UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

NEW MEXICO UNITED FOOD AND COMMERCIAL WORKERS UNION'S AND EMPLOYERS' HEALTH AND WELFARE TRUST FUND, on behalf of itself and all others similarly situated,

Plaintiff,

v.

ASTELLAS PHARMA US, INC.,

Defendant.

CIVIL ACTION NO. 11-11621

PLAINTIFF DEMANDS A JURY TRIAL ON ALL COUNTS

COMPLAINT AND JURY DEMAND

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I. INTRODUCTION

1. When a drug company faces the imminent entry of generic competitors and the loss of nearly 90% of revenue, it has two choices: it can do nothing, and rest on the monopolistic profits already reaped during the product's patent life; or, it can resort to baseless tactics to extend its monopoly. This is a case where the drug company chose the latter.

2. The product that is the subject of this suit is Prograf, a branded form of tacrolimus. In 1984, Japanese researchers discovered tacrolimus in the fermentation broth of soil fungus that they had collected at the foot of Mt. Tsukubu. Experimental data suggesting that tacrolimus had immunosuppressive properties were published three years later, and in 1994, the FDA approved tacrolimus as an immunosuppressant drug to help prevent organ rejection in patients who have received a heart, kidney, or liver transplant.

3. Defendant Astellas Pharma US, Inc. ("Astellas") manufactures and sells Prograf. And for roughly 15 years, Astellas has been the sole producer and seller of tacrolimus. In order to increase its profits at the expense of patients and the healthcare community, Astellas unlawfully abused the generic drug approval regulatory process and fraudulently delayed the introduction of cheaper generic versions of tacrolimus to compete with Prograf. As a result of its efforts, Astellas unlawfully extended its monopoly in the market for tacrolimus for nearly two additional years, forestalling the entry of generic competitors and selling hundreds of millions of dollars of Prograf at an inflated cost during that time. By delaying generic availability for two years, Astellas

has also caused and is causing generic tacrolimus purchasers to pay a higher price than they would have had the competitive generic market started earlier.

4. Plaintiff New Mexico United Food and Commercial Workers Union's and Employers' Health and Welfare Trust Fund, ("NMUFCW") brings this nationwide class action against Defendant Astellas on behalf of itself and a proposed class of indirect purchasers of the prescription drug Prograf and its generic equivalent, tacrolimus. As a result of its anticompetitive conduct to keep generic versions of Prograf off the market and in violation of antitrust and consumer protection laws, Astellas: (a) illegally maintained monopoly power in the market for tacrolimus in the United States for up to two years; (b) maintained and even increased the price of Prograf above competitive levels; and (c) illegally caused the Plaintiff and other members of the proposed class of indirect purchasers of tacrolimus to pay millions of dollars more than they would have had there been unrestricted competition and access to cheaper generic versions of tacrolimus.

5. This class action is brought on behalf of all end-payors (*i.e.*, consumers and third-party payors that pay for prescriptions for family members, employees, or insureds) who purchased or paid for tacrolimus products including Prograf after September 21, 2007.

6. Plaintiff and the Class seek damages for the Defendant's violations of the antitrust and/or deceptive practice statutes of Arizona, California, District of Columbia, Florida, Iowa, Kansas, Maine, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Nebraska, Nevada, New Mexico, New York, North Carolina, North Dakota,

Pennsylvania, South Dakota, Tennessee, Vermont, West Virginia, and Wisconsin (collectively, the "Indirect Purchaser States").

7. Plaintiff and the Class also seek a judgment pursuant to §16 of the Clayton Act, 15 U.S.C. § 26, enjoining the continuation of the Defendant's unlawful monopolistic practices in violation of § 2 of the Sherman Act, 15 U.S.C. §2. Neither Plaintiff nor the Class seek any relief under §4 of the Clayton Act, 15 U.S.C. § 15.

8. Plaintiff and the Class also seek equitable remedies to redress the Defendant's unjust enrichment.

I. PARTIES

9. Plaintiff New Mexico United Food and Commercial Workers Union's and Employers' Health and Welfare Trust Fund, ("NMUFCW") is a Taft-Hartley fund with its principal place of business in Albuquerque, New Mexico.

10. During the Class Period, NMUFCW paid for prescriptions of Prograf and generic tacrolimus and has suffered damages as a result of Defendants' illegal and wrongful conduct alleged herein.

11. NMUFCW brings this class action on behalf of itself and a proposed class of indirect purchasers of the prescription drug Prograf and its generic equivalent, tacrolimus. The allegations in this Complaint are based on: (a) personal knowledge as to matters relating to Plaintiff; (b) the investigation of Plaintiff's counsel, including review of Defendant's citizen petition and other filings with the United States Food and Drug Administration ("FDA"), and court papers and court opinions filed in connection

with Defendant's motions for Temporary Restraining Order and Preliminary Injunction; and (c) information and belief as to all other matters.

12. Defendant Astellas Pharma US, Inc. ("Defendant" or "Astellas") is a Delaware Corporation with its principal offices located at Three Parkway North, Deerfield, Illinois. Astellas is the US affiliate of Astellas Pharma Inc., Tokyo, Japan, a corporation created by the merger of Yamanouchi Pharmaceutical Co., Ltd. and Fujisawa Pharmaceutical Co., Ltd. in 2005. Astellas regularly sells its drug products in the Commonwealth of Massachusetts, owns and operates a facility in the Commonwealth, and maintains full-time employees within the Commonwealth.

II. JURISDICTION AND VENUE

13. This Court has jurisdiction over this action based upon 28 U.S.C. § 1332(a), in that the matter in controversy exceeds the sum or value of $75,000 (exclusive of interests and costs), and that NMUFCW, which resides in New Mexico, and Astellas, a Delaware corporate with its principal place of business in Illinois, are citizens of different states.

14. Additionally, this Court also has jurisdiction over this action based upon the Class Action Fairness Act of 2005 ("CAFA"), 28 U.S.C. §§ 1332(d), in that: (a) the matter in controversy, aggregating all individual class members' claims, exceeds the sum or value of $5,000,000 (exclusive of interests and costs); (b) this is a class action in which NMUFCW, a member of the class which resides in New Mexico, and Defendant Astellas, a Delaware corporate with its principal place of business in Illinois, are citizens of different states; (c) there are more than 100 members of all proposed plaintiff classes;

and (d) fewer than two-thirds of the members of all proposed plaintiff classes in the aggregate are citizens of the state in which the action was originally filed.

15. Plaintiff also brings this action pursuant to § 2 of the Sherman Act, 15 U.S.C. § 2, and § 4 and § 16 of the Clayton Act, 15 U.S.C. §§ 15 & 26. This Court thus also has jurisdiction over this action based upon 28 U.S.C. §§ 1331 & 1337(a) and 15 U.S.C. § 15.

16. Venue is proper in this judicial district pursuant to 15 U.S.C. § 22 and 28 U.S.C. § 1391 in that Astellas transacts business in this judicial district and can be found in this judicial district.

III. LEGAL BACKGROUND

A. The Regulatory Structure for Approval of Generic Drugs

17. Under the Federal Food, Drug, and Cosmetic Act ("FDCA"), codified at 21 U.S.C. §§ 301-392, manufacturers who create a new drug product must obtain the approval of the FDA to sell the new drug by filing a New Drug Application ("NDA"). An NDA must include submission of specific data concerning the safety and effectiveness of the drug, as well as any information on applicable patents. 21 U.S.C. § 355(a), (b).

18. In 1984, Congress modified the FDCA by enacting the Drug Price Competition and Patent Term Restoration Act, Pub. L. No. 98-417, 98 Stat. 1585 (1984). The modification, more typically known as the Hatch-Waxman Amendments, simplified the regulatory hurdles for prospective generic manufacturers eliminating the need to file a lengthy and costly NDA in order to obtain the FDA approval. Instead, the

FDA provides an expedited review process by which generic manufacturers file an abbreviated application (an "ANDA") which relies in substantial part on the scientific finding of safety and effectiveness included by the brand named manufacturer in the NDA for the same drug. 21 U.S.C. § 3550(j).

19. Two primary goals motivated the enactment of the Hatch-Waxman Amendments. First, where a generic product could be developed that did not infringe any existing legitimate patent, Congress sought to expedite the entry of generic competitors and thereby reduce healthcare expenses nationwide. Second, Congress wanted to protect the incentive of pharmaceutical companies to create new and innovative products. The Hatch-Waxman Amendments achieved both goals, substantially advancing the rate of generic product launches, and ushering in an era of historic high profit margins for brand name pharmaceutical companies.

20. Under the terms of the FDCA and the Hatch-Waxman Amendments, a prospective generic manufacturer must demonstrate to the FDA that the generic drug it proposes to market is bioequivalent to the brand named drug. 21 U.S.C. § 355(j)(2)(A)(iv). The FDCA and Hatch-Waxman Amendments operate on the presumption that bioequivalent drug products containing identical amounts of the same active ingredients in the same route of administration and dosage form, and meeting applicable standards of strength, quality, purity and identity; are therapeutically equivalent and may be substituted for one another. Thus, bioequivalence demonstrates that the active ingredient of the proposed generic drug

would be present in the blood of a patient to the same extent and for the same amount of time as the branded counterpart. 21 U.S.C. § 355(j)(8)(B).

21. In reviewing what scientific method it might consider in determining bioequivalence of drugs, the FDA may - but is not required to - issue a guidance document articulating the agency's current thinking on the issue. However, no regulation requires the FDA to issue such a guidance document. Guidance documents, where they exist, do not bind either the FDA or the public, as they do not establish legally enforceable rights or responsibilities. Rather, guidance documents are just that - they embody the FDA's current thinking on a subject and provide guidance to the public. The FDA's obligation to make a determination as to whether an individual ANDA meets statutory requirements and thus should be approved depends in no part on whether or not a guidance document relevant to that ANDA exists, or whether the ANDA complies with the recommendations made in the guidance document.

22. As a counter-balance to this abbreviated approval procedure for bioequivalent generic drugs, the Hatch-Waxman Amendments streamlined the process for brand name manufacturers to enforce legitimate patents they hold against infringement by generic manufacturers. Beyond traditional patent rights, the Hatch-Waxman Amendments also provide manufacturers of brand name drugs with several means to obtain legitimate protection from generic competition for set, and specifically limited, periods of time. For example, each approved NDA provides the owner of that drug with three years of exclusivity during which time no generic manufacturer can even file an ANDA. 21 U.S.C. § 355(j)(5)(F)(iii). Pioneer drugs or truly new or

innovative drugs that make use of a never-before-approved chemical entity or moiety receive even more time: a "New Chemical Entity" ("NCE") exclusivity period of five years. 21 U.S.C. § 355(j)(5)(F)(ii).

