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IN THE UNITED STATES DISTRICT COURT

DISTRICT OF UTAH, CENTRAL DIVISION

UNITED STATES OF AMERICA, Plaintiff, v. ISOMERIC PHARMACY SOLUTIONS, LLC, a limited liability company, and WILLIAM O. RICHARDSON, RACHAEL S. CRUZ, and JEFFERY D. BROWN, individuals, Defendants	Case No. 2:17-cv-00852-RJS **COMPLAINT FOR PERMANENT INJUNCTION** Judge Robert J. Shelby

The United States of America, Plaintiff, by and through its undersigned counsel, and on behalf of the United States Food and Drug Administration ("FDA"), respectfully represents as follows:

1. This statutory injunction proceeding is brought under the Federal Food, Drug, and Cosmetic Act (the "Act"), 21 U.S.C. § 332(a), and this court's inherent equitable authority, to permanently enjoin the defendants, Isomeric Pharmacy Solutions, LLC ("Isomeric"), a limited liability company, and William O. Richardson, Rachael S. Cruz, and Jeffery D. Brown, individuals (collectively, "Defendants") from: (a) violating 21 U.S.C. § 331(a) by introducing or causing to be introduced, or delivering or causing to be delivered for introduction, into interstate commerce, articles of drug that are adulterated within the meaning of 21 U.S.C. §§ 351(a)(2)(A) and 351(a)(2)(B), and/or that are misbranded within the meaning of 21 U.S.C. § 352(f)(1); (b) violating 21 U.S.C. § 331(k) by causing articles of drug to become adulterated within the meaning of 21 U.S.C. §§ 351(a)(2)(A) and 351(a)(2)(B), and/or to become misbranded within the meaning of 21 U.S.C. § 352(f)(1), while such drugs are held for sale after shipment of one or more of their components in interstate commerce; and (c) violating 21 U.S.C. § 331(d) by introducing or causing to be introduced, or delivering or causing to be delivered for introduction, into interstate commerce, new drugs, as defined by 21 U.S.C. § 321(p), that are neither approved under 21 U.S.C. § 355, nor exempt from approval.

2. Isomeric has a history of manufacturing injectable and ophthalmic drug products under conditions that fall short of the minimum requirements to ensure safety and quality. Despite FDA's repeated attempts to obtain Isomeric's voluntary compliance with the Act, the company continued to demonstrate that it was unwilling or unable to implement sustainable corrective actions to assure the sterility of its drug products and comply with the Act. The history of serious violations of the Act, and the likelihood that violations will continue in the absence of court action, demonstrate that permanent injunctive relief is necessary.

Jurisdiction and Venue

3. This Court has jurisdiction over the subject matter and all parties to this action under 28 U.S.C. §§ 1331, 1337, and 1345, and 21 U.S.C. § 332(a).

4. Venue in this district is proper under 28 U.S.C. §§ 1391(b) and (c).

Defendants and Their Operations

5. Isomeric Pharmacy Solutions, LLC, is a limited liability company located at 2401 South Foothill Drive, Suite D, Salt Lake City, Utah, 84109, within the jurisdiction of this Court. Isomeric obtained pharmacy licenses from the Utah Division of Occupational and Professional Licensing, Utah Board of Pharmacy for retail and manufacturing and distribution operations.

6. William O. Richardson is Isomeric's Chief Executive Officer and co-owner (through the "William Richardson Utah 101 Trust"). Defendant Richardson is the person most responsible for Isomeric's operations, including, but not limited to, manufacturing and quality operations, and has the authority to prevent, detect, and correct violations. Defendant Richardson has ultimate authority over regulatory activities and product safety. Defendant Richardson has the authority to approve capital expenditures and hire and fire employees. Defendant Richardson performs his duties at Isomeric, within the jurisdiction of this Court.

7. Rachael S. Cruz is Isomeric's Chief Sales Officer and co-owner (through the "Rachael Cruz Utah 101 Trust"). Defendant Cruz shares the authority to prevent, detect, and correct violations, and has the authority to halt production operations when problems arise. Defendant Cruz is also responsible for overseeing Isomeric's handling of customer complaints. Defendant Cruz performs her duties at Isomeric, within the jurisdiction of this Court.

8. Jeffery D. Brown is Isomeric's Chief Operating Officer. Defendant Brown shares the authority to prevent, detect, and correct violations; halt production operations when problems arise; and approve expenditures for capital improvements, and hire and fire employees. Defendant Brown assumed his role as Chief Operating Officer in July 2016. In 2015, Defendant Brown had worked as a consultant for a consulting firm hired by Isomeric. Brown worked with Isomeric during his time as a consultant and the company hired him as Vice President of Quality

Assurance in January 2016. Defendant Brown performs his duties at Isomeric, within the jurisdiction of this Court.

