IN THE UNITED STATES DISTRICT COURT
FOR THE MIDDLE DISTRICT OF FLORIDA
OCALA DIVISION

UNITED STATES OF AMERICA, Plaintiff, v. FRANCK'S LAB, INC., d.b.a. FRANCK'S COMPOUNDING LAB, a corporation, and PAUL W. FRANCK, an individual Defendants.	Civil Action No. 5:10-cv-00147-Oc-32GRJ MEMORANDUM OF LAW IN SUPPORT OF PLAINTIFF'S MOTION FOR PRELIMINARY INJUNCTION

I. INTRODUCTION

Plaintiff, the United States of America, files this memorandum in support of its motion for preliminary injunction pursuant to 21 U.S.C. § 332(a). The Federal Food, Drug, and Cometic Act, 21 U.S.C. § 301, et. seq. (the "Act"), and its implementing regulations prohibit compounding animal drugs from bulk drug substances. Animal drugs compounded from bulk substances are unsafe within the meaning of the Act, and are adulterated and misbranded. It violates the Act to cause a drug to become adulterated or misbranded while it is held for sale after shipment in interstate commerce, and to introduce an adulterated or misbranded drug into interstate commerce, 21 U.S.C. §§ 331(a) and (k). Defendants have been compounding the overwhelming majority, if not all, of their animal drugs from bulk drug substances, and have been distributing compounded animal drugs nationwide. On April 19, 2009, 21 polo horses died after being administered an illegal compounded animal drug that Defendants had compounded, which contained a dose 100 times the veterinarian-prescribed amount of selenium. Defendants

have been warned that their practices are illegal, yet they continued to regularly compound animal drugs from bulk drug substances until they voluntarily agreed to suspend these practices almost one month after the filing of the government's Complaint, on May 14, 2010, as part of settlement discussions. At this time, the parties have determined that they will proceed with litigation. Accordingly, notwithstanding Defendants' assertions that they will continue to voluntarily suspend their practices, FDA believes that a preliminary injunction is necessary to ensure that Defendants comply with the Act.

II. STATEMENT OF FACTS

A. Post-Filing Discussions

Since the filing of the Complaint in this case on April 16, 2010, the parties have been engaged in settlement discussions. The parties filed a Joint Status Report on May 18, 2010, informing this Court that Defendants had agreed to voluntarily suspend their animal drug compounding practices, which the government asserted in its Complaint are illegal. Defendants have represented to the government that they will continue to abide by the terms of the voluntary suspension for now as litigation moves forward. However, the suspension, by its written terms, can be withdrawn at any time with 48 hours notice.

Additionally, Defendants have attempted to ensure that their customers, who were buying the illegally compounded products at issue in the Complaint, will have other outlets to receive these illegal products by assisting at least one other compounding pharmacy to fill its client requests. Declaration of Emma R. Singleton ("Singleton Decl.") ¶ 8 and Exhibit A thereto (Attachment 1). The government is investigating these activities, but to the extent they are occurring, the government believes that a preliminary injunction is appropriate. Id.

B. An Overview Of Drug Compounding

"Drug compounding," has been defined by the United States Supreme Court as "a process by which a pharmacist or doctor combines, mixes, or alters ingredients to create a medication tailored to the needs of an individual patient." Thompson v. Western States Med. Ctr., 535 U.S. 357, 360-61 (2002). In Western States, the Court explained that "[c]ompounding is typically used to prepare medications that are not commercially available, such as medication for a patient who is allergic to an ingredient in a mass-produced product." Id. at 361. Other traditional uses for compounding include, but are not limited to, flavoring medications or altering dosage strength or dosage form for a particular patient's needs. Declaration of William T. Flynn ("Flynn Decl.") ¶ 15 (attachment 2). FDA's Center for Veterinary Medicine ("CVM") is responsible for the regulation of animal drugs, including those produced by compounding. FDA/CVM has long recognized that traditional pharmacy compounding in response to a valid prescription accommodates a particular human or animal patient's specialized medical needs. Id. at ¶¶ 17, 25. But some compounders are circumventing, and thus undermining, the Act's drug approval process by conducting large-scale drug manufacturing enterprises under the guise of pharmacy compounding. Id. at ¶¶ 18-23. The practice of compounding animal drugs from bulk drug substances poses heightened health risks to human and animal consumers of those products because the safeguards built into the new animal drug approval process are not implemented. Flynn Decl. ¶ 23. Additionally, the unchecked proliferation of such illegal activities creates disincentives for drug sponsors to develop necessary and useful animal drugs, having internalized that any investment in drug development, research, and clinical trials, could be undermined by the cost-savings enjoyed by illegal compounders. Id. at ¶ 23.

