarly, FDA applies a judgmental policy when approving ANDAs for generic products that include an active ingredient that is a different hydrate or polymorph of the active ingredient in the reference product. Generally, FDA considers all hydrates and polymorphs to be the same, despite physical differences from the form of the active ingredient in the reference product, “unless the differences in physical structure found in the polymorphs result in inequivalent safety and efficacy profiles.”<sup>35</sup> Thus, as in the case of proteins, FDA has read into the statutory requirement for sameness the authority to permit differences in polymorphs and hydrates that it views as clinically insignificant.

**b. Differences in Labeling**

The statute requires a generic drug to have the “same” labeling as its reference drug, with only four exceptions. Labeling can vary to reflect (1) differences approved in a suitability petition,<sup>36</sup> (2) differences because the generic drug and the reference drug “are produced or distributed by different manufacturers,”<sup>37</sup> (3) an intentional difference in the rate of the drug’s absorption;<sup>38</sup> and (4) omission of a pediatric indication or other aspect of labeling related to pediatric use that is protected by patent or by three-year Hatch-Waxman exclusivity.<sup>39</sup>

In theory, FDA strongly supports the requirement that generic drugs have the same labeling as

---

<sup>35</sup> See *Zenith Laboratories Inc. v. Abbott Laboratories*, No. 96-1661, 1996 U.S. Dist. LEXIS 22567, at \*32 (D.N.J. Aug. 5, 1996) (quoting FDA response to a citizen petition).

<sup>36</sup> FDCA § 505(j)(2)(A)(v) & (4)(G); 21 U.S.C. § 355(j)(2)(A)(v) & (4)(G).

<sup>37</sup> FDCA § 505(j)(2)(A)(v) & (4)(G); 21 U.S.C. § 355(j)(2)(A)(v) & (4)(G).

<sup>38</sup> FDCA § 505(j)(8)(B)(ii); 21 U.S.C. § 355(j)(8)(B)(ii).

<sup>39</sup> See Section 11 of the “Best Pharmaceuticals for Children Act,” signed by President Bush January 4, 2002.

the innovator drugs they copy, having declared that “[c]onsistent labeling will assure physicians, health professionals, and consumers that a generic drug is as safe and effective as its brand-name counterpart.”<sup>40</sup> In practice, however, FDA deviates from the sameness requirement when necessary to allow the approval of generic versions.

Despite the apparent narrow statutory exceptions to the requirement that generics have the same labeling as their reference drugs, FDA has interpreted the statutory provision that allows for differences when the drugs “are produced or distributed by different manufacturers” to allow for a wide variety of labeling differences. Accordingly, the agency has promulgated regulations that permit generic drug manufacturers: to use labeling with different information on expiration dates, formulation, bioavailability, and pharmacokinetics; to make labeling revisions to comply with current FDA labeling guidance; and to omit any labeling material that is protected by patents or Hatch-Waxman exclusivity.<sup>41</sup>

Many of those permitted labeling differences are impossible to reconcile with the statutory exception for differences due to different manufacturers. The statutory exception was plainly meant to cover information regarding the manufacturer’s identity. The differences in labeling pertaining to formulation, bioavailability, pharmacokinetics, and other factors permitted by FDA regulations, however, are necessitated by differences between the generic and innovator products themselves, rather than by a difference between the products’ manufacturers.

While some of those labeling differences may be inconsequential, FDA has shown little restraint in allowing labeling differences when necessary for approval of a generic product. For example, FDA approved a generic version of Diprivan<sup>®</sup> (propofol) with a different

---

<sup>40</sup> See 57 Fed. Reg. 17950, 17961 (Apr. 28, 1992).

<sup>41</sup> See 21 C.F.R. § 314.94(a)(8)(iv).

preservative than the innovator drug, even though the different preservative required a labeling warning (because it was a sulfite) not applicable to the labeling of the innovator product.<sup>42</sup> In approving the generic version, the agency arbitrarily and capriciously disregarded its previous ruling that a new warning statement that is necessary to accommodate a different inactive ingredient in a generic product would violate the same-labeling requirement.<sup>43</sup>

Another example of FDA's violation of the statutory requirement for same labeling is the draft guidance document that would allow a generic drug to use a previously approved but since discontinued version of a reference drug's labeling if use of the discontinued labeling is necessary to avoid the innovator's exclusivity rights over its current labeling.<sup>44</sup> The draft guidance recognizes that different labeling will cause "confusion in the marketplace" and therefore proposes to limit use of discontinued labeling to situations where use of the labeling is necessary to allow approval of a generic drug.<sup>45</sup> As in the case of the requirement for the same active ingredients, FDA has converted a clear statutory requirement into a mere objective that the agency should comply with to the extent that it does not interfere with the approval of generic products.

**c. Differences in Dosage Forms**

The statute generally requires a generic drug to have the same dosage form as its reference drug, but allows for differences in dosage forms if approved by FDA through a

---

<sup>42</sup> See *Zeneca, Inc. v. Shalala*, 213 F.3d 161, 165-66 (4th Cir. 2000).

<sup>43</sup> See 54 Fed. Reg. 28872, 28884 (July 10, 1989).

<sup>44</sup> See U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research, Draft Guidance for Industry: Referencing Discontinued Labeling for Listed Drugs in Abbreviated New Drug Applications (Oct. 2000); see also 63 Fed. Reg. 64225 (Oct. 26, 2000) (regarding notice of availability).