9. During their regular course of business, Defendants manufacture, process, pack, label, hold, and distribute articles of drug, within the meaning of 21 U.S.C. § 321(g)(1). Their drug products, by virtue of their labeling and/or route of administration, purport to be or are expected to be sterile. Sterile drugs include drugs that are required to be sterile under Federal or state law or drugs that, by nature of their intended use or method of administration, are expected to be sterile ("sterile drugs"). *See* 21 U.S.C. § 353b(d)(5). Defendants' sterile drugs include, for example, injectable hormones (containing testosterone), injectable corticosteroids, and ophthalmic drops.

10. The majority of Defendants' sterile injectable drug products are aseptically processed, which involves filling drug products, which have been rendered sterile by filtration or heat sterilization, into their final containers in a manner that maintains sterility.

11. Defendants' facility contains "cleanrooms" where the production of purportedly sterile drugs occurs. The cleanrooms contain "ISO 5" and "ISO 7" processing areas (referring to International Standards Organization classifications for clean rooms). ISO 5 processing areas are critical zones that, by designation, have the highest level of cleanliness within the facility. Defendants' ISO 5 areas purport to have sufficient protection from contamination during the aseptic processing of sterile drugs.

12. Since approximately March 2016, Isomeric ceased receiving patient-specific prescriptions and began filling orders for compounded drug products for "office use," often referred to as "office stock" (i.e., compounded drugs prepared and distributed not pursuant to a patient-specific prescription).

13. Defendants distribute most of their drugs directly to physicians throughout the United States, including to New York and Arizona. Isomeric obtained licenses (which were

pharmacy, wholesaler, manufacturer, and/or distributor licenses, depending on state regulations) from several states, including Alabama, New Jersey, Oregon, and West Virginia, where they shipped finished products, even when the out-of-state license had expired.

14. Defendants manufacture drugs at Isomeric using components that were shipped in interstate commerce, including components from California, Alabama, and Oklahoma.

Requirements of the Act

15. Under the Act, a "drug" includes any article that is "intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease" or that is "intended to affect the structure or any function of the body." 21 U.S.C. §§ 321(g)(1)(B), (g)(1)(C).

16. A drug is deemed to be adulterated "if it has been prepared, packed, or held under insanitary conditions whereby it may have been contaminated with filth, or whereby it may have been rendered injurious to health." 21 U.S.C. § 351(a)(2)(A).

17. The Act requires that drugs be manufactured in accordance with current good manufacturing practice ("CGMP"). 21 U.S.C. § 351(a)(2)(B); 21 C.F.R. § 210.1(b). A drug is deemed to be adulterated if the methods used in, or the facilities or controls used for, its manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with CGMP to assure that it meets the requirements of the Act as to safety and that it has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess, regardless of whether the drug is actually defective in some way. FDA has promulgated CGMP regulations for drugs at 21 C.F.R. Parts 210 and 211.

18. A drug is deemed to be misbranded unless its labeling bears "adequate directions for use." 21 U.S.C. § 352(f)(1).

19. The Act requires that drug manufacturers obtain FDA approval of a new drug application ("NDA"), an abbreviated new drug application ("ANDA"), or an investigational new

drug ("IND") exemption, with respect to any new drug they introduce into interstate commerce. 21 U.S.C. §§ 331(d), 355(a). A "new drug" includes any drug "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 drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof." 21 U.S.C. § 321(p)(1).

Exemptions in the Act for Compounded Drugs

20. Compounding generally refers to the practice in which a licensed pharmacist or physician (or, in the case of an "outsourcing facility," a person under the direct supervision of a licensed pharmacist) combines, mixes, or alters ingredients to create a drug. Compounded drugs generally are tailored to the needs of identified individual patients, although outsourcing facilities are not required to obtain prescriptions for identified individual patients.