C. Defendants

Franck's Lab, Inc., d.b.a. Franck's Compounding Lab ("Franck's"), has been incorporated under Florida law since 2003, and conducts its business at 1210 SW 33rd Avenue, Ocala, Florida. Singleton Decl. ¶ 4. Franck's markets itself as a compounding pharmacy on its website and in promotional materials, see e.g., https://secure.francks.com/?action=from_the_president (last visited July 2, 2010), and has claimed to be a compounding pharmacy in an amicus brief filed in the United States District Court for the Western District of Texas (attachment 3). Franck's is licensed by the State Board of Pharmacy in Florida and in all but three states in the country, and manufactures and distributes a wide variety of drugs for both human and animal use to customers across the United States. Singleton Decl. ¶ 4. The firm manufactures the vast majority of its animal drugs from active pharmaceutical ingredients ("API," hereinafter referred to interchangeably with "bulk drugs"), which are bulk drug substances within the meaning of 21 C.F.R. § 207.3(4), that it purchases from suppliers outside of Florida, including Minnesota and Texas. Id. Franck's has annual gross sales of roughly $8 million, $3.5 million related to veterinary drugs, and filled more than 37,600 veterinary prescriptions between February 1 and December 4, 2009. Id.

Paul W. Franck is the owner and Chief Executive Officer of Franck's. Id. at ¶ 5. He is involved in the firm's day-to-day activities, and is responsible for providing the final approval on all decisions concerning its operations. Id. He maintains an office and performs his duties at the firm's headquarters, and has participated in each FDA inspection. Id.

Defendants maintain a website at www.francks.com, from which individuals can place orders for products. Id. at ¶ 6. This website advertises hundreds of different products,

comparing many of them to FDA-approved drugs. Id.; see also Franck's Pharmacy, http://catalog.digicatalog.com/showmag.php?mid=wqggrw&spid=-3#/page2/ (last visited July 2, 2010). The website contains a "Product List," which is a chart of the "most common compounds requested," well over 200 different items, and includes the following categories: Defendants' "drug name;" the "trade name;" the "drug classification;" and the "dosage forms available." Singleton Decl. ¶ 6. The firm's website also claims that "Franck's Pharmacy is the nation's premier veterinary compounder," id.; see also Franck's Pharmacy, http://catalog.digicatalog.com/showmag.php?mid=wqggrw&spid=-3#/page4/ (last visited July 2, 2010), and states that "Franck's Compounding Lab specializes in compounded medications . . . allowing the specialist to custom prescribe for an individual patient, the exact drug and dosage form to be used." See About Franck's Pharmacy, https://secure.francks.com/?action=from_the_president (last visited July 2, 2010). There are numerous other statements throughout the website demonstrating that Franck's products are intended to cure, mitigate, treat, or prevent various diseases. Singleton Decl. ¶ 6.

None of Defendants' products is the subject of an approved new animal drug application ("NADA"), an abbreviated new animal drug application ("ANADA"), or a conditional approval, nor are any of them listed in an index for use in minor species, which could permit them to be legally marketed under 21 U.S.C. § 360b(a)(1). Likewise, none of Defendants' products meets the conditions for an investigational new animal drug exemption under 21 U.S.C. § 360b(j). Flynn Decl. ¶ 31. Their products include, but are not limited to, injectables, powders, capsules, suspensions, tablets, and topicals, which they compare to brand-name drugs on their website, for example: Stanazolol (injectable and capsule), which is compared to the brand-name drug

Winstrol-V; cyclosporine (suspension), which is compared to the brand-name drug Optimmune; medroxyprogesterone (injectable), which is compared to the brand-name drug Depo-Provera; estrone aqueous (injectable), which is compared to the brand-name drug Estrone; flunixin meglumine (powder), which is compared to the brand-name drug Banamine; phenylbutazone/dexamethasone (topical), which is compared to the brand-name drug Azium; methimazole (topical), which is compared to the brand-name drug Tapazole; and pergolide mesylate (tablet), which is compared to the brand-name drug Permax. Singleton Decl. ¶ 7. Each of the products listed in the preceding sentence is made using API. Id. By comparing their products to brand-name drugs, Defendants are adopting the claims for those drugs, demonstrating that they intend them for use as drugs.