B. Generic Drugs Offer Significant Savings and Take Significant Sales from Brand Name Drugs

23. Drugs proven to meet bioequivalence requirements through *in vivo* (clinical) and/or *in vitro* (laboratory) testing receive an "AB" rating from the FDA, indicating they are therapeutically equivalent to other drugs with the same rating in the same category. For example, Sandoz Inc.'s tacrolimus capsules are AB-rated generic versions of Astellas's Prograf, indicating the drugs are therapeutically equivalent and bioequivalent to one another.

24. Typically, manufacturers of AB-rated generic versions of brand name drugs price their drugs significantly below the brand name counterparts. Because of the price differential and certain institutional features within the pharmaceutical market that seek to capitalize on this price differential, AB-rated generic versions are rapidly and substantially substituted for their brand name counterparts.

25. Under the statutory regime enacted by Congress (*i.e.*, the Hatch-Waxman Amendments) and as found in most state legislatures (*i.e.*, Drug Product Selection, or "DPS" laws), pharmacists may - and, in most states, must - substitute an AB-rated generic version of a drug for the brand name drug without seeking or obtaining

permission from the prescribing doctor.[1] Congress and state legislatures actively encourage generic substitution of brand name drugs because of the enormous cost savings to purchasers and consumers generated.[2]

26. Once a physician writes a prescription for a brand name drug such as Prograf, the prescription defines and limits the available options to the named drug and its AB-rated generic equivalent(s). Only drugs that carry the FDA's AB generic rating in that category may be substituted by pharmacists for a physician's prescription for a brand name drug.

27. Generic competition enables the purchase of generic versions of brand name drugs at substantially lower prices. Such competition also results in reduced prices for, and thus savings on purchases of, the brand name drug (as the brand manufacturer lowers prices in an attempt to maintain market share). Prior to entry of an AB-rated generic and competition, however, a brand name manufacturer can charge supra-competitive prices without losing all, or a substantial portion, of its brand name sales. Consequently, brand name drug manufacturers have strong incentives to delay the introduction of AB-rated generic competition into the market.

[1] The exception to this general rule appears when the prescribing physician writes "dispense as written" or "DAW" on the prescription. In such instances, pharmacists may not substitute a generic version of the drug.

[2] Federal and state legislatures also recognize that the economics of the pharmaceutical industry prevent generic manufacturers from engaging in the heavy promotion or "detailing" typically done by brand name manufacturers.

C. Citizen Petitions to the FDA

28. Recognizing the central role that healthcare and pharmaceutical drugs play in the United States, Congress enacted federal regulations governing the FDA that allow individuals to express genuine concerns about safety, scientific, or legal issues regarding a product any time before, or after, its market entry. Under these regulations, any person or entity, including a pharmaceutical company, may file a citizen petition with the FDA requesting that the FDA take, or refrain from taking, any administrative action. 21 C.F.R. § 10.30.

29. The citizen petition must contain not only a statement of what action is being requested, but also a justification for that action, including, if appropriate, convincing scientific data and other information. The submitter of the citizen petition also includes a certification stating that the petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner that are unfavorable to the views expressed in the citizen petition. *Id.*

30. Reviewing and responding to these petitions often requires the use of substantial time and resources because the FDA must, in addition to its already-existing workload: (a) research the subject matter of the citizen petition; (b) examine scientific, medical, legal, and sometimes economic issues; (c) consider public responses to the citizen petition; and (d) coordinate internal agency review and clearance of the petition response. These activities can and do strain the FDA's limited resources.

D. Manufacturers of Branded Products Use Citizen Petitions to Forestall Generic Competition

31. In recent years, a number of brand name pharmaceutical manufacturers abused the citizen petition process, using it as a tactic to extend their monopolies on name brand drugs.[3] Citizen petitions by rival companies rarely raise legitimate concerns about the safety or efficacy of generic products, and instead only seek to preserve monopolies after the end of a statutorily granted patent or the FDA exclusivity period. Companies frequently file these citizen petitions on the eve of the FDA approval of an ANDA for a competing AB-rated generic drug, even though the petitioner could have made the same arguments months, or even years, earlier. This results in delay of final approval of a pending ANDA for several months or more while the FDA evaluates the merits of the citizen petition.

32. The resulting delay of generic competition can be lucrative for an incumbent brand name manufacturer facing impending competition from an AB-rated generic. The cost of filing an improper or "sham" citizen petition and the potential injury to company goodwill are dwarfed by the high profits reaped by an indefinite extension of the monopoly.

33. In recent years, only about 7% of citizen petitions regarding the approvability of generic products led to any change in the FDA's policy based on actual data or information submitted in the petition. Yet prior to 2007, the FDA maintained a

[3] *See* Comment of the Staff of the Bureau of Competition and of Policy Planning of the Federal Trade Commission, March 2, 2000, *available at* http://www.ftc.gov/be/v000005.pdf, at 1, *et seq.*

practice, well known in the pharmaceutical industry, of considering and responding to relevant citizen petitions prior to approval of an ANDA to assure itself that the petitions did not present any new issues or issues of concern.

34. Under the FDA's regulations, it should respond to citizen petitions within six months. During the time involved in this case, and regardless of the merit of the arguments made in the citizen petition, it was common for the FDA to take longer than six months to respond, especially if the citizen petition raised numerous technical issues that would require input from various disciplines.

35. Until changed by legislation enacted in 2007, a brand name drug manufacturer that filed a citizen petition appearing to contain substantive issues relating to a pending ANDA often slowed down the FDA's approval process because of the FDA's general policy, responding to the citizen petition before or at the time of the approval of related ANDAs. Brand name drug firms were well aware that filing of a citizen petition, regardless of merit, would delay ANDA approval and delay generic competition and they used this tactic to effect.

36. In a July 20, 2006 statement before the Senate Special Committee on Aging, Gary Buehler, Director of the FDA's Office of Generic Drugs ("OGD"), acknowledged that the FDA waits for a thorough review of citizen petitions before approval of related ANDAs, and he discussed an assessment of recent uses of citizen petitions regarding pending ANDAs:

> Although it is not required that a Citizen Petition response be issued before approval of a related ANDA, it is important that FDA comprehensively assess the scientific issues prior

> to approval of the ANDA. It is very rare that petitions present new issues that CDER has not fully considered, but the Agency must nevertheless assure itself of that fact by reviewing the citizen petitions.
>
> A high percentage of the petitions OGD reviews are denied. An analysis of petitions answered between calendar years 2001 and 2005, raising issues about the approvability of generic products (42 total responses), showed that FDA denied 33, denied three in part, and granted six. It should be noted that when petitions are granted, wholly or in part, it is often because FDA already has the proposed scientific or legal standard in place or is already planning to take the action that the petition requests. While the citizen petition process is a valuable mechanism for the Agency to receive information from the public, it is noteworthy that very few of these petitions on generic drug matters have presented data or analysis that significantly altered FDA's policies. Of the 42 citizen petition responses examined, only three petitions led to a change in Agency policy on the basis of data or information submitted in the petition.[4]

37. The abuse of the citizen petition process helped lead Congress to enact the FDA Amendments Act of 2007, 21 U.S.C. § 355(q) (the "2007 Amendments"). In pertinent part, the 2007 Amendments provide that the FDA shall not delay approval of a pending ANDA because of a citizen petition unless the FDA determines that a delay is necessary to protect the public health. The 2007 Amendments also authorize the FDA to summarily deny any citizen petition whose primary purpose, as determined by the FDA, is to delay competition. Signed into law on September 27, 2007, these revisions were not yet in effect at the time the FDA was considering the petitions at issue here.[5]

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[4] *FDA Efforts to Expedite Generic Drug Approvals, Hearing Before the Senate Special Comm. on Aging*, 109 Cong. 109-28 (2006), Statement of Gary Buehler, Director of Office of Generic Drugs, July 26, 2006, *available at* http://www.fda.gov/NewsEvents/Testimony/ucm161497.htm.

IV. FACTUAL BACKGROUND

A. Organ Transplantation and Immunosuppressant Therapy

38. Transplantation is the replacement of organs, tissues, or cells in a body. When the transplantation moves one part of the body to another area in the same person, the transplant is called an "autograft." Skin transplants and stem cell transplants are examples of possible autografts. When the transplantation occurs across species, such as from pig to human, the transplant is called a "xenograft." Some heart valve replacements and cartilage replacements are xenografts. When the transplantation occurs within the same species, such as from one person to another unrelated person, the transplant is called an "allograft."

39. Allografts account for many human transplants. Heart, lungs, heart/lung, kidneys, pancreas, liver are the most common organs transplanted. Allografts are obtained from cadaveric, living related, and living unrelated donors.

40. Currently more than over 100,000 patients await organ transplant.[6] Kidney (85,450) and liver (16,094) have the largest waiting list for organ donors. *Id*. In 2009, however, only about 28,500 transplants were conducted (21,850 with organs from deceased donors, and nearly 6,600 organs from living donors).[7]

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[5] In January 2009, the FDA issued a Draft Guidance for Industry regarding the 2007 amendments, entitled "Citizen Petitions and Petitions for Stay of Action Subject to Section 505(q) of the Federal Food, Drug and Cosmetic Act" ("Citizen Petitions Guidance"). *See* 74 Fed. Reg. 3611 (Jan. 21, 2009). The Citizen Petitions Guidance, which is available at http://www.fda.gov/OHRMS/DOCKETS/98fr/FDA-2009-D-0008-gdl.pdf, makes clear the FDA's thinking that the 2007 Amendments "only" apply to [citizen] petitions that are submitted on or after September 27, 2007." Citizen Petitions Guidance at 5, lines 169-70.

[6] *See* 2009 Donor, Transplant and Waiting List Numbers published by the U.S. Department of Health & Human Services, *available at* http://optn.transplant.hrsa.gov/data/.

[7] *See id.* at http://optn.transplant.hrsa.gov/data/data_resources.asp.

41. Given the scarcity of organs, every effort must be made to ensure that that the patient remains in good health and that the body does not reject the transplant. Organ rejection occurs when the body has an immune response to the transplanted organ, that is, the body's immune system recognizes the allograft as foreign and attacks the allograft, leading to transplant failure and removal of the transplant from the body.

42. Rejection can be minimized through serotyping before transplant: matching the compatibility of the donor to the recipient based on various markers (*e.g.,* blood type, and other factors) and through the use of drugs that suppress the immune system (immunosuppressants).

