

**Review of FDA Law Related to Pharmaceuticals: The Hatch-Waxman Act,
Regulatory Amendments and Implications for Drug Patent Enforcement.**

Author: Laba Karki¹

Neifeld IP Law P.C.

¹ Ph.D., Patent Agent, J.D., George Washington University. The author would like to thank Dr. Richard Neifeld for helpful comments. I can be reached *via* <http://www.neifeld.com> or *via* telephone at 703-415-0012.

TABLE OF CONTENTS

Part I: Introduction:1

Part II: Historical Background of the FDA Statutory Framework.....3

 A: The Federal Food, Drug and Cosmetic Act (FDCA 1938).....3

 B: 1962 FDCA Amendments.....4

 C: 1962 FDCA New Drug Approval Process.....4

 D: Impact of the 1962 FDCA on Patent Law for Pharmaceuticals.....6

 E: Impact on Generic Drug Manufacturers.....7

 F: Roche Decision.....8

Part III: Summary of the Hatch-Waxman Act.....9

 A: Amendments to the Patent Statutes of 35 USC.....10

 B: Non-Patent Exclusivity.....12

 C: Generic ANDA Filing and FDA Approval Process.....14

 D: Paragraph IV Provisions.....16

 E: Hatch-Waxman and Generic Drug Manufacturers.....17

 F: ANDA Paragraph IV Certification Controversy.....17

Part IV: New Amendments to FDA Law.....20

 A: New Rule Changes in FDA Law.....20

 B: New Legislative Amendments to the Hatch-Waxman Act.....21

Part V: Conclusion.....24

APPENDIX: Statutes and Regulations cited.....

Part I: Introduction

Pharmaceutical drug approval and marketing is regulated by two huge independent regulatory systems: the patent system of the United States Patent and Trademark Office (USPTO) and the regulatory system of the Food and Drug Administration (FDA).² While the primary purpose of the patent system is to protect the intellectual property rights on the pharmaceutical drug, the core function of the drug regulatory system is to protect consumers from products that are unsafe, ineffective or fraudulently marketed.³ The patent holders in the drug and medical device sectors are required prior approval by the FDA in enforcing their intellectual property and marketing exclusivity rights.

For the pharmaceutical industry, patents are its lifeblood. While generating reward for its investment in research and development, patents afford monopoly rights for a limited time. Patents also help pharmaceutical companies to secure continued investment from investors. As such, pharmaceutical companies depend upon these intellectual property protections not only to spur investment in research and development of new drugs, but also to recuperate the cost of bringing the patented drug into market, including the cost of hundreds of pro-drugs that typically die during the clinical trial phases.⁴

The rising cost of prescription medicines, however, is of great concern especially to the ageing senior citizens and indigent population including those afflicted with rare diseases such as

² See, e.g., Rebecca Eisenberg, *Patents, Product Exclusivity, And Information Dissemination: How Law Directs Biopharmaceutical Research and Development*, 72 Fordham L. Rev. 477 (2003).

³ *Id.*

⁴ See, e.g., Bruce Kuhlik, *The Assault on Pharmaceutical Intellectual Property*, 71 U. Chi. L. Rev. 93 (2004).

Alzheimer's disease and HIV/AIDS.⁵ In view of the need to provide greater accessibility and affordability to brand name prescription drugs, Congress has enacted and amended legislation in the area of regulatory and patent laws related to pharmaceutical drugs. For example, the 1984 Drug Price Competition and Patent Term Restoration Act, commonly referred to as the "Hatch-Waxman Act"⁶ represents a major compromise between the competing interests of pioneer drug companies and the generic drug manufacturers that represented the general public interest.⁷ The Hatch-Waxman Act provided an expedited generic drug approval process by allowing generic drug manufacturers to file an abbreviated new drug application (ANDA) to produce low-cost generic alternates, while simultaneously granting pioneer drug manufacturers extension of their intellectual property rights on their drugs.⁸

Despite such success, the legal framework created by the Hatch-Waxman Act continues to raise controversy. There is ongoing debate among various stakeholders including the pharmaceutical research companies, generic manufacturers, the consumers, and Congress over how to optimize the drug regulatory and patent systems to balance various competing interests. Some leaders in the pharmaceutical industry have argued that the recent legislative developments beginning from the Hatch-Waxman Act have eroded the value and length of time for drug patent enforcement.⁹ The consumers, on the other hand, still decry the astronomically high drug prices

⁵ See, e.g., Brian Urevig *Hatch-Waxman-Thoughtful Planning Or Just Piling On: A Consideration of the Federal Trade Commission's Proposed Changes*, 4 Minn. Intell. Prop. Rev. 367 (2003).

⁶ Drug Price Competition and Patent Term Restoration Act of 1984 Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified as amended in 21 U.S.C. §355, 35 U.S.C. §156, 35 U.S.C. §271 (e)(1) (2000)). See end notes.

⁷ See, e.g., Janet A. Gongola, *Prescriptions for change: The Hatch-Waxman Act and New Legislation To Increase The Availability of Generic Drugs to Consumers*, 36 Ind. L. Rev. 787 (2003).

⁸ *Id.*

⁹ See, e.g., *supra*, Notes 1 and 2.

and call for more regulatory and legislative changes so that drugs continue to become more affordable.¹⁰ As a result of this tug-of-war, the landscape for drug patent enforcement continues to be redefined through changes in the FDA regulatory system.

This article reviews the historical and legislative background of the drug regulatory system, the Hatch-Waxman Act, and the recent amendments to this Act. Part II delves into the historical background of the FDA statutory framework. Part III summarizes the main provisions of the Hatch-Waxman Act. Part IV discusses the new rule changes in the FDA regulations and the recent amendments to the Hatch Waxman Act.

Part II: Historical Background of the FDA Statutory Framework

A: The Federal Food, Drug and Cosmetic Act (FDCA 1938): The FDCA passed in 1938 revised the 1906 drug law and created the modern FDA.¹¹ In light of the “Elixir Sulfanilamide” tragedy, the crux of the Act was to designate certain drugs as “new drugs”.¹² A new drug was defined as “[o]ne not generally recognized by experts as safe for use under the conditions prescribed, recommended or suggested in the labeling thereof.”¹³ In order for a new drug to be marketed it had to be the subject of an “effective” new drug application (NDA) under section 505(a).¹⁴ This new rule provided the agency with authority to review the safety of any “new drug” prior to it being introduced into commerce.¹⁵

¹⁰ See, e.g., Nora Flaherty “*Medicaid Preferred Drug Lists*”: *Florida as a Model For Analysis*, 11 Elder L. J. 77 (2003).

¹¹ See, FDCA §505 (codified as 21 U.S.C. § 355). See end notes.

¹² PETER B. HUTT & RICHARD A. MERRILL, *FOOD AND DRUG LAW* 476 (Foundation Press (2001), (1991).

¹³ *Id.* at 467.

¹⁴ *Id.*

¹⁵ *Id.*

B: 1962 FDCA Amendments: In 1962, Congress amended the 1938 Food, Drug, and Cosmetics Act (FDCA) rather hurriedly in the crisis atmosphere of another drug tragedy- the “Thalidomide Tragedy.”¹⁶ The new statute required the FDA to affirmatively determine that new agents have been demonstrated by “substantial evidence” to be effective and safe.¹⁷ The statute defines “substantial evidence” of effectiveness as “[e]vidence consisting of adequate and well controlled investigations...by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved...”¹⁸ The amendments also required FDA to review all NDAs and find that the drug is effective for its intended use.¹⁹

C: 1962 FDCA New Drug Approval Process: One major amendment of the 1962 Act was that it required pharmaceutical companies to conduct clinical trials on new drugs and submit the results to the FDA along with their NDAs.²⁰ In order for the drug to become approved, it had to pass the preclinical and three clinical trial phases. During the preclinical trial phase, the drug manufacturer must generate *in vitro* and animal data about the drug, including chemical structure, safety, efficacy, and toxicology of the drug so that the drug is sufficiently promising to study in humans.²¹ This stage lasts anywhere between one to four years.²²

Once the drug candidate passes the pre-clinical screening phase, it undergoes the investigational new drug ("IND") phase, which involves three clinical research trial phases.

¹⁶ *Id.* at 478. See, also Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 780 (1962).

¹⁷ Hutt & Merril, *supra*, Note 12, at 525, See also FDA §505(d).

¹⁸ *Id.*

¹⁹ *Id.*

²⁰ *Id.*

²¹ See, Hutt and Merrill, *supra*, Note 12 at 513. See, also Laura Giles, *Promoting General Drug Availability: Reforming the Hatch-Waxman Act to Prevent Unnecessary Delays to Consumers*, 75 St. Johns L. Rev. 357 (2001).

²² Hutt and Merrial, *supra*, Note 12 at 514.

These trials are conducted to determine human safety and efficacy of the new drug.²³ In phase I of the clinical trial, the clinical pharmacologist has the responsibility of administering the drug to a human for the first time. This phase is designed to determine the safety and side effects of the drug. Phase II of the clinical trial is designed to determine the effectiveness of the drug on patients with the specific disease, which the drug is designed to treat.²⁴ Phase II trials are typically conducted on a larger population of adults who have the specific medical condition to determine whether the drug has the desired therapeutic effect, the dose range, and whether there are any adverse side effects.²⁵ Lack of efficacy results in drug abandonment at this phase.²⁶

In Phase III trials, however, hundreds and even thousands of patients are investigated.²⁷ Phase III of the clinical trial is intended to gather additional information about the efficacy and safety of the drug that is necessary for evaluating the overall benefit-risk relationship of the drug. Typically, the three clinical research phase trials take between four to six years.²⁸ Upon culmination of Phase III trials, the company can file a New Drug Application ("NDA") with the FDA.²⁹ Generally, only one out of ten drug candidates will have sufficient merit to file an NDA.³⁰ The FDA scrutinizes the NDA extensively and decides whether the submitted data warrant marketing of the new drug. The FDA evaluation and approval process of the NDA

²³ Hutt and Merrill, *supra*, Note 12 at 516-519.

²⁴ *Id.*

²⁵ *Id.*

²⁶ *Id.*

²⁷ *Id.*

²⁸ *Id.* at 514.

²⁹ *Id.*

³⁰ *Id.*

could take anywhere between two to three years.³¹ Overall, the process beginning from the pre-clinical phase to FDA drug approval could take about seven to thirteen years.³²

D: Impact of the 1962 FDCA on Patent Law for Pharmaceuticals:

The 1962 amendments significantly impacted the patent law on pharmaceuticals. Under the current patent statutes, once the USPTO issues a patent, the term for exclusivity is 20 years from the date of filing.³³ Generally, most pharmaceutical companies file and receive their patents during the pre-clinical phase, and therefore, the patent clock starts ticking at this point.³⁴

However, the changes created by the 1962 amendments required the brand name company to undertake years of research and study to demonstrate the safety and efficacy that resulted in significant delay for a pioneer drug company to begin reaping benefits in the marketplace.³⁵ The Amendment effectively eroded the term of patent right exclusivity provided to pharmaceutical manufacturers while also increasing their research and development expenditure.³⁶ For example, a study concluded that for the period between 1966 to 1979, the patent enforcement and marketing period of a patent had declined from 13.6 to 9.5 years.³⁷

³¹ *Id.*

³² *Id.*

³³ 35 U.S.C. §156 (2000). It is interesting to note that prior to 1861, the patent term lasted only fourteen years. After 1861 the patent term lasted for 17 years until June 7, 1995 when it was changed to 20 years from date of filing. See, Alan D. Lourie, *Patent Term Restoration*, 66 J. Pat. & Trademark Off. Socy' 533 (1984).

³⁴ See, e.g., Gerald J. Mossinghoff, *Overview of the Hatch-Waxman Act and its Impact on the Drug Development Process*, 54 Food Drug L. J. 187 (1999).

³⁵ *Id.*

³⁶ Elizabeth Scotland Weiswasser & Scott D. Danzis, *The Hatch-Waxman Act: History, Structure, and Legacy*, 71 Antitrust L. J. 585 (2003).

³⁷ See, Alan D. Lourie, *supra*, Note 33.

Inevitably, this effect was borne out by the consumers who had to pay higher premiums for their drugs and thereby creating increased accessibility and affordability problems.³⁸

In light of the fact that the drug approval process runs in tandem with the patent clock, one could potentially maximize the term on the drug patent by using strategic filing methods. For example, a provisional application could be filed first once a potential drug candidate is found during the basic research or pre-clinical screening phase.³⁹ This filing delays the start of the nominal 20-year term while preserving the priority date. Also, depending on the circumstances one may file continuations and/or divisional applications of the parent application, while gaining priority to the earlier filed application(s).⁴⁰

E: Impact on Generic Drug Manufacturers: Besides impacting the pharmaceutical drug patent law, the new 1962 amendment also affected the entry of generic or “me-too” drug manufacturers.⁴¹ The 1962 amendments required generic pharmaceutical companies seeking to sell copies of pioneer drugs to perform the same studies to show the safety and efficacy of the generic products.⁴² The FDCA required that companies selling generic post-1962 drugs through

³⁸ See, e.g., Joseph P. Reid, *A Generic Drug Price Scandal: Too Bitter A Pill For the Drug Price Competition and Patent Term Restoration Act to Swallow?* 75 Notre Dame L. Rev. 309, 330-31 & n. 126 (1999).

³⁹ Generally large applications with many claims may slow down the examination at the USPTO and this delay may be cured by successful patent term appeals (PTA).

⁴⁰ It should be noted that the Federal Circuit recently held that restriction imposed by a patent examiner upon a patent application disclosing and claiming certain compounds, methods, and compositions, requiring applicant to elect either compound claims or method and composition claims, did not carry over to continuation application, for purpose of plaintiffs' claim protection from a double patenting defense. See *Bristol Myers Squibb Co. & Research Corp Technologies v. Pharmachemie B.V.* 361 F.3d 1343 (Fed. Cir. 2004), (70 U.S.P.Q.2d 1097 (2004)).

⁴¹ Hutt & Merrill, *supra*, Note 12 at 478.

