VENABLE, BAETJER, HOWARD & CIVILETTI, LLP
Including professional corporations

1201 New York Avenue, N W., Suite 1000
Washington, D.C 20005-3917
(202) 962-4800, Fax (202) 962-8300
www.venable.com

OFFICES IN

WASHINGTON, D C
MARYLAND
VIRGINIA

VENABLE
ATTORNEYS AT LAW

David G. Adams
(202) 216-8014
dgadams@venable.com

April 9, 2003

VIA HAND DELIVERY & FEDERAL EXPRESS

Dockets Management Branch
Food and Drug Administration
Room 1-23
12420 Parklawn Drive
Rockville, MD 20857

01137 '03 APR -9 P4:28

Re: Docket Number 02P-0447 (Citizen Petition) - Submission of Comments by Dr. Reddy's Laboratories, Inc.

Dear Sir or Madam:

Please accept the attached comments (in four copies) submitted on behalf of Dr. Reddy's Laboratories, Inc., in response to the Citizen Petition filed by Pfizer, Inc., on October 11, 2002.

Sincerely,

David G. Adams

02P-0447

C1

April 9, 2003

VIA HAND DELIVERY & FEDERAL EXPRESS

Dockets Management Branch
Food and Drug Administration
5630 Fishers Lane
Room 1061 (HFA-305)
Rockville, MD 20852

Re: Docket Number 02P-0447 (Citizen Petition) - Submission of Comments by Dr. Reddy's Laboratories, Inc.

Dear Sir or Madam:

These comments are submitted on behalf of Dr. Reddy's Laboratories, Inc., (Reddy) in response to the Citizen Petition filed by Pfizer, Inc., (Pfizer) on October 11, 2002 (Pfizer Petition). The petition requests that the Commissioner revoke FDA's acceptance for filing of, and/or deny approval of, NDA 21-435 for Reddy's amlodipine maleate product (Reddy NDA).

As set forth below, the petition must be denied based on the following grounds:

1. The statute permits FDA to rely on the approval of an NDA to approve a modified ANDA under section 505(b) of the Act.

2. FDA's reliance on the approval of an NDA to approve a modified ANDA under section 505(b)(2) of the Act does not result in an unconstitutional taking.

3. FDA's scientific determinations regarding Pfizer's NDA for Norvasc® (amlodipine besylate) (Norvasc) are applicable to Reddy's NDA.

BACKGROUND

Pfizer's petition seeks to overturn the agency's seventeen-year-old interpretation of the 1984 Amendments of the Food Drug, and Cosmetic Act (1984 Amendments) regarding NDAs submitted under section 505(b)(2) of the Act. Although this petition specifically challenges Reddy's 505(b)(2) NDA for amlodipine maleate, Pfizer actually seeks to nullify FDA's entire system for approving modified versions of ANDAs under the NDA provisions of the statute. For these modified versions of ANDAs, FDA relies

on the approval of the reference listed drug (RLD) in the same manner that it relies on the RLD to approve an unmodified ANDA.[1]

Pfizer would have FDA remove from the market many important products and many important labeling amendments that have been approved under section 505(b)(2) based on reliance on other RLDs. Although the precise numbers of these approvals cannot be determined based on publicly available data, it appears that the following original NDAs[2] may have been approved or tentatively approved under section 505(b)(2) based on reliance on RLDs:

Drug	**Company**	**Indications**
10% Calcium Chloride Injection, USP in 10mL Plastic Syringe	Abbott Labs Inc.	Treatment of hypocalcemia in those conditions requiring a prompt increase in plasma calcium levels.
Advicor (niacin extended-release and lovastatin) Tablets 500mg/20mg, 750mg/20mg, and 1000mg/20mg.	Kos	Treatment of primary hypercholesterolemia (heterozygous familial and nonfamilial) and mixed dyslipidemia (Fredrickson Types IIA and IIB).
Alavert (loratadine) orally disintegrating tablets)[3]	Whitehall-Robbins	Temporary relief of symptoms of hay fever or other upper respiratory allergies
Altocor (lovastatin) ER tablets	Aura Labs, Inc.	For lowering total cholesterol and LDL-C to target levels as an adjunct to diet and exercise, to slow the progression of atherosclerosis in patients with coronary heart disease, and to reduce Total-C, LDL-C, Apo B and triglycerides and to increase HDL-C in patients with Fredrickson types IIa and IIb dyslipoproteinemia.
CP2D (Anticoagulant Citrate Phosphate Double Dextrose)	Haemonetics	To be used only with automated apheresis devices for collecting human blood and blood components.

[1] Pfizer reargues a petition filed in July of 2001 (Docket No. 01P-0323) in which Pfizer and Pharmacia Corporation challenged FDA's authority to approve 505(b)(2) NDAs that rely on the agency's approval of other NDAs.

[2] A table of supplemental NDAs approved under section 505(b)(2) is attached as Appendix A (Tab 1). The approval letters do not indicate whether the supplements were approved based on literature or based on an RLD.

[3] Tentative approval.

Asimia (paroxetine mesylate) Tablets[4]	Synthon Pharmaceuticals Ltd.	For major depressive disorder, obsessive compulsive disorder, and panic disorder.
Avandamet (rosiglitazone maleate/metformin HCI) Tablets	GlaxoSmith-Kline	Adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus who are already treated with combination rosiglitazone and metformin, or who are not adequately controlled on metformin alone.
Avinza (morphine sulfate extended-release)	Elan Drug Delivery, Inc.	Relief of moderate to severe pain requiring continuous, around-the-clock opioid therapy for an extended period of time.
Avita (tretinoin)	Penederm Inc.	Indicated for topical application in the treatment of acne vulgaris.
Canasa (mesalamine) Suppositories	Axcan Pharma Inc.	Treatment of active ulcerative proctitis.
Cenestin (synthetic conjugated estrogen)	Barr	Treatment of moderate-to-severe vasomotor symptoms associated with menopause.
Cernevit-12 (multivitamins for infusion)	Baxter Healthcare	For (1) a daily multivitamin maintenance dosage for adults and children age 11 years and above receiving parenteral nutrition and (2) for situations where the administration by the intravenous route is required.
Children's Advil Cold (100mg per 5ml ibuprofen and 15mg per 5ml pseudoephedrine hydrochloride) Suspension, 4 fl. oz., Grape Flavor	Wyeth Consumer Healthcare	Temporary relief of symptoms associated with the common cold, sinusitis, or flu, including nasal congestion, headache, fever, body aches and pains, in children 2 to 11 years of age.
(clindamycin phosphate) Topical Gel, 1%	Target Research Assocs.	Once a day treatment of acne vulgaris.
Diltiazem (Once Daily)	Hoechst	Antihypertensive
GlucaGen (glucagon rDNA)	Novo Nordisk Pharmaceuticals Inc.	Treatment of hypoglycemia, and for use as a diagnostic aid.