21. Under the Act, 21 U.S.C. § 353a, compounded drugs may be exempt from three specified provisions of the Act: CGMP requirements (21 U.S.C. § 351(a)(2)(B)); "adequate directions for use" (21 U.S.C. § 352(f)(1)); and premarket approval of new drugs for humans (21 U.S.C. § 355), so long as the drugs comply with all of the conditions set forth in 21 U.S.C. § 353a. Among other things, section 353a requires that the drug product be "compounded for an identified individual patient based on the receipt of a valid prescription order or a notation, approved by the prescribing practitioner, on the prescription order that a compounded product is necessary for the identified patient." 21 U.S.C. § 353a(a). Moreover, the compounding must be by a licensed pharmacist or physician either "on the prescription order for such individual patient" or "in limited quantities before the receipt of a valid prescription order for such individual patient" and "based on a history of" the pharmacist or physician "receiving valid prescription orders for the compounding of the drug product." 21 U.S.C. § 353a(a)(1) & (2).

22. Under the Act, an "outsourcing facility" is a facility that engages in the compounding of sterile drugs, registers as an outsourcing facility pursuant to 21 U.S.C. § 353b(b) and complies with all of the requirements of 21 U.S.C. § 353b. *See* 21 U.S.C. § 353b(d)(4)(A). Unlike drugs produced by firms under 21 U.S.C. § 353a, outsourcing facilities are not required to obtain patient-specific prescriptions for their compounded drug products. 21 U.S.C. § 353b(d)(4)(C).

23. Under the Act, 21 U.S.C. § 353b, drug products compounded in a registered outsourcing facility can qualify for certain exemptions from the Act, including the requirements for "adequate directions for use" (21 U.S.C. § 352(f)(1)), and premarket approval of new drugs for humans (21 U.S.C. § 355), so long as the drugs compounded by the outsourcing facility are compounded in accordance with all of the conditions set forth in 21 U.S.C. § 353b. *See* 21 U.S.C. § 353b(a)(11).

24. Drug products compounded by outsourcing facilities are *not* exempt from the Act's CGMP requirements (21 U.S.C. § 351(a)(2)(B)).

25. Neither 21 U.S.C. § 353a nor 353b exempts compounded drugs from 21 U.S.C. § 351(a)(2)(A), which deems drugs to be adulterated if they are prepared, packed, or held under insanitary conditions whereby they may have been contaminated with filth or rendered injurious to health.

26. On July 14, 2015, Isomeric registered with FDA as an outsourcing facility and, thereafter, its operations were subject to the requirements of 21 U.S.C. § 353b. Isomeric continues to be subject to 21 U.S.C. § 353b, and most recently re-registered as an outsourcing facility on January 25, 2017. Isomeric's operations are also subject to the Act's adulteration provisions regarding CGMP (21 U.S.C. § 351(a)(2)(B)) in addition to insanitary conditions (21 U.S.C. § 351(a)(2)(A)).

FDA's 2017 Inspection

27. FDA conducted its most recent inspection at Isomeric between February 22 and March 24, 2017 ("2017 Inspection") as a follow-up to a previous violative inspection that culminated in FDA's issuance of a Warning Letter on December 12, 2016.

28. During the 2017 Inspection, FDA investigators documented that Defendants manufacture drug products under insanitary conditions whereby they may have become contaminated with filth or may have been rendered injurious to health, and in a manner that does not conform to CGMP. The FDA investigators' inspectional observations were listed in a Form FDA-483, List of Inspectional Observations ("FDA 483"), which was provided to the company at the conclusion of the inspection. The FDA investigators discussed each of the inspectional observations with the individual Defendants.

Adulteration Based on Insanitary Conditions

29. FDA investigators observed that Isomeric's own documentation revealed that the company repeatedly recovered several types of microorganisms in the air and on surfaces used for sterile processing, as well as on personnel engaged in product manufacturing, demonstrating that products manufactured in those areas were prepared, packed, or held under insanitary conditions. On approximately 21 occasions in January 2017 alone, Isomeric's environmental and personnel monitoring in its ISO 5 areas detected microbes in excess of their "action limit" (i.e., a level of contamination high enough to trigger a response such as an investigation and corrective action). Several of the "microbial excursions" (microbial levels in excess of Isomeric's "action limit") occurred in the critical processing areas (inside the ISO 5 processing hoods) or on personnel in the immediate vicinity of the ISO 5 areas. The microbial contamination identified by Isomeric included, but was not limited to, bacteria (*Bacillus megaterium, Paenibacillus glucanolyticus, Paenibacillus turicensis,* and *Staphylococcus*

epidermidis) and fungus (*Chaetomium sp.*). If any of these organisms are present in an injectable product and administered to a patient, they are capable of causing serious adverse effects.

30. Defendants disregarded the potential adverse impact of the microbial contamination on patients. For example, on February 6, 2017, after detecting fungus (*Chaetomium sp.*) on surfaces in the ISO 5 area used for aseptically processing Triamcinolone Acetonide 40 milligrams per milliliter (40 mg/mL) Preservative-Free Injection (Lot 12004), Defendants released the product for distribution.