43. One class of immunosuppressant medications is the calcineurin inhibitors. Calcineurin is an enzyme that activates "cytotoxic T-cells", a group of white blood cells that are part of the immune system. These T-cells attack foreign cells in the body, such as virally infected cells and tumor cells. Activated cytotoxic T-cells are also implicated in organ transplant rejection - *i.e.,* they recognize the transplanted organ as foreign cells and attempt to destroy it. Calcineurin inhibitors inhibit the T-cell activation via the calcineurin pathway, and thereby prevent the immune system cascade that leads to organ rejection. Calcineurin inhibitors used to prevent organ transplant rejection are cyclosporine, tacrolimus, and sirolimus (rapamycin) (indicated for kidney transplants only).

44. These immunosuppressants are administered in combination with other agents, including immunosuppressants (such as corticosteroids and antimetabolites); antifungal, antibacterial, and antiviral agents to support the patient's weakened and

suppressed immune state; and agents for the management of other diseases (*e.g.*, diabetes, hypertension, etc.).

45. Narrow therapeutic index ("NTI") drugs are drugs for which the minimum toxic concentration and the minimum effective concentration are within a two-fold range.[8] A "critical dose drug" is a drug with an NTI; that requires blood level monitoring; for which dosing is based, on highly individualized parameters; for which serious clinical consequences of overdosing (toxicity) or underdosing (lack of effect) can occur; and that has a steep dose-response relationship for either efficacy or toxicity, or both. Small changes in systemic concentration can have a significant difference in pharmacodynamic and clinical response. Monitoring blood levels of NTI drugs is critical to ensure that that the optimum dosage is maintained and adverse events are avoided.

46. The FDA considers cyclosporine an NTI drug; however, the FDA has not made a determination whether to characterize tacrolimus as an NTI drug. For tacrolimus and cyclosporine, sub-therapeutic blood levels may result in transplant rejection and death of the patient; elevated blood levels may lead to toxicity-associated adverse events such as impaired kidney function and neurotoxicity.

[8] FDA uses the term "Narrow Therapeutic Ratio" to describe drugs for which, *inter alia*, there is a less than twofold difference in the minimum toxic concentrations and the minimum effective concentrations in the blood and safe and effective use requires careful monitoring of blood concentrations and patient monitoring.

B. Prograf

47. Astellas manufactures, markets, and sells Prograf (tacrolimus), a brand name prescription drug. Tacrolimus, the active ingredient, is an immunosuppressant indicated for the prevention (prophylaxis) of organ rejection in patients who have had liver, kidney and heart transplants. Tacrolimus is derived from a metabolite produced by the bacteria *Streptomyces tsukubaensis*.

48. The FDA approved Astellas's NDA-050708 for the sale of 1 mg and 5 mg capsules of Prograf on April 8, 1994.[9] (The FDA also approved NDA-050709, for Prograf injection the same day.) On August 24, 1998, the FDA approved the use of 0.5 mg capsules of Prograf.

49. Prograf is administered orally twice daily, in capsule form (though it is also available for intravenous injection.) The labeling includes a boxed warning for the healthcare professional that highlights special information or possible complications associated with the drug. The warning states: only physicians experienced with immunosuppressive therapy and management of organ transplant patients should prescribe Prograf; patients receiving Prograf should be carefully monitored in an appropriate medical setting; and physicians should monitor and follow-up with patients taking Prograf. The labeling further states that patients administered Prograf injection should be observed for at least thirty minutes after the start of the infusion for signs of anaphylaxis, and frequent intervals thereafter.

[9] On March 29, 2006, FDA granted an Orphan Drug Exclusivity for Prograf (capsules and injection) for the prevention of organ rejection post-heart transplantation. This exclusivity ends on March 29, 2013.

50. Immediately post transplant, higher dosages of tacrolimus are administered; by six months post transplant; the dosages are reduced.

51. Further monitoring of the tacrolimus blood concentration with other laboratory and clinical tests are essential for patient management to evaluate possible organ rejection, drug toxicity, the need for dose adjustments and/or lack of patient compliance. Monitoring is required for as long as the patient is on immunosuppressant therapy, although the initial frequency is reduced to about once per month the longer the patient remains on therapy.

52. Prior to entry of generic forms of tacrolimus, Prograf held 100% of the relevant market. Astellas marketed and sold Prograf in the U.S., yielding annual sales of approximately $929 million for the twelve months ending April 2009, according to IMS Health.

53. As a sophisticated and long-standing pharmaceutical manufacturer, Astellas knew that generic manufactures would seek approval from the FDA to market a generic version of the Prograf.

54. On December 28, 2006, just that happened: Sandoz Inc. filed an ANDA to market and sell tacrolimus capsules in 0.5 mg, 1 mg, and 5 mg dosages.

C. The FDA's Preparation for Approval of Generic Competition for Prograf

55. The goal of bioequivalence testing between an innovator (or reference) product and a test (such as a generic) product is to determine whether there is a "lack of significant difference" in the rate and extent of absorption of the drug between the

brand name, and proposed generic. Federal statutes require that, in evaluating generic drugs for approval, the FDA use its own scientific judgment in determining the methods used to uncover whether a significant difference between the innovator and generic products exists and if the tests, methods, and data are sufficient to approve or deny the ANDA application. To communicate to the public what information the FDA considers appropriate to demonstrate bioequivalence, the FDA may publish documents called Guidance for Industry ("Guidance").

56. An FDA Guidance serves as just that: a guide for industry and other interested parties on the FDA's latest thinking on certain topics. As the FDA website and each guidance specifically state: "Guidance documents represent the Agency's current thinking on a particular subject. They do not create or confer any rights for or on any person and do not operate to bind the FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both."[10]

57. Guidance documents do not bind the FDA and they do not restrict the FDA's ability to consider methodologies or processes other than those articulated therein. They serve only as recommendations. The FDA's obligation to make a determination as to whether an individual ANDA meets statutory requirements and thus should be approved depends in no part on whether a guidance on the topic or the

[10] *See* "Guidances (Drugs)," available at http://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/guidances/default.htm.

drug exists or whether the application complied with the thinking outlined in any relevant guidance. *See generally* 21 CFR 10.115(d).

58. In October 2000, the FDA published *Guidance for Industry, Bioavailability and Bioequivalence Studies for Orally Administered Drug Products-General Considerations* ("General Bioequivalence Guidance"), which provided the FDA's then current view on *in vitro* and *in vivo* testing for establishing bioavailability and bioequivalence in NDAs and ANDAs for orally administered drug products.[11]

59. The General Bioequivalence Guidance provided recommendations for establishing bioequivalence, offering thoughts on *in vitro* and *in vivo* study design, dissolution testing, bioavailability comparisons, *etc*.

60. For bioequivalence determinations, FDA recommends single-dose bioequivalence studies conducted in healthy subjects, as opposed to multi-dose studies[12] or those conducted in transplant patients. FDA believes that single dose studies in healthy subjects are more sensitive at detecting the differences in formulation and other product-related characteristics that may affect the bioequivalence of assessment. Using transplant patients introduces variability related to disease state that might confound or impede the analysis of bioequivalence. Studies in transplant patients do not yield any greater ability to detect differences in formulation that might

[11] The FDA published a revised version of this Guidance in March 2003.

[12] Multiple-dose or steady state bioequivalence studies "are generally conducted in patients" as opposed to healthy volunteers. Janet Woodcock, Director of FDA's Center for Drug Evaluation and Research, to William Fitzsimmons, Astellas Pharma USA Inc. Senior Vice President, re. Docket No. FDA-2007-P-0111, dated August 10, 2009 ("FDA Petition Response") at 7.

have clinical significance and that bioequivalence studies in healthy subjects would not otherwise detect. Similarly, for systemically acting drugs (like tacrolimus), single-dose studies are typically more sensitive in assessing release of a drug substance from the drug product into systemic circulation. Consequently, the General Bioequivalence Guidance recommended that pharmacokinetic and pharmacodynamic studies designed to assess bioequivalence be conducted as single-dose studies in healthy adult subjects representative of the general population, taking into account age, sex, and race.

61. The FDA's recommendation for using healthy subjects to establish bioequivalence had been available since 2000 and was the criteria for approval for generic versions of other immunosuppressants, including cyclosporine.

62. In May 2007, the FDA published a Guidance for Industry, Bioequivalence Recommendations for Specific Products for tacrolimus ("the Tacrolimus Guidance"). (Before that time, the FDA provided specific guidance on the design of bioequivalence studies only when requested by ANDA applicants.) Guidances for specific products were developed by the FDA to address bioequivalence with particular drugs that were not addressed in a general guidance.

63. The Tacrolimus Guidance, first drafted in July 2006, recommended sponsors demonstrate bioequivalence of generic tacrolimus through two clinical studies. Both would be single dose, two-treatment, two-period crossover studies; both would use the 5 mg dose; and both would be in healthy volunteers. The difference: one would be a fasting study and one would be a fed study. The Tacrolimus Guidance, like the General Bioequivalence Guidance, did not require bioequivalence studies in

transplant patients as tests in transplant patients introduce disease state variability unrelated to potential differences in the innovator and generic products that may skew bioequivalence determinations.

64. Under the Tacrolimus Guidance, sponsors were directed to measure tacrolimus in whole blood, with bioequivalence of tacrolimus using the standard bioequivalence criteria of 80-125% for both peak blood concentration (Cmax) and the area under the plasma-time concentration curve (AUC) at the 90% confidence interval. Studies in the 0.1 mg and 1.0 mg dosages were not necessary if acceptable bioequivalence was shown with the 5.0 mg strength, and where proportional similarity across the strengths was shown and the sponsor provided acceptable dissolution tests of all strengths.

D. Astellas's Unlawful Attempt to Delay Generic Competition for Prograf

65. On September 21, 2007, Astellas filed a citizen petition with the FDA seeking to delay the FDA approval of generic tacrolimus capsules. Astellas Citizen Petition ("Petition"), dated September 21, 2007. Astellas stated that the petition was filed in response to the FDA's publication of the Tacrolimus Guidance. Astellas filed a supplement to the citizen petition on September 11, 2008. Astellas Supplement to Citizen Petition ("Petition Supplement"), dated September 11, 2008.

66. Astellas's citizen petition did not address the adequacy of Sandoz's ANDA, present any evidence that Sandoz's tacrolimus failed to demonstrate

bioequivalence to Prograf, or raise any valid concerns about public health—the issues for which citizens petitions were primarily implemented.

67. As stated in the petition, Astellas filed the document in response to the FDA's "recently published draft guidance" the 2006 and 2007 Tacrolimus Guidance. Petition at 7.