D. FDA Inspection History And Prior Notice

Defendants have a history, dating back to at least 2004, of violating the Act by compounding new animal drugs from bulk drug substances. Singleton Decl. ¶¶ 9-13. FDA has warned Defendants, both verbally and in writing, of their violations. Id. at ¶¶ 10-14. Defendants consistently responded that they disagreed with FDA's interpretation of the law, and that they believed FDA lacks jurisdiction over their compounding activities. Id. at ¶¶ 10, 12, 13, 15. They had not ceased their illegal activity, which has resulted in animal deaths, as of the date of this lawsuit. Id. at ¶ 16. They only agreed to suspend their activities nearly a month after this case was initiated. See Joint Status Report at ¶ 1.

1. Inspections

a. December 1 - 4, 2009

FDA most recently inspected Defendants from December 1 - 4, 2009. Id. at ¶ 10. During the inspection, FDA investigators observed that Defendants continued to compound animal drugs from API,, and Mr. Franck confirmed that between 95 and 99.9% of the animal drugs Defendants compound are made from API. Id. Many of these drugs are unapproved copies of FDA-approved drugs. Id. At the inspection's conclusion, the FDA investigators discussed their observations with Mr. Franck, informed him that his firm's activities violated the law, and provided him with a copy of FDA's Compliance Policy Guide 608.400, entitled "Compounding of Drugs for Use in Animals" ("CPG"). Id.

b. June 18 - 23, 2009

FDA previously inspected Defendants' facility from June 18 - 23, 2009. Id. at ¶ 11. During that inspection, FDA investigators collected document samples of API that Defendants use in their normal course of compounding animal drugs. Id. At that time, Mr. Joseph Kraatz, Franck's Inventory Control Coordinator, told FDA investigators that 95% of the firm's veterinary drugs are made from bulk API. Id.

c. September 29 - October 4, 2004 and Subsequent Warning Letter

FDA conducted a previous inspection of Defendants' animal drug compounding operations from September 29 through October 4, 2004. Id. at ¶ 13. During that inspection, Mr. Franck admitted that 70% of the firm's business related to veterinary drug compounding and 90% of those animal drugs were compounded from bulk materials. Id. The FDA investigator explained that this practice violated the Act, and Mr. Franck replied that he disagreed with

FDA's interpretation of the law. Id. An FDA Form 483, List of Inspectional Observations ("Form 483") was issued to Defendants citing, for example, ten veterinary drugs that were illegally compounded from API. Id.

After this inspection, on January 5, 2005, FDA issued a Warning Letter to Defendants notifying them that they were violating the Act by compounding veterinary drugs from API in conjunction with: (1) distributing to third-parties for resale; (2) compounding drugs when an approved drug would appropriately treat the animal; and (3) allowing their drugs to be used in food-producing animals, which could expose humans who eventually ingested the food, to residues of any illegal drugs. Id. at ¶ 14.

Defendants' counsel responded by letter dated January 27, 2005, contending that compounding from bulk substances should be legal, and that his clients would comply with a new CPG only if it permitted such activity:

> It is my understanding that the FDA allows compounding by bulk chemicals for human use, so the same should apply to veterinary compounding . . . . It is further my understanding that the FDA/CVM is in the process of revising their . . . CPG which should allow for bulk compounding. Franck's believes it is in compliance now, but will most certainly comply with the new CPG . . . .

Id. at ¶ 15 and Exhibit E attached thereto. Defendants' counsel ignored the statutory differences between regulation of compounding for human and animal use; the Act expressly permits compounding from bulk drug substances for human drugs, but contains no such provisions for animal drugs. Compare 21 U.S.C. § 360b and 21 U.S.C. § 353a.

d. Other Relevant Inspections

FDA inspected Defendants' operations on May 4 - 20, 2009, in response to allegations that one of their products caused the deaths of 21 polo horses on April 19, 2009. Id. at ¶ 12. During this inspection, Defendants admitted that they had been asked by a veterinarian to compound a product that was unapproved in the United States, but that is known elsewhere as Biodyl, and is prescribed for fatigue in horses. Id. Defendants further admitted that they had not previously compounded this product, and they made a miscalculation resulting in the concentration of selenium being 100 times what should have been administered. Id. In horses, toxic amounts of selenium can damage multiple organs including lung, liver, and heart. Flynn Decl. ¶ 33. This can result in respiratory distress, liver malfunction, and cardiovascular collapse, which can lead to death. Id. In addition to reviewing the documents relevant to the compounding of the drug implicated in the horses' deaths, the FDA investigators randomly selected and reviewed six other incidents from Defendants' complaint files. Singleton Decl. ¶ 12. Several of these incident reports documented that dispensed products compounded by Franck's were the incorrect strength. Id. FDA issued a five-item Form 483 and discussed the items with Mr. Franck at the inspection's close. Id. The observations all related to the processes and controls used in Defendants' compounding activities. Id. In response to the Form 483, Defendants sent a letter, dated June 12, 2009, arguing that FDA did not have jurisdiction over the firm's practices because it was a compounding pharmacy and only subject to state regulation rather than FDA oversight. Id.