<sup>45</sup> *Id.* at lines 196-98.

suitability petition.<sup>46</sup> Despite this available statutory procedure, there have been several instances in which FDA has adopted dubious interpretations of the “same dosage form” to permit approval of generic drugs without use of the petition process.

For example, FDA approved a generic version of Dilantin<sup>®</sup> (phenytoin) as a capsule, even though the generic drug was in fact a tablet inserted into a capsule shell, rather than powder in a capsule as is the case for the innovator version.<sup>47</sup> In another instance, FDA reversed its position on the dosage form of the innovator drug Neoral<sup>®</sup> (cyclosporin for microemulsion) when an ANDA applicant proposed a version that did not fit the definition of Neoral’s dosage form. FDA not only ruled that the innovator and the generic products were the same dosage form, but it also ordered the innovator to change its labeling to accommodate the new policy.<sup>48</sup> FDA has also requested comments on an extraordinarily significant possible change in dosage form classification that would consider tablets and capsules to be the same dosage form.<sup>49</sup>

It is noteworthy that FDA’s departures from congressional intent in determining whether a generic product has the same dosage form as the innovator are not for the purpose of permitting approval of the generic product. Since the suitability petition process allows for approval of different dosage forms, FDA could recognize differences in dosage forms and nevertheless approve the generic products through ANDAs. FDA’s conclusion, in questionable

---

<sup>46</sup> Generic drug manufacturers may also use suitability petitions to gain FDA approval of products that differ from a reference drug in terms of active ingredients, route of administration, and dosage strength. *See* FDCA § 505(j)(2)(C); 21 U.S.C. § 355(j)(2)(C).

<sup>47</sup> *See Warner-Lambert Co. v. Shalala*, 202 F.3d 326, 327-28 (D.C. Cir. 2000).

<sup>48</sup> *See* Letter from FDA to Novartis Pharmaceuticals Corporation (Nov. 2, 1998), (on file in FDA Docket No. 96P-0459).

<sup>49</sup> 62 Fed. Reg. 14917 (Mar. 28, 1997).

circumstances, that generic products share the “same” dosage form appears to be for the sole reason of enhancing the competitive position of the generic drugs in the marketplace. Only drugs with the same dosage form are “A” rated (“therapeutically equivalent”) in the FDA *Orange Book* and thus obtain the benefit of pharmacist substitution. FDA’s blatant foray into assisting the competitive position of generic drugs by manipulating the structure of dosage form designations has no statutory basis and is entirely impermissible.

**d. Use of Limited Confirmatory Studies**

The statutory suitability petition process allows FDA to permit ANDAs for products that differ in certain respects from the reference products but not if “investigations must be conducted to show the safety and effectiveness of the [generic] drug.”<sup>50</sup> To evade that restriction, FDA has adopted a policy allowing for “limited confirmatory tests” to show that the proposed changes “do not alter [the generic drug’s] safety and effectiveness.”<sup>51</sup>

This practice allows FDA to approve through the ANDA process new types of products about which it has safety or effectiveness concerns – and which therefore require studies – while purportedly remaining faithful to the statutory injunction against using studies to support an ANDA. FDA’s position, which finds no basis in the statutory text, is that the law prohibits only studies intended to answer “basic safety or effectiveness questions” and that “simple studies intended to rule out unlikely problems” are permissible.<sup>52</sup>

FDA later expanded its policy to allow for “limited confirmatory tests” in support of ANDAs outside of the suitability petition process. Consistent with the statute, FDA’s general

---

<sup>50</sup> FDCA § 505(j)(2)(C)(i); 21 U.S.C. § 355(j)(2)(C)(i).

<sup>51</sup> See 54 Fed. Reg. 28872, 28880 (July 10, 1989); see also 57 Fed. Reg. 17950, 17957-58 (Apr. 28, 1992).

<sup>52</sup> See 54 Fed. Reg. 28872, 28880 (July 10, 1989).

rule is that an ANDA cannot be supported by studies on safety or effectiveness. This policy is clearly embodied in the statute, which specifies the required content of an ANDA and expressly prohibits FDA from requiring any additional information.<sup>53</sup> None of the information required to be included in an ANDA relates to showing the safety and effectiveness of the product, other than the required bioequivalence studies. In the case of the menotropins ANDA, however, FDA required the applicant to submit three animal studies to determine whether unidentified proteins in its proposed product raised a safety issue.<sup>54</sup> FDA justified these as limited confirmatory tests and therefore supposedly permissible.

FDA's improper use of studies to support ANDAs is a companion to its policy of deviating from the statutory sameness requirements. The agency knows that differences between the innovator product and a proposed generic version can raise safety and effectiveness concerns. Notwithstanding the statutory proscriptions against studies supporting an ANDA, FDA adopted the ruse of "limited confirmatory tests" to afford the benefits of the ANDA process to generic drugs that differ from the reference drugs they purport to copy, while providing some comfort to itself that the differences probably do not have untoward clinical effects.

## 2. Bioequivalence

In addition to sameness, the other core statutory requirement for approval of a generic drug is bioequivalence to the reference drug. The statute defines bioequivalence by specifying that a drug "shall be considered to be bioequivalent" to its reference drug if there is no significant difference in the "rate and extent of absorption of the drug" compared to the reference

---

<sup>53</sup> See FDCA § 505(j)(2)(A); 21 U.S.C. § 355(j)(2)(A) (sentence following clause (viii)).