68. Astellas's citizen petition requested that the FDA:

> 1) require ANDA applicants for immunosuppressant drugs such as tacrolimus demonstrate bioequivalence to innovator products in transplant patients, in addition to healthy subjects, in direct contradiction to the FDA's longstanding practice of requiring the demonstration of bioequivalence only in healthy subjects in order to reduce the introduction of confounding variables (like disease state) on bioequivalence studies;
>
> 2) require labeling changes for all orally administered immunosuppressant drugs used in transplant patients that are characterized as having a narrow therapeutic index, which Astellas argued included tacrolimus, to add warnings and precautions regarding the substitution of generics for the innovator product, even though AB-rated generic products are bioequivalent to the innovator product and it has long been the FDA's practice to treat such products as interchangeable;
>
> 3) add a section to the Orange Book that highlights risks associated with switching patients among different oral formulations of immunosuppressants, such as tacrolimus despite the FDA's practice, and many states' requirements, of complete interchangeability of innovator and AB-rated generic products; and
>
> 4) require generic manufacturers to distinguish their product from branded products by use of different color capsules or container closure.

Id. at 1-2.

69. For scientific support of its requests, Astellas cited articles on cyclosporine for the proposition that current bioequivalence studies in healthy subjects may not be sufficient to support interchangeability between generic and innovator products in transplant patients.

70. Astellas first recounted the approval history and withdrawal from the market of cyclosporine. Novartis obtained approval for Sandimmune (cyclosporine) for immunosuppression in transplant patients in 1983. Novartis subsequently marketed a different formulation of cyclosporine, called Neoral, in 1995. A generic form of Neoral, called SangCya, marketed by SangStat, was approved in 1998. After discovering that SangCya was not bioequivalent to Neoral when taken with apple juice per label instructions, SangStat voluntarily withdrew the product from the market in 2000; however, other generic versions of Neoral became available that year. Generic versions of the earlier formulation, Sandimmune, were approved in 2002 and 2004. *Id*. at 7.

71. Astellas described five studies comparing branded and generic cyclosporine in transplant patients, arguing that they suggested that bioequivalence in healthy volunteers does "not necessarily translate to clinical equivalence when comparing both generic and branded [immunosuppressants] in transplant patients." *Id.* These included:

- Roza and colleagues (2002) compared fifty kidney transplant patients on Neoral who were converted to generic cyclosporine on a dose per dose basis, then two weeks later converted back to Neoral. According to Astellas, "no dosing adjustments were required following conversion between formulations of cyclosporine" and there were no differences in the pharmacokinetic parameters (C_{max}, AUC, T_{max} and C_{min}). Astellas concluded that

although the "study was not powered to show statistical differences between subpopulations," the authors found no differences in pharmacokinetics of cyclosporine based on gender, race, or presence of diabetes with either the generic or branded cyclosporine.

- Carnahan and colleagues (2003) also reported a study comparing the conversion of forty-one kidney transplant patients from branded to generic cyclosporine. The authors found no significant differences observed in patients whose blood levels showed therapeutic levels of cyclosporine. No changes in dose were required when the patient was converted to the generic form.

- Fradette and colleagues (2005) evaluated the pharmacokinetics of conversion between branded and generic cyclosporine in thirty-seven stable kidney transplant patients. Patients were converted to generic cyclosporine on a dose per dose basis, and after two weeks of treatment, were converted to the brand product. "On average, Cmax and AUC observed after administration of branded or generic cyclosporine were not statistically different." Some intra-patient variability was observed after treatment with the generic product when compared to the branded product; however this variability was not significantly significant.

- Taber and colleagues (2005) reported on 188 kidney transplant patients treated with either branded (n=100) or generic (n=88) cyclosporine. Patients on the branded product were studied from January 1999 to May 2001; patients on generic product were studied between May 2001 and July 2002. Patients received the same initial dose of cyclosporine and were targeted to have the same "trough levels" in the blood. Adjunctive agents (corticosteroids and mycophenolate mofetil) were allowed in both groups. Six months post transplant, patients receiving generic cyclosporine had statistically significant higher proportion of acute rejection (39% v. 25%).

- Qazi and coworkers (2006) revaluated 82 kidney transplant patients who were converted from branded to generic cyclosporine on a dose for dose basis. Seventy-three patients switched to the generic, while nine remained on the brand cyclosporine and served as a control group. The authors reported that 18% of the patients on the generic cyclosporine required dose adjustments, whereas none of the control group did.

Id. at 7-10.

72. Astellas acknowledged that three of the five studies showed no difference between branded and generic cyclosporine. Nevertheless, it still asserted that studies in healthy volunteers are inconclusive at best, or are insufficient to establish bioequivalence in transplant patients. *Id.* at 10. Given the literature on the subject, Astellas argued that "questions arise as to whether the current standard for bioequivalence is sufficient to support indiscriminate substitution of alternate formulations of immunosuppressants in vulnerable transplant patients." *Id.* at 7.

73. For further support for its requests for additional testing in transplant patients, Astellas cited to reports from the National Kidney Foundation (1999) recommending that, among other items, tacrolimus be designated on the "critical drug category," mandating further studies in transplant populations and subpopulations for demonstrating bioequivalence, and recommending patient and physician education regarding the risks associated with switching to a generic immunosuppressant. *Id.* at 10. According to the petition, the American Society of Transplantation ("AST") published similar recommendations in 2003; however, the experts here acknowledged that with proper patient follow-up and monitoring, generic immunosuppressants, including those with NTI, appeared to provide adequate immunosuppression. *Id.* at 10-11.

74. The petition then argued that "limited clinical data" and the recommendations of the two organizations demonstrated that bioequivalence established in healthy volunteers could result in significant risks to transplant patients

who are "indiscriminate[ly]" switched to generics without notice to the patient or physician. *See id.*

75. According to Astellas, high intrapatient variability in transplant patients also mandated the conclusion that bioequivalence studies in healthy volunteers may not sufficiently predict blood levels in individual patients. Petition at 12. Again citing to the Taber study, Astellas argued that bioequivalence of generic to branded cyclosporine in a population of healthy volunteers did not correlate to bioequivalence within an individual patient. Petition at 12. Further, bioequivalence studies in healthy volunteers between branded and generic cyclosporine reported suboptimal blood levels in volunteers receiving generic product (18% on AVC; 38% on C_{max}). *Id.*

76. Astellas concluded that not only does bioequivalence in healthy patients not adequately correlate to bioequivalence in transplant patients as a whole, it does not translate to interchangeability in the individual patient. *Id.* The remedy suggested by Astellas was to add bioequivalence studies in transplant patients for bioequivalence determinations. *Id.* at 14.

77. Astellas also cited several journal articles that described factors that impact the ability to maintain adequate blood levels of tacrolimus. *Id.* at 14-18. These factors included patient disease state, time since transplant, concurrent medications, organ transplanted, rate, age, and whether the drug was taken in a fasted or fed state, and with a particular meal (high fat, low carbohydrate). Since differences may exist between generic and innovator products, Astellas requested that these factors be considered in designing bioequivalence studies in patients. *Id.* at 18. "[T]aking into

account the limitations of current bioequivalence standards in assessing the impact of switches at the individual level, along with interpatient factors discussed above, the performance of studies in healthy volunteers only is inadequate to insure patient safety." *Id.*

78. The petition then recounted Astellas's difficulties in demonstrating bioequivalence for an extended-release form of tacrolimus, called Advagraf, which would provide the same total daily dose as the immediate-release Prograf. According to Astellas, despite meeting the FDA's bioequivalence requirements in healthy volunteers, significant differences were observed in *de novo* kidney and liver transplant patients: extended-release tacrolimus showed significantly reduced blood levels on day one. Thus, bioequivalence in healthy volunteers did not predict the pharmacokinetics of the drug in transplant patients early after surgery. *Id.* at 18-19. According to Astellas, the FDA bioequivalence studies should require pharmacokinetic monitoring immediately after the transplant to ensure that adequate blood levels are maintained. *Id.*

79. Astellas then requested that patients and physicians be notified of any substitution of branded tacrolimus for generic tacrolimus, as a way to mitigate potential risks to the patient on the theory that notification would ensure that physicians would increase the monitoring of patients who were switched to a generic tacrolimus. Astellas included suggested wording for black box warnings that the physician should be consulted before a substitute for the branded product was made. *Id.* at 20. Astellas suggested additional warnings be included in the Dosage and Administration section of

the prescribing information to state that substitutions to other formulations was an indication that additional monitoring was necessary and that the Precautions section should also include warnings that substitutions should be under a physician's direction because additional monitoring was necessary. Petition at 20. Similar notifications of substitutions and additional monitoring should be included in the Orange Book. *Id.* at 20-21.

80. Astellas's final request asked the FDA to require manufacturers of generic versions of NTI drugs, which it believed included tacrolimus, to differentiate their products from Prograf by color/shape of capsule, container closure, packaging, and source so that patients and pharmacists would be aware of a change in source of the drug. *Id.* at 21. Such a differentiation would reduce the potential for medication errors Astellas contended. *Id.*

81. The petition ended with the certification required under 21 C.F.R. § 10.30: "The undersigned certifies to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information know to the petitioner that are unfavorable to the petition." *Id.* at 22. The petition was signed by William E. Fitzsimmons, Pharm.D., M.S., Senior Vice President, Research and Development, Astellas Pharma US, Inc.

82. Astellas filed a supplement on September 11, 2008, requesting that the FDA consider comments from the AST that had been submitted to the FDA during development of a draft guidance document for tacrolimus.

83. Astellas further supplemented its petition with submissions from several third parties, all of whom had significant economic reasons to prevent generic competition for tacrolimus. One submission was from David C. Cronin II, M.D., Director of Liver Transplantation at The Medical College of Wisconsin. Dr. Cronin had received significant sums of money from Astellas in connection with the marketing of Prograf, and he knew that the marketing budget for Prograf would dry up if there were any generic competition. Accordingly, Dr. Cronin colluded with Astellas and submitted a letter, dated September 8, 2008, supporting the citizen petition with the intent of preventing the availability of generic tacrolimus. Dr. Cronin's letter parroted the same arguments as those in Astellas's citizen petition; the letter cited to no data, research, or published writings. Nevertheless, Dr. Cronin and Astellas both knew that a letter from a distinguished and seemingly independent "expert" would lend an air of legitimacy to Astellas's arguments. They also knew that the letter could add to the delay caused by the petition if FDA wanted to separately address Dr. Cronin's remarks.