[4] Tentative approval.

Glucovance (glyburide and metformin HCI tablets)	Bristol-Myers Squibb	Initial therapy, as an adjunct to diet and exercise, to improve glycemic control in patients with type 2 diabetes whose hyperglycemia cannot be satisfactorily managed with diet and exercise alone; Second-line therapy when diet, exercise, and initial treatment with sulfonylurea or metformin do not result in adequate glycemic control in patients with type 2 diabetes.
Ibuprofen capsules	Banner Pharmaceuticals Inc.	Temporary relief of minor aches and pains due to headache, muscle aches, minor pain of arthritis, toothache, backache, the common cold, menstrual cramps and temporarily reduces fever.
Mucinex (guaifenesin) Extended-Release 600mg Tablets	Adams Labs, Inc.	Expectorant for patients 12 years and above.
Multi-12 (Multiple Vitamins for Infusion)	Sabex Inc.	Daily multivitamin maintenance supplement for adults and children aged 11 years and older receiving parenteral nutrition or in other situations in which administration by intravenous route is required.
Mupirocin Ointment, 2%	Clay-Park Labs, Inc.	Topical treatment of impetigo due to *Staphylococcus aureus* and *Streptococcus pyogenes*.
Olux (clobetasol propionate) Foam, .05%	Connetics Corp.	Short-term topical treatment of the inflammatory and pruritic manifestations of moderate to severe corticosteroid-responsive dermatoses of the scalp
Pamidronate disodium Injection	Bedford Labs	Treatment of moderate or severe hypercalcemia associated with malignancy; Treatment of patients with moderate to severe Paget's disease of bone; Treatment of osteolytic bone metastases of breast cancer and osteolytic lesions of multiple myeloma in conjunction with standard antineoplastic therapy.
Repronex (menotropins for injection, USP)	Ferring Pharmaceuticals Inc.	Use in conjunction with hCG for multiple follicular development (controlled ovarian stimulation) and ovulation induction in patients who have previously received pituitary suppression.

Roxicodone (oxycodone hydrochloride)	Roxane Labs, Inc.	Management of moderate to severe pain where use of an opioid analgesic is appropriate.
Sulfa-methoxazole/ trimethoprim/ USP and phena-zopyridine hydrochloride tablets	ABLE Labs, Inc.	Treatment of urinary tract infections and for the symptomatic relief of pain, burning, urgency, frequency, and other discomforts arising from irritation of the lower urinary tract mucosa caused by infection.
Tavist Allergy/Sinus/ Headache (0.335mg clemastine fumarate/30mg pseudo-ephedrine sulfate/500mg acetaminophen) Tablets	Novartis Consumer Health	Temporary relief of symptoms associated with hay fever, allergic rhinitis, and the common cold.
Testim 1% (testosterone gel)	Auxilium Pharmaceuticals Inc.	Testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone: Primary hypogonadism and Hypogonadotropic hypogonadism.
Thalomid (thalidomide) Capsules	Steve Thomas, Ph.D.	Use in acute treatment of the cutaneous manifestations of moderate to severe erythema leprosum (ENL) and as maintenance therapy for prevention and suppression of the cutaneous manifestations of ENL recurrences.
Tri-Nasal (triamcinolone acetonide) Nasal Spray	Muro Pharmaceuticals Inc.	Treatment of nasal symptoms of seasonal and perennial allergic rhinitis in adults and children 12 years of age or older.
Versed injection and Versed syrup	Roche Labs, Inc.	Preoperative sedation/anxiolysis/amnesia; indication of general anesthesia; agent for sedation/anxiolysis/amnesia prior to or during diagnostic or therapeutic procedures.
Visicol (sodium phosphate monobasic monohydrate, USP and sodium phosphate dibasic anhydrous, USP) Tablets	InKine Pharmaceutical Co., Inc.	Cleansing of the bowel as a preparation for colonoscopy, in adults 18 years of age and older.

Xopenex (levalbuterol HCl) Inhalation Solution	Sepracor Inc.	Treatment or prevention of bronchospasm in adults and adolescents 12 years of age and older with reversible obstructive airway disease.
Zerit XR Extended Release (stavudine) Capsules	Bristol-Myers Squibb Co.	Treatment of HIV-1 infection in adults as part of a combination regimen.
20% ProSol—sulfite free (Amino Acid) Injection	Baxter Healthcare	Adjunct in the offsetting loss or in the treatment of negative nitrogen balance in certain patients; To reduce fluid intake in patients who require both fluid restriction and total parenteral nutrition.

Pfizer's remarkable challenge to these products and to FDA's generic drug approval process is without merit and Pfizer's petitions should be rejected by the agency.

DISCUSSION

I. The Statute Permits Submission of an Original Application for a Modified Version of an ANDA under Section 505(b)(2).

A. The Relationship Between ANDAs and 505(b)(2) NDAs

When Congress amended the Federal Food, Drug, and Cosmetic Act (FDCA) in 1984,[5] it provided a new statutory approval mechanism for companies seeking to market generic drugs. Under this mechanism, Congress directed FDA to rely on the approval of an NDA for one drug (i.e., an RLD) to approve a similar or identical generic drug in order to avoid requiring generic applicants to replicate safety and efficacy studies that have already been done. This reliance was conditioned, however, on statutory delays in approving the generic drugs, which were designed to reward the RLD manufacturers for product innovations (five-year and three-year exclusivity) and to protect patent rights (patent certifications and 30-month stays in approval).

The approval process introduced in 1984 distinguished closely related generic drugs that could be approved under ANDAs based on bioequivalence to RLDs from other generic drugs that must be approved under NDAs to allow a broader assessment of their safety and efficacy and, where necessary, to require new clinical studies. For generic drugs that are approved based on RLDs but that must be reviewed under NDAs rather than ANDAs, Congress defined a hybrid NDA in section 505(b)(2) of the Act.

For both these classes of generic drugs (drugs approved under ANDAs and drugs approved under 505(b)(2) NDAs), Congress provided trade-off protections for the RLDs

[5] Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984).

that are relied upon for the generic approvals. For generic drugs approved under ANDAs, Congress provided patent and exclusivity protections in sections 505(j)(2(A) and (j)(5)(D). In the case of NDAs submitted under section 505(b)(2), Congress provided the same patent and exclusivity protections accorded under the ANDA provisions of the Act. Congress required in section 505(b)(2)(A) of the Act that the 505(b)(2) applicant to provide the patent certifications identical to those required under section 505(j)(2)(A).[6] In section 505(c)(3)(D), Congress subjected 505(b)(2) applications to exclusivity restrictions that are identical to those imposed on ANDAs under section 505(j)(5)(D). Thus, Congress permitted FDA to rely on the data supporting approved NDAs under both section 505(j) and section 505(b)(2), and provided precisely the same patent and exclusivity protections to the NDA holders whose data are relied upon.