<sup>54</sup> See *Serono Laboratories*, 158 F.3d at 1325.

drug.<sup>55</sup> Because it interpreted “absorption” to mean systemic absorption, FDA found the statutory definition too restrictive – if “absorption” means systemically, the statute provided no basis for approving generic versions of drugs that are not systemically absorbed (such as inhaled drugs). FDA therefore adopted additional definitions of bioequivalence beyond what appears in the statute. FDA also promulgated regulations allowing it to waive bioequivalence testing in certain circumstances, even though no waiver authority can be found in the statute.<sup>56</sup>

In defending its actions, FDA argued that, in using the words “shall be considered to be bioequivalent,” the statute simply provided a safe harbor for how bioequivalence could be shown, and that the method described in the statute was not the exclusive method for demonstrating bioequivalence.<sup>57</sup> In FDA’s view, it had unlimited authority to define bioequivalence.<sup>58</sup> It is a mystery why Congress would have granted FDA unlimited authority to

---

<sup>55</sup> FDCA § 505(j)(8); 21 U.S.C. § 355(j)(8). In general, two drugs are considered bioequivalent when their rate and extent of absorption into the bloodstream do not differ significantly. Traditionally, FDA has concluded that no significant difference exists between a generic and reference pioneer drug so long as the absorption profile of the generic falls within a range that is between 80-125 per cent of the reference drug. *See, e.g.*, 65 Fed. Reg. 64225 (Oct. 26, 2000); Guidance for Industry, Bioavailability and Bioequivalence Studies for Orally Administered Drug Products -- General Considerations at 21 (Oct. 2000). There are products where a differential within the 80-125 per cent range is significant, and where more rigorous parameters are needed to ensure that a generic drug is truly bioequivalent to the pioneer drug. Moreover, permitting absorption to range from 80 to 125 per cent of the reference drug could be clinically significant for generic-generic substitution. For example, if a patient fills a prescription with generics, the patient might get a generic product with an absorption profile 80 per cent of the reference drug one month, and a different generic another month with an absorption profile of 125 per cent. The latter generic is more than 50 per cent more potent than the former, and the two cannot reasonably be considered to be clinically equivalent.

<sup>56</sup> *See Fisons Corp. v. Shalala*, 860 F. Supp. 859 (D.D.C. 1994).

<sup>57</sup> *See Schering Corp. v. FDA*, 51 F.3d 390 (3d Cir. 1995); *see also Schering Corp. v. Sullivan*, 782 F. Supp. 645 (D.D.C. 1992), *vacated as moot*, 995 F.2d 1103 (D.C. Cir. 1993).

<sup>58</sup> *See id.*

define bioequivalence, yet at the same time have so little faith in the agency that it enacted a safe harbor to require FDA to recognize the most obvious test of bioequivalence. Reviewing courts have nevertheless deferred to FDA's interpretation.

FDA's aggressive interpretation of the statutory bioequivalence provisions has led to court challenges that might have been avoided had the agency adopted positions that were more consistent with the statutory language. For example, FDA might have attempted to work within the term "absorption" without determining that the term meant only systemic absorption. Although courts have upheld FDA's position by invoking the *Chevron* doctrine to defer to agency interpretation of an ostensibly ambiguous statute, an FDA policy more aligned with the statute would have suggested a more even-handed approach to Hatch-Waxman than the current rules designed to facilitate the approval of generic drugs regardless of the statutory language.

### 3. **Other Standards**

In addition to the basic requirements of sameness in the products' key aspects and bioequivalence, generic drugs are subject to other requirements, such as the safety of inactive ingredients, limits on impurities in active ingredients, adequate containers and closures, and compliance with good manufacturing practices.<sup>59</sup> Although much of how FDA applies these requirements to particular products is not public, it is evident that FDA applies disparate standards. Specifically, generic products and manufacturers are often held to lesser requirements than innovator products and manufacturers.

FDA has not established an integrated review staff for both innovator and generic drugs but instead has two separate operations. Not surprisingly, this has led to inconsistent

---

<sup>59</sup> See FDCA § 505(j)(4); 21 U.S.C. § 355(j)(4).

standards in practice, with the new drug divisions applying more rigorous requirements than the Office of Generic Drugs (“OGD”).

For example, the two divisions have instituted inconsistent requirements for clinical studies. When the manufacturer of Diprivan<sup>®</sup> (propofol) wanted to add a preservative to the product, FDA required clinical studies to support the change. By contrast, FDA approved a generic version of propofol, containing a different preservative, without requiring any clinical studies.<sup>60</sup> In another instance, the new drug division required an innovator manufacturer to conduct studies to support conversion of its product from glass to plastic packaging, while OGD approved a generic version of the same drug in plastic packaging without any studies. A further example involves the OGD approval of the ANDA for a complex drug (menotropins) despite a recommendation by the new drug division that additional safety studies be required.<sup>61</sup>

Product specification requirements also differ between the two divisions. When OGD reviews the chemistry of a proposed generic product, it does not compare the proposed specifications to those of the innovator product. Instead, it relies on compendia monographs and published literature.

Furthermore, FDA implements variant factory inspection standards. It is widely understood – although of course difficult to document – that FDA applies less demanding standards in inspecting facilities of generic drug manufacturers than those of innovator companies. The issue is particularly acute with respect to the production of bulk active

---

<sup>60</sup> See *Zeneca, Inc.*, 213 F.3d at 165-66.