31. FDA investigators observed that Isomeric's documentation also revealed that the company repeatedly recovered non-viable particles (e.g., particulate contamination from non-microbial sources) during environmental monitoring of the ISO 5, ISO 7, and ISO 8 processing areas, demonstrating that products manufactured in those areas were prepared, packed, or held under insanitary conditions. Defendants released for distribution over 100 batches of purportedly sterile finished products that had been processed in one or more of the areas containing particulates in excess of its own "action limit" for particulates.

32. FDA investigators observed that, upon recovering and identifying the microbial and particulate contamination, Defendants failed to adequately investigate or take corrective action to alleviate the insanitary conditions that caused the presence of these microorganisms in the facility's aseptic processing areas. Despite their findings of contamination during personnel and environmental monitoring, Defendants continued to manufacture and distribute products expected to be sterile.

33. On April 6, 2017, Isomeric voluntarily recalled all lots of non-expired drug products expected to be sterile that it compounded and distributed nationwide between October 4, 2016 and February 7, 2017, because of FDA's concerns regarding a lack of sterility assurance.

34. FDA investigators observed and documented other evidence of insanitary conditions during the 2017 Inspection, including but not limited to the following:

a. Failure to conduct smoke studies in ISO 5 processing areas under dynamic (i.e., operational) conditions. Smoke studies must be conducted under dynamic conditions to assess the airflow patterns necessary to maintain unidirectional flow of sufficient velocity from areas of higher air quality (e.g., ISO 5) to areas of lower air quality (e.g., ISO 7) to prevent microbial contamination of sterile drug products during processing. Without adequate smoke studies, there is no assurance that the air quality in the aseptic processing areas is tightly controlled and continuously maintained, which, in turn, puts drug products being processed in those areas at risk of contamination; and

b. Detection of microbial growth, including spore-forming bacteria, in media fills. Media fill runs are process simulations that are conducted to demonstrate the effectiveness of a company's aseptic processes, to ensure that product will not be contaminated during actual sterile drug production. Bacteria in media fills indicate the presence of significant breaches in aseptic processing; these breaches raise concerns that other aseptically produced products are at a similar risk of becoming contaminated.

35. The insanitary conditions that FDA investigators observed at Isomeric's facility during FDA's 2017 Inspection establish that drugs manufactured and distributed by Defendants are adulterated within the meaning of 21 U.S.C. § 351(a)(2)(A), in that they are prepared, packed, or held under insanitary conditions whereby they may have been contaminated with filth or whereby they may have been rendered injurious to health.

36. Defendants violate 21 U.S.C. § 331(a) by introducing or delivering for introduction into interstate commerce articles of drug that are adulterated within the meaning of 21 U.S.C. § 351(a)(2)(A).

37. Defendants violate 21 U.S.C. § 331(k) by causing articles of drug to become adulterated within the meaning of 21 U.S.C. § 351(a)(2)(A), while such drugs are held for sale after shipment of one or more of their components in interstate commerce.

Adulteration Based on CGMP Violations

38. During the 2017 Inspection, FDA investigators documented significant deviations from CGMP requirements in Defendants' sterile drug manufacturing operations, including but not limited to the following:

a. Failure to establish and follow appropriate written procedures, including validation of all aseptic and sterilization processes, designed to prevent microbiological contamination of drug products purporting to be sterile (*see* 21 C.F.R. § 211.113(b)). As described above, Isomeric detected microbial and non-viable contamination at actionable levels in ISO 5 processing areas during environmental and personnel monitoring and also failed to conduct adequate smoke studies to ensure that aseptic operations do not contaminate sterile drug products during processing. In addition, the company changed the aseptic processing steps for Phenylephrine HCl/Tropicamide Ophthalmic Solution, but failed to perform media fills to demonstrate that the changes did not increase the risk of contamination during processing. Furthermore, Isomeric did not calibrate or qualify its in-house testing unit used to verify the integrity of the sterile filters used to sterilize drugs (to confirm that the filter has maintained its ability to sterilize throughout the filtration process), but nevertheless produced approximately 120 lots of drug products that relied on this testing unit for filter-integrity testing;