2. Additional Prior Notice

Defendants have been told repeatedly that their conduct violates the law and that continued violations could lead to regulatory action. See Id. at ¶¶ 10, 14. FDA issued to Defendants a Form 483 in 2004, documenting multiple violations related to compounding animal drugs from bulk drug substances. Id. at ¶ 13. They also received from FDA a Warning Letter in 2005 addressing those same violations, and stating that enforcement action could follow without further notice. Id. at 14 and Exhibit D attached thereto. Defendants again responded that they thought compounding animal drugs from bulk substances should be legal. Id. at ¶ 15 and Exhibit E attached thereto. FDA investigators verbally warned Defendants of their continued violations during the December 2009 inspection, and again Mr. Franck disputed FDA's interpretation of the law, while acknowledging that Defendants' activities are in violation under the Agency's interpretation. Id. at ¶ 10. He stated that he would have to stop making products from API to bring his operations into compliance. Id. Despite these warnings, Defendants' violations have persisted. Based on Defendants' responses and continued illegal activities, it is clear that Defendants do not intend to voluntarily comply with the Act.

III. LEGAL ANALYSIS AND ARGUMENT

A. Standard For Preliminary Injunction

This action seeks injunctive relief under the Act, 21 U.S.C. § 332(a). When, as here, the United States seeks a preliminary injunction to prevent the violation of a federal statute that expressly provides for injunctive relief, the court applies a different standard than that applied to private litigants. The Eleventh Circuit has stated that "[w]here . . . an injunction is authorized by statute and the statutory conditions are satisfied . . . the usual prerequisite of irreparable injury

need not be established and the agency to whom the enforcement of the right has been entrusted is not required to show irreparable injury before obtaining an injunction." Gresham v. Windrush Partners, Ltd., 730 F.2d 1417, 1423 (11th Cir. 1984) (quoting United States v. Hayes Int'l Corp., 415 F.2d 1038, 1045 (5th Cir. 1969)).

Instead, the government must show only that the defendants have violated the statute and there is some "cognizable danger of recurrent violations" to obtain a statutory injunction. United States v. W.T. Grant Co., 345 U.S. 629, 633 (1953); United States v. Supporting Solutions, Inc., 2009 U.S. Dist. LEXIS 59993 at *16 (S.D. Fla. 2009) (holding that the Government need not establish the usual prerequisites for a preliminary injunction when the W.T. Grant test is met); United States v. Sene X Eleemosynary Corp., 479 F. Supp. 970, 981 (S.D. Fla. 1979) (irreparable harm is presumed); United States v. Diapulse Corp. of America, 457 F.2d 25, 27-28 (2d Cir. 1972) (where a federal statute is involved, irreparable harm is presumed). Additionally, the law is clear that cessation of illegal activity in the face of litigation does not bar an injunction. W. T. Grant, 345 U.S. at 633 ("the court's power to grant injunctive relief survives discontinuance of the illegal conduct").

Examining Defendants' past record of noncompliance is the best way to predict the likelihood of future violative conduct. Id.; Diapulse Corp., 457 F.2d at 28. Injunctive relief is particularly appropriate where, despite repeated warnings, systemic violations have persisted. United States v. Endotec, 2009 U.S. Dist. LEXIS 93985 at *22 (M.D. Fla. 2009) (holding that preliminary injunction is appropriate when the W.T. Grant factors are met); United States v. Kasz Enterprises, Inc., 855 F. Supp. 534, 544, amended on other grounds, 862 F. Supp. 717 (D.R.I. 1994). The standard for preliminary injunction is virtually identical to the permanent

injunction standard except that in a preliminary injunction, the moving party meets its burden by demonstrating likely success on the merits instead of actual success. United States v. Prater, 2005 U.S. Dist. LEXIS 24952 at *9 (M.D. Fla. 2005).

In this case, the United States is entitled to an injunction because the Defendants have repeatedly violated the Act and this illegal activity continues. As noted, Defendants have been warned multiple times over the course of many years that they are violating the law. Despite these warnings from FDA, Defendants continue to violate the law, and have asserted that FDA does not have jurisdiction over their activities. And although the government acknowledges that the Defendants voluntarily suspended their activities during initial discussions, that suspension could be revoked with 48 hours notice. Additionally they continue to assist at least one other compounding pharmacy to fill orders that the government has alleged are illegal. Where, as here, the evidence establishes a persistent pattern of failure to comply with the Act despite numerous warnings, preliminary injunctive relief is proper and, indeed, necessary.

