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UNITED STATES OF AMERICA

UNITED STATES DISTRICT COURT

FOR THE CENTRAL DISTRICT OF CALIFORNIA

WESTERN DIVISION

UNITED STATES OF AMERICA, Plaintiff, v. MED-PHARMEX, INC., a corporation, GERALD P. MACEDO and VINAY M. RANGNEKAR, PH.D., individuals, Defendants.	Case No. 2:20-cv-09844 **COMPLAINT FOR PERMANENT INJUNCTION**

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

1. This action is brought by the United States of America under the Federal Food, Drug, and Cosmetic Act ("FDCA" or the "Act"), 21 U.S.C. § 332(a), to stop Med-Pharmex, Inc. ("MPX" or "the company"), a corporation, Gerald P. Macedo and Vinay M. Rangnekar, Ph.D., individuals (collectively, "Defendants"), from distributing potentially dangerous animal drugs. Specifically, the United States seeks to enjoin and restrain Defendants from: (a) violating 21 U.S.C. § 331(a), by introducing or causing the introduction or delivery for introduction into interstate commerce of animal drugs that are adulterated within the meaning of 21 U.S.C. § 351(a)(2)(B); and (b) violating 21 U.S.C. § 331(k), by causing animal drugs to become adulterated within the meaning of 21 U.S.C. § 351(a)(2)(B) while such animal drugs are held for sale after shipment of one or more of their components in interstate commerce.

JURISDICTION AND VENUE

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

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

DEFENDANTS

4. Defendant Med-Pharmex, Inc., a California corporation, is a contract manufacturer and own-label distributor of sterile and non-sterile animal drugs, including sterile injectable pharmaceuticals and non-sterile ointments, oral solutions, suspensions, and powders, at and from its manufacturing facility at 2727 Thompson Creek Road, Pomona, California 91767, within the jurisdiction of this Court.

5. According to MPX's corporate filings with the California Secretary of State, Defendant Gerald P. Macedo is the company's Chief Executive Officer and one of the company's two Directors.[1] He is also MPX's President and owns 50% of the company. He is the most responsible person at the company, and his duties include

[1] *See* MPX's Statement of Information (Apr. 28, 2013) (listing Macedo as CEO and a Director); MPX's Statement of Information No Change (Jul. 31, 2020) ("There has been no change in any of the information contained in the previous complete Statement of Information filed with the California Secretary of State.").

oversight of all operations, research and development, accounting, personnel, facility improvements, and capital expenditures. He has the ultimate authority for initiating product recalls. He has the responsibility, duty, power, and authority to prevent, detect, and correct any violations of the FDCA. Macedo performs his duties at and from the manufacturing facility at 2727 Thompson Creek Road, Pomona, California 91767, within the jurisdiction of this Court.

6. According to MPX's corporate filings with the California Secretary of State, Defendant Vinay M. Rangnekar, Ph.D. is one of the company's two Directors.[2] He is also the company's Vice President of Quality Control. He is responsible for MPX's quality control laboratories and reports directly to Macedo. Rangnekar is responsible for writing standard operating procedures, validation protocols (chemistry methods, process, and cleaning), equipment qualification protocols, and method validation review. He has the authority to approve data generated by MPX's chemistry and microbiology laboratories, and to make expenditures to support facilities and quality operations. Rangnekar performs his duties at and from the manufacturing facility at 2727 Thompson Creek Road, Pomona, California 91767, within the jurisdiction of this Court.

7. Defendants receive at least 95 percent of the components used to manufacture their finished products from outside of California, including from New Jersey. Defendants distribute approximately 92 percent of their finished products outside of California.

REGULATORY FRAMEWORK

8. MPX's products are animal drugs within the meaning of 21 U.S.C. § 321(g)(1)(B) and (C) because they are "intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals" or are "intended to affect the structure or any function of the body of man or other animals." 21 U.S.C.