<sup>61</sup> See *Serono Laboratories*, 158 F.3d at 1317.

ingredients, which are typically manufactured for generic companies in other countries – often Third World countries. Investigations have uncovered extensive problems with such facilities.<sup>62</sup>

**B. Citizen Petitions**

Innovator manufacturers have sometimes submitted citizen petitions to FDA to suggest appropriate bioequivalence testing and other approval criteria for particular generic drugs. FDA regulations in place since the 1970s permit the submission of citizen petitions on any subject and require FDA to respond to the petitions.<sup>63</sup> Unlike ordinary correspondence, the regulations treat the response to a citizen petition as the official position of the agency.

FDA has proposed to curtail dramatically the subjects on which citizen petitions may be submitted.<sup>64</sup> Under the proposal, citizen petitions could propose changes in regulations or could oppose administrative orders already issued, but could not address administrative actions pending for decision. The proposal specifically mentions petitions raising “detailed scientific concerns about a particular product’s safety or bioequivalence.” These petitions would be permissible only after product approval under FDA’s proposal.

The proposal recommends that outside parties raise their concerns via letter or e-mail instead of a citizen petition, stating that the different format does not “mean that it will receive less attention from FDA.”<sup>65</sup> In clear contradiction to that assurance, however, the proposal complains that part of the problem with the citizen petition process is that “FDA must

---

<sup>62</sup> See, e.g., *Continuing Concerns Over Imported Pharmaceuticals: Hearings Before the Subcomm. on Oversight and Investigations of the House Comm. on Energy and Commerce*, 107<sup>th</sup> Cong. (2001).

<sup>63</sup> 21 C.F.R. § 10.30

<sup>64</sup> See 64 Fed. Reg. 66822 (Nov. 30, 1999).

<sup>65</sup> See *id.* at 66824.

research the petition's subject, [and] examine scientific, medical, legal, and sometimes economic issues.”<sup>66</sup> This reluctance to investigate generic drug approval standards as they apply in particular cases is difficult to square with FDA's statutory obligations to protect the public health.

The generic industry's well-worn refrain that frivolous petitions delay the approval of generic drugs is no more than an urban legend. FDA is fully capable of disposing with frivolous petitions. Behind the generic industry's bluster is that simple but important fact that FDA's criteria for approval of some generic drugs raise serious scientific and medical issues, and the NDA holder for the drug, which has extensive knowledge about it, is often in the best position to bring to FDA's attention issues regarding appropriate standards.

Moreover, the citizen petition process is desirable because it is a welcome manifestation of the principles of open government. Citizen petitions, comments filed concerning petitions, and FDA's responses to petitions are all public documents. FDA should not be permitted to backslide on its sunshine-in-government policies and conceal from the public its handling of safety and effectiveness issues relating to generic drugs by foreclosing the use of a public process to air those concerns.

**C. Section 505(b)(2) Applications**

Under section 505(b)(2) of the FDCA, NDAs that rely on clinical trials for which the applicant lacks a right of reference are subject to the same patent certification process as ANDAs (including delay in approval if patent litigation ensues).<sup>67</sup> This provision is based on FDA's pre-1984 “paper NDA” policy which referred to NDAs that are supported in whole or in

---

<sup>66</sup> *See id.* at 66822.

<sup>67</sup> FDCA § 505(b)(2)(A); 21 U.S.C. § 355(B)(2)(A).

part by published literature rather than by clinical trials conducted by the sponsor. The paper NDA was developed by FDA prior to the Hatch-Waxman Act as a mechanism to provide a basis for approval of generic drugs. It was based on the theory that published articles can constitute the statutorily required “full reports of clinical investigations” proving safety and effectiveness and that, by relying on published literature, an applicant need not rely on the innovator’s confidential and proprietary data. Of course, even with the use of published literature there may be applicable patents at issue. The Hatch-Waxman Act therefore applied the same patent certification procedures to paper NDAs as to ANDAs to close a possible loophole through which an applicant for a generic drug might avoid the certification process (*i.e.*, by submitting its application in the form of a paper NDA instead of an ANDA).

Although on its face section 505(b)(2) does nothing more than apply the patent certification procedures to paper NDAs, FDA has signaled that it will somehow construe it as a substantive grant of authority to approve a new class of applications.<sup>68</sup> Under this interpretation, FDA has asserted in its regulations and in a draft guidance that it is authorized to approve not only NDAs that are based on reports of studies in the published literature, but also NDAs based

---

<sup>68</sup> *See, e.g.*, U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research, Draft Guidance for Industry: Applications Covered by Section 505(b)(2) (“Draft Guidance on Section 505(b)(2)”), at 2 (Oct. 1999). The draft guidance states that section 505(b)(2) “expressly permits FDA to rely, for approval of an NDA, on data not developed by the applicant.” FDA plainly overinterprets section 505(b)(2). Contrary to the assertion in the draft guidance, section 505(b)(2) does not “expressly” permit FDA to rely on data not developed by the applicant. Rather, it only expressly requires certain patent certifications. The provision does *imply* that FDA has authority under section 505(b)(1) to allow NDAs to contain reports of investigations for which the applicant lacks a right of reference, but that by itself is unremarkable. Section 505(b)(1) merely requires “full reports of investigations which have been made . . . .” The reference to studies “which have been made” has always permitted the submission of studies that were not conducted by the sponsor. There is no textual support for FDA’s assertion that section 505(b)(2) created a new class of drug applications.

on a previous FDA finding of safety and/or effectiveness for a drug.<sup>69</sup> FDA would require only those “bridging studies” that it determines are necessary to apply the previous FDA finding to the new product.