Further, in filing their recent Motion to Dismiss (Def.'s Mot. Dismiss, Doc. No. 13), the Defendants have launched a challenge to the FDA's regulatory jurisdiction over the compounding practices in question. The government presumes that these arguments will also be at the heart of the defense to this Motion For Preliminary Injunction. Because of this litigation strategy by the Defendants, and because there has been little substantive progress towards a negotiated final consent decree, which has been under discussion since early May, the United States sees little benefit in any further forbearance from submitting these issues to this Court. Indeed, a decision by this Court on these legal questions, which go to the heart of FDA's regulatory authority over Defendants' practices, will clarify the issues for the parties.

B. Regulatory Framework For Compounded Animal Drugs

The Act defines "drug" at 21 U.S.C. § 321(g)(1)(B) as "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals." Whether a product is a "drug" under the Act depends on the product's intended use. See 21 U.S.C. § 321(g)(1); National Nutritional Foods Ass'n v. Mathews, 557 F.2d 325, 333-34 (2d Cir. 1977).

The Act defines "new animal drug" at 21 U.S.C. § 321(v) as:

> any drug intended for use for animals . . . the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of animal drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof . . . .

When a pharmacist compounds a drug for use in animals, by definition, he or she creates a "new animal drug" within the meaning of the Act because the compounded drug is not "generally recognized, among experts . . . as safe and effective." See 21 U.S.C. § 321(v)(1); Weinberger v. Hynson, Westcott & Dunning, 412 U.S. 609, 629-30 (1973) (holding that a drug cannot be "generally recognized" as safe and effective without the adequate and well-controlled studies that would be required for its approval); Medical Center Pharmacy v. Mukasey, 536 F.3d 383, 394-95 (5th Cir. 2008). To obtain approval to market a new animal drug, a drug's sponsor must submit to FDA a new animal drug application ("NADA"), which demonstrates, through adequate and well-controlled studies, the drug's safety and efficacy for particular uses and, among other things, describes its manufacturing processes. 21 U.S.C. § 360b(b). As part of the NADA approval, FDA approves those uses for which the drug can be marketed, based on the data submitted in the

NADA. Flynn Decl. ¶ 12. Manufacturers of approved drugs must meet certain requirements, such as registering with FDA, validating their chemistry and manufacturing processes, and complying with post-approval obligations, including reporting adverse events. 21 C.F.R. Part 514. An animal drug without approval, and without an effective exception is unsafe, and therefore "adulterated," within the meaning of the Act. See 21 U.S.C. § 351(a)(5). Such exceptions include, but are not limited to, an index listing for use in a minor species, a conditional approval, or an investigational new animal drug exemption. None of these exemptions apply in this case.

In 1994, Congress amended the Act by passing the Animal Medicinal Drug Use Clarification Act ("AMDUCA"), which permits certain uses of FDA-approved drugs for indications that are not listed in the drugs' FDA-approved labeling, if validly prescribed by a veterinarian. 21 U.S.C. §§ 360b(a)(4)(A) and (a)(5). If the requirements of AMDUCA are not met, the drug is not excepted from being deemed "unsafe" within the meaning of 21 U.S.C. § 360b(a)(1). FDA has promulgated regulations implementing AMDUCA, which specifically address compounding. 21 C.F.R. Part 530. The regulations permit compounding drugs for animal use only if such drugs are compounded from "approved animal or human drugs" and state that "[n]othing in this part shall be construed as permitting compounding from bulk drugs." 21 C.F.R. § 530.13. A "bulk drug substance" is defined in 21 C.F.R. § 207.3(a)(4) as:

> any substance that is represented for use in a drug and that, when used in the manufacturing, processing, or packaging of a drug, becomes an active ingredient or a finished dosage form of the drug, but the term does not include intermediates used in the synthesis of such substances.

The prohibition on compounding animal drugs from bulk differs from the regulation of compounded human drugs, in which there is some limited statutory allowance for compounding from bulk drug substances, so long as certain requirements are met. See 21 U.S.C. § 353a.

In 2003, to further clarify its interpretation and intent to apply AMDUCA and its corresponding regulations, FDA issued the current CPG. Flynn Decl. ¶ 27 and Exhibit A attached thereto. In the CPG, FDA recognizes the use of compounding within certain areas of veterinary practice, while explaining that some compounders intentionally circumvent the drug approval process and create the potential for an unacceptable lack of quality control and appropriate manufacturing standards. Id. The CPG sets out FDA's interpretation of the Act and implementing regulations, under which compounding from bulk drug substances or unapproved drugs renders the compounded drugs unsafe as a matter of law, and thus adulterated in violation of 21 U.S.C. § 351(a)(5). Id. It also provides by way of example, a non-inclusive, 13-item list of factors that the Agency may consider in deciding whether to exercise its enforcement discretion with regard to compounded animal drugs. Id. Compounding from bulk drug substances or other unapproved drugs is one of the factors, especially as that practice is not allowed under the regulations, 21 C.F.R. § 530.13. Id.