⁴² See, e.g., Alfred B. Engelberg, *Special Patent Provisions for Pharmaceuticals: Have they Outlived Their Usefulness?* 39 IDEA 389, 396-97 (1999); See also U.S. FOOD AND DRUG ADMINISTRATION, THE EVOLUTION OF US DRUG LAW, available at <http://www.fda.gov/fdac/special/newdrug/benlaw.html>

the “ANDA” route, could not begin the FDA approval process for their generic pharmaceuticals until after the brand name patent had expired.⁴³

However, at the end of the 1970s, the FDA adopted a policy to approve an “ANDA” for any generic version of a pre-1962 pioneer drug that had been found effective under the Drug Efficacy Study Implementation (DESI) program.⁴⁴ Also, in 1980, the FDA allowed generic manufacturers to file a “paper” NDA of approved either pre-1962 or post-1962 drug.⁴⁵ The “paper” NDA was based solely on published scientific or medical literature that demonstrated that the chemical compound was safe thereby avoiding full studies on safety and efficacy.⁴⁶ However, because of scant and inadequate literature on most post-1962 drugs, the new FDA policy applied only to a handful of post-1962 drugs. As a result of the higher regulatory standard, lengthy time, inadequate scientific literature of drug data, and huge expenses involved, very few generic drugs appeared on the market. Therefore, this situation restricted generics access to the drug market allowing the pioneering drug pharmaceutical industry to enjoy greater monopoly on their drug prices.⁴⁷

F: Roche Decision: The conflict between the pioneering and generic pharmaceutical industry came to a head in Roche Products, Inc. v. Bolar Pharmaceutical Co., Inc.⁴⁸ Bolar applied to the FDA for a generic version of the Roche’s patented sleeping drug Dolamine prior to the expiry of

⁴³ *Id.*

⁴⁴ Hutt & Merrill, *supra*, Note 12, at 484-486

⁴⁵ *Id.*

⁴⁶ *Id.* See, also 21 U.S.C. §355 b (2).

⁴⁷ See, e.g., Jian Xiao, *Carving Out a Biotechnology Research Tool Exception to the Safe Harbor Provision of 35 USC§ 271 (e) (1)*, 12 Tex. Intell. Prop. L. J. 23 (2003).

⁴⁸ Roche Products, Inc. v. Bolar Pharmaceuticals Co. Inc. 733 F.2d 858, 221 U.S.P.Q.2d (BNA) 937 (Fed. Cir.1984).

the patent.⁴⁹ Bolar then began to perform bioequivalency studies on Roche's patented drug during the last six months of the patent term.⁵⁰ In response, Roche sued Bolar for patent infringement. The district court held that the use of Roche's patented drug fell under the experimental use exception doctrine under §102 (b).⁵¹

On appeal, the Federal Circuit acknowledged two significant distortions in patent law as a result of the new 1962 FDA regulation.⁵² First, the court noted that the regulatory approval process at the FDA reduced the effective term of a patent.⁵³ Second, the court noted Bolar's argument that pioneer drug manufacturers enjoyed a greater time period of monopoly by preventing generic drug manufacturers from using their patented drugs for testing purposes until after the patent had expired.⁵⁴ Notwithstanding these important policy considerations, the Federal Circuit reversed the district court's decision, and held that Bolar's use of Roche's patented drug for testing purposes constituted patent infringement under existing law.⁵⁵

Part III: Summary of the Hatch-Waxman Act

In response to the lobbying efforts of pioneer and generic drug manufacturers following the Roche decision, Congress enacted the Drug Price Competition and Patent Term Restoration Act of 1984, popularly known as the Hatch-Waxman Act, (named after Congressman Henry Waxman and Senator Orin Hatch) in an attempt to control the escalating drug prices and create a compromise between the conflicting interests of pioneer drug developers and generic drug

⁴⁹ See, *Id.* at 860.

⁵⁰ *Id.*

⁵¹ Roche Products, Inc. v. Bolar Pharmaceuticals Co. Inc. 572 F. Supp 255, 256 (E.D.N.Y 1983).

⁵² 733 F.2d at 863-865.

⁵³ *Id.* at 864.

⁵⁴ *Id.*

⁵⁵ *Id.* at 863, 867.

manufacturers.⁵⁶ The Act balances two policy objectives: It simplifies and expedites the market entry of generic versions, while providing pioneering drug manufacturers with increased lengths of market exclusivity to compensate them for the patent exclusion time lost while their drugs were undergoing regulatory approval at the FDA.⁵⁷

A: Amendments to Patent Statutes of 35 U.S.C. : With respect to pharmaceuticals, the Hatch-Waxman Act contains two titles. Title I of the Act modifies the FDCA and carves out a provision for generic drug manufacturers.⁵⁸ Title II covers the provision regarding patent term extension and safe harbor provision.⁵⁹ Title I enabled generic drug manufacturers to file an "Abbreviated New Drug Application" ("ANDA"), whereby generic drug firms could introduce copies of pioneer drugs to the marketplace without repeating expensive and lengthy clinical trials.⁶⁰ The ANDA process enabled generic manufacturers simply to show that their drugs were the "same" as and "bioequivalent" to the Orange Book⁶¹ listed patented drug.⁶² The "sameness" requirement provides that the active ingredient, route of administration, dosage form, strength, and labeling must all be the same as the pioneer drug product.⁶³

⁵⁶ See, Drug Price Competition and Patent Term Restoration Act of 1984, *supra*, Note 6. See, also Weiswasser & Danzis, *supra*, Note 36.

⁵⁷ See, e.g., Mossinghoff, *supra*, Note 34.

⁵⁸ Title I was codified into 21 U.S.C. §355. See end notes.

⁵⁹ Title II was codified into 35 U.S.C. §§ 156 & 271 (e) (1). See end notes 37 C.F.R. §§ 1.710-1.791.

⁶⁰ 21 U.S.C. §355 (j) (2) (A); 21 CFR §314.94(a) (5).

⁶¹ FDA, Orange Book available at <http://www.fda.gov/cder/ob/obfaqs.htm>. The "Orange Book" is an annual FDA publication that lists drug products with related information that have been approved for safety and efficacy. See discussion in text *infra*.

⁶² See, 21 U.S.C. §355 (j) (2) (A); 21 CFR §314.94(a) (5).

⁶³ *Id.* "Active ingredient" refers to the "Active ingredient in the finished drug product prior to its administration" 54 Fed. Reg. 28,881 (July 10, 1989).

The patent term extension and restoration provision of Title II of the Act, codified in 35 U.S.C. §156, arose out of Congress's recognition that the FDA pre-market approval requirements reduced the effective patent term of pioneer drugs, and therefore, provides additional marketing exclusivity to make up for the lost time.⁶⁴ The Act established five eligibility requirements for patent term restoration: (1) the patent term must not yet have expired; (2) the patent term must not have previously been extended; (3) a patent extension application must be submitted; (4) the product claimed by the patent and/or the product whose use is claimed by the patent must have been subject to a regulatory review period prior to commercial marketing or use; and (5) the particular commercial marketing or use must be the first such marketing or use of the product.⁶⁵

Importantly, the Act amended 35 U.S.C. in part by extending a patent term for the length of the "regulatory review period" subject to three important limitations. The regulatory review period is defined as half of the IND-phase (*i.e.*, half of human clinical trial study) period, plus the whole period during NDA review by the FDA.⁶⁶ These three limitations are as follows. First, the maximum extension for the delay during the regulatory review process cannot exceed five years (one exception to this rule is that if a "pipeline" drug, whose regulatory review period spans the enactment date of the legislation, this limitation is two years).⁶⁷ (It should be noted here that this extension is separate and distinct from the adjustment of the patent term granted due to the USPTO's delay in processing the application).⁶⁸ Second, the total effective patent life, *i.e.*, from the date of the pioneer *NDA approval* to the end of the enforceable term of the patent, with the

⁶⁴ See, H.R. Report No. 98-857, pt. 1 at 15 and pt .2, at 5-6 (1984). See also Xiao, *Supra*, Note 46.

⁶⁵ 35 U.S.C. §156 (a).

⁶⁶ *Id.* See Hutt & Merrill, *supra*, Note 12 at 574. Thus, if the IND time is 6 years and the NDA time is 2 years, the regulatory review period would be five years ($\frac{1}{2} * 6 + 2$).

⁶⁷ *Id.*

⁶⁸ See, 35 U.S.C. §154 (b).

addition of the extended patent term obtained from the above rules, may not exceed a total of fourteen years.⁶⁹ Third, the regulatory review time is subject to a reduction if the industry fails to exercise “due diligence” to gain FDA approval of the NDA.⁷⁰ Moreover, in order to benefit from the patent term extension provisions of the Act, the patent holder must submit an application to the USPTO within sixty days of approval of the NDA.⁷¹ Since that application is burdensome, the evidence necessary to support it should be prepared in anticipation of grant of NDA.⁷² The principal benefit of these non-patent-based exclusivity provisions was to ensure that the research based pharmaceutical company gained some valuable patent life that was lost during the FDA drug approval process.

B: Non-Patent Exclusivity: Apart from the patent term restoration, the Act amended FDCA to provide further market exclusivity periods for certain innovative drugs. For example, the patent holder of an approved NDA is entitled to 5 years of exclusivity for NCEs (new chemical entities) if “no active ingredient, (including any ester or salt of the active ingredient) [of the drug] has been approved in any other application.”⁷³ For purposes of the five-year exclusivity, the FDA defines a “NCE” to mean “a drug that contains no active moieties that has been approved by the FDA in any other application.”⁷⁴ Thus ANDA for post-enactment NCE drugs cannot be submitted or accepted by the FDA for five years following the date of approval of the pioneer’s NDA.⁷⁵

⁶⁹ *Id.*

⁷⁰ *Id.*

⁷¹ *Id.*

⁷² See, 37 C.F.R. §1.710.

⁷³ 21 U.S.C. §355 (c) (3) (D) (ii), j (5) (D) (ii). See also Weiswasser and Danzis, *supra*, Note 36.

⁷⁴ 21 C.F.R. §314.108 (a).

⁷⁵ See, Hutt & Merril, *supra*, Note 12 at 573.

Moreover, a NDA that does not contain a NCE but which “contains reports of new clinical investigations, other than bioavailability studies essential to the approval of the application and conducted or sponsored by the applicant” is entitled to three years of exclusivity from the approval date.⁷⁶ These exclusivity periods are independent of patent term restoration and run in tandem with any remaining patent life beginning on the date of marketing approval.

Another advantage to pioneer drug companies that the Act provides is that it allows pioneer companies to tack an additional six months onto their patent term in exchange for testing their drugs in the pediatric population, so-called “pediatric exclusivity”.⁷⁷ The FDA forbids approval of generic version of the drug during this six-month period.

Concurrent with the Hatch-Waxman Act, Congress amended the “Orphan Drug Act” in 1985 to provide a seven-year market exclusivity and tax credits to the pioneer drug manufacturer if their drug met the “orphan drug” status.⁷⁸ Orphan drugs are defined as those that are intended to treat “rare diseases or condition” such as lupus.⁷⁹ Furthermore, this status is attributed to a drug that treats a disease that afflicts fewer than 200,000 people in the United States.⁸⁰ This benefit was intended to encourage research and development of new life saving drugs that are less lucrative unlike some “blockbuster” drugs in the market.⁸¹

⁷⁶ 21 U.S.C. §355 (c) (3) (D) (iii), j (5) (D) (iii). See also Hutt & Merrill, *supra*, Note 12 at 573.

⁷⁷ 21 U.S.C. 355 (a) (2000). See also Thomas Parker & Amy Manning, *Best Pharmaceuticals for Children Act is Now Law*, Nat'l L. J., Apr. 15, 2002 at C8.

⁷⁸ 21 U.S.C. §360 (c) (2000).

⁷⁹ See, Hutt & Merrill, *supra*, Note 12 at 566.

⁸⁰ William E. Holtz, *Reassessing Hatch-Waxman Incentives*, Update Mag. (Federal Food and Drug Law Institute, Washington, D.C.) Mar. 2001, at 47-48.

⁸¹ *Id.*

Moreover, the safe harbor provision of Title II of the Hatch-Waxman Act is encoded in 35 U.S.C. §271 (e)(1). Through the enactment of the safe harbor provision, Congress overruled the Roche holding that a generic drug developer's use of a patented drug for the FDA approval process constituted patent infringement.⁸² Section 271 (e)(1) states in part that it shall not be an act of infringement to use a patented invention solely for uses reasonably related to the development and submission of information under a federal law which regulates the manufacture, use, or sale of drugs.⁸³ Thus, Congress enacted this provision hoping that less expensive generic equivalents of brand name drugs become available as soon as possible after the expiry date of the patent.⁸⁴

C: Generic ANDA Filing and FDA Approval Process: Realizing the importance of timing for bringing generic versions of the patented drug, Congress created the abbreviated new drug application (ANDA) process in the Hatch-Waxman Act and permitted the use of patented drugs for regulatory approval of generic version of the patented drugs.⁸⁵ The listing of patents in the FDA “Orange Book” provides the basis on which pioneer drug company protect and enforce their patent rights prior to generic approval and market entry. The “Orange Book” is an annual publication of the FDA, which contains a list of: (1) Approved prescription drugs; (2) approved over the counter (OTC) drugs (3) biologics; and (4) products that were approved but were

⁸² See H.R. Rep No. 98-857, pt. 2, at 27 (1984) (stating that ‘[t]he provision of 271 (e)(1) have the net effect of reversing the holding of the court in[Roche]’)

⁸³ See, 35 U.S.C. §271 (e)(1).

⁸⁴ See, Courtenay C. Brincherhoff, *Can the Safe Harbor of 35 USC 271 (e) (1) Shelter Pioneer Drug Manufacturers?* 35 Food Drug L. J. 643, 645 (1998).

⁸⁵ See, e.g., Colman B. Ragan, *Saving the Lives of Drugs: Why Procedural Amendments in Hatch – Waxman Litigation and Certification of Markman Hearings For Interlocutory Appeal Will Help Lower Drug Prices*, 13 Fed. Circuit B. J. 411 (2003-2004).

revoked.⁸⁶ Hence, under the Act, an ANDA filer seeking to market a generic copy of a pioneer drug must "certify" pursuant to 21 U.S.C. §355(j) by any of Paragraph 1-IV route, to each patent listed in the Orange Book for that drug by the approved NDA holder that the conditions stipulated in any of the Paragraph 1-IV route is met.⁸⁷ In addition to demonstrating that the generic drug product has the same active ingredient, route of administration, dosage form and strength, and proposed labeling as the brand-name drug, the ANDA also must contain sufficient information to demonstrate that the generic drug is "bioequivalent" to the relevant brand-name product.⁸⁸

Specifically, under the statute, a generic applicant is required to provide one of the four certifications for each patent listed in the Orange Book for the innovator product:⁸⁹

(I) Paragraph I: that there are no patents listed in the Orange Book for the drug;

(II) Paragraph II: that the relevant patents have expired;

(III) Paragraph III: that the generic manufacturer will not seek approval of the ANDA until after expiration of the relevant patent; or

(IV) Paragraph IV: that such a patent is invalid or will not be infringed by the manufacture, use, or sale of the new generic drug for which the ANDA is submitted.