84. Another submission was a letter from the American Society of Transplantation ("AST") dated September 20, 2007. The AST letter was also submitted in support of the petition. The AST claims to represent the "majority of professionals engaged in the field of solid organ transplantation"—professionals who, like Dr. Cronin, earned significant income from Astellas in connection with the marketing of Prograf. The AST itself earned significant sums of money directly from Astellas in the form of grants, although this conflict of interest was not disclosed in the letter. Astellas provides enough money to the AST each year to qualify as a "Gold" sponsor, and no

corporate sponsors occupy a higher level than Astellas. Like Dr. Cronin's letter, the AST letter repeats the same arguments as the petition, without disclosing any research, data, or published writings to justify them. Like Dr. Cronin, the AST wanted to maintain Astellas's monopoly in order to keep the grant money and other emoluments coming, and thus it too colluded with Astellas. Astellas and the AST knew that that the FDA would have to pay close attention to the AST's position, as the AST is one of two preeminent professional societies in the field of transplantation, boasting twice as many members as its older counterpart, the American Society of Transplant Surgeons. The intended effect of this letter was further delay of the FDA's response to the citizen petition.

E. The FDA Sees Astellas's Citizen Petition for What It Is: A Blatant Attempt to Slow the Process of Approval of Generic Competitors

85. The FDA denied Astellas's citizen petition on August 10, 2009, nearly two years after Astellas filed it, in a detailed fifteen-page letter. Janet Woodcock, Director of FDA's Center for Drug Evaluation and Research, to William Fitzsimmons, Astellas Pharma USA Inc. Senior Vice President, re. Docket No. FDA-2007-P-0111, dated August 10, 2009 ("FDA Petition Response"). Astellas's citizen petition had not changed or altered any FDA actions. On the same day, the FDA also approved Sandoz's ANDA for generic tacrolimus capsules, filed nearly three years earlier.

86. In its letter, the FDA recounted the history of generic cyclosporine products. Cyclosporine is available as an oral solution and in oral capsules. Generic formulations of both forms established bioequivalence to the branded product using *in*

vivo bioequivalence studies conducted in healthy volunteers under fasted and fed conditions. The standard bioequivalence criteria of 80-125% for both maximum drug concentration (C_{max}) and area under the curve (AUC) at the 90% confidence interval were used. *Id* at 3.

87. The FDA reiterated its position, consistent with the General Bioequivalence Guidance and the Tacrolimus Guidance, that ANDA applicants need not conduct additional clinical trials for bioequivalence in transplant patients. The goal of bioequivalence is to determine if significant differences exist in the rate and extent of absorption between innovator and generic formulations. Once bioequivalence is demonstrated, the generic product can be substituted for the innovator product and can be expected to have the same safety profile and clinical effect as the innovator product. *Id.* at 6-7.

88. With regards to tacrolimus, FDA found that Astellas's proposed additional studies, involving multiple doses in specific transplant subpopulations, were not justified. *Id.* At 7. And this was for good reason. The single-dose bioequivalence studies the FDA uses in healthy volunteers are free from the confounders related to disease state that arise when testing multiple doses in patients. Thus, single-dose bioequivalence studies are more sensitive at detecting differences that may affect bioequivalence. And there was insufficient scientific evidence to indicate that tacrolimus behaved any differently. Stating the obvious, FDA pointed out that the patient-related factors Astellas claimed would affect bioequivalence were all related to

the active ingredient. Thus they could not alter bioequivalence, since generic tacrolimus contains the same amount of active ingredient as Prograf.

89. Turning to the scientific literature, the FDA noted that Astellas did "not provide sufficient evidence to show that the current the FDA standards for generic approval of immunosuppressants such as tacrolimus, fail to support substitution of alternate formulations of these drugs in transplant patients." *Id.* at 9. If anything, Astellas merely succeeded in demonstrating what the FDA knew—that studies in healthy volunteers were predictive of bioequivalence. In sum, Astellas citizens petition was based on 2 studies which directly contradicted its position and 3 studies from which no conclusions could be drawn:

- Roza provided information on the bioequivalence of a generic cyclosporine with the innovator product in stable renal transplant patients. The Roza findings actually suggest that a bioequivalence in healthy volunteers can be predictive of bioequivalence in stable renal transplant patients. *Id.* at 9.

- The Carnahan study did not provide any meaningful conclusion on the interchangeability of generic cyclosporine with the innovator product. *Id*.

- Fradette's data was consistent with Roza's data, showing that bioequivalence in healthy subjects was predictive of bioequivalence in renal transplant patients. Further, the FDA found Astellas's conclusions from this study baseless since they were not supported by any data. *Id*. 8-9.

- For the Taber study, the FDA replied that Astellas failed to cite important limitations. First, the studies compared patients transplanted at different times creating a high likelihood of selection bias. Second, information related to dosing changes and adjustments was not taken into consideration. Therefore, differences in dosing strategies could very likely explain any observed intrapatient observation. *Id*.

- Astellas should have known better than to rely on the Qazi study and its obviously questionable design and analysis. Qazi provided insufficient information regarding basic clinical trial elements such as patient randomization, treatment group sample size or data analysis to provide any meaningful conclusions regarding safety and efficacy of the generic product and innovator product. *Id*. at 9.

90. The FDA found Astellas's use of data comparing its extended-release tacrolimus formulation (Advagraf) to immediate-release Prograf "not applicable to the approval of generic tacrolimus." *Id.* at 11. The reason was simple: Astellas ignored the critical fact that these two formulations, extended- and immediate-release, were "different types of products" that were obviously not pharmaceutically equivalent and therefore not bioequivalent. Thus pharmacokinetic differences noted between two entirely different products cannot, obviously, support the conclusion that pharmacokinetic differences could arise between bioequivalent products in different patient populations. *Id.* At 10-11.

91. Turning to the AST comment, as submitted by Astellas, FDA noted that AST merely reiterated Astellas's position while providing "no new scientific or clinical data to support their comments." *Id.* at 6. This is not surprising, given the grant relationship between AST and its Gold-level supporter Astellas. Since AST reiterated Astellas's position, FDA reiterated its own. First, patient-related factors are related to the active ingredient, which is identical in generic and reference product, and thus their impact would not differ between the two. "Since a generic product will contain identical amounts of the same active ingredient in the same dosage form as the [innovator product], the impact of patient related factors on drug exposure is not

expected to differ between the [generic] and [innovator] products." *Id.* at 11. Second, bioequivalence studies in transplant patients are subject to additional sources of disease-state-related variation and are thus less sensitive for determining bioequivalence. Thus, there is no need to undertake additional bioequivalence studies in transplant patients.

92. As to additional warnings on the label and in the Orange Book, the FDA obviously denied these requests. If a generic drug is bioequivalent, then it is interchangeable with the branded counterpart. Additional warnings are not needed: the "ANDA review process [is] sufficient to ensure that the generic versions of immunosuppressant drugs...are equivalent with respect to their safety and efficacy for use under conditions suggested in their labeling." *Id.* at 14.

93. The FDA denied Astellas's request to require differentiation between branded and generic tacrolimus by shape, color, or some other method of distinguishing. Again, since a generic product is substitutable for its branded product, differentiation between the two is unnecessary.

94. Finally, since the FDA requires differentiation among dosages, it is entirely unsurprising that it would do so with generic tacrolimus. *Id.* at 14-15. Astellas's request that the FDA continue to do as it had always done was just as baseless as the rest of its petition.

F. Astellas Continued the Charade and Filed Motions for a Temporary Restraining Order and Preliminary Injunction; the Court Summarily Denied Them.

95. On August 11, 2009, one day after the FDA denied Astellas's citizen petition requests and approved Sandoz's ANDA, Astellas filed a motion for a temporary restraining order ("TRO") in the District of Columbia, seeking to stay the FDA approval of the generic product and block the FDA from approving generic tacrolimus capsules. Sandoz's generic capsules came to market the same day.

96. Astellas's court briefing raised the very same issues that the FDA comprehensively rejected and further argued that the FDA's rejection was arbitrary and capricious. Astellas argued that, contrary to the FDA's dismissal of its scientific evidence, Astellas's evidence was "compelling" in showing the need for bioequivalence testing in transplant patients and that the FDA's response was "inadequate to the point of being arbitrary and capricious." Memorandum of Points and Authorities in Support of Application of Plaintiff Astellas for a Temporary Restraining Order and a Preliminary Injunction, Astellas v. Food & Drug Admin., No. 09-01511, Document No. 3-1 (D.D.C. Aug. 10, 2009) ("Astellas TRO Motion") at 22-23. Similarly, it argued the FDA's failure to warn of generic substitution was arbitrary and capricious and denied the safety and efficacy issues that Astellas raised. *Id*. at 25.

97. Astellas, further argued that absent the TRO, it would suffer irreparable harm in the form of lost sales, price erosion, loss of goodwill and harm to reputation. The balance of harms, Astellas argued, favored Astellas. The FDA would suffer no

harm; a delay would also not harm Sandoz. Astellas implied that allowing Sandoz generic tacrolimus to come to market would destroy Astellas's business. *Id.* at 30.

98. Astellas argued that injunctive relief served the public interest because (i) it would require the FDA to comply with the law and (ii) the public has an interest in safe and effective generic products, (here, through additional patient monitoring to ensure that the warning signs for overdose (toxicity) or underdose (organ rejection) are caught early).

99. The FDA opposed the motion on August 12, 2009; the same day, and without oral argument, the court denied the TRO. *Astellas v. Food & Drug Admin.*, 642 F. Supp. 2d 10, 24 (D.D.C. 2009).

100. In its briefing, the FDA stated that its process for approving generic tacrolimus used the appropriate methods and standards and was based on a thorough and rigorous review of relevant scientific evidence. Defendants' Memorandum in Opposition to Plaintiffs Motion for a Temporary Restraining Order and a Preliminary Injunction, Astellas v. Food & Drug Admin., No. 09-01511, Document No. 6 (D.D.C. Aug. 12, 2009) at 2 ("FDA Opposition").

101. Furthermore, the FDA argued that Astellas's citizen petition delayed the approval of a generic: "Sandoz' [ANDA] was pending for over [2 ½] years. At least part of this period was directly attributable to the need to evaluate and respond" to Astellas's citizen petitions. Astellas's citizen petition arguments were "yet another instance in which a manufacturer of a pioneer drug product in fear of losing its

lucrative monopoly has attempted to block generic competition by challenging the scientific basis for the FDA's approval of a generic." *Id.*

102. The FDA is due a high degree of deference in its decision-making. The FDA's decision was based on evaluation of the scientific evidence that is within its area of expertise. Courts have roundly rejected challenges to the FDA's scientific judgment in determining appropriate measures for establishing bioequivalence. *Id.* at 11.