Multiple professional and industry groups have acknowledged FDA's regulatory structure as described above. For example, the American Veterinary Medical Association distributes a brochure stating that compounding can only legally be done from approved drugs. See, http://www.avma.org/issues/drugs/compounding/veterinary_compounding_brochure.pdf. Additionally, the American Association of Equine Practitioners has developed "Equine Veterinary Compounding Guidelines," which state:

> The veterinarian must realize that the use of bulk drugs in preparation of compounded medications is, under strict interpretation of the Federal Food Drug and Cosmetic Act, illegal because it results in the production of an unapproved new animal drug. Preparation, sale, distribution, and use of unapproved new animal drugs is in violation of the Act. The preparation of compounded medication from bulk drugs may be permissible in medically necessary situations when there is no approved product available or the needed compounded preparation cannot be made from an FDA-approved drug. Therefore legal compounding can only begin with FDA-approved drugs in compliance with federal extra-label drug use regulations. . . .

Equine Veterinary Compounding Guidelines,

http://www.aaep.org/pdfs/drug_compounding_guidelines.pdf (last visited July 2, 2010).

C. Defendants' Practices Violate The Act

The Act prohibits introducing into interstate commerce drugs that are adulterated or misbranded. 21 U.S.C. § 331(a). It further prohibits doing any act to a drug while it is held for sale after shipment of one or more of its components in interstate commerce that causes the drug to become adulterated or misbranded. 21 U.S.C. § 331(k). Thus, the relevant inquiries are:

(1) Whether Defendants' products are drugs;

(2) Whether the products or their component parts travel in interstate commerce; and

(3) Whether the products are adulterated or misbranded.

1. Defendants' Products Are Both "Drugs" And "New Animal Drugs" As Defined In The Act.

a. "Drug"

As stated above in Section III.B, the Act defines "drug" at 21 U.S.C. § 321(g)(1)(B) as "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals." Whether a product is a "drug" under the Act depends on its intended use.

See 21 U.S.C. § 321(g)(1); National Nutritional Foods Ass'n v. Mathews, 557 F.2d at 333-34. A product's intended use may be determined from any relevant source, including product advertising and labeling, which may include labels, promotional material, and oral or written representations by the vendor, and the circumstances surrounding the product's distribution. See 21 C.F.R. § 201.128; United States v. Articles of Drug for Veterinary Use, 50 F.3d 497, 500 (8th Cir. 1995); National Nutritional Foods Ass'n v. Mathews, 557 F.2d 325, 334 (2d Cir. 1977); United States v. 216 Cartoned Bottles . . . "Sudden Change", 409 F.2d 734, 739 (2d Cir. 1969); United States v. Hohensee, 243 F.2d 367, 370 (3d Cir. 1957).

Defendants' products are unquestionably intended for use as drugs. As explained above in section II. C., Defendants' website lists many of their products compared to brand name drugs, and claims that "Franck's Compounding Lab specializes in compounded medications . . . ." Defendants make multiple claims that their products are to be used in the cure, mitigation, or treatment of diseases. Thus, Defendants' products are "drugs."

b. "New Animal Drug"

The Act defines "new animal drug" at 21 U.S.C. § 321(v), as a drug for use in animals that is not generally recognized as safe and effective ("GRAS/GRAE") for the uses in its labeling. For a drug to be GRAS/GRAE, it must be the subject of published adequate and well-controlled studies showing that the drug is safe and effective for the use(s) set out in its labeling, and be recognized as safe and effective by qualified experts whose opinions are based on the publicized studies. See 21 U.S.C. § 360b(d). The government need not establish that a drug actually "is either unsafe or ineffective in order to establish that it is a new drug. Rather, the government must demonstrate only that [the drug] is not generally recognized as safe and

effective by qualified experts for use as promoted by defendants." United States v. Sene X Eleemosynary Corp., 479 F. Supp. 970, 977 (S.D. Fla. 1979) (citations omitted). Therefore, "the purpose of the normal inquiry [into whether a drug is generally recognized among qualified experts as safe and effective for its intended uses] is not to determine the [actual] safety and effectiveness at all, but to ascertain the drug's general reputation in the scientific community for such characteristics." United States v. Articles of Food and Drug (Coli-Trol 80 Medicated), 372 F. Supp. 915, 920 (N.D. Ga. 1974), aff'd, 518 F.2d 743 (5th Cir. 1975).