The first three certifications do not involve challenge to existing patents, and so they do not typically raise any patent disputes. Thus, if there are no patents listed in the Orange Book, if the patent have expired, or if the generic manufacturer plans to market its product only after

⁸⁶ FDA, Orange Book *available at* <http://www.fda.gov/cder/ob/obfaqs.htm>

⁸⁷ 21 U.S.C. §355 (j) (2) (A) (i) (explaining that the application and approval process for abbreviated new drug applications).

⁸⁸ 21 U.S.C. §355 (j) (2) (A) (ii). See, also 21 C.F.R. §314.94.

⁸⁹ See, 21 U.S.C. §355 (j) (2) (A) (vii) (I) through (IV) (2000). Also, 21 C.F.R. §314.94 (a)(12). See end notes.

expiration of the relevant patents, then the generic drug manufacturer can produce and market the generic copies after satisfying the FDA requirements.

D: Paragraph IV Provisions: In contrast, however, the fourth certification, “Paragraph IV” certification route, applies when the generic drug manufacturer claims either that the patent is invalid or that its product does not infringe the unexpired patent. Filing an ANDA under paragraph IV certification route is a *de jure* act of infringement under 35 U.S.C. §271 and gives rise to case or controversy, which is a requirement for filing an infringement suit.⁹⁰ This provision triggers a number of additional provisions of the Act and typically results in litigation between the pioneer and generic drug manufacturer. When an ANDA contains a paragraph IV certification, the applicant is required to provide notice to the FDA and the patent holders, including a detailed statement of the factual and legal basis for the ANDA filer's assertion that the patent is invalid or will not be infringed.⁹¹

Procedurally, the Act provides that if the patent holder files a lawsuit for patent infringement within 45 days of the notice, the FDA automatically stays approval of the ANDA for thirty months.⁹² Once this occurs, FDA approval of the generic drug is stayed until "the earliest of: (1) the date the patent(s) expire; (2) a final determination of non-infringement or patent invalidity by a court in the patent litigation; or (3) the expiration of 30 months from the receipt of notice of the paragraph IV certification."⁹³ If the branded manufacturer fails to file suit within this 45 day time period, the FDA can approve the generic manufacturer's ANDA.

⁹⁰ 35 U.S.C. §271 (e)(2).

⁹¹ 21 U.S.C. §355 (j) (2) (B) (i) (2000).

⁹² 21 U.S.C. §355 (j) (5) (B) (iii) (2003).

⁹³ See, e.g., Federal Trade Commission, *Generic Drug Entry Prior to Patent Expiration: An FTC Study*.

Available at <http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf>

Additionally, the Act provides that the first generic applicant who files an ANDA with the FDA is eligible for 180 days of marketing exclusivity, during which time the FDA is not allowed to approve any other ANDAs for the same pharmaceutical drug.⁹⁴ The 180 days of exclusivity was intended for the ANDA filer to recover the expense of patent litigation.⁹⁵

E: Hatch-Waxman and Generic Manufacturers: In effect, the Hatch-Waxman amendments created the modern generic drug industry.⁹⁶ One of the underlying themes of the Act was that competition would ultimately lead to lowering of the drug prices. As a result of the Act, generic manufacturers can avoid the huge costs associated with developing a new drug. For example, the cost of bringing a generic drug to market costs only about \$1 million, as opposed to about \$800 million typically involved in bringing a new brand name drug to market.⁹⁷ As a result of the Act, the generic prescriptions now comprise over 47% of the total prescriptions.⁹⁸ Thus, since the Act's passage, generic drug companies have mushroomed and flourished thereby increasing consumer access to affordable generic drugs.

E: ANDA Paragraph IV Certification Controversy: The ANDA certification process and paragraph IV certification in particular has become controversial in recent years.⁹⁹ The USPTO requires that the disclosure is novel, non-obvious and useful before it issues the patent.¹⁰⁰ However, the FDA which traditionally only required safety and efficacy evaluations, now essentially opens the door to challenge existing drug patents on grounds of validity and non-

⁹⁴ 21 U.S.C. §355 (j) (5) (B) (iv) 2000.

⁹⁵ See, e.g., Weiswasser & Danzis, *Supra*, Note 36.

⁹⁶ *Id.*

⁹⁷ See, e.g., Laura Robinson, *Analysis of Recent Proposals to Reconfigure Hatch-Waxman*, 11 J. Intell. Prop. L. 47 (2003).

⁹⁸ *Id.*

⁹⁹ See, e.g., James Gongola, *supra*, Note 7.

¹⁰⁰ See, e.g., 35 U.S.C. §§101,102 & 103.

infringement placing the burden on the judiciary to resolve the patent disputes. This provision has inadvertently created a patent litigation “cottage industry”, with generics exploiting the exclusivity grants as a revenue source.¹⁰¹ Because of the lucrative drug market and the possibility to get 180-days of marketing exclusivity, generic manufacturers are inclined to file an ANDA for patented drugs in hopes that they can later prevail in the ensuing litigation.

The Federal Trade Commission (FTC) study found that for a period between 1992 and 2000, 104 NDAs were the subject of paragraph IV certification patent challenges.¹⁰² While some challenges have been legitimate and resulted in success for the generic company as for Barr Labs against Eli Lilly’s in the Prozac[®] (fluoxetine hydrochloride) case, others have been unsuccessful.¹⁰³ Of the patent challenges brought to court and decided as of June 1, 2002, the patent was determined to be invalid in 11 cases, not infringed in 14 cases, while twenty cases settled out of court.¹⁰⁴ While the FTC study indicates the generic’s high success rate, these numbers also raise questions as to whether the USPTO has lowered the patentability bar for pharmaceutical drug patents.

There is also a growing concern that the very rules that increased competition may have increased incentive for brand-name and generic manufacturers to engage in collusive anti-competitive tactics.¹⁰⁵ Besides the 180-month exclusivity, one particularly controversial provision under the Hatch-Waxman Act is the automatic 30-month stay, which is vulnerable to strategies by brand-name manufacturers to prolong this stay with anticompetitive effects.¹⁰⁶ The 30-month stay of FDA approval of the generic drug is granted upon a brand-name company bringing a patent infringement suit within 45 days of receiving notice of the generic’s ANDA

¹⁰¹ See, e.g., Alison Young & Meredith Smith Andrus, *Pharmaceutical Pricing and Hatch-Waxman Reform: The Right Prescription*, J. Gen. Med. 1, 228-237 (2004).

filing at the FDA.¹⁰⁷ The stay was designed to allow time to resolve all patent disputes and infringement issues prior to the generic manufacturer entering the market.¹⁰⁸

The FTC study has identified that brand name manufacturers have been able to exploit loopholes in the 30-month stay provision of the Act. Under the Act, the pioneer manufacturer can list additional patents for the same brand-name drug in the Orange Book even after a generic company has already filed an ANDA. The effect of the later listings is that the generic applicant is required submit a new paragraph IV certification (*i.e.*, repeat the ANDA process) for the later listed patents. If the brand-name company sues for this ANDA re-certification within the 45 days, then another 30-month stay is triggered for the same drug. Some pharmaceutical companies have flagrantly exploited this loophole. For example, Smith Kline obtained five lengths of stays (total 65 months) against Aptoex, a generic manufacturer seeking to manufacturer the generic version of the anti-depressant medication Paxil®.¹⁰⁹ Thus, this “patent ever-greening”¹¹⁰ strategy may have anticompetitive effects to the generic’s entry into the

¹⁰² See, FTC study, *supra*, Note 90.

¹⁰³ Maureen Rouhi, *Beyond Hatch-Waxman* 80, 53-59 Chem. & Eng. News. September 2002.

¹⁰⁴ FTC study, *supra* Note

¹⁰⁵ See, e.g., Julia Rosenthal, *Hatch- Waxman Use or Abuse? Collusive Settlements between Brand-Name and Generic Drug Manufacturers*, 17 Berkeley Tech L. J. 317 (2002).

¹⁰⁶ See, Melissa K. Davis, *Monopolistic Tendencies of Brand-Name Drug Companies in the Pharmaceutical Industry*, 15 J.L. & Com. 357, 365 (1995).

¹⁰⁷ 21 U.S.C. §355 (j)(5)(B)(iii)(2000).

¹⁰⁸ See, Weiswasser & Danzis, *supra* , Note 36.

¹⁰⁹ See, e.g., Sarah E. Eurek, *Hatch-Waxman Reform and Accelerated Market Entry of Generic Drugs: Is Faster Necessarily Better?* Duke L & Tech Rev. 18 (2003).

¹¹⁰ See, e.g., Pamela Bertani, *Evergreening Patents*, available at <http://www.wientraub.com/12-10-04%20PWB.pdf>. Also, see e.g., Robert Schulman, *A review of Significant Federal Circuit Decisions Affecting Chemical, Pharmaceutical and Biotech Inventions*, 16 No. 3 J. Proprietary Rts. 1(2004).

market, which has since raised eyebrows in Congress and elicited further proposals for reforming the Hatch-Waxman Act.

Part IV: New Amendments to FDA Law

A: New Rule Changes in FDA Law: In response to the FTC study and recommendations to tighten the loopholes in the Hatch-Waxman Act, the FDA proposed new regulations that would alter the delicate compromise that Hatch-Waxman sought to achieve between pharmaceutical companies and their generic competitors.¹¹¹ These new FDA rules were finalized in June 2003.

The new FDA regulations make two major changes to Hatch-Waxman Act. These changes were recommended by the FTC study.¹¹² First, they clarify the types of patents that are to be listed in the Orange Book in an attempt to curtail frivolous, attenuated or tangential patents.¹¹³ The regulation clearly outlines what types of patents are appropriate for Orange Book listing. Such patents consist of patents that claim the drug product (formulation and composition), product by process patents, and patents that claim a method of use.¹¹⁴ Process patents, patents claiming packaging, patents claiming metabolites, and patents claiming intermediates are not covered by this section and information on these patents may not be submitted to the FDA.¹¹⁵ The new rules also require the person submitting an NDA, an amendment to the NDA, or an NDA supplement to submit a signed declaration as part of its

¹¹¹ See, e.g., Robinson, *Supra*, Note 94.

¹¹² *Id.* See, also FTC study *supra* Note 90. See <http://www.fda.gov/OHRMS/DOCKETS/98fr/PATENT.pdf>

¹¹³ Applications for FDA Approval to Market a New Drug: Patent Listing Requirements and Application of 30-Month Stays on Approval of Abbreviated New Drug Applications Certifying That a Patent Claiming a Drug is Invalid or Will Not be Infringed, 67 Fed. Reg. 65448 (proposed Oct. 24, 2002) (to be codified as 21 C.F.R. pt. 314.)

¹¹⁴ *Id.*

¹¹⁵ 21 C.F.R. §314.53 (b)(2002). See <http://www.fda.gov/OHRMS/DOCKETS/98fr/PATENT.pdf>

submission of patent information, if the patent covers the drug's formulation, composition, and/or method of use.¹¹⁶ Among other things, the new rules include a claim-by-claim declaration requirement.¹¹⁷

Second, the new FDA regulation limits pharmaceutical companies to only one thirty-month stay.¹¹⁸ Specifically, the new rule re-interprets 21 U.S.C. §355 (b)(3)(C), which says in part that if an ANDA application is amended to include a paragraph IV certification, then notice to the NDA holder or patent owner is required.¹¹⁹ Under the new rule, any amendment to that ANDA application to include additional paragraph IV certifications (to later listed patents) would not require notice to the NDA holder because the original application was not amended to include a paragraph IV certification; it had included one all along.¹²⁰

B: New Legislative Amendments to the Hatch-Waxman Act

While the FDA regulation tweaked some of the existing problems of the Hatch-Waxman Act, some House representatives proposed further legislative changes to the Act by introducing bills such as the Greater Access to Affordable Pharmaceuticals (GAAP) in Congress.¹²¹ In response, Congress recently enacted and the president signed into law on December 8, 2003, the

¹¹⁶ 21 C.F.R. §314.53 (c)(2)(i)(2002). See <http://www.fda.gov/OHRMS/DOCKETS/98fr/PATENT.pdf>

¹¹⁷ *Id.*

¹¹⁸ 21 C.F.R. §314 (2002).

¹¹⁹ *Id.* See, 21 U.S.C. §355 (b)(3)(C)

¹²⁰ *Id.*

¹²¹ The Greater Access to Affordable Pharmaceuticals Act, S. 812, 107th Cong. (2002); The Greater Access to affordable Pharmaceuticals Act S. 54, 108th Cong. (2003).

Medicare Prescription Drug Improvement and Modernization Act, which also implements important changes clarifications to the Hatch-Waxman Act.¹²²

One of the major changes under the new law is that only one 30-month stay per ANDA is allowed as codified under 21 U.S.C. §355 (j)(2) and (5).¹²³ Before, if additional patents were added to the Orange Book after an applicant filed an ANDA, that applicant would need to make a new paragraph IV certification and the NDA holder or patent owner could then file a second patent infringement action which would automatically result in a new 30-month stay of approval. The Act also clarifies that it is the district court's decision, rather than the appeals court decision that suffices to end the thirty-month stay.¹²⁴ This new rule will eliminate any incentives for patent holders to prolong the 30-month stay by listing additional patents in the Orange Book to obtain successive 30-month stays.

Additionally, a new provision under 21 U.S.C. §355 (j) (2) (B) (ii), of the Hatch-Waxman Act amendments requires an ANDA applicant that makes the certification to give notice of its application to the NDA holder and the patent holder within 20 days of receiving notice from the FDA that its application has been filed, whereas previously the law was silent as to when the notice could be given.¹²⁵ Further, under the amendments to 21 U.S.C. §355 (j) (5) (C) (i), (also codified as amended at 35 USC 271 (e) (5)), an ANDA applicant may bring a declaratory judgment action against an NDA holder if the NDA holder does not institute a patent

¹²² See, Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MPDIMA) § 1101-04.. Pub L No. 108-173, 117 Stat 2066. See, also Micahel Padden & Thomas Jenkins, *Hatch-Waxman Changes*, Nat'l L. J., Feb. 23, 2004. See, also Weiswasser and Danzis, *Supra*, Note 36.

¹²³ *Id.* This was the recommendation made by the FTC study. See end notes 21 U.S.C. § 355 J (2) and (5).