103. The FDA rejected Astellas's labeling arguments as unnecessary because the existing product labeling reflected the need for physicians to closely monitor transplant patients on immunosuppressant therapy. *Id.* at 15.

104. The FDA observed that Astellas's economic loss was insufficient to demonstrate it would suffer irreparable harm. The "bald assertions", made without support, were speculative at best and therefore did not meet the level of scrutiny required by courts for this type of harm. *Id.* at 16.

105. Finally, Astellas's argument that delaying approval for generic tacrolimus served public interests failed because the FDA correctly found that higher branded drug prices for consumers thwart the public interest.

106. In denying Astellas's request for a TRO and preliminary injunction, the Court found that "the FDA produced a comprehensive response to the plaintiff's Citizen Petition, in which it specifically addressed the plaintiff's arguments and provided a detailed justification for its conclusion that additional bioequivalency testing was not needed." *Astellas v. Food & Drug Admin.*, 642 F. Supp. 2d 10, 20 (D.D.C. 2009).

107. The Court recognized that the FDA is accorded a high degree of deference in evaluations of scientific data within its area of expertise and that judgment of what constitutes safety and efficacy of drugs "falls squarely within the ambit of the FDA's expertise and merits deference from the courts." *Id.* at 19. The FDA produced a comprehensive response to the citizen petition and provided detailed reasoning for its position that additional bioequivalence testing was unnecessary. Astellas provided no evidence that "FDA's conclusion was irrational, implausible or contrary to existing scientific consensus." *Id.* at 20. "Given the high level of deference that must be afforded to the FDA in choosing which methodologies to employ to test bioequivalency for a given drug, the court concludes that [Astellas] has presented insufficient evidence" that the FDA's actions in denying the citizen petition requests were arbitrary or capricious. *Id.* (internal citations omitted).

108. This high degree of deference awarded to the FDA carries over into its rationale for not granting Astellas's label change requests, the court observed, as labeling is within the FDA's mandate on bioequivalence. *Id*. at 21.

109. Moreover, Astellas failed to demonstrate irreparable harm absent the injunctive relief. The court reiterated that that economic loss alone is in sufficient to show irreparable harm. Astellas failed to demonstrate to what extent it would lose sales to generic competition, or that it would not be able to recover lost market share through competition. The public interest favors generic competition. "Indeed, the evidence presented to the court strongly suggests that the interests of the public, and of

transplant patients more specifically, will be served by permitting generic competition with the name brand version of tacrolimus." *Id.* at 23-24.

110. On August 17, 2009, the Court issued its opinion describing its reasoning for denying the TRO and Preliminary Injunction. On August 19, 2009, Sandoz moved to intervene in the case; the Court granted on this motion August 21, 2009. On November 24, 2009, rather than continuing its legal pursuit, Astellas voluntarily dismissed the case.

G. Astellas's Anticompetitive Conduct

111. Astellas's petition and court actions were a sham. Astellas could not reasonably have expected to prevail on the substance of the petition or the lawsuit.

112. The arguments in Astellas's citizen petitions were objectively baseless from regulatory and scientific perspectives. Any pharmaceutical industry stakeholder, including Astellas, was aware that Astellas's arguments would fail at the FDA. The citizen petition was filed with the intent to delay the FDA approval of generic tacrolimus capsules. According to the FDA, the petition delayed the approval of generic tacrolimus capsules.

113. Astellas made arguments in the citizen petition that have been repeatedly rejected when other innovator citizen petitions sought to prevent generic approval. The arguments were knowingly frivolous.

114. The statutory and regulatory bases for bioequivalence are clear: if the generic product has the same dose, strength and route of administration, form and blood plasma levels as innovator product, the generic is fully substitutable for the

branded product. 21 U.S.C. § 355(j)(2)(A). The generic product is relying on the findings of safety and efficacy of the branded drug. Thus, with tacrolimus any safety and efficacy issues with the branded product, including dose management issues in transplant patients, would apply to the generic product as well. As the FDA said, as long as the generic has the same dosage, strength and route of administration as the branded product, the issues with interpatient variability apply equally to both innovator and generic product. This is consistent with the law and the regulations. The FDA has repeated these statements in many citizen petition responses and multiple draft guidance documents, including the guidance documents for oral dosage forms generally, and specifically for tacrolimus.

115. Astellas's own briefing further demonstrates that their argument lacks merit. Astellas cites the studies of cyclosporine as support for the need to conduct bioequivalence studies in transplant patients. However, as the FDA stated, the cyclosporine studies failed to support Astellas's assertion outright or were inconclusive because of study design. The FDA noted that some of the studies of bioequivalence for cyclosporine generics were conducted on healthy patients and were in fact predictive of bioequivalence in transplant patients.

116. Astellas clearly was aware of the information in these studies as it cherry picked the information from them to present to the FDA in support of its arguments. Astellas cited to cyclosporine bioequivalence articles that were either inconclusive or demonstrated that bioequivalence assessments in healthy volunteers *were* transferrable to transplant patients, positions which are contrary to its arguments. Furthermore,

Astellas failed to include in its argument that the authors in the Taber study acknowledged the critical limitations of their conclusions.

117. Had Astellas accurately discussed the journal articles or disclosed the limitations of the Taber article's conclusions, Astellas's arguments for the petition simply would not have existed.

118. The misrepresented conclusions and omissions of key information from these articles in support of its own arguments render false the certification signed by Astellas acknowledging its duty to supply information contrary to its position.

119. Astellas's argument that drugs such as tacrolimus and cyclosporine have special problems requiring additional bioequivalence studies in transplant patients ignores the fact that the FDA has experience in assessing bioequivalence in this class of drugs: cyclosporine has several generics on the market. The FDA has also published guidance documents for the industry on assessing bioequivalence in this class of drugs.

120. Astellas's own package insert contradicts its argument that neither healthy volunteers nor a single-dose study was sufficient for bioequivalence studies. Astellas used healthy volunteers to assess bioequivalence between the 1 mg and 5 mg capsules: "A single dose study conducted in 32 healthy volunteers established the bioequivalence of the 1mg and 5 mg capsules. Another single dose study in 32 healthy volunteers established the bioequivalence of the 0.5 mg and 1 mg capsules."

121. The request for labeling changes to alert caregivers and patients of switching between generic and branded product is also baseless. Because by law the approved generic product is the same as the branded product, the labeling

requirements of the branded product apply to the generic. In this particular class of drugs, doctors are routinely monitoring patients for changes and would detect any problems, whether related to dose, source, rejection, or disease state. For example, the prescribing information highlights, in a prominent black box warning, the requirement for routine monitoring of blood concentration, renal and liver function testing, and tissue biopsies.

122. The remaining requests were also baseless. Generics are supposed to be interchangeable from branded reference products, and thus there were no grounds to petition the FDA to have the different sources of tacrolimus identified by color or container closure. The request to have different pill strengths identified was also unwarranted and unnecessary. The FDA was already well aware of the risk of dosage mix-ups. It routinely requires different dosage forms of the same drug to be distinguishable and would have so required in this case without the need for citizen petition. This request was nothing more than a truism.

123. Astellas knew that the FDA and the courts would not find in its favor. Astellas, as a sophisticated pharmaceutical company, is aware, or should have been aware, of the long line of cases that provide deference to the FDA on determining scientific methods it uses to establish drug approvals. Additionally, such a sophisticated pharmaceutical company would have been aware that courts were routinely finding for the FDA in court challenges over its citizen petition denials.[13]

[13] *FDA Racks Up Another Win in Bioequivalence Litigation; This Time Over Generic EFUDEX*, FDA Law Blog, Oct. 19, 2009, *available at* http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2009/10/fda-racks-

124. The FDA itself recognized Astellas's citizen petition as a sham designed to delay generic competition: "Sandoz' [ANDA] was pending for over two-and-one-half years. At least part of this period was directly attributable to the need to evaluate and respond" to Astellas's citizen petition. Astellas's citizen petition arguments were "yet another instance in which a manufacturer of a pioneer drug product in fear of losing its lucrative monopoly has attempted to block generic competition by challenging the scientific basis for the FDA's approval of a generic." FDA Opposition at 2.

125. Further underscoring that the purpose of the citizen petition was solely to delay competition, Astellas filed the citizen petition only a few days before the new law that eliminated just this type of abuse became effective. *See* ¶ 37, *supra*.

V. ASTELLAS'S ANTICOMPETITIVE ACTIONS HARMED PLAINTIFF AND CLASS MEMBERS

126. Although the FDA rebuffed Astellas's citizen petition in a fifteen-page letter, the petition and the various related submissions had their desired effect and extended the company's monopoly in the United States, perhaps by as long as almost two years. Tellingly, Covington & Burling LLP, Astellas's legal counsel for the citizen petition and the litigation that followed, touts these items on its website as a *success*, when in substance they were abject failures.[14]

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up-another-win-in-bioequivalence-litigation-this-time-over-generic-efudex.html ("The district court's decision leaves intact FDA's stellar batting average in bioequivalence decision court challenges. Courts have uniformly held that FDA's bioequivalence determinations fall squarely within the broad discretion of the Agency.").

[14] *See* Covington & Burling LLP, Hatch-Waxman & Biosimilars, available at http://www.cov.com/practice/food_and_drug/hatch_waxman/ (last accessed September 13, 2011 at 4:06 pm).

127. Astellas did not make its petition requests to the FDA to influence FDA policy or address any legitimate concern about the efficacy or safety of generic tacrolimus. Rather, Astellas meant solely to forestall generic competition in the United States market for tacrolimus during the time it would take the FDA to evaluate and respond to the petition. Astellas, with full knowledge that the FDA was very likely in the process of considering the bioequivalency of one or more generic products, waited until nearly the last possible moment before the law on citizen petitions changed to curb this type of abuse to submit its citizen petition to the FDA, hoping to impose significant delay into the consideration by the FDA of any generic competition. Although it argued that the petition was in response to the Tacrolimus Guidance, this guidance had been published four months earlier and was publically available fourteen months earlier.

128. Given the FDA's limited resources and practice at that time of carefully considering all citizen petitions before granting final approval to ANDAs, Astellas knew that the filing of a citizen petition would immediately derail the FDA process for approving generic versions of Prograf. Astellas made its submissions to the FDA not to influence the FDA policy or procedure but instead to delay the FDA approval of generic Prograf and unlawfully extend the company's monopoly for Prograf products in the United States.