Courts have recognized a three-part test to determine general recognition of safety and effectiveness. First, the drug must have at least "substantial evidence" of effectiveness for approval, including adequate and well-controlled studies as defined at 21 C.F.R. § 314.126. See Weinberger v. Hynson, Westcott, & Dunning, Inc., 412 U.S. at 629; United States v. Atropine Sulfate . . . Dey-Dose, 843 F.2d 860, 862 (5th Cir. 1988); United States v. Article of Drug . . . 4,860 Pails, 725 F.2d 976, 985 (5th Cir. 1984). Second, the studies must be published in the scientific literature so that they are made generally available to the community of qualified experts. See Weinberger v. Bentex Pharm., Inc., 412 U.S. 645, 652 (1973); 4,860 Pails, 745 F.2d at 987; Premo Pharm. Labs., Inc., 629 F.2d 795, 803 (2d Cir. 1980). Finally, there must be a consensus by qualified experts, which is based on the published studies, that the drug is safe and effective for the indications set out in its labeling. United States v. Undetermined Quantities of . . . Equidantin, 675 F.2d 994, 1001 (8th Cir. 1992); Dey-Dose, 843 F.2d at 862;4,860 Pails, 725 F.2d at 985. Failure to meet any one of these criteria establishes that the drug is not GRAS/GRAE, and renders the drug a "new drug" as a matter of law. See United States v. 118/110 Tablet Bottles, 662 F. Supp. 511, 513 (W.D. La. 1987); see also 21 U.S.C. § 321(p)(1).

Compounded drugs, such as Defendants', have not been studied in adequate and well-controlled investigations. Flynn Decl. ¶ 19. Because there is no published scientific literature, qualified experts cannot reach a consensus concerning these drugs' safety and effectiveness. Weinberger v. Henson, 412 U.S. at 629-30. Therefore, compounded animal drugs cannot be GRAS/GRAE and are, thus, "new animal drugs." Med Ctr. Pharm, 536 F.3d at 394-95. The three appellate courts that have considered this issue have each held that compounded drugs are new drugs. Id. at 405, 407-08 (finding both that compounded human and compounded animal drugs are "new drugs" and the Act "contains no blanket 'implicit exemption' for animal drugs produced by compounding"); United States v. Algon Chemical, Inc., 879 F.2d 1154, 1158 (3d Cir. 1989) (finding that "[t]he statutory definition of a "new drug". . . does not exempt drugs that are compounded by veterinarians"); United States v. 9/1 Kg. Containers, More or Less . . ., 854 F.2d 173, 177-78 (7th Cir. 1988) (holding that the Act "forbids the sale, in any form, of drugs formulated or put to new uses after 193[8], without the approval of FDA"). As a result, all of Defendants' compounded veterinary drugs are "new animal drugs."

2. Defendants' Drugs Or Their Components Travel In Interstate Commerce

As explained above, Defendants ship their compounded drugs nationwide. Singleton Decl. at ¶ 4. Such shipments constitute the introduction or delivery for introduction of drugs into interstate commerce within the meaning of 21 U.S.C. § 331(a).

Defendants also purchase the components used to manufacture their drugs, including API, from firms located in states other than Florida, including Minnesota and Texas. Id. Defendants' use of these components to manufacture adulterated and misbranded drugs violates 21 U.S.C. § 331(k). See United States v. Dianovin Pharm., Inc., 475 F.2d 100, 103 (1st Cir. 1973) (use of

components shipped in interstate commerce to make drugs brings activities within 21 U.S.C. § 331(k)), cert. denied, 414 U.S. 830 (1973).

3. Defendants' Drugs Are Adulterated Under 21 U.S.C. § 351(a)(5) Because They Do Not Qualify For Any Exemption, And Are Deemed Unsafe Under 21 U.S.C. § 360b.

The Act provides that a drug is adulterated if "it is a new animal drug which is unsafe within the meaning of [21 U.S.C. § 360b]." 21 U.S.C. § 351(a)(5). The Act, 21 U.S.C. § 360b(a)(1), further states that a new animal drug shall be deemed unsafe unless the drug, its labeling, and its use conform to: (1) an FDA-approved application; (2) a conditional approval; or (3) an index listing for use in a minor species. Defendants have no approvals or conditional approvals for any of their drugs and their drugs are not listed in any minor species index. Flynn Decl. ¶ 31. Moreover, they do not meet the conditions for an investigational new animal drug exemption under 21 U.S.C. § 360b(j). Id. Thus Defendants' drugs are unsafe within the meaning of 21 U.S.C. § 360b. Id.