¹²⁴ *Id.*

¹²⁵ *Id.* MPDIMA 1101 (a) (1) (B) (ii). See, e.g., Barry Marenberg, *Changes to the Hatch-Waxman Act Following the "Medicare Prescription Drug, Improvement and Modernization Act of 2003"* 23 *Biotechnology L. Rep.* 277 (2004). See, 21 U.S.C. §355 (j) (2) (B) (ii).

infringement lawsuit within the required 45-day time period.¹²⁶ Before, if the NDA holder did not file suit the generic would have to complete its ANDA approval and market the generic drug before a district court would determine that the product infringed the patented drug.¹²⁷ The declaratory judgment affords the generic manufacturer to obtain legal certainty while seeking FDA approval, thereby avoiding the risk of selling a potentially infringing product.¹²⁸

Moreover, under 21 U.S.C. §355 (j) (5) (C) (ii), an ANDA applicant can assert a counterclaim seeking an order requiring the NDA holder “to correct or delete” patents listed in the Orange Book, on the grounds that the patent does not claim the approved drug or an approved method of using the drug.¹²⁹ This counterclaim can be asserted only when the ANDA applicant has been sued for infringement and does not provide an independent cause of action. This provision will simplify and expedite the resolution of the Paragraph IV litigation process.

Another important amendment to 21 U.S.C. §355 (j) (5) (B) (iv) clarifies that the 180-day exclusivity period does not begin until the date of first commercial marketing.¹³⁰ The amendment also stipulates that the exclusivity period begins upon the applicant’s marketing of either the NDA product or the ANDA product.¹³¹ However, under the “Forfeiture” clause codified in 21 U.S.C. §355 (j) (5) (D) & (I), a “First Applicant” may forfeit its 180-day exclusivity if it fails to market its product within 75 days after it receives FDA approval or 30 months after ANDA submission whichever is earlier; or 75 days after a non-appealed favorable

¹²⁶ See, MPDIMA §1101. See, 21 U.S.C. §355 (j) (5) (C) (i)

¹²⁷ MPDIMA §1101 (d).

¹²⁸ *Id.*

¹²⁹ MPDIMA §1101 (a) 2) (C). See, 21 U.S.C. §355 (j) (5) (C) (ii)

¹³⁰ See, MPDIMA §1102 (a). See, 21 U.S.C. §355 (j) (5) (B) (iv)

¹³¹ *Id.* The subtleties take care of the situation where a first applicant agrees to market the brand-name product instead of its own generic product.

district court or favorable Federal Circuit court decision has been rendered; or 75 days after a favorable settlement has been entered; or 75 days after the patent expires or is withdrawn.¹³²

Previously, the law was silent in this issue. The new law appears to be favorable to the generic manufacturer because it allows the generic manufacturers to only begin manufacturing after obtaining a favorable ruling without having to sacrifice part of its exclusivity period. In sum, the new law refines and irons out some of the loopholes and ambiguities of the Hatch-Waxman Act, tilting the balance in favor of the generic drug manufacturers.

Part V: Conclusion:

The interface between the pharmaceutical drug patent and FDA regulatory systems has emerged as a contentious area where reforms and legislative changes continuously redefine the legal contours. It is widely accepted among the public, industry leaders, and politicians that the Hatch-Waxman Act has generally achieved the dual goal of greatly expanding consumer access to low-cost generic pharmaceutical drugs and providing incentives to pioneer pharmaceutical drug manufacturers to continue producing innovative drugs. Nonetheless, public policy enacted through the Hatch-Waxman Act, FDA legislation, and the recent amendments appear to compromise the patent laws as calculated mechanisms to balance new policy issues. In light of the ANDA certifications especially Paragraph IV provisions, and the new FDA regulations, it also appears that the FDA is increasing its authority in the area of intellectual property rights and patent enforcement of pharmaceutical drugs. In conclusion, it is likely that as new issues surface, the intersection of pharmaceutical drug regulatory and patent laws will continue to evolve in order to strike further compromises for the major stakeholders.

¹³² *Id.*

APPENDIX: STATUTES AND REGULATIONS CITED

Title II of the Hatch Waxman Act: 35 U.S.C.A. § 156

35 U.S.C.A. § 156

(a) The term of a patent which claims a product, a method of using a product, or a method of manufacturing a product shall be extended in accordance with this section from the original expiration date of the patent, which shall include any patent term adjustment granted under [section 154\(b\)](#), if--

(1) the term of the patent has not expired before an application is submitted under subsection (d)(1) for its extension;

(2) the term of the patent has never been extended under subsection (e)(1) of this section;

(3) an application for extension is submitted by the owner of record of the patent or its agent and in accordance with the requirements of paragraphs (1) through (4) of subsection (d);

(4) the product has been subject to a regulatory review period before its commercial marketing or use;

(5)(A) except as provided in subparagraph (B) or (C), the permission for the commercial marketing or use of the product after such regulatory review period is the first permitted commercial marketing or use of the product under the provision of law under which such regulatory review period occurred;

(B) in the case of a patent which claims a method of manufacturing the product which primarily uses recombinant DNA technology in the manufacture of the product, the permission for the commercial marketing or use of the product after such regulatory review period is the first permitted commercial marketing or use of a product manufactured under the process claimed in the patent; or

(C) for purposes of subparagraph (A), in the case of a patent which--

(i) claims a new animal drug or a veterinary biological product which (I) is not covered by the claims in any other patent which has been extended, and (II) has received permission for the commercial marketing or use in non-food-producing animals and in food-producing animals, and

(ii) was not extended on the basis of the regulatory review period for use in non-food-producing animals,

the permission for the commercial marketing or use of the drug or product after the regulatory review period for use in food-producing animals is the first permitted commercial marketing or use of the drug or product for administration to a food-producing animal.

The product referred to in paragraphs (4) and (5) is hereinafter in this section referred to as the "approved product".

(c) The term of a patent eligible for extension under subsection (a) shall be extended by the time equal to the regulatory review period for the approved product which period occurs after the date the patent is issued, except that--

(1) each period of the regulatory review period shall be reduced by any period determined under subsection (d)(2)(B) during which the applicant for the patent extension did not act with due diligence during such period of the regulatory review period;

(2) after any reduction required by paragraph (1), the period of extension shall include only one-half of the time remaining in the periods described in paragraphs (1)(B)(i), (2)(B)(i), (3)(B)(i), (4)(B)(i), and

(5)(B)(i) of subsection (g);

(3) if the period remaining in the term of a patent after the date of the approval of the approved product under the provision of law under which such regulatory review occurred when added to the regulatory review period as revised under paragraphs (1) and (2) exceeds fourteen years, the period of extension shall be reduced so that the total of both such periods does not exceed fourteen years; and

(4) in no event shall more than one patent be extended under subsection (e)(1) for the same regulatory review period for any product.

(d)(1) To obtain an extension of the term of a patent under this section, the owner of record of the patent or its agent shall submit an application to the Director. Except as provided in paragraph (5), such an application may only be submitted within the sixty-day period beginning on the date the product received permission under the provision of law under which the applicable regulatory review period occurred for commercial marketing or use. The application shall contain--

(5)(A) If the owner of record of the patent or its agent reasonably expects that the applicable regulatory review period described in paragraph (1)(B)(ii), (2)(B)(ii), (3)(B)(ii), (4)(B)(ii), or (5)(B)(ii) of subsection (g) that began for a product that is the subject of such patent may extend beyond the expiration of the patent term in effect, the owner or its agent may submit an application to the Director for an interim extension during the period beginning 6 months, and ending 15 days, before such term is due to expire. The application shall contain--

(i) the identity of the product subject to regulatory review and the Federal statute under which such review is occurring;

(ii) the identity of the patent for which interim extension is being sought and the identity of each claim of such patent which claims the product under regulatory review or a method of using or manufacturing the product;

(iii) information to enable the Director to determine under subsection (a)(1), (2), and (3) the eligibility of a patent for extension;

(iv) a brief description of the activities undertaken by the applicant during the applicable regulatory review period to date with respect to the product under review and the significant dates applicable to such activities; and

(v) such patent or other information as the Director may require.

E) Any interim extension granted under this paragraph shall terminate at the end of the 60-day period beginning on the date on which the product involved receives permission for commercial marketing or use, except that, if within that 60-day period the applicant notifies the Director of such permission and submits any additional information under paragraph (1) of this subsection not previously contained in the application for interim extension, the patent shall be further extended, in accordance with the provisions of this section--

(i) for not to exceed 5 years from the date of expiration of the original patent term; or

(ii) if the patent is subject to subsection (g)(6)(C), from the date on which the product involved receives approval for commercial marketing or use.

(g) For purposes of this section, the term "regulatory review period" has the following meanings:

(1)(A) In the case of a product which is a new drug, antibiotic drug, or human biological product, the term means the period described in subparagraph (B) to which the limitation described in paragraph (6) applies.

(B) The regulatory review period for a new drug, antibiotic drug, or human biological product is the sum of--

(i) the period beginning on the date an exemption under subsection (i) of section 505 or subsection (d) of section 507 became effective for the approved product and ending on the date an application was initially submitted for such drug product under section 351, 505, or 507, and

(ii) the period beginning on the date the application was initially submitted for the approved product under section 351, subsection (b) of section 505, or section 507 and ending on the date such application was approved under such section.

(2)(A) In the case of a product which is a food additive or color additive, the term means the period described in subparagraph (B) to which the limitation described in paragraph (6) applies.

35 U.S.C.A. § 271

(e)(1) It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention (other than a new animal drug or veterinary biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Act of March 4, 1913) which is primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques) solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.

(2) It shall be an act of infringement to submit--

(A) an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act or described in section 505(b)(2) of such Act for a drug claimed in a patent or the use of which is claimed in a patent, or
(B) an application under section 512 of such Act or under the Act of March 4, 1913 ([21 U.S.C. 151-158](#)) for a drug or veterinary biological product which is not primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques and which is claimed in a patent or the use of which is claimed in a patent, if the purpose of such submission is to obtain approval under such Act to engage in the commercial manufacture, use, or sale of a drug or veterinary biological product claimed in a patent or the use of which is claimed in a patent before the expiration of such patent.

Patent Term Extension For Regulatory Review. Codes of Federal Regulation

37 CFR § 1.710 :Patents Subject to Extension of the Patent Term.

(a) A patent is eligible for extension of the patent term if the patent claims a product as defined in paragraph (b) of this section, either alone or in combination with other ingredients that read on a composition that received permission for commercial marketing or use, or a method of using such a product, or a method of manufacturing such a product, and meets all other conditions and requirements of this subpart.

(b) The term "product" referred to in paragraph (a) of this section means--

(1) The active ingredient of a new human drug, antibiotic drug, or human biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act) including any salt or ester of the active ingredient, as a single entity or in combination with another active ingredient; or

(2) The active ingredient of a new animal drug or veterinary biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Virus-Serum-Toxin Act) that is not primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes including site specific genetic manipulation techniques, including any salt or ester of the active ingredient, as a single entity or in combination with another active ingredient; or

(3) Any medical device, food additive, or color additive subject to regulation under the Federal Food, Drug, and Cosmetic Act.

37 C.F.R. § 1.720 Conditions for Extension of Patent Term.

The term of a patent may be extended if:

(a) The patent claims a product or a method of using or manufacturing a product as defined in § 1.710;

(b) The term of the patent has never been previously extended, except for extensions issued pursuant to §§ 1.701, 1.760, or § 1.790;

(c) An application for extension is submitted in compliance with § 1.740;

(d) The product has been subject to a regulatory review period as defined in [35 U.S.C. 156\(g\)](#) before its commercial marketing or use;

(e) The product has received permission for commercial marketing or use and--

(1) The permission for the commercial marketing or use of the product is the first received permission for commercial marketing or use under the provision of law under which the applicable regulatory review occurred, or

(2) In the case of a patent other than one directed to subject matter within § 1.710(b)(2) claiming a method of manufacturing the product that primarily uses recombinant DNA technology in the manufacture of the product, the permission for the commercial marketing or use is the first received permission for the commercial marketing or use of a product manufactured under the process claimed in the patent, or

(3) In the case of a patent claiming a new animal drug or a veterinary biological product that is not covered by the claims in any other patent that has been extended, and has received permission for the commercial marketing or use in non-food-producing animals and in food-producing animals, and was not extended on the basis of the regulatory review period for use in non-food-producing animals, the permission for the commercial marketing or use of the drug or product after the regulatory review period for use in food-producing animals is the first permitted commercial marketing or use of the drug or product for administration to a food-producing animal.

(f) The application is submitted within the sixty-day period beginning on the date the product first received permission for commercial marketing or use under the provisions of law under which the applicable regulatory review period occurred; or in the case of a patent claiming a method of manufacturing the product which primarily uses recombinant DNA technology in the manufacture of the product, the application for extension is submitted within the sixty-day period beginning on the date of the

first permitted commercial marketing or use of a product manufactured under the process claimed in the patent; or in the case of a patent that claims a new animal drug or a veterinary biological product that is not covered by the claims in any other patent that has been extended, and said drug or product has received permission for the commercial marketing or use in non-food-producing animals, the application for extension is submitted within the sixty-day period beginning on the date of the first permitted commercial marketing or use of the drug or product for administration to a food-producing animal;

(g) The term of the patent, including any interim extension issued pursuant to § 1.790, has not expired before the submission of an application in compliance with § 1.741; and

(h) No other patent term has been extended for the same regulatory review period for the product.

37 C.F. R § 1.775 :Calculation of patent term extension for a human drug, antibiotic drug or human biological product.

(a) If a determination is made pursuant to § 1.750 that a patent for a human drug, antibiotic drug or human biological product is eligible for extension, the term shall be extended by the time as calculated in days in the manner indicated by this section. The patent term extension will run from the original expiration date of the patent or any earlier date set by terminal disclaimer (§ 1.321).

(b) The term of the patent for a human drug, antibiotic drug or human biological product will be extended by the length of the regulatory review period for the product as determined by the Secretary of Health and Human Services, reduced as appropriate pursuant to paragraphs (d)(1) through (d)(6) of this section.

(c) The length of the regulatory review period for a human drug, antibiotic drug or human biological product will be determined by the Secretary of Health and Human Services. Under [35 U.S.C. 156\(g\)\(1\)\(B\)](#), it is the sum of--

(1) The number of days in the period beginning on the date an exemption under subsection (i) of section 505 or subsection (d) of section 507 of the Federal Food, Drug, and Cosmetic Act became effective for the approved product and ending on the date the application was initially submitted for such product under those sections or under section 351 of the Public Health Service Act; and

(2) The number of days in the period beginning on the date the application was initially submitted for the approved product under section 351 of the Public Health Service Act, subsection (b) of section 505 or section 507 of the Federal Food, Drug, and Cosmetic Act and ending on the date such application was approved under such section.