B. Modifications to Drugs Approved under ANDAs

One of FDA's first responsibilities after passage of the 1984 Amendments was to explain how the new statutory provisions were to be applied with regard to modifications to generic drugs that were already approved under ANDAs. Products approved under ANDAs, like products approved under NDAs, may later be modified with regard to formulation, dosage form, labeling, etc. These modifications may require new bioequivalence studies or, in some instances, new safety and efficacy studies. Thus, for some ANDAs, the agency is required to review supplements that contain clinical data. In the case of supplements requiring new safety and efficacy data, the agency had, prior to the 1984 Amendments, applied the same approval standard to both ANDAs and NDAs -- the applicant was required to demonstrate that the *modification* to the product is safe and effective.[7] Neither the NDA applicant nor the ANDA applicant was required to reinvent the wheel by reestablishing the safety and effectiveness of the originally approved version of the product.[8] The original ANDA, supplemented with clinical data, were reviewed and approved as a single application.

Soon after passage of the 1984 Amendments the agency addressed how such clinical supplements to ANDAs would be handled where Congress had provided separate statutory processes for NDAs and ANDAs and had limited ANDA approvals to evaluations of bioequivalence. FDA determined that these sorts of clinical supplements to approved ANDAs should be approved under section 505(b)(2).[9]

---

[6] *See* comparison of patent certification provisions for ANDAs and 505(b)(2) NDAs in Appendix B (Tab 2).

[7] *See* P. Bryan and G. Knapp, "Problems in Implementing Paper NDA's and Post-1962 ANDA's: FDA Perspectives," at 20 (1982) (Tab 3).

[8] *Id.*

[9] ANDAs for estradiol and estropipate were modified in this manner to add an osteoporosis indication. *See, e.g.*, Review and Evaluation of Clinical Data, ANDA 83-220 (estropipate) (Mar. 30, 1990).

The next question for the agency to address was the question of whether this two-step process involving an (1) initial approval of an original ANDA and (2) a subsequent approval of a supplement could be streamlined by allowing an applicant to submit a single, original application for a modified version of a product that could be approved under an ANDA. The agency determined that it would make no sense to require an applicant seeking approval for such a product to first obtain an ANDA for a product the applicant did not intend to market and then file a supplement for the modified version. Rather than requiring a two-step process, the agency determined that an original application consisting of the same data and information that would be contained in an approved ANDA with a clinical supplement could be approved under section 505(b)(2) in the same manner as an ANDA with a subsequently filed clinical supplement.

The agency communicated this determination in a 1987 letter to all NDA and ANDA holders and applicants signed by Dr. Paul Parkman (the 1987 Parkman Letter).[10] The agency explained in the letter that an original application for a drug that would have been approvable in a supplement to an approved ANDA should be submitted as an NDA described in section 505(b)(2). The agency noted that, because the new application is essentially a modified ANDA, the data required for approval would be the same data that would be required for approval of an original ANDA plus the data that would be required for approval of an ANDA supplement for the modification.[11] The agency also noted that the patent and exclusivity protections that would have attached under the ANDA process would attach under identical patent and exclusivity provisions related to 505(b)(2) NDAs.[12] The hybrid NDA described in section 505(b)(2), allowing approval of generic drugs based in part on the safety and effectiveness of other drugs, and conditioned on the same types of patent and exclusivity protections provided in the ANDA process, clearly encompassed drugs that were modified versions of ANDA products.

The agency again discussed this policy in the preamble to the agency's proposed regulations implementing the 1984 Amendments.[13] The agency repeated the analysis in the 1987 Parkman Letter, stating that a two-stage procedure requiring the initial approval of an ANDA that the company did not intend to market "would be inconsistent with the legislative purposes of the 1984 Amendments because it would serve as a disincentive to

---

[10] Letter to all NDA and ANDA holders and applicants from Paul D. Parkman, M.D., dated April 10, 1987.

[11] The agency stated:

> Like similar supplements to approved ANDAs, these applications will rely on the approval of the listed drug together with the clinical data needed to support the change. The applicant will thus be relying on the approval of the listed drug only to the extent that such reliance would be allowed under section 505(j): to establish the safety and effectiveness of the underlying drug.

Id.

[12] *Id.*

[13] 54 Fed. Reg. 28,872, 28,875, 28,892-93 (1989).

innovation and could require needless duplication of research."[14] No comment was submitted in opposition to the policy or to the provision of the proposed new regulation implementing the policy (21 C.F.R. 314.54).[15]

C. Pfizer's Belated Objection

Subsequent to the issuance of the Parkman letter, Pfizer filed its NDA for Norvasc. Pfizer does not appear to have objected to the policy announcement in the Parkman Letter. Two years later FDA proposed its regulation implementing the 505(b)(2) policy announced in the Parkman letter.[16] Neither Pfizer nor any other NDA holder appears to have commented on the proposed regulation implementing section 505(b)(2). Pfizer continued to seek approval of its Norvasc NDA. On April 26, 1992, the agency issued the final regulation implementing the policy.[17] Pfizer still pursued approval of its Norvasc NDA and received its approval on July 31, 1992. It was not until after the approval of the Norvasc NDA that Pfizer first expressed disagreement with the agency over section 505(b)(2) and proffered a contrary reading of the text and legislative history of the 1984 Amendments. Pfizer misreads both sources.

1. FDA May Rely on "Innovator Data" under Both 505(b) and 505(j).

Pfizer first argues that FDA cannot approve a modified ANDA submitted as an original application under section 505(b)(2) because "[s]ection 505(j), exclusively, authorizes FDA to rely on innovator data in order to expedite approval of a generic drug . . . ."[18] Pfizer seriously misconstrues the statute. Section 505(b)(2) expressly describes an NDA for a generic drug in which the applicant relies on studies that the applicant did not perform and for which the applicant has no right of reference. This clearly acknowledges that FDA can approve an NDA based on studies on an RLD without any right of reference.[19]

Moreover, Pfizer fails to appreciate the broader statutory structure. As discussed above, where generic drug applicants rely on data supporting an RLD under section 505(b)(2), Congress provided precisely the same patent and exclusivity protections that are provided where an ANDA relies on an RLD. Congress required in section 505(b)(2)(A) of the Act that the 505(b)(2) applicant to provide the patent certifications

---

[14] *Id.* at 28,892.