AMDUCA offers a limited exception to the approval mechanism outlined above for the use of approved drugs for indications not listed in their approved labeling ("extralabel use"). 21 U.S.C. §§ 360b(a)(4), (a)(5). As explained above, the Act provides that a new animal drug is deemed to be unsafe if its use does not conform to its approved, conditionally approved, or indexed indications. Pursuant to AMDUCA and corresponding regulations, an approved new animal or human drug intended to be used for an extralabel purpose in an animal will not be deemed unsafe under 21 U.S.C. § 360b if the use is "by or on the lawful . . . order of a licensed veterinarian within the context of a valid veterinarian-client-patient relationship, and in compliance with [21 C.F.R. Part 530]." 21 C.F.R. § 530.10. Part 530 includes regulations

relating to, among other things, keeping appropriate veterinary records, required labeling, and conditions in which extralabel use is not allowed due to safety or other concerns. Where, as here, there are no relevant product approvals, this exception does not apply.

Within the AMDUCA implementing regulations, 21 C.F.R. Part 530, there is a provision that specifically addresses compounded drugs, and makes clear that it does not permit compounding from bulk drugs:

> This part applies to compounding of a product from approved animal or human drugs by a veterinarian or a pharmacist on the order of a veterinarian within the practice of veterinary medicine. Nothing in this part shall be construed as permitting compounding from bulk drugs.

21 C.F.R. § 530.13(a) (emphasis added). The regulation further states that extralabel use from the compounding of approved new animal or human drugs is permissible only when certain criteria are met. 21 C.F.R. § 530.13(b). Again, Defendants have no drug approvals and do not compound their drugs from other approved drugs, therefore, they cannot find any safe harbor in the AMDUCA language.

Defendants compound the overwhelming majority, if not all, of their veterinary drugs from bulk drugs, which are not approved. Singleton Decl. ¶ 10. Therefore, these drugs do not meet the requirements of 21 C.F.R. Part 530, and do not qualify for an exemption under AMDUCA. Consequently, they are unsafe within the meaning of 21 U.S.C. § 360b and are thus adulterated within the meaning of 21 U.S.C. § 351(a)(5).

4. Defendants' Drugs Are Misbranded Because They Do Not Bear Adequate Directions For Use.

A drug is misbranded within the meaning of 21 U.S.C. § 352(f)(1) unless its labeling bears "adequate directions for use." FDA has defined "adequate directions for use" as "directions under which the layman can use a drug safely and for the purpose for which it is intended." 21 C.F.R. § 201.5(a); see also United States v. Articles of Drug . . . Rucker, 625 F. 2d 665, 671-75 (5th Cir. 1980). Adequate directions for use must be based on animal and clinical data derived from extensive, scientifically controlled testing. United States v. Miami Serpentarium Lab., [1981-1982 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38, 931 (S.D. Fla. 1982). As stated above in section III.C.1.b., compounded drugs, such as Defendants', do not have any well-controlled clinical trial data. Therefore, adequate directions under which a layman can safely use Defendants' drugs cannot be written, and the drugs are misbranded within the meaning of 21 U.S.C. § 352(f)(1).

Moreover, unapproved prescription new animal drugs, such as those distributed by Defendants, lack adequate directions for use as a matter of law. A new animal drug is exempt from the adequate directions for use requirement only if several requirements are met, including that the drug bears the precise labeling authorized by its approved NADA. See 21 C.F.R. § 201.105(c)(2). Thus, any prescription new animal drug that lacks an approved NADA cannot satisfy this condition for exemption from the adequate directions of use requirement and is misbranded until such time as it becomes the subject of an FDA-approved NADA. See Rucker, 625 F.2d at 675 (discussing the theory in the human drug context); United States v. Premo Pharm. Labs., Inc., 511 F. Supp. 958, 977 n.23 (D.N.J. 1981) ("A drug is misbranded if it is a

prescription drug that is an unapproved new drug, because a prescription drug cannot bear the adequate directions for use required by such statute . . . and the lack of an approved new drug application means that there is no exemption from the adequate directions for use requirement.") (citations omitted). Because Defendants do not have approvals for any drugs, including any of their prescription drugs, all of their prescription drugs are misbranded as a matter of law.

IV. CONCLUSION

For the foregoing reasons, Plaintiff respectfully requests that this Court grant the preliminary injunctive relief requested by Plaintiff in its Motion for Preliminary Injunction for Defendants' violations of 21 U.S.C. §§ 331(a) and (k).

Respectfully submitted,

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