(d) The term of the patent as extended for a human drug, antibiotic drug or human biological product will be determined by--

(1) Subtracting from the number of days determined by the Secretary of Health and Human Services to be in the regulatory review period:

(i) The number of days in the periods of paragraphs (c)(1) and (c)(2) of this section which were on and before the date on which the patent issued;

(ii) The number of days in the periods of paragraphs (c)(1) and (c)(2) of this section during which it is determined under [35 U.S.C. 156\(d\)\(2\)\(B\)](#) by the Secretary of Health and Human Services that applicant did not act with due diligence;

(iii) One-half the number of days remaining in the period defined by paragraph (c)(1) of this section after that period is reduced in accordance with paragraphs (d)(1)(i) and (ii) of this section; half days will be ignored for purposes of subtraction;

(2) By adding the number of days determined in paragraph (d)(1) of this section to the original term of the patent as shortened by any terminal disclaimer;

(3) By adding 14 years to the date of approval of the application under section 351 of the Public Health Service Act, or subsection (b) of section 505 or section 507 of the Federal Food, Drug, and Cosmetic Act;

(4) By comparing the dates for the ends of the periods obtained pursuant to paragraphs (d)(2) and (d)(3) of this section with each other and selecting the earlier date;

(5) If the original patent was issued after September 24, 1984,

(i) By adding 5 years to the original expiration date of the patent or any earlier date set by terminal disclaimer; and

(ii) By comparing the dates obtained pursuant to paragraphs (d)(4) and (d)(5)(i) of this section with each other and selecting the earlier date;

- (6) If the original patent was issued before September 24, 1984, and
- (i) If no request was submitted for an exemption under subsection (i) of section 505 or subsection (d) of section 507 of the Federal Food, Drug, and Cosmetic Act before September 24, 1984, by--
 - (A) Adding 5 years to the original expiration date of the patent or earlier date set by terminal disclaimer; and
 - (B) By comparing the dates obtained pursuant to paragraphs (d)(4) and (d)(6)(i)(A) of this section with each other and selecting the earlier date; or
 - (ii) If a request was submitted for an exemption under subsection (i) of section 505 or subsection (d) of section 507 of the Federal Food, Drug, or Cosmetic Act before September 24, 1984 and the commercial marketing or use of the product was not approved before September 24, 1984, by--
 - (A) Adding 2 years to the original expiration date of the patent or earlier date set by terminal disclaimer; and
 - (B) By comparing the dates obtained pursuant to paragraphs (d)(4) and (d)(6)(ii)(A) of this section with each other and selecting the earlier date.

Title I of the Hatch Waxman Act: 21 U.S.C.A. § 355.

21 U.S.C.A. § 355

(b) Filing application; contents

(2) An application submitted under paragraph (1) for a drug for which the investigations described in clause (A) of such paragraph and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted shall also include--

(A) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the drug for which such investigations were conducted or which claims a use for such drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under paragraph (1) or subsection (c) of this section--

(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; and

(B) if with respect to the drug for which investigations described in paragraph (1)(A) were conducted information was filed under paragraph (1) or subsection (c) of this section for a method of use patent which does not claim a use for which the applicant is seeking approval under this subsection, a statement that the method of use patent does not claim such a use.

(3) Notice of opinion that patent is invalid or will not be infringed

(A) Agreement to give notice

An applicant that makes a certification described in paragraph (2)(A)(iv) shall include in the application a statement that the applicant will give notice as required by this paragraph.

(B) Timing of notice

An applicant that makes a certification described in paragraph (2)(A)(iv) shall give notice as required under this paragraph--

(i) if the certification is in the application, not later than 20 days after the date of the postmark on the notice with which the Secretary informs the applicant that the application has been filed; or

(ii) if the certification is in an amendment or supplement to the application, at the time at which the applicant submits the amendment or supplement, regardless of whether the applicant has already given notice with respect to another such certification contained in the application or in an amendment or supplement to the application.

(C) Recipients of notice

An applicant required under this paragraph to give notice shall give notice to--

(i) each owner of the patent that is the subject of the certification (or a representative of the owner designated to receive such a notice); and

(ii) the holder of the approved application under this subsection for the drug that is claimed by the patent or a use of which is claimed by the patent (or a representative of the holder designated to receive such a notice).

(D) Contents of notice

A notice required under this paragraph shall--

(i) state that an application that contains data from bioavailability or bioequivalence studies has been submitted under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of the drug before the expiration of the patent referred to in the certification; and

(ii) include a detailed statement of the factual and legal basis of the opinion of the applicant that the patent is invalid or will not be infringed.

(4)(A) An applicant may not amend or supplement an application referred to in paragraph (2) to seek approval of a drug that is a different drug than the drug identified in the application as submitted to the Secretary.

(B) With respect to the drug for which such an application is submitted, nothing in this subsection or subsection (c)(3) of this section prohibits an applicant from amending or supplementing the application to seek approval of a different strength.

(5)(A) The Secretary shall issue guidance for the individuals who review applications submitted under paragraph (1) or under [section 262 of Title 42](#), which shall relate to promptness in conducting the review, technical excellence, lack of bias and conflict of interest, and knowledge of regulatory and scientific standards, and which shall apply equally to all individuals who review such applications.

(B) The Secretary shall meet with a sponsor of an investigation or an applicant for approval for a drug under this subsection or [section 262 of Title 42](#) if the sponsor or applicant makes a reasonable written request for a meeting for the purpose of reaching agreement on the design and size of clinical trials intended to form the primary basis of an effectiveness claim. The sponsor or applicant shall provide information necessary for discussion and agreement on the design and size of the clinical trials. Minutes of any such meeting shall be prepared by the Secretary and made available to the sponsor or applicant upon request.

(C) Any agreement regarding the parameters of the design and size of clinical trials of a new drug under this paragraph that is reached between the Secretary and a sponsor or applicant shall be reduced to writing and made part of the administrative record by the Secretary. Such agreement shall not be changed after the testing begins, except--

(i) with the written agreement of the sponsor or applicant; or

(ii) pursuant to a decision, made in accordance with subparagraph (D) by the director of the reviewing division, that a substantial scientific issue essential to determining the safety or effectiveness of the drug has been identified after the testing has begun.

(D) A decision under subparagraph (C)(ii) by the director shall be in writing and the Secretary shall provide to the sponsor or applicant an opportunity for a meeting at which the director and the sponsor or applicant will be present and at which the director will document the scientific issue involved.

(E) The written decisions of the reviewing division shall be binding upon, and may not directly or

indirectly be changed by, the field or compliance division personnel unless such field or compliance division personnel demonstrate to the reviewing division why such decision should be modified.

(F) No action by the reviewing division may be delayed because of the unavailability of information from or action by field personnel unless the reviewing division determines that a delay is necessary to assure the marketing of a safe and effective drug.

(G) For purposes of this paragraph, the reviewing division is the division responsible for the review of an application for approval of a drug under this subsection or [section 262 of Title 42](#) (including all scientific and medical matters, chemistry, manufacturing, and controls).

(C) Period for approval of application; period for, notice, and expedition of hearing; period for issuance of order

(1) Within one hundred and eighty days after the filing of an application under subsection (b) of this section, or such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall either--

(A) Approve the application if he then finds that none of the grounds for denying approval specified in subsection (d) of this section applies, or

(B) Give the applicant notice of an opportunity for a hearing before the Secretary under subsection (d) of this section on the question whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

(2) If the patent information described in subsection (b) of this section could not be filed with the submission of an application under subsection (b) of this section because the application was filed before the patent information was required under subsection (b) of this section or a patent was issued after the application was approved under such subsection, the holder of an approved application shall file with the Secretary the patent number and the expiration date of any patent which claims the drug for which the application was submitted 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. If the holder of an approved application could not file patent information under subsection (b) of this section because it was not required at the time the application was approved, the holder shall file such information under this subsection not later than thirty days after September 24, 1984, and if the holder of an approved application could not file patent information under subsection (b) of this section because no patent had been issued when an application was filed or approved, the holder shall file such information under this subsection not later than thirty days after the date the patent involved is issued. Upon the submission of patent information under this subsection, the Secretary shall publish it.

(3) The approval of an application filed under subsection (b) of this section which contains a certification required by paragraph (2) of such subsection shall be made effective on the last applicable date determined by applying the following to each certification made under subsection (b)(2)(A) of this section:

(A) If the applicant only made a certification described in clause (i) or (ii) of subsection (b)(2)(A) of this section or in both such clauses, the approval may be made effective immediately.

(B) If the applicant made a certification described in clause (iii) of subsection (b)(2)(A) of this section, the approval may be made effective on the date certified under clause (iii).

(C) If the applicant made a certification described in clause (iv) of subsection (b)(2)(A) of this section,

the approval shall be made effective immediately unless, before the expiration of 45 days after the date on which the notice described in subsection (b)(3) of this section is received, an action is brought for infringement of the patent that is the subject of the certification and for which information was submitted to the Secretary under paragraph (2) or subsection (b)(1) of this section before the date on which the application (excluding an amendment or supplement to the application) was submitted. If such an action is brought before the expiration of such days, the approval may be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under subsection (b)(3) of this section or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that--

(i) if before the expiration of such period the district court decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity), the approval shall be made effective on--

(I) the date on which the court enters judgment reflecting the decision; or

(II) the date of a settlement order or consent decree signed and entered by the court stating that the patent that is the subject of the certification is invalid or not infringed;

(ii) if before the expiration of such period the district court decides that the patent has been infringed--

(I) if the judgment of the district court is appealed, the approval shall be made effective on--

(aa) the date on which the court of appeals decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity); or

(bb) the date of a settlement order or consent decree signed and entered by the court of appeals stating that the patent that is the subject of the certification is invalid or not infringed; or

(II) if the judgment of the district court is not appealed or is affirmed, the approval shall be made effective on the date specified by the district court in a court order under [section 271\(e\)\(4\)\(A\) of Title 35](#);

(iii) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective as provided in clause (i); or

(iv) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent has been infringed, the approval shall be made effective as provided in clause (ii).

In such an action, each of the parties shall reasonably cooperate in expediting the action.

(D) Civil action to obtain patent certainty

(i) Declaratory judgment absent infringement action

(I) In general

No action may be brought under [section 2201 of Title 28](#), by an applicant referred to in subsection (b)(2) of this section for a declaratory judgment with respect to a patent which is the subject of the certification referred to in subparagraph (C) unless--

(aa) the 45-day period referred to in such subparagraph has expired;

(bb) neither the owner of such patent nor the holder of the approved application under subsection (b) of this section for the drug that is claimed by the patent or a use of which is claimed by the patent brought a civil action against the applicant for infringement of the patent before the expiration of such period; and

(cc) in any case in which the notice provided under paragraph (2)(B) relates to noninfringement, the notice was accompanied by a document described in subclause (III).

(II) Filing of civil action

If the conditions described in items (aa), (bb), and as applicable, (cc) of subclause (I) have been met, the applicant referred to in such subclause may, in accordance with [section 2201 of Title 28](#), bring a civil action under such section against the owner or holder referred to in such subclause (but not against any owner or holder that has brought such a civil action against the applicant, unless that civil action was dismissed without prejudice) for a declaratory judgment that the patent is invalid or will not be infringed by the drug for which the applicant seeks approval, except that such civil action may be brought for a declaratory judgment that the patent will not be infringed only in a case in which the condition described in subclause (I)(cc) is applicable. A civil action referred to in this subclause shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

(III) Offer of confidential access to application

For purposes of subclause (I)(cc), the document described in this subclause is a document providing an offer of confidential access to the application that is in the custody of the applicant referred to in subsection (b)(2) of this section for the purpose of determining whether an action referred to in subparagraph (C) should be brought. The document providing the offer of confidential access shall contain such restrictions as to persons entitled to access, and on the use and disposition of any information accessed, as would apply had a protective order been entered for the purpose of protecting trade secrets and other confidential business information. A request for access to an application under an offer of confidential access shall be considered acceptance of the offer of confidential access with the restrictions as to persons entitled to access, and on the use and disposition of any information accessed, contained in the offer of confidential access, and those restrictions and other terms of the offer of confidential access shall be considered terms of an enforceable contract. Any person provided an offer of confidential access shall review the application for the sole and limited purpose of evaluating possible infringement of the patent that is the subject of the certification under subsection (b)(2)(A)(iv) of this section and for no other purpose, and may not disclose information of no relevance to any issue of patent infringement to any person other than a person provided an offer of confidential access. Further, the application may be redacted by the applicant to remove any information of no relevance to any issue of patent infringement.

(ii) Counterclaim to infringement action

(I) In general

If an owner of the patent or the holder of the approved application under subsection (b) of this section for the drug that is claimed by the patent or a use of which is claimed by the patent brings a patent infringement action against the applicant, the applicant may assert a counterclaim seeking an order requiring the holder to correct or delete the patent information submitted by the holder under subsection (b) of this section or this subsection on the ground that the patent does not claim either--

(aa) the drug for which the application was approved; or

(bb) an approved method of using the drug.

(II) No independent cause of action

Subclause (I) does not authorize the assertion of a claim described in subclause (I) in any civil action or proceeding other than a counterclaim described in subclause (I).

(iii) No damages

An applicant shall not be entitled to damages in a civil action under clause (i) or a counterclaim under clause (ii).

(E)(i) If an application (other than an abbreviated new drug application) submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of another application for a drug for which the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted effective before the expiration of ten years from the date of the approval of the application previously approved under subsection (b) of this section.

(ii) If an application submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, is approved after September 24, 1984, no application which refers to the drug for which the subsection (b) application was submitted and for which the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted may be submitted under subsection (b) of this section before the expiration of five years from the date of the approval of the application under subsection (b) of this section, except that such an application may be submitted under subsection (b) of this section after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in clause (iv) of subsection (b)(2)(A) of this section. The approval of such an application shall be made effective in accordance with this paragraph except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (C) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

(iii) If an application submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application approved under subsection (b) of this section, is approved after September 24, 1984, and if such application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under subsection (b) of this section for the conditions of approval of such drug in the approved subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) of this section if the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

(iv) If a supplement to an application approved under subsection (b) of this section is approved after September 24, 1984, and the supplement contains reports of new clinical investigations (other than

bioavailability [\[FN1\]](#) studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under subsection (b) of this section for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b) of this section if the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

(v) If an application (or supplement to an application) submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection and for which the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted and which refers to the drug for which the subsection (b) application was submitted effective before the expiration of two years from September 24, 1984.

(4) A drug manufactured in a pilot or other small facility may be used to demonstrate the safety and effectiveness of the drug and to obtain approval for the drug prior to manufacture of the drug in a larger facility, unless the Secretary makes a determination that a full scale production facility is necessary to ensure the safety or effectiveness of the drug.