[15] The agency's policy was further explained in its Guidance for Industry: Applications Covered by Section 505(b)(2): Draft Guidance (1999).

[16] 54 Fed. Reg. at 28,919.

[17] 57 Fed. Reg. 17,950, 17,954-55 (1992).

[18] Pfizer Petition at 6.

[19] In fact, Pfizer states that section 505(b)(2) was intended to encompass NDAs that were previously described by FDA as "paper NDAs" (Pfizer Petition at 8). These "paper NDAs" were NDAs for generic drugs that relied, without permission, on published studies of innovator drugs.

identical to those required under section 505(j)(2)(A). In section 505(c)(3)(D), Congress subjected 505(b)(2) applications to exclusivity restrictions that are identical to those imposed on ANDAs under section 505(j)(5)(D). In the absence of reliance on the approval of an RLD under section 505(b)(2), there would have been no reason for Congress to provide the types of countervailing patent and exclusivity protections that are provided under the ANDA provisions of the Act.

Pfizer also argues that the "process and logic" of section 505(j) cannot be applied to section 505(b)(2) because the modified products approved under section 505(b)(2) may have different chemical structures (in the case of salts) and different adverse event profiles.[20] Pfizer misses the point in a rather profound way. The "process and logic" of section 505(j) is that, where a generic drug can be approved based on bridging studies without requiring the needless duplication of full safety and effectiveness studies on the underlying moiety, the government should not require generic manufacturers to reinvent the wheel. The government should instead provide the RLD manufacturers with statutory patent and exclusivity protections. This logic and process was provided under section 505(j) and under section 505(b)(2).

The only difference between the two processes is that, where certain generic drugs have differences that may require an assessment going beyond the narrow examination of bioequivalence permitted in an ANDA, FDA is allowed to conduct a more open-ended inquiry under section 505(b)(2). This is where Congress placed the review of generic drugs containing modified active ingredients such as salts and esters of the RLDs (ANDA's must contain the same active ingredient). In the case of Reddy's NDA for amlodipine maleate, FDA can require whatever clinical or preclinical data are necessary to determine that Reddy's *modification* is safe and effective. Thus the logic and process of reliance on an RLD (for the *unmodified* aspects of the generic drug that are the same as the RLD) is precisely the same under an ANDA or under a 505(b)(2) NDA.

2. The ANDA Suitability Process Remains Alive and Well.

Pfizer argues that FDA's interpretation of 505(b)(2) "eliminates entirely the public petition process set forth in section 505(j)."[21] In fact, the ANDA suitability petition process remains vital under the agency's interpretation of the statute. Under the ANDA provisions of the Act, Congress created a narrowly circumscribed process in which FDA is *required* to approve generic drugs based *solely* on a demonstration of bioequivalence (and safe and suitable inactive ingredients).[22] This circumscribed process is available, however, only to duplicates of RLDs and to certain specified modifications of RLDs (e.g., strength, dosage form, route of administration, and certain active

---

[20] Pfizer Petition at 6.

[21] *Id.* at 7.

[22] *See* FDCA § 505(j)(2) (FDA "may not require that an abbreviated application contain information in addition to that required by clauses (1) through (vii)").

ingredients). These specific types of modifications are allowed into the ANDA process only after FDA determines through a public petition process that the modified version can be approved based solely on bioequivalence. If FDA determines that it must examine additional data such as clinical safety or efficacy data, the applicant must file an NDA, which would ordinarily be a 505(b)(2) NDA.

The NDA approval process under section 505(b)(2) is significantly different from the ANDA suitability process. Unlike the ANDA process, the submission of an NDA under section 505(b)(2) permits the agency to make a full inquiry into safety and efficacy and to require whatever data it deems necessary, including clinical data. Congress did not provide a public petition process under section 505(b)(2) to review whether the modification could be approved based solely on bioequivalence because Congress did not require under section 505(b)(2) that FDA approve the modification based solely on bioequivalence. Because, under section 505(b)(2), as under section 505(b)(1), FDA can require whatever data it deems necessary to determine safety and effectiveness, there is no need for any public determination of any form of "suitability."

Section 505(b)(2) hardly renders the ANDA suitability process meaningless. FDA receives numerous suitability petitions each year from generic drug applicants seeking to have their products reviewed under the limited, bioequivalence standard of the ANDA process.

3. Section 505(b)(2) Does Not Conflict with Section 505(l).

Pfizer attempts to find support for its position in the disclosure provisions of section 505(l). Section 505(l) provides that the safety and effectiveness data in an NDA shall be made available to the public in certain enumerated circumstances, unless the NDA holder can show "extraordinary circumstances."[23] One of the bases for making the data available for disclosure is the approval of an ANDA or the passage of enough time for approval of an ANDA. Because section 505(l) does not provide a similar trigger for disclosure based on the approval of a 505(b)(2) NDA in addition to the ANDA trigger,

---

[23] Section 505(l) provides as follows:

> Safety and effectiveness data and information which has been submitted in an application under subsection (b) for a drug and which has not previously been disclosed to the public shall be made available to the public, upon request, unless extraordinary circumstances are shown -
>
> (1) if no work is being or will be undertaken to have the application approved,
> (2) if the Secretary has determined that the application is not approvable and all legal appeals have been exhausted,
> (3) if approval of the application under subsection (c) is withdrawn and all legal appeals have been exhausted,
> (4) if the Secretary has determined that such drug is not a new drug, or
> (5) upon the effective date of the approval of the first application under subsection (j) which refers to such drug or upon the date upon which the approval of an application under subsection (j) which refers to such drug could be made effective if such an application had been submitted.

Pfizer argues that FDA's interpretation of section 505(b)(2) renders section 505(l) "meaningless."[24]

Pfizer misunderstands section 505(l). Section 505(l) provides public access to safety and efficacy data in an NDA after the NDA holder's statutory exclusivity protections have been exhausted (when the first ANDA is or could have been approved). Congress did not provide a second trigger for disclosure based on the date that a 505(b)(2) NDA could be approved because such an additional trigger would have been unnecessary and potentially confusing. Congress was obviously aware that it had drafted statutory exclusivity protections for 505(b)(2) NDAs that were identical to those for ANDAs. This meant that that the potential date of approval for a 505(b)(2) NDA would be the same as that for an ANDA and that there would be no point in providing an additional trigger in section 505(l) based on the date that a 505(b)(2) NDA could have been approved.