FDA’s position that a previous finding of safety and effectiveness for one drug can be relied upon for approval of another, separate NDA has no statutory support. The requirements for an NDA are set forth in section 505(b)(1) and require “full reports of clinical investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective for use.” There is simply no reading of this language that would permit a previous agency finding for a non-identical drug to be considered a “full report of clinical investigations.”

The effect of FDA’s interpretation of section 505(b)(2) is to expand the circumstances in which an innovator’s proprietary safety and effectiveness studies are relied on to support the approval of competitive products. When the Hatch-Waxman bargain was struck, the only such circumstances apparent in the statute were for identical products approved through ANDAs and permissible variations authorized, without the submission of new studies, through suitability petitions. The trade-offs in Hatch-Waxman having been agreed to long ago, FDA now asserts that there is a vast new category of potential products for which FDA can rely on the proprietary data submitted in NDAs. This draft administrative interpretation is inconsistent with the statute and should be withdrawn.

---

<sup>69</sup> 21 C.F.R. § 314.54; Draft Guidance on Section 505(b)(2) at 3.

**D. Patent Listing and Litigation**

**1. Listable Patents**

One of the key elements of Hatch-Waxman is its procedure for litigating patent disputes prior to FDA approval of an allegedly infringing product.<sup>70</sup> NDA holders are required to list all patents in the FDA Orange Book. ANDA applicants must notify the NDA holder and patent holder if they seek approval prior to expiration of the listed patents. If the patent holder sues the ANDA applicant after receiving such notice, FDA is prohibited from approving the ANDA involved until the patent litigation is resolved, all the listed patents have expired, or 30 months have passed, whichever is earlier.

Since the applicability of this procedure depends on whether a patent is listed in the Orange Book, there has been substantial controversy over the criteria for listability. The statute requires NDA applicants to list any patent “which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug.”<sup>71</sup> Patents issued after approval of an NDA must be submitted to FDA within 30 days for listing.<sup>72</sup>

**a. Listing Patents That Do Not Cover the Approved Product**

The primary ambiguity in this statutory language – and the source of much of the controversy – is its requirement to list patents that claim “the drug.” That term, which appears frequently in the Federal Food, Drug, and Cosmetic Act, has multiple potential meanings.

---

<sup>70</sup> FDCA §§ 505(c)(3)(C) & (j)(5)(B)(iii); 21 U.S.C. §§ 355(c)(3)(C) & (j)(5)(B)(iii).

<sup>71</sup> FDCA § 505(b)(1); 21 U.S.C. § 355(b)(1).

<sup>72</sup> FDCA § 505(c)(2); 21 U.S.C. § 355(c)(2).

Historically, FDA has sometimes interpreted the term “drug” as meaning the active ingredient or active moiety of a product and sometimes as meaning the entire drug product, with the particular meaning determined from the context of its use in the statute. For example, FDA interprets “drug” in the statutory provision on orphan drug exclusivity to mean active moiety,<sup>73</sup> while it interprets “drug” in the new drug approval provisions to mean drug product.<sup>74</sup> In addition, “drug” is defined in the statute as including the components of a product.<sup>75</sup>

With respect to drug formulation patents, FDA has adopted a pro-generic interpretation of the listing requirements that unduly narrows the scope of patents that can be listed in the Orange Book. This interpretation is exemplified by the result in the *Pfizer* case.<sup>76</sup> Pfizer held patents on nifedipine in both tablet and capsule formulations but sold only the capsule version. Pfizer sought to list both patents because, under the suitability petition process for changes in dosage form, FDA could rely on Pfizer’s data for its capsule product to approve a competitive generic tablet product.

FDA refused to allow the listing of the tablet patent. The agency recognized that the patent listing provision was directly linked to use of the innovator’s data to approve a competitive product. Despite acknowledging this link, FDA refused to list Pfizer’s tablet patent even though the safety and effectiveness data for the capsule product were to be used as the only such data supporting the generic tablet product. FDA’s restrictive interpretation of the patent

---

<sup>73</sup> See *Baker Norton Pharmaceuticals, Inc. v. FDA*, 132 F. Supp. 2d 30, 34-35 (D.D.C. 2001)

<sup>74</sup> See *U.S. v. Generix Drug Corp.*, 460 U.S. 453, 459-60 (1983).

<sup>75</sup> FDCA § 201(g)(1); 21 U.S.C. § 321(g)(1).

<sup>76</sup> See *Pfizer, Inc. v. FDA*, 753 F. Supp. 171 (D. Md. 1990).

listing provisions is in no way compelled by the statutory language and cannot be reconciled with its purpose, as acknowledged by the agency.

Even under FDA's restrictive implementation of the listing provisions, room is available to list some patents that do not apply to the approved product. The controversy surrounding the listing of such patents does not indicate that the listings are necessarily improper. While the following discussion is not intended to be exhaustive on this matter, two examples can be identified.

First, FDA regulations provide that all patents covering the "drug substance" of a drug product (*i.e.*, the active ingredient) must be listed. In the case of polymorphs and hydrates, FDA generally considers all variations to be the same, and the official names for the resulting drug products may not even identify the particular polymorph or hydrate involved. Consequently, a court has held that patents on hydrates and polymorphs are listable, even though an approved product may use only one of the forms of the active ingredient.<sup>77</sup>

The court's interpretation is fully consistent with the purposes of the pre-approval litigation procedure. If an active ingredient occurs in a variety of crystalline forms, all of which are patented by the NDA holder and all of which are considered interchangeable by FDA, it hardly makes sense to allow a generic applicant to avoid the pre-approval litigation process by selecting a form different from that used in the innovator's product.