(j) Abbreviated New Drug Applications

(2)(A) An abbreviated application for a new drug shall contain--

(i) information to show that the conditions of use prescribed, recommended, or suggested in the labeling proposed for the new drug have been previously approved for a drug listed under paragraph (7) (hereinafter in this subsection referred to as a "listed drug");

(ii)(I) if the listed drug referred to in clause (i) has only one active ingredient, information to show that the active ingredient of the new drug is the same as that of the listed drug;

(II) if the listed drug referred to in clause (i) has more than one active ingredient, information to show that the active ingredients of the new drug are the same as those of the listed drug, or

(III) if the listed drug referred to in clause (i) has more than one active ingredient and if one of the active ingredients of the new drug is different and the application is filed pursuant to the approval of a petition filed under subparagraph (C), information to show that the other active ingredients of the new drug are the same as the active ingredients of the listed drug, information to show that the different active ingredient is an active ingredient of a listed drug or of a drug which does not meet the requirements of [section 321\(p\)](#) of this title, and such other information respecting the different active ingredient with respect to which the petition was filed as the Secretary may require;

(iii) information to show that the route of administration, the dosage form, and the strength of the new drug are the same as those of the listed drug referred to in clause (i) or, if the route of administration, the dosage form, or the strength of the new drug is different and the application is filed pursuant to the approval of a petition filed under subparagraph (C), such information respecting the route of administration, dosage form, or strength with respect to which the petition was filed as the Secretary may require;

(iv) information to show that the new drug is bioequivalent to the listed drug referred to in clause (i), except that if the application is filed pursuant to the approval of a petition filed under subparagraph (C), information to show that the active ingredients of the new drug are of the same pharmacological or therapeutic class as those of the listed drug referred to in clause (i) and the new drug can be expected to have the same therapeutic effect as the listed drug when administered to patients for a condition of use referred to in clause (i);

(v) information to show that the labeling proposed for the new drug is the same as the labeling approved for the listed drug referred to in clause (i) except for changes required because of differences approved under a petition filed under subparagraph (C) or because the new drug and the listed drug are produced or distributed by different manufacturers;

(vi) the items specified in clauses (B) through (F) of subsection (b)(1) of this section;

(vii) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the listed drug referred to in clause (i) or which claims a use for such listed drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under subsection (b) or (c) of this section--

(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; and

(viii) if with respect to the listed drug referred to in clause (i) information was filed under subsection (b) or (c) of this section for a method of use patent which does not claim a use for which the applicant is seeking approval under this subsection, a statement that the method of use patent does not claim such a use.

The Secretary may not require that an abbreviated application contain information in addition to that required by clauses (i) through (viii).

(B) Notice of opinion that patent is invalid or will not be infringed

(i) Agreement to give notice

An applicant that makes a certification described in subparagraph (A)(vii)(IV) shall include in the application a statement that the applicant will give notice as required by this subparagraph.

(ii) Timing of notice

An applicant that makes a certification described in subparagraph (A)(vii)(IV) shall give notice as required under this subparagraph--

(I) if the certification is in the application, not later than 20 days after the date of the postmark on the notice with which the Secretary informs the applicant that the application has been filed; or

(II) if the certification is in an amendment or supplement to the application, at the time at which the applicant submits the amendment or supplement, regardless of whether the applicant has already given notice with respect to another such certification contained in the application or in an amendment or supplement to the application.

(iii) Recipients of notice

An applicant required under this subparagraph to give notice shall give notice to--

(I) each owner of the patent that is the subject of the certification (or a representative of the owner designated to receive such a notice); and

(II) the holder of the approved application under subsection (b) of this section for the drug that is claimed by the patent or a use of which is claimed by the patent (or a representative of the holder designated to receive such a notice).

(iv) Contents of notice

A notice required under this subparagraph shall--

(I) state that an application that contains data from bioavailability or bioequivalence studies has been submitted under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of the drug before the expiration of the patent referred to in the certification; and

(II) include a detailed statement of the factual and legal basis of the opinion of the applicant that the patent is invalid or will not be infringed.

(C) If a person wants to submit an abbreviated application for a new drug which has a different active ingredient or whose route of administration, dosage form, or strength differ from that of a listed drug, such person shall submit a petition to the Secretary seeking permission to file such an application. The Secretary shall approve or disapprove a petition submitted under this subparagraph within ninety days of the date the petition is submitted. The Secretary shall approve such a petition unless the Secretary finds--

(i) that investigations must be conducted to show the safety and effectiveness of the drug or of any of its active ingredients, the route of administration, the dosage form, or strength which differ from the listed drug; or

(ii) that any drug with a different active ingredient may not be adequately evaluated for approval as safe and effective on the basis of the information required to be submitted in an abbreviated application.

(D) (i) An applicant may not amend or supplement an application to seek approval of a drug referring to a different listed drug from the listed drug identified in the application as submitted to the Secretary.

(ii) With respect to the drug for which an application is submitted, nothing in this subsection prohibits an applicant from amending or supplementing the application to seek approval of a different strength.

(iii) Within 60 days after December 8, 2003, the Secretary shall issue guidance defining the term "listed drug" for purposes of this subparagraph.

(5)(A) Within one hundred and eighty days of the initial receipt of an application under paragraph (2) or within such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall approve or disapprove the application.

(B) The approval of an application submitted under paragraph (2) shall be made effective on the last applicable date determined by applying the following to each certification made under paragraph (2)(A)(vii):

(i) If the applicant only made a certification described in subclause (I) or (II) of paragraph (2)(A)(vii) or

in both such subclauses, the approval may be made effective immediately.

(ii) If the applicant made a certification described in subclause (III) of paragraph (2)(A)(vii), the approval may be made effective on the date certified under subclause (III).

(iii) If the applicant made a certification described in subclause (IV) of paragraph (2)(A)(vii), the approval shall be made effective immediately unless, before the expiration of 45 days after the date on which the notice described in paragraph (2)(B) is received, an action is brought for infringement of the patent that is the subject of the certification and for which information was submitted to the Secretary under subsection (b)(1) or (c)(2) of this section before the date on which the application (excluding an amendment or supplement to the application), which the Secretary later determines to be substantially complete, was submitted. If such an action is brought before the expiration of such days, the approval shall be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under paragraph (2)(B)(i) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that--

(I) if before the expiration of such period the district court decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity), the approval shall be made effective on--

(aa) the date on which the court enters judgment reflecting the decision; or

(bb) the date of a settlement order or consent decree signed and entered by the court stating that the patent that is the subject of the certification is invalid or not infringed;

(II) if before the expiration of such period the district court decides that the patent has been infringed--

(aa) if the judgment of the district court is appealed, the approval shall be made effective on--

(AA) the date on which the court of appeals decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity); or

(BB) the date of a settlement order or consent decree signed and entered by the court of appeals stating that the patent that is the subject of the certification is invalid or not infringed; or

(bb) if the judgment of the district court is not appealed or is affirmed, the approval shall be made effective on the date specified by the district court in a court order under section 271(e)(4)(A) of Title 35;

(III) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective as provided in subclause (I); or

(IV) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent has been infringed, the approval shall be made effective as provided in subclause (II).

In such an action, each of the parties shall reasonably cooperate in expediting the action.

(iv) 180-day exclusivity period

(I) Effectiveness of application

Subject to subparagraph (D), if the application contains a certification described in paragraph (2)(A)(vii)(IV) and is for a drug for which a first applicant has submitted an application containing such a certification, the application shall be made effective on the date that is 180 days after the date of the first commercial marketing of the drug (including the commercial marketing of the listed drug) by any first applicant.

(II) Definitions

In this paragraph:

(aa) 180-day exclusivity period

The term "180-day exclusivity period" means the 180-day period ending on the day before the date on which an application submitted by an applicant other than a first applicant could become effective under this clause.

(bb) First applicant

As used in this subsection, the term "first applicant" means an applicant that, on the first day on which a substantially complete application containing a certification described in paragraph (2)(A)(vii)(IV) is submitted for approval of a drug, submits a substantially complete application that contains and lawfully maintains a certification described in paragraph (2)(A)(vii)(IV) for the drug.

(cc) Substantially complete application

As used in this subsection, the term "substantially complete application" means an application under this subsection that on its face is sufficiently complete to permit a substantive review and contains all the information required by paragraph (2)(A).

(C) Civil action to obtain patent certainty

(i) Declaratory judgment absent infringement action

(I) In general

No action may be brought under section 2201 of Title 28, by an applicant under paragraph (2) for a declaratory judgment with respect to a patent which is the subject of the certification referred to in subparagraph (B)(iii) unless--

(aa) the 45-day period referred to in such subparagraph has expired;

(bb) neither the owner of such patent nor the holder of the approved application under subsection (b) of this section for the drug that is claimed by the patent or a use of which is claimed by the patent brought a civil action against the applicant for infringement of the patent before the expiration of such period; and

(cc) in any case in which the notice provided under paragraph (2)(B) relates to noninfringement, the notice was accompanied by a document described in subclause (III).

(II) Filing of civil action

If the conditions described in items (aa), (bb), and as applicable, (cc) of subclause (I) have been met, the applicant referred to in such subclause may, in accordance with section 2201 of Title 28, bring a civil action under such section against the owner or holder referred to in such subclause (but not

against any owner or holder that has brought such a civil action against the applicant, unless that civil action was dismissed without prejudice) for a declaratory judgment that the patent is invalid or will not be infringed by the drug for which the applicant seeks approval, except that such civil action may be brought for a declaratory judgment that the patent will not be infringed only in a case in which the condition described in subclause (I)(cc) is applicable. A civil action referred to in this subclause shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

(ii) Counterclaim to infringement action

(I) In general

If an owner of the patent or the holder of the approved application under subsection (b) of this section for the drug that is claimed by the patent or a use of which is claimed by the patent brings a patent infringement action against the applicant, the applicant may assert a counterclaim seeking an order requiring the holder to correct or delete the patent information submitted by the holder under subsection (b) or (c) of this section on the ground that the patent does not claim either--

(aa) the drug for which the application was approved; or

(bb) an approved method of using the drug.

(II) No independent cause of action

Subclause (I) does not authorize the assertion of a claim described in subclause (I) in any civil action or proceeding other than a counterclaim described in subclause (I).

(iii) No damages

An applicant shall not be entitled to damages in a civil action under clause (i) or a counterclaim under clause (ii).

(D) Forfeiture of 180-day exclusivity period

(i) Definition of forfeiture event

In this subparagraph, the term "forfeiture event", with respect to an application under this subsection, means the occurrence of any of the following:

(I) Failure to market

The first applicant fails to market the drug by the later of--

(aa) the earlier of the date that is--

(AA) 75 days after the date on which the approval of the application of the first applicant is made effective under subparagraph (B)(iii); or

(BB) 30 months after the date of submission of the application of the first applicant; or

(bb) with respect to the first applicant or any other applicant (which other applicant has received tentative approval), the date that is 75 days after the date as of which, as to each of the patents with respect to which the first applicant submitted and lawfully maintained a certification qualifying the first applicant for the 180-day exclusivity period under subparagraph (B)(iv), at least 1 of the following has occurred:

(AA) In an infringement action brought against that applicant with respect to the patent or in a declaratory judgment action brought by that applicant with respect to the patent, a court enters a final decision from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken that the patent is invalid or not infringed.

(BB) In an infringement action or a declaratory judgment action described in subitem (AA), a court signs a settlement order or consent decree that enters a final judgment that includes a finding that the patent is invalid or not infringed.

(CC) The patent information submitted under subsection (b) or (c) of this section is withdrawn by the holder of the application approved under subsection (b) of this section.

(ii) Forfeiture

The 180-day exclusivity period described in subparagraph (B)(iv) shall be forfeited by a first applicant if a forfeiture event occurs with respect to that first applicant.

(iii) Subsequent applicant

If all first applicants forfeit the 180-day exclusivity period under clause (ii)--

(I) approval of any application containing a certification described in paragraph (2)(A)(vii)(IV) shall be made effective in accordance with subparagraph (B)(iii); and

(II) no applicant shall be eligible for a 180-day exclusivity period.

TITLE I: CODES OF FEDERAL REGULATIONS

21 C.F.R. § 314.107 Effective Date of Approval of a 505(b)(2) Application or Abbreviated New Drug Application Under Section 505(j) of the act.

(a) General. A drug product may be introduced or delivered for introduction into interstate commerce when approval of the application or abbreviated application for the drug product becomes effective. Except as provided in this section, approval of an application or abbreviated application for a drug product becomes effective on the date FDA issues an approval letter under § 314.105 for the application or abbreviated application.

(b) Effect of patent on the listed drug. If approval of an abbreviated new drug application submitted under section 505(j) of the act or of a 505(b)(2) application is granted, that approval will become effective in accordance with the following:

(1) Date of approval letter. Except as provided in paragraphs (b)(3), (b)(4), and (c) of this section, approval will become effective on the date FDA issues an approval letter under § 314.105 if the applicant certifies under § 314.50(i) or § 314.94(a)(12) that:

(i) There are no relevant patents; or

(ii) The applicant is aware of a relevant patent but the patent information required under section 505 (b) or (c) of the act has not been submitted to FDA; or

(iii) The relevant patent has expired; or

(iv) The relevant patent is invalid, unenforceable, or will not be infringed.

(2) Patent expiration. If the applicant certifies under § 314.50(i) or § 314.94(a)(12) that the relevant patent will expire on a specified date, approval will become effective on the specified date.

(3) Disposition of patent litigation.

(i)(A) Except as provided in paragraphs (b)(3)(ii), (b)(3)(iii), and (b)(3)(iv) of this section, if the applicant certifies under § 314.50(i) or § 314.94(a)(12) that the relevant patent is invalid, unenforceable, or will not be infringed, and the patent owner or its representative or the exclusive patent licensee brings suit for patent infringement within 45 days of receipt by the patent owner of the notice of certification from the applicant under § 314.52 or § 314.95, approval may be made effective 30 months after the date of the receipt of the notice of certification by the patent owner or by the exclusive licensee (or their representatives) unless the court has extended or reduced the period because of a failure of either the plaintiff or defendant to cooperate reasonably in expediting the action; or

(B) If the patented drug product qualifies for 5 years of exclusive marketing under § 314.108(b)(2) and the patent owner or its representative or the exclusive patent licensee brings suit for patent infringement during the 1-year period beginning 4 years after the date the patented drug was approved and within 45 days of receipt by the patent owner of the notice of certification, the approval may be made effective at the expiration of the 7 1/2 years from the date of approval of the application for the patented drug product.