129. Astellas's unlawful conduct denied Plaintiff and the Class the benefits of free and unrestrained competition in the market for tacrolimus from September 21, 2007, the date of Astellas's petition, until August 10, 2009, the date the FDA approved

generic tacrolimus for sale in the United States. Further, the effects of Astellas's anticompetitive scheme extended beyond August 10, 2009 as the full extent and benefit of generic penetration does not occur immediately upon generic market entry.

130. Astellas's unlawful actions denied Plaintiff and members of the Class the opportunity to purchase lower-priced AB-rated generic versions of Prograf and thus forced Plaintiff and members of the Class to pay supra-competitive prices for tacrolimus.

131. Astellas's actions are part of, and in furtherance of, the illegal monopolization scheme alleged herein, and were authorized, ordered, or done by Astellas's officers, agents, employees, or representatives while actively engaged in the management of Astellas's affairs.

VI. INTERSTATE COMMERCE

132. Astellas's efforts to monopolize and restrain competition in the market for tacrolimus substantially affected interstate and foreign commerce.

133. At all material times, Astellas manufactured, promoted, distributed, and sold substantial amounts of Prograf in a continuous and uninterrupted flow of commerce across state and national lines and throughout the United States.

134. At all material times, Astellas transmitted funds as well as contracts, invoices, and other forms of business communications and transactions in a continuous and uninterrupted flow of commerce across state and national lines in connection with the sale of Prograf.

135. In furtherance of its efforts to monopolize and restrain competition in the market for Prograf and generic forms of Prograf, Astellas employed the United States mails and interstate and international telephone lines, as well as means of interstate and international travel.

VII. RELEVANT MARKET

136. Direct proof that Astellas had monopoly power over the price of tacrolimus in the United States exists. Such direct evidence includes transactional data showing a significant, non-transitory decline in prices of tacrolimus immediately upon entry of generic versions of the drug. Such a significant, non-transitory decline in prices did not occur until generic entry into the market. This direct evidence of monopoly power obviates the need to define a relevant product market in assessing whether Astellas had monopoly power.

137. The only seller of tacrolimus products in the United States could and would impose a significant, non-transitory price increase without losing sufficient sales to render the price increase unprofitable, as demonstrated by Astellas's ability to earn profits charging supra-competitive prices during the period in which it was without generic competition. There were no reasonably interchangeable drug products available to prescribing physicians for the indications for which tacrolimus is prescribed.

138. To the extent that the law requires Plaintiff to prove monopoly power circumstantially by first defining a relevant product market, Plaintiff alleges that the

relevant market is all tacrolimus capsule products - *i.e.,* Prograf (in all its dosage strengths) and AB-rated bioequivalent tacrolimus capsule products.

139. The relevant geographic market is the United States and its territories.

140. Prior to generic entry in August 2009, Astellas held 100% market share in the relevant market. Following market entry by generic manufacturers and much cheaper generic version of Prograf, Astellas's market share for tacrolimus products declined dramatically in a short period of time.

VIII. MARKET EFFECTS

141. Astellas's acts and practices, as herein alleged, had the purpose and effect of unreasonably restraining and injuring competition by protecting Prograf from generic competition in the relevant market.

142. Had generic competitors been able to enter the relevant market and compete with Astellas, Plaintiff and the Class would have paid for lower-priced generics in place of the higher-priced brand name drug, resulting in far fewer dollars paid for tacrolimus products between September 2007 and August 2009, if not beyond. Regulations generally permit – and sometimes even mandate - pharmacists to substitute generic drugs for their branded counterparts, unless the prescribing physician has directed that the branded product be dispensed. Similarly, many third-party payors of prescription drugs (*e.g.*, managed care plans) encourage or insist on the use of generic drugs whenever possible, thus creating a ready market for generic products.

143. The initial entry of generic products generally leads to a significant erosion of a branded drug's sales within the first year as generic drugs can quickly and

efficiently enter the marketplace at substantial discounts. Astellas itself recognizes the effects of market entry of generic versions of a drug - both generally and in the specific instance of Prograf competition: affidavits from Astellas in its litigation to block entry of a generic version of Prograf state that the company expected to lose a significant amount of the $74 million per month in North American sales. Astellas TRO Motion at 9 (citing to Declaration of P. Shea).

144. By preventing generic competitors from entering the market, Astellas injured Plaintiff and the other members of the Class in their business or property by causing them to pay more for tacrolimus products than they otherwise would have paid, Astellas's unlawful conduct deprived Plaintiff and other indirect purchasers of tacrolimus products of the benefits of competition that Congress designed federal antitrust laws to preserve.

IX. CLASS ACTION ALLEGATIONS

145. NMUFCW, on behalf of itself and the proposed Class, seeks monetary damages against Astellas based on allegations of anticompetitive conduct in the market for Prograf and its AB-rated generic equivalents.

146. NMUFCW brings this action on behalf of itself and, under Fed. R. Civ. P. 23(a), (b)(2) and (b)(3), as representative of a Class defined as follows:

> All persons or entities in the United States and its territories who purchased, paid and/or reimbursed for Prograf (tacrolimus capsules), intended for consumption by themselves, their families, or their members, employees or insureds (the "Class") during the period from September 21, 2007 through such time in the future as the effects of Defendants' illegal conduct, as alleged herein, have ceased (the "Class Period"). Excluded from the Class are all Defendants and their respective subsidiaries and

> affiliates, all governmental entities, and all persons or entities that purchased Prograf (tacrolimus capsules): (i) for purposes of resale, or (ii) directly from the Defendant. For purposes of the Class definition, individuals and entities "purchased" Prograf if they paid some or the entire purchase price.

147. Excluded from the Class are Astellas, and its predecessors, officers, directors, management, employees, subsidiaries, parent or affiliates, and all federal governmental entities.

148. Members of the Class are so numerous that joinder is impracticable. NMUFCW believes there are at least 10,000 Class members spread across the United States. Moreover, members of the Class are readily identifiable from information and records that are in the possession of Astellas.

149. NMUFCW's claims are typical of the claims of the members of the Class. Plaintiff and all members of the Class were damaged in the same way by the same wrongful conduct of Astellas, *i.e.*, they paid artificially inflated prices for tacrolimus and were deprived of the benefits of competition from cheaper generic versions of Prograf as a result of Astellas's wrongful conduct.

150. NMUFCW will fairly and adequately protect and represent the interests of the Class. Plaintiffs' interests are coincident with, and not antagonistic to, those of the Class.

151. NMUFCW is represented by counsel who are experienced and competent the prosecution of class action antitrust litigation, and have particular experience with class action antitrust litigation in the pharmaceutical industry.

152. Questions of law and fact common to the members of the Indirect Purchaser Class predominate over questions, if any, that may affect only individual Class members because Astellas has acted on grounds generally applicable to the entire Class thereby making monetary and equitable relief with respect to the Class as a whole appropriate. Such generally applicable conduct is inherent in Astellas's wrongful conduct.

153. Questions of law and fact common to the Class include:

(a) Whether Astellas delayed or prevented generic manufacturers from coming to market in the United States;

(b) Whether the petitioning to the FDA by the Astellas was objectively baseless;

(c) Whether Astellas maintained its monopoly power by improperly delaying generic entry through, *inter alia*, the filing of sham citizen petitions with the FDA;

(d) Whether direct proof of Astellas's monopoly power is available, and if available, whether it is sufficient to prove Astellas's monopoly power without the need to also define a relevant market;

(e) The definition of relevant market or markets, to the extent on is necessary;

(f) Whether the activities of Astellas as alleged herein have substantially affected interstate commerce; and

(g) Whether, and to what extent, Astellas's conduct caused antitrust injury to the business or property of Plaintiff and the members of the Class, and if so, the appropriate measure of damages.

154. Class action treatment is a superior method for the fair and efficient adjudication of the controversy. Such treatment will permit a large number of similarly

situated persons to prosecute their common claims in a single forum simultaneously, efficiently; and without the unnecessary duplication of evidence, effort, and expense that numerous individual actions would engender. The benefits of proceeding through the class mechanism, including providing injured persons or entities with a method for obtaining redress on claims that it might not be practicable to pursue individually, substantially outweigh any difficulties that may arise in management of this class action.

155. NMUFCW knows of no difficulty to be encountered in the maintenance of this action that would preclude its maintenance as a class action.

X. COUNT I: CLAIM FOR COMPENSATORY AND MULTIPLE DAMAGES UNDER THE ANTITRUST AND/OR CONSUMER PROTECTION STATUTES OF THE INDIRECT PURCHASER STATES

156. NMUFCW repeats, and incorporates by reference, the allegations above in ¶¶ 1 – 155 above.

157. Defendant's conduct described herein constitutes unlawful acts of monopolization and attempts to monopolize, as well as prohibited practices and unconscionable conduct under the antitrust and/or unfair and deceptive trade practices acts of the Indirect Purchaser States, as follows:

(a) Arizona: The aforementioned practices by the Defendant were and are in violation of the Arizona Uniform State Antitrust Act, Ariz. Rev. Stat. § 44-1401, *et seq.*, the Arizona Consumer Fraud Act, Ariz. Rev. Stat § 44-1521, *et seq.*, and the Constitution of the State of Arizona, Article 14, §15;

(b) California: The aforementioned practices by the Defendant were and are in violation of the Cartwright Act, Cal. Bus. & Prof. Code § 16700, *et seq.*, and the California Unfair Competition Act, Cal. Bus. & Prof. Code § 17200, *et seq.*;

(c) District of Columbia: The aforementioned practices by the Defendant were and are in violation of the District of Columbia Antitrust Act, D.C. Code § 28-4501, *et seq.*;

(d) Florida: The aforementioned practices by the Defendant were and are in violation of the Florida Antitrust Act, Fla. Stat. Ann. § 542.15, *et seq.*, and the Florida Deceptive and Unfair Trade Practices Act, Fla. Stat. Ann. § 501.201, *et seq.*;

(e) Illinois: The aforementioned practices by the Defendant were and are in violation of 740 Ill. Comp. Stat. 10/7(2).

(f) Iowa: The aforementioned practices by the Defendant were and are in violation of the Iowa Competition Law, Iowa Code §§ 553.4, 553.5 (1997);

(g) Kansas: The aforementioned practices by the Defendant were and are in violation of the Kansas Monopolies and Unfair Trade Act, Kan. Stat. Ann. § 50-101, *et seq.*;

(h) Massachusetts: The aforementioned practices by the Defendant were and are in violation of the Massachusetts Consumer Protection Act, Mass. Gen. Laws ch. 93A, § 11.