Furthermore, the approval of a modified ANDA submitted under section 505(b)(2) can hardly be deemed to render section 505(l) meaningless. Section 505(l) goes well beyond FDA's limited use of data to approve another product. The provision is designed to allow *full public disclosure* of the data *to anyone for any purpose.*[25] Section 505(l) thus provides special mechanisms for protecting the data in "extraordinary circumstances," which is so broadly construed by the agency that the agency appears never to have released data under this provision.[26]

4. Section 505(b)(2) Is Not Limited to Publicly Available Reports.

Pfizer argues that section 505(b)(2) should not be read in terms of its plain meaning, but should be interpreted to embody an unstated restriction -- that the studies "relied upon" be published and publicly available. This limitation is not found in section 505(b)(2) and would render the provision meaningless.

Pfizer first asserts that the limitation comes from the plain meaning of the statute. Pfizer's task is difficult here because the wording of section 505(b)(2) is broad and contains no such restriction. Section 505(b)(2) describes the following type of application:

> An application for which the investigations described in [section 505(b)(1)(A)] and relied upon by the applicant for approval of the application were not

---

[24] Pfizer Petition at 7.

[25] The Supreme Court has recognized he important difference between an agency's internal use of one company's data in reviewing the application of another company and an agency's disclosure of the data for any use by a competitor. *See Ruckelshaus v. Monsanto Company*, 467 U.S. 986 (1984) ("It is important to distinguish at the outset public disclosure of trade secrets from use of those secrets entirely within [the agency]. Internal use may undermine [the company's] competitive position within the United States, but it leaves [the company's] position in foreign markets undisturbed").

[26] *See, e.g., Public Citizen Health Research Group v. FDA*, 997 F. Supp. 56, 69-71 (D.D.C. 1998).

> 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 . . . .

This wording neither states nor suggests that the studies relied upon must be published or publicly available.[27] The clear wording of the statute words instead expresses the absence of such a limitation.

Pfizer also seeks to rely on the legislative history of the 1984 Amendments to support its position, arguing that the legislative history "makes plain that section 505(b)(2) was intended to codify FDA's 'paper NDA' policy."[28] In fact, the legislative history demonstrates just the opposite. FDA's paper NDA policy, published in 1981, was a limited policy designed to assist the agency in approving generic drugs based on NDAs that were approved after passage of the 1962 Amendments. Under the original paper NDA policy, FDA relied on published reports of studies to approve generic drugs in narrowly tailored circumstances designed to mimic an ANDA.[29] Such applications could be submitted only where the generic application (1) identified an approved NDA (i.e., RLD) and (2) demonstrated that the generic drug in the paper NDA was a duplicate of the product approved in the original NDA.[30]

In enacting section 505(b)(2), Congress clearly chose to avoid these restrictions that defined the original paper NDA policy. Rather than codify FDA's 1981 paper NDA policy, Congress adopted its own, new definition of a "paper NDA":

> *Paper NDAs are defined as any application submitted under section 505(b)(2) of the FFDCA* in which the investigations relied upon by the applicant to show safety and effectiveness were not conducted by or for the applicant and the applicant has not obtained a right of reference or use from the person who conducted the studies or for whom the studies were conducted.[31]

---

[27] Pfizer argues that the statute supports its position because the statute refers in section 505(b)(2) to investigations for which the applicant has no "right of reference or use." Pfizer Petition at 8, n.12. Pfizer argues that this description forecloses approval of a 505(b)(2) NDA based on a "reference" to an approved RLD. A closer look at the language of section 505(b)(2), however, demonstrates the opposite. Congress made clear there that the provisions of section 505(b)(2) applied where "applicant has not obtained a right of reference or use *from the person by or for whom the investigations were conducted.*" In expressly referring to studies for which there is no right of reference from the owner, Congress appears to have rejected Pfizer's further limitation that there be no reference to the RLD in the manner expressly allowed under the ANDA provisions of the Act.

[28] Pfizer Petition at 8.

[29] 46 Fed. Reg. 27,396 (1981).

[30] *Id.*

[31] H.R. Rep. No. 857 (Part I), 98 Cong. 2d Sess., at 32 (1984) (emphasis added).

Thus, as FDA explained in the preamble to its regulation implementing section 505(b)(2), Congress created a new type of "paper NDA" that was significantly different from the agency's old definition of that term:

> The 1984 amendments also amended section 505(b) of the act (21 U.S.C. § 355(b)) to create another type of application. These applications, known as 505(b)(2) applications, are similar to applications under the agency's "paper NDA" policy. Unlike the paper NDA policy, however, section 505(b)(2) of the act applies to applications that contain investigations relied upon by the applicant to provide full reports of safety and effectiveness where the investigations were not conducted by or for the applicant and the applicant has not obtained a right of reference or use from the person who conducted the investigations. (See 21 U.S.C. § 355(j)(2). *Thus, section 505(b)(2) of the act is not restricted to literature-supported NDA's for duplicates of approved drugs; it covers all NDA's for drug products that rely on studies not conducted by or for the applicant or for which the applicant does not have a right of reference.*[32]

This interpretation is not only consistent with the wording of the statute and with Congress' definition of "paper NDA" in the legislative history, it is required to give meaning to section 505(b)(2).[33] Had Congress limited section 505(b)(2) to applications described under FDA's 1981 paper NDA policy, it would have rendered section 505(b)(2) superfluous. The agency's 1981 paper NDA policy was an effort to create what amounted to an ANDA for generic versions of "pioneer" drugs that were approved after 1962.

Prior to the passage of the 1984 Amendments, FDA had created an administrative mechanism for approving generic drugs based on bioequivalence to pioneer drugs that were approved prior to the 1962 Amendments to the FDCA. The 1962 Amendments required that all NDAs be approved based on a demonstration of effectiveness as well as safety. Because this requirement was retroactive for NDAs approved prior to 1962, FDA created a public process known as DESI[34] to assess effectiveness data for all pre-1962 NDAs. The agency applied its DESI determinations to all identical, similar, and related drugs and created an abbreviated new drug application that allowed for the approval of certain identical, similar, or related drug based on bioequivalence to the drug approved in the pioneer NDA. Although these abbreviated new drug applications were known as ANDAs and did not contain safety and effectiveness data, they were still considered to be NDAs submitted under section 505(b) of the Act.

---

[32] 57 Fed. Reg. 17,950, 17,952 (April 28, 1992) (emphasis added).

[33] FDA is required to interpret the statute in a manner that gives meaning to all of its provisions. *United States v. Nordic Village, Inc.*, 503 U.S. 30, 35-36 (1992).

[34] Drug Effectiveness Study Implementation.

While this DESI ANDA process enabled FDA to approve generic versions of pre-1962 pioneer drugs, it did not address generic versions of pioneer drugs approved after the 1962 Amendments. For post-1962 pioneer drugs, which were not addressed in DESI, FDA developed a "paper NDA" policy. Although this policy mimicked the ANDA process, it was more narrowly circumscribed and allowed approval of generic drugs only where there were published studies and only for generic drugs that were "duplicates" of drugs approved after 1962. The policy was so narrow that it was unavailable to the vast majority of post-1962 drugs.