(ii) If before the expiration of the 30-month period, or 7 1/2 years where applicable, the court issues a final order that the patent is invalid, unenforceable, or not infringed, approval may be made effective on the date the court enters judgment;

(iii) If before the expiration of the 30-month period, or 7 1/2 years where applicable, the court issues a final order or judgment that the patent has been infringed, approval may be made effective on the date the court determines that the patent will expire or otherwise orders; or

(iv) If before the expiration of the 30-month period, or 7 1/2 years where applicable, the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug product until the court decides the issues of patent validity and infringement, and if the court later decides that the patent is invalid, unenforceable, or not infringed, approval may be made effective on the date the court enters a final order or judgment that the patent is invalid, unenforceable, or not infringed.

(v) In order for an approval to be made effective under paragraph (b)(3) of this section, the applicant must receive an approval letter from the agency indicating that the application has received final approval. Tentative approval of an application does not constitute "approval" of an application and cannot, absent a final approval letter from the agency, result in an effective approval under paragraph (b)(3) of this section.

(4) Multiple certifications. If the applicant has submitted certifications under § 314.50(i) or § 314.94(a)(12) for more than one patent, the date of approval will be calculated for each certification, and the approval will become effective on the last applicable date.

(c) Subsequent abbreviated new drug application submission.

(1) 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, 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.

(2) For purposes of paragraph (c)(1) of this section, the "applicant submitting the first application" is the applicant that submits an application that is both substantially complete and contains a certification that the patent was invalid, unenforceable, or not infringed prior to the submission of any other application for the same listed drug that is both substantially complete and contains the same certification. A "substantially complete" application must contain the results of any required bioequivalence studies, or, if applicable, a request for a waiver of such studies.

(3) For purposes of paragraph (c)(1) of this section, if FDA concludes that the applicant submitting the first application is not actively pursuing approval of its abbreviated application, FDA will make the approval of subsequent abbreviated applications immediately effective if they are otherwise eligible for an immediately effective approval.

(4) For purposes of paragraph (c)(1)(i) of this section, the applicant submitting the first application shall notify FDA of the date that it commences commercial marketing of its drug product. Commercial marketing commences with the first date of introduction or delivery for introduction into interstate commerce outside the control of the manufacturer of a drug product, except for investigational use under part 312 of this chapter, but does not include transfer of the drug product for reasons other than sale within the control of the manufacturer or application holder. If an applicant does not promptly notify FDA of such date, the effective date of approval shall be deemed to be the date of the commencement of first commercial marketing.

(d) Delay due to exclusivity. The agency will also delay the effective date of the approval of an abbreviated new drug application under section 505(j) of the act or a 505(b)(2) application if delay is required by the exclusivity provisions in § 314.108. When the effective date of an application is delayed under both this section and § 314.108, the effective date will be the later of the 2 days specified under this section and § 314.108.

(e) Notification of court actions. The applicant shall submit a copy of the entry of the order or judgment to the Office of Generic Drugs (HFD-600), or to the appropriate division in the Office of Drug Evaluation I (HFD-100) or Office of Drug Evaluation II (HFD-500), whichever is applicable, within 10 working days of a final judgment.

(f) Computation of 45-day time clock.

(1) The 45-day clock described in paragraph (b)(3) of this section begins on the day after the date of receipt of the applicant's notice of certification by the patent owner or its representative, and by the approved application holder. When the 45th day falls on Saturday, Sunday, or a Federal holiday, the 45th day will be the next day that is not a Saturday, Sunday, or a Federal holiday.

(2) The abbreviated new drug applicant or the 505(b)(2) applicant shall notify FDA immediately of the filing of any legal action filed within 45 days of receipt of the notice of certification. If the applicant submitting the abbreviated new drug application or the 505(b)(2) application or patent owner or its representative does not notify FDA in writing before the expiration of the 45-day time period or the completion of the agency's review of the application, whichever occurs later, that a legal action for patent infringement was filed within 45 days of receipt of the notice of certification, approval of the abbreviated new drug application or the 505(b)(2) application will be made effective immediately upon expiration of the 45 days or upon completion of the agency's review and approval of the application, whichever is later. The notification to FDA of the legal action shall include:

(i) The abbreviated new drug application or 505(b)(2) application number.

(ii) The name of the abbreviated new drug or 505(b)(2) application applicant.

(iii) The established name of the drug product or, if no established name exists, the name(s) of the active ingredient(s), the drug product's strength, and dosage form.

(iv) A certification that an action for patent infringement identified by number, has been filed in an appropriate court on a specified date.

The applicant of an abbreviated new drug application shall send the notification to FDA's Office of Generic Drugs (HFD-600). A 505(b)(2) applicant shall send the notification to the appropriate division in the Center for Drug Evaluation and Research reviewing the application. A patent owner or its representative may also notify FDA of the filing of any legal action for patent infringement. The notice should contain the information and be sent to the offices or divisions described in this paragraph.

(3) If the patent owner or approved application holder who is an exclusive patent licensee waives its opportunity to file a legal action for patent infringement within 45 days of a receipt of the notice of certification and the patent owner or approved application holder who is an exclusive patent licensee submits to FDA a valid waiver before the 45 days elapse, approval of the abbreviated new drug application or the 505(b)(2) application will be made effective upon completion of the agency's review and approval of the application. FDA will only accept a waiver in the following form:

(Name of patent owner or exclusive patent licensee) has received notice from (name of applicant) under (section 505(b)(3) or 505(j)(2)(B) of the act) and does not intend to file an action for patent infringement against (name of applicant) concerning the drug (name of drug) before (date on which 45 days elapses). (Name of patent owner or exclusive patent licensee) waives the opportunity provided by (section 505(c)(3)(C) or 505(j)(B)(iii) of the act) and does not object to FDA's approval of (name of applicant)'s (505(b)(2) or abbreviated new drug application) for (name of drug) with an immediate effective date on or after the date of this letter.

21 CFR § 314.94 :Content and format of an abbreviated application.

Abbreviated applications are required to be submitted in the form and contain the information required under this section. Three copies of the application are required, an archival copy, a review copy, and a field copy. FDA will maintain guidance documents on the format and content of applications to assist applicants in their preparation.

(a) Abbreviated new drug applications. Except as provided in paragraph (b) of this section, the applicant shall submit a complete archival copy of the abbreviated new drug application that includes the following:

(1) Application form. The applicant shall submit a completed and signed application form that contains the information described under § 314.50(a)(1), (a)(3), (a)(4), and (a)(5). The applicant shall state whether the submission is an abbreviated application under this section or a supplement to an abbreviated application under § 314.97.

(2) Table of contents. The archival copy of the abbreviated new drug application is required to contain a table of contents that shows the volume number and page number of the contents of the submission.

(3) Basis for abbreviated new drug application submission. An abbreviated new drug application must refer to a listed drug. Ordinarily, that listed drug will be the drug product selected by the agency as the reference standard for conducting bioequivalence testing. The application shall contain:

(i) The name of the reference listed drug, including its dosage form and strength. For an abbreviated new drug application based on an approved petition under § 10.30 of this chapter or § 314.93, the reference listed drug must be the same as the listed drug approved in the petition.

(ii) A statement as to whether, according to the information published in the list, the reference listed drug is entitled to a period of marketing exclusivity under section 505(j)(4)(D) of the act.

(iii) For an abbreviated new drug application based on an approved petition under § 10.30 of this chapter or § 314.93, a reference to FDA-assigned docket number for the petition and a copy of FDA's correspondence approving the petition.

(4) Conditions of use.

(i) A statement that the conditions of use prescribed, recommended, or suggested in the labeling proposed for the drug product have been previously approved for the reference listed drug.

(ii) A reference to the applicant's annotated proposed labeling and to the currently approved labeling for the reference listed drug provided under paragraph (a)(8) of this section.

(5) Active ingredients.

(i) For a single-active-ingredient drug product, information to show that the active ingredient is the same as that of the reference single-active-ingredient listed drug, as follows:

(A) A statement that the active ingredient of the proposed drug product is the same as that of the reference listed drug.

(B) A reference to the applicant's annotated proposed labeling and to the currently approved labeling for the reference listed drug provided under paragraph (a)(8) of this section.

(ii) For a combination drug product, information to show that the active ingredients are the same as those of the reference listed drug except for any different active ingredient that has been the subject of an

approved petition, as follows:

(A) A statement that the active ingredients of the proposed drug product are the same as those of the reference listed drug, or if one of the active ingredients differs from one of the active ingredients of the reference listed drug and the abbreviated application is submitted under the approval of a petition under § 314.93 to vary such active ingredient, information to show that the other active ingredients of the drug product are the same as the other active ingredients of the reference listed drug, information to show that the different active ingredient is an active ingredient of another listed drug or of a drug that does not meet the definition of "new drug" in section 201(p) of the act, and such other information about the different active ingredient that FDA may require.

(B) A reference to the applicant's annotated proposed labeling and to the currently approved labeling for the reference listed drug provided under paragraph (a)(8) of this section.

(6) Route of administration, dosage form, and strength.

(i) Information to show that the route of administration, dosage form, and strength of the drug product are the same as those of the reference listed drug except for any differences that have been the subject of an approved petition, as follows:

(A) A statement that the route of administration, dosage form, and strength of the proposed drug product are the same as those of the reference listed drug.

(B) A reference to the applicant's annotated proposed labeling and to the currently approved labeling for the reference listed drug provided under paragraph (a)(8) of this section.

(ii) If the route of administration, dosage form, or strength of the drug product differs from the reference listed drug and the abbreviated application is submitted under an approved petition under § 314.93, such information about the different route of administration, dosage form, or strength that FDA may require.

(7) Bioequivalence.

(i) Information that shows that the drug product is bioequivalent to the reference listed drug upon which the applicant relies; or

(ii) If the abbreviated new drug application is submitted under a petition approved under § 314.93, the results of any bioavailability or bioequivalence testing required by the agency, or any other information required by the agency to show that the active ingredients of the proposed drug product are of the same pharmacological or therapeutic class as those in the reference listed drug and that the proposed drug product can be expected to have the same therapeutic effect as the reference listed drug. If the proposed drug product contains a different active ingredient than the reference listed drug, FDA will consider the proposed drug product to have the same therapeutic effect as the reference listed drug if the applicant provides information demonstrating that:

(A) There is an adequate scientific basis for determining that substitution of the specific proposed dose of the different active ingredient for the dose of the member of the same pharmacological or therapeutic class in the reference listed drug will yield a resulting drug product whose safety and effectiveness have not been adversely affected.

(B) The unchanged active ingredients in the proposed drug product are bioequivalent to those in the reference listed drug.

(C) The different active ingredient in the proposed drug product is bioequivalent to an approved dosage form containing that ingredient and approved for the same indication as the proposed drug product or is bioequivalent to a drug product offered for that indication which does not meet the definition of "new drug" under section 201(p) of the act.

(iii) For each in vivo bioequivalence study contained in the abbreviated new drug application, a description of the analytical and statistical methods used in each study and a statement with respect to each study that it either was conducted in compliance with the institutional review board regulations in part 56 of this chapter, or was not subject to the regulations under § 56.104 or § 56.105 of this chapter and that each study was conducted in compliance with the informed consent regulations in part 50 of this chapter.

(12) Patent certification--

(i) Patents claiming drug, drug product, or method of use.

(A) Except as provided in paragraph (a)(12)(iv) of this section, a certification with respect to each patent issued by the United States Patent and Trademark Office that, in the opinion of the applicant and to the best of its knowledge, claims the reference listed drug or that claims a use of such listed drug for which the applicant is seeking approval under section 505(j) of the act and for which information is required to be filed under section 505(b) and (c) of the act and § 314.53. For each such patent, the applicant shall provide the patent number and certify, in its opinion and to the best of its knowledge, one of the following circumstances:

(1) That the patent information has not been submitted to FDA. The applicant shall entitle such a certification "Paragraph I Certification";

(2) That the patent has expired. The applicant shall entitle such a certification "Paragraph II Certification";

(3) The date on which the patent will expire. The applicant shall entitle such a certification "Paragraph III Certification"; or

(4) That the patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the abbreviated application is submitted. The applicant shall entitle such a certification "Paragraph IV Certification". This certification shall be submitted in the following form:

I, (name of applicant), certify that Patent No. _____ (is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of) (name of proposed drug product) for which this application is submitted.

The certification shall be accompanied by a statement that the applicant will comply with the requirements under § 314.95(a) with respect to providing a notice to each owner of the patent or their representatives and to the holder of the approved application for the listed drug, and with the requirements under § 314.95(c) with respect to the content of the notice.

(B) If the abbreviated new drug application refers to a listed drug that is itself a licensed generic product of a patented drug first approved under section 505(b) of the act, the appropriate patent certification under paragraph (a)(12)(i) of this section with respect to each patent that claims the first-approved patented drug or that claims a use for such drug.

(ii) No relevant patents. If, in the opinion of the applicant and to the best of its knowledge, there are no patents described in paragraph (a)(12)(i) of this section, a certification in the following form:

In the opinion and to the best knowledge of (name of applicant), there are no patents that claim the listed drug referred to in this application or that claim a use of the listed drug.

(iii) Method of use patent.

(A) If patent information is submitted under section 505(b) or (c) of the act and § 314.53 for a patent claiming a method of using the listed drug, and the labeling for the drug product for which the applicant is seeking approval does not include any indications that are covered by the use patent, a statement explaining that the method of use patent does not claim any of the proposed indications.

(B) If the labeling of the drug product for which the applicant is seeking approval includes an indication that, according to the patent information submitted under section 505(b) or (c) of the act and § 314.53 or in the opinion of the applicant, is claimed by a use patent, an applicable certification under paragraph (a)(12)(i) of this section.

(iv) Method of manufacturing patent. An applicant is not required to make a certification with respect to any patent that claims only a method of manufacturing the listed drug.

(v) Licensing agreements. If the abbreviated new drug application is for a drug or method of using a drug claimed by a patent and the applicant has a licensing agreement with the patent owner, a certification under paragraph (a)(12)(i)(A)(4) of this section ("Paragraph IV Certification") as to that patent and a statement that it has been granted a patent license.

(vi) Late submission of patent information. If a patent on the listed drug is issued and the holder of the approved application for the listed drug does not submit the required information on the patent within 30 days of issuance of the patent, an applicant who submitted an abbreviated new drug application for that drug that contained an appropriate patent certification before the submission of the patent information is not required to submit an amended certification. An applicant whose abbreviated new drug application is submitted after a late submission of patent information, or whose pending abbreviated application was previously submitted but did not contain an appropriate patent certification at the time of the patent submission, shall submit a certification under paragraph (a)(12)(i) of this section or a statement under paragraph (a)(12)(iii) of this section as to that patent.

(vii) Disputed patent information. If an applicant disputes the accuracy or relevance of patent information submitted to FDA, the applicant may seek a confirmation of the correctness of the patent information in accordance with the procedures under § 314.53(f). Unless the patent information is withdrawn or changed, the applicant shall submit an appropriate certification for each relevant patent.