b. Failure to have written procedures for production and process control designed to ensure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess (*see* 21 C.F.R. § 211.100(a)). Isomeric has not validated the process for manufacturing injectable suspension drug products to demonstrate that proper controls are in place to ensure particle-size consistency for, among others, all Methylprednisolone Acetate and Triamcinolone products. Isomeric received customer complaints about product clumping and difficulties drawing up product into a syringe and, on several occasions, the company documented that it failed to achieve homogenization (consistent

particle-size range) during processing. Although the homogenization failures were linked to product clumping, Isomeric neither validated the homogenization process nor qualified the homogenizer units. Instead, the company continued to manufacture and distribute injectable suspension drug products. For example, on October 10, 2016, after concluding that the homogenization process was the root cause of clumping in Methylprednisolone Acetate/Lidocaine HCl 40/10 mg/ml (Lot 09007), Defendants simply reprocessed the product, which was released by Isomeric's quality assurance unit;

c. Failure to establish adequate control systems necessary to prevent contamination during aseptic processing, including but not limited to an air supply filtered through high-efficiency particulate air (HEPA) filters under positive pressure (*see* 21 C.F.R. § 211.42(c)(10)(iii)), and a system for cleaning and disinfecting the room and equipment to produce aseptic conditions (*see* 21 C.F.R. § 211.42(c)(10)(v)). Isomeric re-installed the grates protecting the HEPA filters in the ISO 5 area processing hoods after they were removed for cleaning, but did not re-certify the processing hoods to ensure the integrity of the HEPA filters after removal and re-installation. In addition, Defendants' employees placed the disinfectant fogging unit that cleans the ISO processing areas directly into the ISO areas from an unclassified (non-ISO) area without first cleaning the fogger or demonstrating that the unit itself is not a source of contamination;

d. Failure to ensure that automatic, mechanical, and electronic equipment used in the manufacture, processing, packing, or holding of a drug product is routinely calibrated, inspected, or checked to assure proper performance, and that written records of those calibration checks and inspections are maintained (*see* 21 C.F.R. § 211.68(a)). Since initial installation in or around January 2015, Defendants have failed to re-calibrate the electronic system used for monitoring non-viable particles, pressure differentials, humidity, and temperature in the ISO 5, 7, and 8 areas. When Defendants ultimately re-calibrated the non-

viable particle counters (i.e., only after FDA investigators pointed out the calibration deficiency during the 2017 Inspection), the firm found that the counters in two ISO 5 hoods were significantly out-of-tolerance, failing size calibration, size setting, and counting efficiency for certain particle sizes, and thus were highly unreliable;

e. Failure to have, for each batch of drug product, appropriate laboratory determination of satisfactory conformance to final specifications for the drug product, including the identity and strength of each active ingredient, prior to release (*see* 21 C.F.R. § 211.165(a)). Visible black particles were detected in vials of an injectable drug product that had "passed" visual inspection conducted by Defendants' employees. On February 22, 2017, a day after Isomeric's visual inspectors rejected only 18 vials of Triamcinolone Acetonide 40 mg/mL Preservative-Free Injection when conducing a 100% inspection of the vials to identify critical defects, including particulates, an Isomeric pharmacist observed black particles in 50-60 additional vials of the preservative-free injectable drug;

f. Failure to thoroughly review and investigate unexplained discrepancies and the failure of a batch or any of its components to meet any of its specification, whether or not the batch has already been distributed (*see* 21 C.F.R. § 211.192). Defendants failed to conduct adequate investigations of the following: black particles observed in vials of product that had "passed" visual inspection; microbial and particulate contamination found in ISO 5 processing areas (on surfaces, in the air, and on personnel); spore-forming bacteria detected in media fills; gross particulate contamination observed during visual inspection (over 50% of a batch was rejected and the remaining vials were released for distribution); and out-of-specification results for commercial and stability batches used to support commercial expiry dates. In addition, after receiving customer complaints about brittling and coring of stoppers (causing rubber fragments to fall into the drug solution after multiple uses) used for Testosterone Cypionate/Testosterone Propionate 200/20 mg/mL Injection, Defendants decided to change the sterilization method for

future batches; however, they did not address product that was within expiration date and still on the market, by investigating the impact of stopper brittling and coring on the lots distributed to customers;

g. Failure to follow written procedures for handling written and oral complaints regarding a drug product (*see* 21 C.F.R. § 198)). Isomeric received serious complaints describing infection, pain, swelling, or knotting at the injection site, but did not conduct adequate investigations to evaluate how the underlying cause(s) may apply to products previously produced, and Defendants' quality control unit continued to approve batches for distribution. Defendants also failed to adequately investigate other customer complaints, including those mentioned above, i.e.: clumping and inability to draw the drug product up in a syringe; black particles or fragments in an injectable drug product; and coring of stoppers used in containers for an injectable drug product;