Another example involves a patent that covers a form of the drug substance that is used in the production of a drug but is not present in the final product. Since FDA regulations

---

<sup>77</sup> In response to a preliminary injunction motion, the court in *Zenith Laboratories, Inc. v. Abbott Laboratories*, found that the plaintiff was unlikely to succeed in showing that the defendant improperly listed a patent, since the patent was for a different polymorph of the active ingredient in the approved product. No. 96-1661, at 13 n.4 (D.N.J. Oct. 2, 1997). *See also Ben Venue Laboratories v. Novartis Pharmaceutical Corp.*, 10 F. Supp. 2d 446 (D.N.J. 1998).

define a drug as including its components, whether or not the component is present in the finished product, a patent covering such a component may meet the definition of a listable patent.<sup>78</sup>

Finally, there is no basis for any FDA refusal to list product-by-process patents, as some generic companies have urged. Process patents are not listable because they neither claim the drug nor a method of using the drug. Product-by-process patents plainly claim the drug, however, and FDA has no authority to refuse their listing.

**b. FDA's Role in Reviewing Patents for Listing**

FDA regulations take the position that the agency's role in listing patents is purely ministerial – that is, the agency does not review patent information submitted for listing to determine whether the patent meets the legal requirements for listing. The only administrative procedure for contested listings is a process by which FDA queries the submitter if the agency receives a complaint about a listed patent. FDA, however, accepts the response of the submitter and will not change the patent information in the Orange Book unless the submitter withdraws or amends its patent information in response to an agency request.<sup>79</sup>

Some in the generic industry have argued that FDA should review individual submissions of patent information to determine whether they meet the legal criteria for listing. Courts have ruled, however, that FDA has no role in that process, asserting that FDA has no

---

<sup>78</sup> See *Ben Venue Laboratories v. Novartis Pharmaceutical Corp.*, 10 F. Supp. 2d 446 (D.N.J. 1998) (the patented pentahydrate form of the active ingredient was used in the manufacturing process of the drug and therefore the patent was listable, even though the active ingredient in the final product was anhydrous).

<sup>79</sup> 21 C.F.R. § 314.53(f).

“statutory franchise” to review proposed patent listings and that FDA’s ministerial role in this regard was the “clear intent of the Hatch-Waxman Amendments.”<sup>80</sup>

The conclusion that FDA is not authorized to review the submissions of patent information has a firm basis in the statutory language. The statute instructs an NDA applicant to submit specified patent information.<sup>81</sup> The statutory direction to FDA is that “Upon approval of the application, [FDA] shall publish information submitted under the previous two sentences.”<sup>82</sup> Similarly, in the case of patent information submitted after approval of an NDA, the statute instructs: “Upon the submission of patent information under this subsection, [FDA] shall publish it.”<sup>83</sup>

If the statute provided that “FDA shall publish information on any patent that claims the drug,” or words to that effect, it might properly be construed as obligating FDA to assess whether the patent met the standard. But the statute does not take that approach, and directs FDA simply to publish whatever is submitted. There is no legal basis for the recommendation that FDA should substantively review patent submissions before including them in the Orange Book. Moreover, this scheme is consistent with the congressional intent of leaving all patent issues to the courts for resolution.

**c. Listing of “Late-Issued” Patents**

If a patent relevant to a drug is issued subsequent to approval of the drug’s NDA, the statute requires the NDA holder to submit information on the patent for listing in the Orange

---

<sup>80</sup> See *Watson Pharmaceuticals, Inc. v. Henney*, 2001 U.S. Dist. LEXIS 2477, at \*7 (D. Md. 2001).

<sup>81</sup> FDCA § 505(b)(1); 21 U.S.C. § 355(b)(1).

<sup>82</sup> FDCA § 505(b)(1); 21 U.S.C. § 355(b)(1).

<sup>83</sup> FDCA § 505(c)(2); 21 U.S.C. § 355(c)(2).

Book within 30 days after the patent is issued.<sup>84</sup> As previously noted, the statute provides that, upon submission of that information, “[FDA] shall publish it.”

Listable patents may be issued after approval of an NDA and, occasionally, long after approval. Some generic companies have argued that FDA should decline to list such patents because they trigger the pre-approval litigation process and thus may delay FDA approval of ANDAs that are pending at FDA or being readied for submission.

There is, however, no legal authority for FDA to refrain from publishing submitted information on patents, regardless of how long after NDA approval a patent is issued. The statute provides, without exception, that “[FDA] shall publish it.” This result is entirely consistent with the purpose of Hatch-Waxman’s pre-approval patent litigation procedure. The procedure is intended to protect innovator companies against FDA approval of infringing generic products. This objective is not dependent on when the patent was issued relative to approval of the NDA or to a generic company’s progress in obtaining FDA approval of a potentially infringing product.

If an NDA holder refrains from listing a patent within thirty days after issuance in order to gain some strategic advantage over ANDA applicants by listing the patent at some later date, FDA has the statutory authority to deny the late listing. FDA can prevent any abuses of that nature. The timing of patent issuance, however, is not controlled by the patent holder, and FDA does not have authority to deny listing to “late-issued” patents. The courts are properly charged with resolving listing issues in the course of patent litigation under the Hatch-Waxman Act.

---

<sup>84</sup> FDCA § 505(c)(2); 21 U.S.C. § 355(c)(2).