(viii) Amended certifications. A certification submitted under paragraphs (a)(12)(i) through (a)(12)(iii) of this section may be amended at any time before the effective date of the approval of the application. However, an applicant who has submitted a paragraph IV patent certification may not change it to a paragraph III certification if a patent infringement suit has been filed against another paragraph IV applicant unless the agency has determined that no applicant is entitled to 180-day exclusivity or the patent expires before the lawsuit is resolved or expires after the suit is resolved but before the end of the 180-day exclusivity period. If an applicant with a pending application voluntarily makes a patent certification for an untimely filed patent, the applicant may withdraw the patent certification for the untimely filed patent. An applicant shall submit an amended certification by letter or as an amendment to a pending application or by letter to an approved application. Once an amendment or letter is submitted, the application will no longer be considered to contain the prior certification.

(A) After finding of infringement. An applicant who has submitted a certification under paragraph (a)(12)(i)(A)(4) of this section and is sued for patent infringement within 45 days of the receipt of notice sent under § 314.95 shall amend the certification if a final judgment in the action against the applicant is entered finding the patent to be infringed. In the amended certification, the applicant shall certify under paragraph (a)(12)(i)(A)(3) of this section that the patent will expire on a specific date. Once an amendment or letter for the change has been submitted, the application will no longer be considered to be one containing a certification under paragraph (a)(12)(i)(A)(4) of this section. If a final judgment finds the patent to be invalid and infringed, an amended certification is not required.

(B) After removal of a patent from the list. If a patent is removed from the list, any applicant with a pending application (including a tentatively approved application with a delayed effective date) who has made a certification with respect to such patent shall amend its certification. The applicant shall certify under paragraph (a)(12)(ii) of this section that no patents described in paragraph (a)(12)(i) of this section claim the drug or, if other relevant patents claim the drug, shall amend the certification to refer only to those relevant patents. In the amendment, the applicant shall state the reason for the change in certification

(that the patent is or has been removed from the list). A patent that is the subject of a lawsuit under § 314.107(c) shall not be removed from the list until FDA determines either that no delay in effective dates of approval is required under that section as a result of the lawsuit, that the patent has expired, or that any such period of delay in effective dates of approval is ended. An applicant shall submit an amended certification. Once an amendment or letter for the change has been submitted, the application will no longer be considered to be one containing a certification under paragraph (a)(12)(i)(A)(4) of this section.

(C) Other amendments.

(1) Except as provided in paragraphs (a)(12)(vi) and (a)(12)(viii)(C)(2) of this section, an applicant shall amend a submitted certification if, at any time before the effective date of the approval of the application, the applicant learns that the submitted certification is no longer accurate.

(2) An applicant is not required to amend a submitted certification when information on a patent on the listed drug is submitted after the effective date of approval of the abbreviated application.

(13) Financial certification or disclosure statement. An abbreviated application shall contain a financial certification or disclosure statement as required by part 54 of this chapter.

(b) Drug products subject to the Drug Efficacy Study Implementation (DESI) review. If the abbreviated new drug application is for a duplicate of a drug product that is subject to FDA's DESI review (a review of drug products approved as safe between 1938 and 1962) or other DESI-like review and the drug product evaluated in the review is a listed drug, the applicant shall comply with the provisions of paragraph (a) of this section.

Orphan-Drug Act Amendments: 21 USCA § 360cc.

(a) Exclusive approval, certification, or license

Except as provided in subsection (b) of this section, if the Secretary--

(1) approves an application filed pursuant to section 355 of this title, or

(2) issues a license under section 262 of Title 42

for a drug designated under section 360bb of this title for a rare disease or condition, the Secretary may not approve another application under section 355 of this title or issue another license under section 262 of Title 42 for such drug for such disease or condition for a person who is not the holder of such approved application or of such license until the expiration of seven years from the date of the approval of the approved application or the issuance of the license. Section 355(c)(2) of this title does not apply to the refusal to approve an application under the preceding sentence.

(3) Redesignated (2)

(b) Exceptions

If an application filed pursuant to section 355 of this title is approved for a drug designated under section 360bb of this title for a rare disease or condition or if a license is issued under section 262 of Title 42 for such a drug, the Secretary may, during the seven-year period beginning on the date of the application approval or of the issuance of the license, approve another application under section 355 of this title or issue a license under section 262 of Title 42, for such drug for such disease or condition for a person who is not the holder of such approved application or of such license if--

(1) the Secretary finds, after providing the holder notice and opportunity for the submission of views, that in such period the holder of the approved application or of the license cannot assure the availability of sufficient quantities of the drug to meet the needs of persons with the disease or condition for which the drug was designated; or

(2) such holder provides the Secretary in writing the consent of such holder for the approval of other applications or the issuance of other licenses before the expiration of such seven-year period.

21 U.S.C.A. § 355a “ Pediatric Exclusivity”

(a) Definitions

As used in this section, the term "pediatric studies" or "studies" means at least one clinical investigation (that, at the Secretary's discretion, may include pharmacokinetic studies) in pediatric age groups (including neonates in appropriate cases) in which a drug is anticipated to be used.

(b) Market exclusivity for new drugs

If, prior to approval of an application that is submitted under section 355(b)(1) of this title, the Secretary determines that information relating to the use of a new drug in the pediatric population may produce health benefits in that population, the Secretary makes a written request for pediatric studies (which shall include a timeframe for completing such studies), and such studies are completed within any such timeframe and the reports thereof submitted in accordance with subsection (d)(2) of this section or accepted in accordance with subsection (d)(3) of this section--

(1)(A)(i) the period referred to in subsection (c)(3)(D)(ii) of section 355 of this title, and in subsection (j)(5)(F)(ii) of such section, is deemed to be five years and six months rather than five years, and the references in subsections (c)(3)(D)(ii) and (j)(5)(F)(ii) of such section to four years, to forty-eight months, and to seven and one-half years are deemed to be four and one-half years, fifty-four months, and eight years, respectively; or

(ii) the period referred to in clauses (iii) and (iv) of subsection (c)(3)(D) of such section, and in clauses (iii) and (iv) of subsection (j)(5)(F) of such section, is deemed to be three years and six months rather than three years; and

(B) if the drug is designated under section 360bb of this title for a rare disease or condition, the period referred to in section 360cc(a) of this title is deemed to be seven years and six months rather than seven years; and

(2)(A) if the drug is the subject of--

(i) a listed patent for which a certification has been submitted under subsection (b)(2)(A)(ii) or (j)(2)(A)(vii)(II) of section 355 of this title and for which pediatric studies were submitted prior to the expiration of the patent (including any patent extensions); or

(ii) a listed patent for which a certification has been submitted under subsections (b)(2)(A)(iii) or (j)(2)(A)(vii)(III) of section 355 of this title,

the period during which an application may not be approved under section 355(c)(3) of this title or section 355(j)(5)(B) of this title shall be extended by a period of six months after the date the patent expires (including any patent extensions); or

(B) if the drug is the subject of a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) of section 355 of this title, and in the patent infringement litigation resulting from the certification the court determines that the patent is valid and would be infringed, the period during which an application may not be approved under section 355(c)(3) of this title or section 355(j)(5)(B) of this title shall be extended by a period of six months after the date the patent expires (including any patent extensions).

21 C.F.R. § 60.3 Definitions.

- (a) The definitions contained in 35 U.S.C. 156 apply to those terms when used in this part.
- (b) The following definitions of terms apply to this part:
 - (2) Active ingredient means any component that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body of man or of animals. The term includes those components that may undergo chemical change in the manufacture of the drug product and be present in the drug product in a modified form intended to furnish the specified activity or effect.
 - (3) Applicant means any person who submits an application or an amendment or supplement to an application under 35 U.S.C. 156 seeking patent term restoration.
 - (4) Application means an application for patent term restoration submitted under 35 U.S.C. 156.
 - (5) Clinical investigation or study means any experiment that involves a test article and one or more subjects and that is either subject to requirements for prior submission to the Food and Drug Administration under section 505(i), 512(j), or 520(g) of the Federal Food, Drug, and Cosmetic Act, or is not subject to the requirements for prior submission to FDA under those sections of the Federal Food, Drug, and Cosmetic Act, but the results of which are intended to be submitted later to, or held for inspection by, FDA as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions of Part 58 regarding nonclinical laboratory studies.

21 C.F.R. § 314.53 Submission of Patent Information.

- (a) Who must submit patent information. This section applies to any applicant who submits to FDA a new drug application or an amendment to it under section 505(b) of the act and § 314.50 or a supplement to an approved application under § 314.70, except as provided in paragraph (d)(2) of this section.
- (b) Patents for which information must be submitted and patents for which information must not be submitted--
 - (1) General requirements. An applicant described in paragraph (a) of this section shall submit the required information on the declaration form set forth in paragraph (c) of this section for each patent that claims the drug or a method of using the drug that is the subject of the new drug application or amendment or supplement to it 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. For purposes of this part, such patents consist of drug substance (active ingredient) patents, drug product (formulation and composition) patents, and method-of-use patents. For patents that claim the drug substance, the applicant shall submit information only on those patents that claim the drug substance that is the subject of the pending or approved application or that claim a drug substance that is the same as the active ingredient that is the subject of the approved or pending application. For patents that claim a polymorph that is the same as the active ingredient described in the approved or pending application, the applicant shall certify in the declaration forms that the applicant has test data, as set forth in paragraph

21 C.F.R. § 314.92 Drug Products for Which Abbreviated Applications May be Submitted.

- (a) Abbreviated applications are suitable for the following drug products within the limits set forth under § 314.93:
 - (1) Drug products that are the same as a listed drug. A "listed drug" is defined in § 314.3. For determining the suitability of an abbreviated new drug application, the term "same as" means identical in active ingredient(s), dosage form, strength, route of administration, and conditions of use, except that conditions of use for which approval cannot be granted because of exclusivity or an existing patent may be omitted. If a listed drug has been voluntarily withdrawn from or not offered for sale by its manufacturer, a person who wishes to submit an abbreviated new drug application for the drug shall comply with § 314.122.

C.F.R. § 314.108 New Drug Product Exclusivity.

(a) Definitions. The following definitions of terms apply to this section:

Active moiety means the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule, responsible for the physiological or pharmacological action of the drug substance.

Approved under section 505(b) means an application submitted under section 505(b) and approved on or after October 10, 1962, or an application that was "deemed approved" under section 107(c)(2) of Pub.L. 87-781.

Clinical investigation means any experiment other than a bioavailability study in which a drug is administered or dispensed to, or used on, human subjects.

Conducted or sponsored by the applicant with regard to an investigation means that before or during the investigation, the applicant was named in Form FDA-1571 filed with FDA as the sponsor of the investigational new drug application under which the investigation was conducted, or the applicant or the applicant's predecessor in interest, provided substantial support for the investigation. To demonstrate "substantial support," an applicant must either provide a certified statement from a certified public accountant that the applicant provided 50 percent or more of the cost of conducting the study or provide an explanation why FDA should consider the applicant to have conducted or sponsored the study if the applicant's financial contribution to the study is less than 50 percent or the applicant did not sponsor the investigational new drug. A predecessor in interest is an entity, e.g., a corporation, that the applicant has taken over, merged with, or purchased, or from which the applicant has purchased all rights to the drug. Purchase of nonexclusive rights to a clinical investigation after it is completed is not sufficient to satisfy this definition.

Date of approval means the date on the letter from FDA stating that the new drug application is approved, whether or not final printed labeling or other materials must yet be submitted as long as approval of such labeling or materials is not expressly required. "Date of approval" refers only to a final approval and not to a tentative approval that may become effective at a later date.

Essential to approval means, with regard to an investigation, that there are no other data available that could support approval of the application.

FDA means the Food and Drug Administration.

New chemical entity means a drug that contains no active moiety that has been approved by FDA in any other application submitted under section 505(b) of the act.

New clinical investigation means an investigation in humans the results of which have not been relied on by FDA to demonstrate substantial evidence of effectiveness of a previously approved drug product for any indication or of safety for a new patient population and do not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness or safety in a new patient population of a previously approved drug product. For purposes of this section, data from a clinical investigation previously submitted for use in the comprehensive evaluation of the safety of a drug product but not to support the effectiveness of the drug product would be considered new.

(b) Submission of and effective date of approval of an abbreviated new drug application submitted under section 505(j) of the act or a 505(b)(2) application.

(1) [Reserved]

(2) If a drug product that contains a new chemical entity was approved after September 24, 1984, in an application submitted under section 505(b) of the act, no person may submit a 505(b)(2) application or abbreviated new drug application under section 505(j) of the act for a drug product that contains the same active moiety as in the new chemical entity for a period of 5 years from the date of approval of the first approved new drug application, except that the 505(b)(2) application or abbreviated application may be submitted after 4 years if it contains a certification of patent invalidity or noninfringement described in § 314.50(i)(1)(i)(A)(4) or § 314.94(a)(12)(i)(A)(4).

(3) The approval of a 505(b)(2) application or abbreviated application described in paragraph (b)(2) of this section will become effective as provided in § 314.107(b)(1) or (b)(2), unless the owner of a patent that claims the drug, the patent owner's representative, or exclusive licensee brings suit for patent infringement against the applicant during the 1-year period beginning 48 months after the date of approval of the new drug application for the new chemical entity and within 45 days after receipt of the notice described at § 314.52 or § 314.95, in which case, approval of the 505(b)(2) application or abbreviated application will be made effective as provided in § 314.107(b)(3).

(4) If an application:

(i) Was submitted under section 505(b) of the act;

(ii) Was approved after September 24, 1984;

(iii) Was for a drug product that contains an active moiety that has been previously approved in another application under section 505(b) of the act; and

(iv) Contained reports of new clinical investigations (other than bioavailability studies) conducted or sponsored by the applicant that were essential to approval of the application, the agency will not make effective for a period of 3 years after the date of approval of the application the approval of a 505(b)(2) application or an abbreviated new drug application for the conditions of approval of the original application, or an abbreviated new drug application submitted pursuant to an approved petition under section 505(j)(2)(C) of the act that relies on the information supporting the conditions of approval of an original new drug application.

(5) If a supplemental application:

(i) Was approved after September 24, 1984; and

(ii) Contained reports of new clinical investigations (other than bioavailability studies) that were conducted or sponsored by the applicant that were essential to approval of the supplemental application, the agency will not make effective for a period of 3 years after the date of approval of the supplemental application the approval of a 505(b)(2) application or an abbreviated new drug application for a change, or an abbreviated new drug application submitted pursuant to an approved petition under section 505(j)(2)(C) of the act that relies on the information supporting a change approved in the supplemental new drug application.