h. Failure to have adequate training for each person engaged in aseptic processing (*see* 21 C.F.R. § 211.25(a)). For example, Defendants did not adequately train and qualify their employees conducting visual inspections of finished sterile injectable drug products for critical defects, including particulates; and

i. Failure to have an adequate quality control unit with the responsibility and authority to approve or reject all components, drug product containers, closures, in-process materials, packaging materials, labeling, and drug products, and the authority to review production records to assure that errors have not occurred or, if errors have occurred, that they have been fully investigated (*see* 21 C.F.R. § 211.22(a)). As described above, Defendants' quality control unit failed to ensure that adequate investigations were conducted and customer complaints were properly handled. Defendants continued to distribute a suspension drug product (Methylprednisolone Acetate) despite ongoing problems with particle-size homogenization and customer complaints about product clumping. Although Isomeric has had similar problems in

the past, and conducted a recall of Betamethasone Acetate/Betamethasone Sodium Phosphate 7 mg/mL in July 2016 because of this issue, Defendants continued to produce a suspension product without first demonstrating that they have successfully validated the production process. In addition, Defendants' quality control unit released a batch of Triamcinolone Acetonide 40 mg/mL Preservative-Free Injection (Lot 11031), even though the aseptic processing time exceeded its established limit. To justify releasing the product, Defendants' quality assurance personnel relied on a subsequently conducted media fill that purported to validate the excessive hold time of the product (Lot 11031).

39. These observations establish that Defendants' drugs are adulterated within the meaning of 21 U.S.C. § 351(a)(2)(B), in that the methods used in, or the facilities or controls used for, their manufacturing, processing, packing, or holding do not comply with CGMP to assure that they meet the requirements of the Act as to their safety and that they have the identity and strength, and meet the quality and purity characteristics, which they purport or are represented to possess.

40. Defendants violate 21 U.S.C. § 331(a) by introducing or delivering for introduction into interstate commerce articles of drug that are adulterated within the meaning of 21 U.S.C. § 351(a)(2)(B).

41. Defendants violate 21 U.S.C. § 331(k) by causing articles of drug to become adulterated within the meaning of 21 U.S.C. § 351(a)(2)(B), while such drugs are held for sale after shipment of one or more of their components in interstate commerce.

Unapproved New Drugs

42. Defendants' products, including Testosterone Cypionate/Testosterone Propionate Injection and Testosterone Cypionate/Testosterone Propionate/Vitamin D_3 Injection (collectively, "Testosterone products"), are drugs within the meaning of the Act because they are

intended "for use in the diagnosis, cure, mitigation, treatment, or prevention of disease" or "to affect the structure or any function of the body" in humans. 21 U.S.C. § 321(g)(1)(B).

43. Defendants' Testosterone products are not generally recognized as safe and effective because there are no published adequate and well-controlled clinical studies of those drugs upon which qualified experts could conclude that the drugs are safe and effective. Therefore, Defendants' Testosterone products are new drugs within the meaning of 21 U.S.C. § 321(p).

44. Defendants' Testosterone products lack an approved NDA or ANDA, as required by 21 U.S.C. § 355, and are not exempt from approval as an investigational new drug under 21 U.S.C. § 355(i).

45. At the time of FDA's 2017 Inspection, Isomeric was registered with FDA under the outsourcing facility exception of 21 U.S.C. § 353b(d)(4)(A). For a drug product compounded in a registered outsourcing facility to qualify for certain exemptions from the Act, including the requirements for premarket approval of new drugs for humans (21 U.S.C. § 355), and "adequate directions for use" (21 U.S.C. § 352(f)(1)), the drug needs to meet all of the statutory elements of 21 U.S.C. § 353b. *See* 21 U.S.C. §§ 353b(a)(11), 353b(d)(4)(A). One of the conditions that must be met for a drug compounded by an outsourcing facility to qualify for those exemptions is that the drug is compounded in an outsourcing facility that does not compound using bulk drug substances unless (a) the bulk drug substance appears on a list established by FDA identifying bulk drug substances for which there is a clinical need ("bulks list"), or (b) the drug compounded from such bulk drug substance appears on the drug shortage list in effect under 21 U.S.C. § 356e at the time of compounding, distribution, and dispensing. *See* 21 U.S.C. §§ 353b(a), 353b(a)(2)(A). The bulks list is currently in development but is not yet established.