Had Congress limited section 505(b)(2) to this small class of drugs as proposed by Pfizer, Congress would have had no need to craft the extensive patent and exclusivity provisions that accompany section 505(b)(2). Congress provided a separate statutory mechanism to address the approval of duplicates of all post-1962 pioneer drugs – the ANDA process of section 505(j). As the legislative history of the 1984 Amendments makes clear, section 505(j) was intended to resolve fully the problem that gave rise to FDA's pre-1984 paper NDA policy by providing an ANDA process for all post-1962 drugs.[35] Congress ensured in section 505(j) that duplicates of post-1962 RLDs no longer require published studies for approval and can be approved based on a simple reference to the approval of the RLD.[36]

Thus, section 505(b)(2) and its related patent and exclusivity provisions would have no purpose if Congress had limited their scope to duplicate products that could be approved under ANDAs. The lengthy and intricate patent and exclusivity protections found in sections 505(b)(2)(A) and 505(b)(2) of the Act, respectively, would be unnecessary because duplicates of RLDs are now approved under the ANDA provisions of the Act, where they are subject to separate patent and exclusivity protections. Section 505(b)(2) and its related patent and exclusivity provisions have meaning because Congress redefined the concept of a "paper NDA." Rather than stating that section 505(b)(2) was intended to codify FDA's 1981 definition of "paper NDA," the legislative history states that "[p]aper NDAs *are defined as any application submitted under section 505(b)(2) of the FFDCA* . . . ."[37]

II. FDA's Reliance on the Norvasc NDA to Approve Reddy's 505(b)(2) NDA Would Not Result in an Unconstitutional Taking.

Pfizer argues that FDA's reliance on the Norvasc NDA to approve Reddy's 505(b)(2) NDA would result in an unconstitutional taking. In support of this claim Pfizer asserts that (1) when it "developed and submitted the [Norvasc] data", the FDA had not yet published its' interpretation of section 505(b)(2) and (2) Pfizer "properly and reasonably understood from the statutory drug approval scheme that its data would be

---

35 H.R. Rep. No. 857 (Part I), 98 Cong. 2d Sess., at 16-17 (1984).

36 In fact, FDA's regulations do not permit the filing of a 505(b)(2) for a generic drug that is a duplicate of an RLD that could be approved under an ANDA. 21 C.F.R. 101(b)(9).

37 *Supra* note 31.

protected . . . ."[38] Pfizer's assertions are erroneous and, even if correct, would not demonstrate a taking.

Generally, regulatory use of information submitted voluntarily by an applicant for economic gain or advantage is not a "taking."[39] To demonstrate a taking in these circumstances, an applicant must demonstrate, *inter alia*, that it had a "reasonable investment-backed expectation" that the information submitted would remain confidential.[40] Moreover as the Supreme Court held in *Ruckelshaus v. Monsanto,*[41] this reasonable expectation of exclusive use must be based on an "explicit guarantee" by the government. The government provided no explicit guarantee to Pfizer that its data would not be relied on by FDA under section 505(b)(2) and, in fact, provided Pfizer with ample notice that its data could be relied on under section 505(b)(2). Because of the nature of the government's use of Pfizer's data and because of the absence of an explicit guarantee of non-use, Pfizer's takings claim is meritless.

A. Pfizer Fails to Demonstrate a Reasonable Investment-Backed Expectation of Non-Use.

1. The Government Did Not Provide Pfizer with an Explicit Guarantee of Exclusive Use.

Pfizer claims that, prior to 1992, when the FDA incorporated 505(b)(2) NDAs, Pfizer had a reasonable expectation of exclusive use because it believed that FDA did not interpret that statute to allow reliance upon approved NDAs and because FDA had not yet published a contrary position on the issue.[42] Pfizer's belief, even if genuinely held, does not give rise to constitutional protections.[43] A constitutionally protected expectation does not arise in the absence of an explicit guarantee that the information submitted by an applicant will remain proprietary and will not be used for any other purpose without the permission of the applicant.[44] Here, no such guarantee was ever made to Pfizer by FDA and, accordingly, no taking can exist.

---

38 Pfizer Petition at 9 (footnote omitted).

39 *National Fertilizer Association v. Bradley*, 301 U.S. 178, 181 (1937); *Westinghouse Electric Corp. v. United States Nuclear Regulatory Commission*, 555 F.2d 82, 95 (3d Cir. 1977).

40 *PruneYard Shopping Center v. Robbins*, 447 U.S. 74, 83 (1980). The court must also examine the character of the governmental action and its economic impact. *Id.*

41 467 U.S. 986 (1984).

42 Pfizer Petition at 9. Pfizer asserts that FDA did not state until 1999 that an applicant could seek approval of a different salt under section 505(b)(2), referring to FDA's *Guidance for Industry: Applications covered by section 505(b)(2): Draft Guidance.*

43 *Webb's Fabulous Pharmacies, Inc. v. Beckwith*, 449 U.S. 155, 161 (1980) ("a reasonable expectation must be more than a unilateral expectation or an abstract need").

44 *Monsanto*, 467 U.S. at 1008-09.

In *Monsanto*, the takings issue involved data submitted under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). The Court examined three sequential versions of that enactment. Under the first version, the act was "silent with respect to the [Environmental Protection Agency's] authorized use and disclosure of data submitted in connection with an application for registration."[45] Examining this version of FIFRA, the Court held that, *in the absence of an explicit guarantee*, Monsanto did not have a reasonable investment-backed expectation that the EPA would keep the data confidential or limit its use exclusively to Monsanto's application.[46] The Court found a taking existed only during the limited period in which the statute had "explicitly guaranteed" confidentiality and exclusive use of the information to applicants.[47]

The United States Court of Appeals for the Fourth Circuit recently confirmed the strictness of the test set forth in *Monsanto*:

> In the period between 1947 and 1972, "FIFRA was primarily a licensing and labeling statute," and it *failed to specify the government's ability to use and disclose data* submitted by pesticide manufacturers. Therefore, manufacturers like Monsanto had no guarantee that their data would be treated confidentially, nor did the government have specific authority to disclose such data. The Court concluded that *without a guarantee of confidentiality*, Monsanto had no reasonable investment-backed expectation that its submitted data would remain secret. Therefore, any disclosures of this data by the government did not constitute an unconstitutional taking of property.[48]

In the only FDA-related case in which a court found an unconstitutional taking, *Tri-Bio Laboratories, Inc. v. United States*,[49] the court found an explicit guarantee of protection against use. That case involved a new drug application for an animal vaccine. The court found a reasonable expectation of confidentiality and exclusive use grounded in an FDA regulation, limited to animal vaccines, that specifically provided that "[a]ny

---

45 *Id.* at 1008.