(i) Maine: The aforementioned practices by the Defendant were and are in violation of the Maine Monopolies and Profiteering Statute, Me. Rev. Stat. Ann. tit. 10, § 1101, *et seq.*,;

(j) Michigan: The aforementioned practices by the Defendant were and are in violation of the Michigan Antitrust Reform Act, Mich. Comp. Laws § 445.771, *et seq.*, and the Michigan Consumer Protection Act, § 445.901, *et seq.*;

(k) Minnesota: The aforementioned practices by the Defendant were and are in violation of the Minnesota Antitrust Law of 1971, Minn. Stat. § 325D.49, *et seq.*, and the Minnesota Consumer Fraud Act, Minn. Stat § 325F.67, *et seq.*;

(l) Mississippi: The aforementioned practices by the Defendant were and are in violation of Miss. Code Ann. § 75-21-1, *et seq.*;

(m) Missouri: The aforementioned practices by the Defendant were and are in violation of the Missouri Merchandising Practices Act, Mo. Rev. Stat. § 407.025;

(n) Nebraska: The aforementioned practices by the Defendant were and are in violation of Ne. Rev. Stat. § 59-801, *et seq.*;

(o) Nevada: The aforementioned practices by the Defendant were and are in violation of the Nevada Unfair Trade Practices Act, Nev. Rev. Stat. § 598A.010, *et seq.*, and the Nevada Deceptive Trade Practices Act, Nev. Rev. Stat. § 598.0903, *et seq.*;

(p) New Mexico: The aforementioned practices by the Defendant were and are in violation of the New Mexico Antitrust Act, N.M. Stat. Ann. § 57-1-1, *et seq.*, and the New Mexico Unfair Practices Act, N.M. Stat. Ann. § 57-12-1, *et seq.*;

(q) New York: The aforementioned practices by the Defendant were and are in violation of the Donnelly Act, N.Y. Gen. Bus. Law § 340, *et seq.*, and the New York Deceptive Acts and Practices Act, N.Y. Gen. Bus. Law § 349, *et seq.*;

(r) North Carolina: The aforementioned practices by the Defendant were and are in violation of North Carolina's antitrust and unfair competition law, N.C. Gen. Stat. § 75-1, *et seq.*;

(s) Pennsylvania: The aforementioned practices by the Defendant were and are in violation of the Pennsylvania Unfair Trade Practices and Consumer Protection Law, 73 Pa. Stat. Ann. § 201-1, *et. seq.*;

(t) North Dakota: The aforementioned practices by the Defendant were and are in violation of the North Dakota Antitrust Act, N.D. Cent. Code § 51-08.1-01, *et seq.*;

(u) South Dakota: The aforementioned practices by the Defendant were and are in violation of South Dakota's antitrust law, S.D. Codified Laws § 37-1-3, *et seq.*;

(v) Tennessee: The aforementioned practices by the Defendant were and are in violation the Tennessee Trade Practices Act, Tenn. Code Ann. § 47-25-

101, *et seq.*, and the Consumer Protection Act, Tenn. Code Ann. § 47-18-101, *et seq.*;

(w) Vermont: The aforementioned practices by the Defendant were and are in violation of the Vermont Consumer Fraud Act, Vt. Stat. Ann. tit. 9, § 2451, *et seq.*;

(x) West Virginia: The aforementioned practices by the Defendant were and are in violation of the West Virginia Antitrust Act, W. Va. Code § 47-18-1.

(y) Wisconsin: The aforementioned practices by the Defendant were and are in violation of the Wisconsin Antitrust Act, Wis. Stat. § 133.01, *et seq.*, and the Wisconsin Unfair Trade Practices Act, Wis. Stat. § 100.20, *et seq.*

158. As a result of the conduct described above, Plaintiff and the Class have sustained and will continue to sustain substantial losses and damage to their businesses and property in the form of, *inter alia*, being deprived of the ability to purchase less expensive, generic versions of Prograf, and paying prices for tacrolimus products that were higher than they would have been but for Defendant's improper actions. The full amount of such damages are presently unknown and will be determined after discovery and upon proof at trial.

159. Plaintiff and the Class seek damages, multiple damages, treble damages, and other damages as permitted by state law, for their injuries caused by these violations pursuant to these statutes.

XI. COUNT II: CLAIM FOR RELIEF – MONOPOLIZATION IN VIOLATION OF SECTION 2 OF THE SHERMAN ACT

160. NMUFCW repeats, and incorporates by reference, the allegations above in ¶¶ 1 – 159 above.

161. Astellas used willful and exclusionary means as part of an overall scheme described herein to improperly maintain and extend its monopoly power in the tacrolimus market, as described above. Astellas accomplished this scheme by filing a baseless citizen petition with the FDA in an attempt to delay generic versions of Prograf from entering the market.

162. The goal, purpose, and effect of Astellas's scheme was to prevent, delay, and/or minimize the success of the entry of AB-rated generic tacrolimus competitors which would have sold generic tacrolimus capsules in the United States at prices significantly below Astellas's prices for Prograf, thereby effectively causing the average market price of tacrolimus to decline dramatically.

163. The goal, purpose, and effect of Astellas's scheme were also to maintain and extend its monopoly power with respect to tacrolimus. Astellas's illegal scheme enabled Astellas to continue charging supra-competitive prices for tacrolimus, without a substantial loss of sales, reaping substantial unlawful monopoly profits.

164. NMUFCW and members of the Class paid and/or reimbursed for substantial amounts of Prograf indirectly from Astellas.

165. As a result of Astellas's illegal conduct, Plaintiff and members of the Class were compelled to pay, and did pay, more than they would have paid for tacrolimus absent Astellas's illegal conduct. But for Astellas's illegal conduct, competitors would have begun marketing generic versions of Prograf well before they actually did.

166. Had manufacturers of generic tacrolimus entered the market and lawfully competed with Astellas in a timely fashion, Plaintiff and other members of the Class would have substituted lower-:priced generic tacrolimus for the higher-priced brand name Prograf for some or all of their tacrolimus requirements, and/or would have paid lower net prices on their remaining Prograf purchases.

167. Consequently, NMUFCW and the Class have sustained damage to their business and property in the form of overcharges. The injury to Plaintiff and the Class is the type of injury antitrust laws were designed to prevent, and the injury flows from Astellas's unlawful conduct.

168. Astellas's scheme was in the aggregate an act of monopolization undertaken with the specific intent to monopolize the market for tacrolimus in the United States, in violation of Section 2 of the Sherman Act, 15 U.S.C. § 2.

XII. COUNT III: CLAIM FOR INJUNCTIVE RELIEF UNDER SECTION 16 OF THE CLAYTON ACT FOR DEFENDANTS' VIOLATIONS OF SECTION 2 OF THE SHERMAN ACT

169. NMUFCW repeats, and incorporates by reference, the allegations above in ¶¶ 1 – 168 above.

170. As alleged above, the Defendant knowingly and willfully engaged in a course of conduct designed to unlawfully maintain and prolong their monopoly

position in the market for tacrolimus products in violation of Section 2 of the Sherman Act, 15 U.S.C. § 2.

171. Plaintiff and the other members of the Class have been injured in their business or property by reason of Defendant's antitrust violation alleged in this Count. Their injury consists of being deprived of the ability to purchase less expensive, generic tacrolimus products, and paying higher prices for Prograf than they would have paid in the absence of the antitrust violation. The injury to Plaintiff and the Class is the type of injury the antitrust laws were designed to prevent, and the injury flows from the Defendant's unlawful conduct. Plaintiff and members of the Class are threatened with further injuries as a result of the Defendant's continuing scheme, as alleged herein.

172. Plaintiff and the Class seek equitable and injunctive relief pursuant to Section 16 of the Clayton Act, 15 U.S.C. § 26, and other applicable law, to correct for the anticompetitive market effects caused by the unlawful conduct of the Defendant, and other relief so as to assure that similar anticompetitive conduct does not occur in the future.

XIII. COUNT IV: CLAIM FOR RESTITUTIONARY RELIEF, DISGORGEMENT, AND CONSTRUCTIVE TRUST TO REDRESS DEFENDANT'S UNJUST ENRICHMENT

173. NMUFCW repeats, and incorporates by reference, the allegations above in ¶¶ 1 – 172 above.

174. As a result of its unlawful conduct described above, the Defendant has been and will continue to be unjustly enriched. Defendant has been unjustly enriched, to the detriment of Plaintiff and the Class by the receipt of, at a minimum, unlawfully

inflated prices and illegal monopoly profits on their sale of Prograf. Defendant has benefitted from its unlawful acts and it would be inequitable for the Defendant to be permitted to retain any of their ill-gotten gains resulting from the overpayments for Prograf made by Plaintiff and the Class.

175. Plaintiff and members of the Class are entitled to the amount of Defendant's ill-gotten gains resulting from Defendant's unlawful, unjust and inequitable conduct. Plaintiff and the Class are entitled to the establishment of a constructive trust consisting of all ill-gotten gains from which Plaintiff and the Class members may make claims on a pro rata basis.

XIV. JURY TRIAL DEMANDED

176. Pursuant to Federal Rule of Civil Procedure 38(b), NMUFCW demands a trial by jury on all issues so triable.

XV. PRAYER FOR RELIEF

WHEREFORE, Plaintiff, on behalf of itself and the Class, respectfully requests that:

(a) The Court determine that this action may be maintained as a class action pursuant to Rule 23 of the Federal Rules of Civil Procedure, and direct that reasonable notice of this action, as provided by Rule 23(c)(2) of the Federal Rules of Procedure, be given to the Class;

(b) The acts alleged herein be adjudged and decreed to be unlawful and willful acts of monopolization in restraint of trade in violation of Section 2 of the Sherman Act, 15 U.S.C. § 2, of the statutes of the Indirect Purchaser States set forth above, and the common law of unjust enrichment;

(c) The Class be awarded three-fold the damages determined to have been sustained by the Class, according to the laws of

the Indirect Purchaser States, including interest, and that judgment be entered against Defendant in favor of the Class;

(d) Plaintiff and each member of the Class recover the amounts by which Defendant has been unjustly enriched;

(e) The Defendant be enjoined from continuing the illegal activities alleged herein;

(f) The Class recover their costs of suit, including reasonable attorneys' fees as provided by law; and

(g) The Class be granted such other, further and different relief as the nature of the case may require or as may be determined to be just, equitable, and proper by this Court.

Respectfully Submitted,

NEW MEXICO UNITED FOOD AND COMMERCIAL WORKERS UNION'S AND EMPLOYERS' HEALTH AND WELFARE TRUST FUND, on behalf of itself and all others similarly situated,

By their attorneys,

Dated: September 14, 2011

/s/ *Thomas M. Greene*

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