46. Testosterone cypionate, a bulk drug substance used in compounding Defendants' Testosterone products, does not appear on the bulks list, as such list does not yet exist, and is not used to compound a drug that appears on FDA's drug shortage list. Therefore, Defendants' Testosterone products are not eligible for the exemptions in 21 U.S.C. § 353b. Additionally, because testosterone cypionate was not nominated for inclusion on the bulks list with sufficient supporting information for FDA to evaluate it, Defendants' Testosterone products are subject to immediate enforcement. *See FDA's Guidance for Industry: Interim Policy on Compounding Using Bulk Drug Substances Under Section 503B of the Federal Food, Drug, and Cosmetic Act* (January 2017), *available at* https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM469122.pdf.

47. Because Defendants' Testosterone products fail to meet at least one of the criteria for qualifying for the exception, they are not exempt from the drug approval requirements. *See* 21 U.S.C. §§ 353b(a), 353b(a)(2). Defendants' Testosterone products are unapproved new drugs, for the reasons described above.

48. Defendants' distribution into interstate commerce of unapproved new drugs violates 21 U.S.C. § 331(d).

Misbranding Based on Lack of Adequate Directions for Use

49. Because of their toxicity or other potentiality for harmful effect, or the method of their use, or the collateral measures necessary to their use, Defendants' Testosterone products are not safe for use except under the supervision of a practitioner licensed by law to administer such drugs. As such, Defendants' Testosterone products are "prescription drugs" within the meaning of 21 U.S.C. § 353(b)(1)(A).

50. "Adequate directions for use" means directions under which a layperson could use a drug safely and effectively for the purposes for which the drug is intended. 21 C.F.R.

§ 201.5. A prescription drug, by definition, cannot bear adequate directions for use by a layperson because such drug must be administered under the supervision of a licensed practitioner. *See* 21 U.S.C. § 353(b)(1). FDA has established exemptions for certain drug products from the requirements that labeling bear adequate directions for use (apart from the exemptions for certain compounded drugs, as discussed in paragraph 45), but Defendants' Testosterone products do not satisfy the conditions for any of these exemptions. *See* 21 C.F.R. §§ 201.115, 201.100.

51. Because Isomeric is registered with FDA as an outsourcing facility, it is required to comply with all of the statutory elements of 21 U.S.C. § 353b to be eligible for the exemption in that provision from the requirement for adequate directions for use (21 U.S.C. § 352(f)(1)). *See* 21 U.S.C. §§ 353b(a)(11), 353b(d)(4)(A). As described above (in paragraphs 45-46), Defendants' Testosterone products are compounded in violation of the requirements of 21 U.S.C. § 353b because testosterone cypionate, a bulk drug substance in Defendants' Testosterone products, does not appear on a bulks list and is not used to compound a drug that appears on FDA's drug shortage list. *See* 21 U.S.C. § 353b(a)(2)(A). Therefore, Defendants' Testosterone products are not eligible for the exemption in 21 U.S.C. § 353b from the requirement for adequate directions for use. Because Defendants' Testosterone products lack adequate directions for use, they are misbranded under 21 U.S.C. § 352(f)(1).

52. Defendants violate 21 U.S.C. § 331(a) by introducing and causing to be introduced, and delivering and causing to be delivered for introduction, into interstate commerce, articles of drug that are misbranded within the meaning of 21 U.S.C. § 352(f)(1), in that their labeling fails to bear adequate directions for use.

53. Defendants violate 21 U.S.C. § 331(k) by causing articles of drug to become misbranded within the meaning of 21 U.S.C. § 352(f)(1), while such drugs are held for sale after shipment of one or more of their components in interstate commerce.

Prior Inspections and Warnings to Defendants

54. FDA previously inspected Isomeric between July 20-29, 2016 (the "2016 Inspection") and observed similar insanitary conditions and CGMP deficiencies. Defendants' insanitary conditions included, but were not limited to: burnt, brown, carbon-like staining on the interior surface of glassware that would come in contact with drug products during sterilization; white stains on the metal grates covering the HEPA filters in two of the ISO 5 hoods; and a failure to demonstrate through appropriate air flow studies (smoke studies) that the hoods provide adequate protection in the ISO 5 areas to protect products against contamination during sterile processing. In a Warning Letter dated December 12, 2016, issued to Defendant Richardson as a result of the 2016 Inspection, FDA put Defendants on notice that their products "may be produced in an environment that poses a significant contamination risk." (December 12, 2016 Warning Letter to Defendant Richardson available at https://www.fda.gov/iceci/enforcementactions/warningletters/2016/ucm534129.htm.**)**