46 *Id.* at 1008-09. The Court reached this decision despite a finding by the district court that the agency had an internal policy precluding internal use of the data to approve a competitor's application. *Id.* at 1009, n.14. The Court upheld the district court's decision because the agency's policy was not publicly known *and* there was no "explicit guarantee of exclusive use" by the agency. *Id.* In *Monsanto* the Supreme Court also noted that "the Trade Secrets Act cannot be construed as any sort of assurance against internal agency use of submitted data during consideration of the application of a subsequent applicant for registration." *Id.* at 1010.

47 *Id.* at 1011. *See also Chevron Chemical Co. v. Costle*, 641 F2d 104 (3rd Cir. 1981) (government's use of pesticide data to approve later applications of generic producers was not a taking because federal law did not create in the submitter a legitimate expectation that the agency would not so use the data).

48 *Philip Morris v. Reilly*, 312 F.3d 24, 33 (4th Cir. 2002) (emphasis added; citations omitted).

49 836 F.2d 135 (3rd Cir. 1988).

reference to information furnished by a person other than the applicant *may not be considered* unless its use is authorized in a written statement signed by the person who submitted it."[50] The statute at issue here provides no such explicit guarantee to Pfizer.

Pfizer cannot establish even an *implicit* guarantee. FDA has made clear that companies that engage in business within the highly regulated drug arena are implicitly on notice that their regulatory status is not static, stating that such companies "cannot object if the legislative scheme is buttressed by subsequent amendments to achieve the legislative end."[51]

In any event, Pfizer cannot establish a reasonable investment-backed expectation in the absence of an explicit guarantee that FDA would not use the data in the Norvasc NDA to approve a competitor's NDA under section 505(b)(2). Because there is no such explicit guarantee, Pfizer cannot claim constitutional protection.

2. Pfizer Received Timely Notice that FDA Could Use Pfizer's Data to Approve Another Drug Under Section 505(b)(2).

Rather than guaranteeing Pfizer that its Norvasc NDA would not be relied on to approve other NDAs, the government told Pfizer the opposite. Pfizer was on notice from the clear wording of section 505(b)(2) and from the legislative history of that provision. As discussed above, section 505(b)(2) describes the rules for approving an NDA based in whole or in part on another applicant's studies without the permission of the other applicant. There is no limitation in section 505(b)(2) to reliance on published studies. Similarly, the legislative history clearly redefines the concept of a "paper NDA" in a manner that provides no limitation to published studies.

More significantly, the 1987 Parkman Letter states the government's interpretation of section 505(b)(2) in the clearest of terms. That letter provided Pfizer with explicit notice that a modified ANDA could be submitted under section 505(b)(2) without regard to whether the underlying safety and efficacy studies were published. The Parkman Letter was issued on April 10, 1987. Pfizer did not submit the Norvasc NDA until later.[52]

---

[50] 21 C.F.R. § 514.7(a) (1987). *See* 836 F.2d. at 140-141.

[51] 61 Fed. Reg. at 44,554 (citing *Connolly v. Pension Benefit Guar. Corp.*, 475 U.S. 211, 227 (1986). It has previously been stated that "[g]iven a long history of Government regulation of an industry, its members are "on notice that [they] might be subjected to different regulatory burdens over time.'" 61 Fed. Reg. at 44, 554 (citing *California Hous. Sec., Inc., v. United States,* 959 F.2d 955, 959 (Fed. Dir.1992)). The FDA has also stated that in order for expectations to be reasonable, they must take into account the regulatory environment, the foreseeability of changes in the regulatory scheme, and the power of the State to regulate in the public interest. 61 Fed. Reg. at 44, 554; 58 Fed. Reg. at 2398 (citing *Pace resources, Inc., v. Shrewsbury Township*, 808 F.2d 1023, 1033 (3rd Cir. 1987) and *Monsanto,* 467 U.S. at 1008).

[52] Pfizer states that it submitted the Norvasc NDA on December 22, 1987. Pfizer Petition at 9.

It is also important to note that the data in the Norvasc NDA were not available for FDA's use in approving other applications until the approval of Norvasc in 1992.[53] Prior to the approval of the Norvasc NDA, the FDA provided further notice to Pfizer in its proposed regulation implementing section 505(b)(2)[54] and in the promulgation of its final regulation in April 1992.[55] Although Pfizer could have withdrawn its pending NDA in response to these notices and thereby prevented any use by FDA of the data it now seeks to protect, Pfizer chose instead to pursue approval. In fact, Pfizer appears not to have even commented on the proposed regulation.[56]

Thus, Pfizer received numerous notices of FDA's policy on using data from approved NDAs to approve other NDAs under section 505(b)(2) and, despite these notices, chose to pursue approval of Norvasc. Pfizer chose to profit from the approval of Norvasc rather than shield its data from possible use by FDA in approving other NDAs. Pfizer's choice can hardly be deemed to be a taking by the government.

---

53 The relevant date in terms of Pfizer's notice is the date of FDA's approval of the Norvasc NDA. Prior to that date, Pfizer could have withdrawn the NDA rather than allow FDA to rely on it to approve another NDA. Because the Parkman Letter was issued before the filing of the Norvasc NDA, Pfizer attempts to argue that the agency's specific policy allowing a section 505(b)(2) NDA for a different salt was not made public until the publication of the 1999 Draft Guidance. The Parkman letter, however, clearly states that "[c]hanges in already approved drugs for which such applications will be accepted include changes in dosage form, strength, route of administration, and *active ingredients* . . . ." Pfizer had ample notice that a new active ingredient in the form of a new salt might be approved under a section 505(b)(2) application. In any event, Pfizer has failed to cite any express guarantee by the government that FDA would not accept a 505(b)(2) NDA for a different salt. *See* Section A, *supra*.