2. **The 30-Month Stay on ANDA Approvals**

a. **Certifications That Trigger the Stay**

When an ANDA applicant submits a Paragraph IV certification with respect to a listed patent, and the patent holder sues within 45 days, FDA is prohibited from approving the ANDA for up to 30 months while the litigation proceeds. FDA has correctly interpreted the statute as establishing a 30-month stay with respect to each Paragraph IV certification. The generic industry's suggestion that FDA should permit only one Paragraph IV certification per ANDA would not be consistent with the statute.

Under the statute, the 30-month stay goes into effect if “an action is brought for infringement of a patent which is the subject of the certification before the expiration of forty-five days from the date the notice [of the Paragraph IV certification] is received.”<sup>85</sup> There is no room for FDA discretion in this language. If an ANDA applicant makes a Paragraph IV certification and the patent holder sues within the specified time, the stay automatically goes into effect.

b. **Termination of the 30-Month Stay**

As noted above, once patent litigation is instituted under the Hatch-Waxman procedure, FDA is prohibited from approving the ANDA for 30 months unless “the court” has determined that the patent is invalid or not infringed prior to the expiration of that period.<sup>86</sup> FDA regulations initially implemented this provision by interpreting “the court” to mean the U.S. Court of Appeals. District courts have held, however, that “the court” means a U.S. district

---

<sup>85</sup> FDCA § 505(j)(5)(B)(iii); 21 U.S.C. § 355(j)(5)(B)(iii). For 505(b)(2) applications, the comparable provision is FDCA § 505(c)(3)(C); 21 U.S.C. § 355(c)(3)(C).

<sup>86</sup> FDCA § 505(c)(3)(C) & (j)(5)(B)(iii); 21 U.S.C. § 355(c)(3)(C) & (j)(5)(B)(iii).

court, thus permitting FDA approval of an ANDA during the 30-month period if a district court rules that a disputed patent is invalid or would not be infringed.<sup>87</sup>

FDA did not obtain review of these decisions by a court of appeals even though a court of appeals decision on a related matter had held that FDA enjoyed substantial discretion in how it interpreted “the court” in this statutory provision.<sup>88</sup> Instead, FDA summarily rescinded its regulation referring to the court of appeals and announced that a district court decision on a patent infringement claim could terminate the 30-month bar to ANDA approvals.<sup>89</sup> The agency instituted this policy without prior notice and opportunity for comment, claiming, without explanation, that the district court decisions (which were not accompanied by an injunction) made its regulation “unenforceable.”<sup>90</sup>

The issue of when the 30-month stay is terminated by a court decision is intertwined with the issue of when the 180-day period for generic drug exclusivity begins, since, under the statute, both are triggered by a decision of “the court.” Generic companies have instituted a great deal of litigation against FDA over the 180-day exclusivity period. FDA’s haste to resolve how the 180-day exclusivity provision operates for generic companies may be responsible for its decision to simply terminate the rights of NDA holders under the separate 30-

---

<sup>87</sup> See *Mylan Pharmaceuticals, Inc. v. Shalala*, 81 F. Supp. 2d 30 (D.D.C. 2000); *Torpharm, Inc. v. Shalala*, No. 97-1925 (D.D.C. Sep. 15, 1997), *vacated on mootness grounds*, 1998 U.S. App. LEXIS 4681 (D.C. Cir. Feb. 5, 1998).

<sup>88</sup> See *Granutec, Inc. v. Shalala*, 1998 WL 153410 at \*9 (4th Cir. Apr. 3, 1998).

<sup>89</sup> See 65 Fed. Reg. 43233 (July 13, 2000); see also U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research, *Guidance for Industry: Court Decisions, ANDA Approvals, and 180-day Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act* (Mar. 2000).

<sup>90</sup> 65 Fed. Reg. at 43235. Despite its asserted lack of discretion, FDA nevertheless stated that its action would have prospective effect only and that the agency would continue to apply the policy in the rescinded regulation to ANDAs filed prior to April 2000.

month stay provision without appealing the court cases or undertaking the required notice and comment rulemaking. If so, it would be another example of how FDA's focus on generic drug approvals in administering Hatch-Waxman has undermined the rights of innovator companies.

**E. Exclusivity**

**1. 5-year Exclusivity**

Hatch-Waxman provides five years of exclusivity for products “no active ingredient (including any ester or salt of the active ingredient) of which has been previously approved by FDA in any other [NDA].”<sup>91</sup> FDA refers to this as new chemical entity exclusivity.<sup>92</sup>

Although the statute's language confers five years of exclusivity on any product with a new “active ingredient” (other than a product containing an ester or salt of a previously approved active ingredient), FDA has chosen to adopt a narrower interpretation of the statute by conferring five years of exclusivity only to products with a new active moiety.<sup>93</sup>

When FDA informally adopted this interpretation prior to the issuance of a regulation, the Court of Appeals for the District of Columbia Circuit declared it invalid as being inconsistent with the statutory language.<sup>94</sup> Likewise, the Court of Appeals for the Federal Circuit struck down a similar interpretation by the Patent and Trademark Office (“PTO”) of similar language in the patent term extension provisions of Hatch-Waxman.<sup>95</sup> The PTO's argument that

---

<sup>91</sup> FDCA §§ 505(c)(3)(D)(ii) & (j)(5)(D)(ii); 21 U.S.C. §§ 355(c)(3)(D)(ii) & (j)(5)(D)(ii).