55. During the 2016 Inspection, FDA investigators also observed serious deviations from CGMP requirements, many of which were subsequently observed during the 2017 Inspection, including but not limited to: failure to establish and follow appropriate written procedures, including validation of all aseptic and sterilization processes, designed to prevent microbiological contamination of drug products expected to be sterile (as exemplified by recurring environmental monitoring excursions; lack of adequate smoke studies; failure to adequately validate the sterilization cycles of equipment used for sterilizing product glassware and utensils and equipment used in processing); failure to establish adequate written procedures for production and process controls designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess, and to record and justify deviations from the written procedures; failure to clean, sanitize, and sterilize equipment and utensils at appropriate intervals to prevent contamination that would alter the safety, identity,

strength, quality, or purity of the drug; and failure to thoroughly review and investigate unexplained discrepancies and the failure of a batch or any of its components to meet any of its specification, whether or not the batch has already been distributed.

56. At the close of the 2016 Inspection, the FDA investigators provided an FDA 483 to Defendants and discussed the inspectional observations with them. Many similar inspectional observations were also included in the December 12, 2016, Warning Letter issued to Defendant Richardson.

57. The Warning Letter also contained a detailed explanation of the deficiencies in the corrective actions proposed by Isomeric.

58. On August 1, 2016, Defendants conducted a voluntary recall of Betamethasone Acetate/Betamethasone Sodium Phosphate Injectable Suspension because of problems with product clumping. Although Defendants were not manufacturing this product at the time of the 2017 Inspection, the same issues persisted in other products that were on the market at that time.

59. Isomeric has responded in writing to the inspectional observations and Warning Letter. These written responses contain repeated promises to take corrective actions.

60. Despite promises to correct their deficiencies, Defendants' violations persisted, as evidenced by the violations observed during FDA's 2017 Inspection.

61. Based on the foregoing, Plaintiff believes that, unless restrained by the Court, Defendants will continue to violate the Act in the manner set forth above.

WHEREFORE, Plaintiff respectfully requests that this Court:

I. Order that Defendants and each and all of their directors, officers, agents, representatives, employees, attorneys, successors, and assigns, and any and all persons in active concert or participation with any of them, cease manufacturing, processing, packing, labeling, holding, or distributing any article of drug unless and until Defendants bring their manufacturing,

processing, packing, labeling, holding, and distribution operations into compliance with the Act and its implementing regulations to the satisfaction of FDA;

II. Order that Defendants and each and all of their directors, officers, agents, representatives, employees, attorneys, successors, and assigns, and any and all persons in active concert or participation with any of them, are permanently restrained and enjoined under 21 U.S.C. § 332(a) from directly or indirectly doing or causing the following acts:

A. Violating 21 U.S.C. § 331(a) by introducing and/or causing to be introduced, and/or delivering or causing to be delivered for introduction, into interstate commerce, any drug that is adulterated within the meaning of 21 U.S.C. §§ 351(a)(2)(A) and/or 351(a)(2)(B), and/or misbranded within the meaning of 21 U.S.C. § 352(f)(1);

B. Violating 21 U.S.C. § 331(k) by causing any drug to become adulterated within the meaning of 21 U.S.C. §§ 351(a)(2)(A) and/or 351(a)(2)(B), and/or misbranded within the meaning of 21 U.S.C. § 352(f)(1), while such drug is held for sale after shipment of one or more of its components in interstate commerce; and

C. Violating 21 U.S.C. § 331(d) by introducing and/or causing the introduction into interstate commerce, and/or delivering and/or causing the delivery for introduction into interstate commerce, of any new drug that is neither approved under 21 U.S.C. § 355, nor exempt from approval;

III. Order that FDA be authorized pursuant to this injunction to inspect Defendants' places of business and all records relating to the receipt, manufacture, processing, packing, labeling, holding, and distribution of any drug to ensure continuing compliance with the terms of the injunction, with the costs of such inspections, including testing and sampling, to be borne by Defendants at the rates prevailing at the time the inspections are accomplished; and

IV. Award Plaintiff costs and other such relief as the Court deems just and proper.

/ / /

DATED this 27th day of July, 2017.

Respectfully submitted,

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District of Utah

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CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on July 27, 2017 I caused to be served a true and correct copy of the foregoing Complaint by email to:

rpontikes@reedsmith.com
ctgrohman@duanemorris.com

/s/ Raquel Toledo
Raquel Toledo
Trial Attorney
Consumer Protection Branch
U.S. Department of Justice