Although in *Monsanto* the Court referred to the reasonable expectations of Monsanto at the time the data were submitted rather than the date the application was approved, this was based on the fact that the relevant 1972 statute allowed regulatory use of the data upon the date of its submission, regardless of approval. 467 U.S. 986, 992 (1984). The statute provided that "data submitted in support of an application shall not, without permission of the *applicant*, be considered by the Administrator in support of any other application for registration unless such other applicant shall have first offered to pay reasonable compensation for producing the test data to be relied upon and such data is not protected from disclosure by section 10(b) [which protected 'trade secrets' from disclosure]." Federal Environmental Pesticide Control Act of 1972, § 3(c)(1)(D), 86 Stat. 973, Public Law 92-516 (current version generally providing for data exclusivity for fifteen years after the date the data is submitted and ten years after date of registration at 7 U.S.C. § 136a(c)(F)) (emphasis added). The 1972 statute clearly distinguishes between "registrants" and "applicants." "Registrant" is defined in the statute as "any person who has registered a pesticide pursuant to the provisions of this Act." *Id.* at § 2(y). In contrast, the term "applicant" is used to describe persons who are seeking a registration. Thus, data could be used in licensing other applications before the data submitter received an approved registration. EPA personnel confirm that EPA currently approves (subject to exclusivities provided for in the 1978 statute) and in the past has approved applications based on data from other, withdrawn or unapproved applications.

54 54 Fed. Reg. at 28919.

55 57 Fed. Reg. at 17982.

56 *Id.*

B. In Any Event, the Nature of the Government's Action Cannot Give Rise to an Unconstitutional Taking.

Even if Pfizer were able to establish a reasonable, investment-backed expectation that its data would not be released, which it cannot, Pfizer would still need to address the negative economic impact[57] and the nature of the government action causing that impact before a regulatory taking could be established. Here the latter factor is particularly important. Pfizer ignores it because the nature of the government's action in using scientific data in the drug approval process weighs against a taking.

As the agency has noted, "[c]ourts have accorded particular deference to government action taken to protect the public interest in health, safety and welfare."[58] As the agency has also noted, "[c]ourts are more likely to find a taking when the interference with property can be characterized as a physical invasion by the Government than when the interference is caused by a regulatory program that 'adjust[s] the benefits and burdens of economic life to promote the common good.'"[59] This is particularly true in government licensing schemes.

FDA has always relied on the approval of old products to approve new, competing therapies. This occurs every time the agency approves a new drug based on an active-controlled trial involving another approved drug. The approval of the new product will be based, at least in part, on the agency's determination that the old product is safe and effective. There is no reason, in the absence of an explicit guarantee to the contrary, for an NDA holder to have a different expectation with regard to a competitor that seeks approval based on a comparative bioavailability, comparative pharmacokinetics, comparative pharmacodynamics, or other comparative parameters. These comparisons are, essentially, comparative clinical trials using a surrogate endpoint (bioavailability) to demonstrate therapeutic equivalence.[60]

---

[57] New generic competition will obviously have an economic impact on a company. FDA has often pointed out with regard to its regulatory actions, however, that the "economic impact may be great without rising to the level of a taking." *See Final Rule: Regulations of Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body*, 65 Fed. Reg. 1000, 1042 (January 6, 2000); *Final Rule: Regulations Restricting the Sale and Distribution of Cigarettes and Smokeless Tobacco to Protect Children and Adolescents,* 61 Fed. Reg. 44,396, 44,553 (August 28, 1996); *Final Rule; Food Labeling; Nutrient Content Claims*, 58 Fed. Reg. 2302, 2399 (January 6, 1993) (explaining in all of these rulemakings that prohibiting the use of some established product names or other proprietary trademarks was not a taking although the economic impact might be substantial). The agency has also stated that "mere denial of the most profitable or beneficial use of the property does not require a finding that a taking has occurred ... [r]ather, courts look for drastic interference with a property's possible uses." 61 Fed. Reg. at 44,553.

[58] 61 Fed. Reg. at 44,552 (citations omitted); 58 Fed. Reg. at 2397 (citations omitted); 65 Fed. Reg. at 1041 (citations omitted).

[59] *Id.*

[60] In fact, it is clear that FDA's 1981 paper NDA policy was predicated on some degree of reliance on the approval of an RLD. Under that policy FDA relied upon published reports that did not contain the actual data that FDA generally requires for approval of an NDA. The agency accepted such paper NDAs

This also goes to a fundamental point regarding the character of the government action. FDA's reliance on that which is established and generally known, such as the safety and effectiveness of a comparable product, is good science and good public health policy. There is no question that the agency may rely on such information in assessing possible risks that a new product may pose. As FDA has noted in rulemaking preambles dismissing this type of takings concern, that "[c]ourts have accorded particular deference to governmental action taken to protect the public interest in health, safety, and welfare.: 61 Fed. Reg. at 44,552 (citations omitted); 58 Fed. Reg. at 2397 (citations omitted); 65 Fed. Reg. at 1041 (citations omitted).

III. FDA's Reliance on the Norvasc NDA to Approve Reddy's 505(b)(2) NDA Would Be Scientifically Appropriate.

Pfizer argues that there is no scientific basis for FDA to rely on data in the Norvasc NDA to approve the Reddy NDA for amlodipine maleate.[61] Pfizer's scientific arguments fare no better than its legal arguments. The data and information in Reddy's NDA demonstrate that FDA's approval of the Norvasc NDA is relevant to Reddy's amlodipine maleate product and that Reddy's product is safe, effective, and therapeutically equivalent to Norvasc.

CONCLUSION

The 1984 Amendments adjusted property rights by creating a statutory process for approving generic drugs based on approved NDAs and by granting specific benefits to those NDA holders. The NDA holders were benefited by statutory exclusivity protections, patent protections including 30-month stays, and patent-term extensions. Pfizer cannot challenge this compromise or its rationale in the context of a modified ANDA submitted under section 505(b)(2), any more than Pfizer can challenge the approval of unmodified ANDAs under section 505(j).

There is no basis in the wording of the statute or in logic to allow FDA to use data supporting an RLD to approve an ANDA but not allow FDA to use the data in the same manner, subject to the same protections, to approve a modified version of the ANDA under section 505(b)(2). Where Congress sought to protect rights to data, it provided patent and exclusivity protections. Where those protections no longer apply, it is

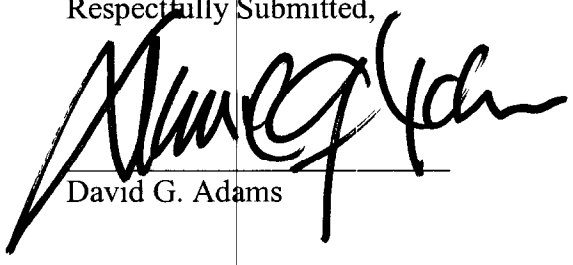
---

only where the paper NDA applicant could identify an approved NDA for the RLD. The requirement of an approved NDA for an RLD meant, by definition, that FDA relied in part on its approval of the RLD (which contained the actual data).

[61] Pfizer Petition at 11-13.

reasonable to expect the government to make determinations regarding the safety and effectiveness of new products based on comparisons to old products that the government has determined to be safe and effective.

Respectfully Submitted,



David G. Adams