<sup>92</sup> Of course, prior to enactment of Hatch-Waxman, innovators had perpetual exclusive rights in their safety and effectiveness data. Thus, rather than *providing* five years of exclusivity, it is more accurate to say that the Hatch-Waxman Act *limited* exclusivity to five years.

<sup>93</sup> 21 C.F.R. § 314.108.

<sup>94</sup> See *Abbott Laboratories v. Young*, 920 F.2d 984, 995-96 (D.C. Cir. 1990).

<sup>95</sup> See *Glaxo Operations UK Ltd. v. Quigg*, 894 F.2d 392, 399-400 (Fed. Cir. 1990).

its interpretation attained a better balancing between the competing purposes of Hatch-Waxman was soundly rejected as a basis for deviating from the plain language of the statute.<sup>96</sup> Despite the adverse decisions by the two courts of appeals, FDA proceeded to codify its unchanged interpretation of the statute through the rulemaking process.<sup>97</sup> The resulting regulation has yet to be challenged in court.<sup>98</sup>

Although no large category of compounds has been denied five years of exclusivity due to FDA's misinterpretation of "active ingredient" to mean "active moiety," some potentially important innovations may be affected. For example, the development of a product based on only one of the enantiomers in a racemic mixture may result in a drug with significantly fewer side effects, but FDA considers an enantiomer of an existing product to be eligible for only three years of exclusivity. Because the development process for enantiomer products is potentially very expensive, FDA itself published a notice in 1997 stating that it was re-evaluating whether it should grant five years of exclusivity to products using a single enantiomer of a previously approved racemate.<sup>99</sup> As is typical of FDA's approach in these matters, however, the notice addressed the issue from a policy rather than legal perspective – asking what period of exclusivity was appropriate to effectuate the various goals of Hatch-Waxman and whether five years of exclusivity would encourage innovative products. FDA has not taken any action to revise its policy in the five years since publication of the notice.

---

<sup>96</sup> *See id.* at 396-97.

<sup>97</sup> *See* 59 Fed. Reg. 50338, 50357-58 (Oct. 3, 1994).

<sup>98</sup> This may be due to the fact that five-year exclusivity is often redundant with patent protection.

<sup>99</sup> 62 Fed. Reg. 2167 (Jan. 15, 1997).

## **2. 3-Year Exclusivity for Supplemental NDAs**

The statute provides three years of exclusivity for changes approved in a supplemental NDA.<sup>100</sup> In the case of supplemental NDAs for labeling changes, FDA has taken numerous steps in violation of statutory provisions to undermine the utility of this right.

First, FDA has narrowed the scope of changes eligible for exclusivity. The only prerequisite set forth in the statute for exclusivity is that there was a clinical study that was necessary for approval of the supplement and that was conducted or sponsored by the applicant. FDA, however, has claimed authority to decide that some supplements that meet that test are nevertheless not worthy of receiving the statutory exclusivity right. The agency has stated, “FDA declines to define in the regulation the kinds of supplemental applications that, if supported by clinical investigations, would warrant 3-year exclusivity.”<sup>101</sup>

Second, as previously discussed, despite the statutory requirement that generic drugs have the same labeling as their reference drugs, FDA has interpreted the exception for labeling differences based on different manufacturers to permit omission of material protected by exclusivity. This makes the 3-year exclusivity essentially worthless for labeling changes, since despite the labeling omissions, generic products will be “A” rated to the innovator and thus seen as fully interchangeable despite the omission of any protected labeling information.

Third, as also previously discussed, FDA has recently proposed to go beyond mere omissions of protected labeling by permitting the substitution of the innovator’s previously approved but discontinued labeling when exclusivity rights preclude a generic drug’s use of the

---

<sup>100</sup> FDCA §§ 505(c)(3)(D)(iv) & (j)(5)(D)(iv); 21 U.S.C. §§ 355(c)(3)(D)(iv) & (j)(5)(D)(iv).

<sup>101</sup> 59 Fed. Reg. 50338, 50357 (Oct. 3, 1994).

current labeling. The purpose of this approach is explicitly to avoid the innovator's three-year exclusivity over labeling changes.

Fourth, when FDA has approved generic products with different labeling because of the innovator's exclusivity rights, it has nonetheless allowed the generic product to have characteristics, such as a special strength, that facilitate its off-label use of the protected uses. For example, FDA approved a generic version of a product that was half the strength of the innovator product, even though there was no medical need for the reduced strength, based on the applicant's assertion that some patients would prefer to take two smaller pills.<sup>102</sup> The generic applicant's true motive was to sell a reduced-strength product that could also be used for the innovator's new and protected indication. Such generic boosterism on the part of FDA is not a victimless crime – it materially diminishes the very incentives for innovation that Congress intended to preserve in the Hatch-Waxman Act in order to support the interests of patients awaiting cures.

### **Conclusion**

The Hatch-Waxman Act is a complex and largely successful piece of legislation. Congress legislated carefully in order to ensure that incentives for innovation would be preserved, especially by providing a process for vindicating patent rights and standards for ensuring that only true generic copies could be approved. The law itself does not now need to be reopened, but many FDA policies have departed from the statutory language and Congress's promises to the research-based industry. The agency should return to the statute and apply it

---

<sup>102</sup> Suitability petition regarding 250 mg hydroxyurea (FDA Docket No. 96P-0407), approved June 10, 1997.

consistently with its language and intent. This approach will not only be faithful to the law but will further Congress's public-health purposes.