[2] *See* MPX's Statement of Information and Statement of Information No Change, *supra* note 1.

§ 321(g)(1)(B), (C). For example, MPX manufactures an injection to reduce the symptoms of diarrhea in pigs, cattle and horses and, among other animal drugs, drops to treat ear infections in dogs.

9. An animal drug is adulterated under the FDCA as a matter of law 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 current good manufacturing practice to assure that such drug meets the requirements of [the FDCA] as to safety and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess[.]" 21 U.S.C. § 351(a)(2)(B).

10. FDA has promulgated regulations establishing current good manufacturing practice ("cGMP") requirements applicable to drugs. *See* 21 C.F.R. Part 211. The cGMP regulations contained in 21 C.F.R. Part 211 apply to both animal and human drug products. *See* 21 C.F.R. § 211.1(a) (Sept. 29, 1978) (defining scope of regulations). The drug cGMP regulations establish requirements for the manufacture of drugs and include sections related to personnel, building and facilities, equipment, control of components and drug product containers and closures, production and process controls, packaging and labeling control, holding and distribution, laboratory controls, records and reports, and returned and salvaged drug products. *See generally* 21 C.F.R. Part 211.

11. The introduction or delivery for introduction, or causing the introduction or delivery for introduction, into interstate commerce of any animal drug that is adulterated violates the FDCA, 21 U.S.C. § 331(a).

12. Causing animal drugs 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 violates the FDCA, 21 U.S.C. § 331(k).

DEFENDANTS' VIOLATIONS OF THE FDCA

13. FDA investigators observed significant violations of cGMP, 21 C.F.R. Part 211, during the most recent inspection of MPX's facility between May 1 and 17, 2019 ("2019 Inspection"). These drug cGMP violations include, but are not limited to, the following:

a. Failure of the quality control unit to investigate complaints, as required by 21 C.F.R. § 211.198(a) (Sept. 29, 1978). Specifically, Defendants failed to adequately investigate complaints associated with adverse events related to their products, including animal deaths. Examples include, but are not limited to: (1) a customer identified 30 baby pigs that became ill after they were injected with MPX-manufactured Iron Dextran, but Defendants failed to investigate their manufacturing operations (including facilities and production and personnel records) to identify the root cause of the adverse event or to develop appropriate corrective action; (2) a horse died after receiving MPX-manufactured Ivermectin Paste, but Defendants did not collect the lot number or perform any investigation; and (3) MPX received a complaint that one of its Ivermectin Paste syringe bodies lacked incremental dosage markings, but Defendants failed to contact the syringe supplier, to describe the event or retain a sample for inspection, to perform a manufacturing or material investigation, or review their processes for receipt and inspection of syringe bodies. The lack of such markings could result in incorrect dosing.

b. Failure to clean and disinfect aseptic processing areas (i.e., where sterile animal drug products are manufactured) and equipment to produce aseptic conditions, as required by 21 C.F.R. § 211.42(c)(10)(v) (Sept. 29, 1978). Specifically, the company applied sporicidal agents only to the floor of their

aseptic processing area, but not to the walls, ceiling, and laminar flow hood.[3] Moreover, additional components in the sterile production area were also not cleaned, including power and data cables and the production belt. FDA investigators observed approximately six black particles on the filling head (the nozzle for filling drug vials) adjacent to the cables during processing of an aseptic product.

c. Failure to investigate unexplained discrepancies to identify a root cause of particulate matter events reported during aseptic filling of sterile drug product, as required by 21 C.F.R. § 211.192 (Sept. 29, 1978). Specifically, during the manufacture of several lots of its purportedly sterile animal drug Iron Dextran in April 2018, MPX reported the presence of particulate matter during aseptic filling. An investigation identified multiple particulate matter events reported by the company's personnel during aseptic filling that had an impact on lots processed afterwards, but the investigation lacked a root cause analysis. Simply put, the cause of those particles was not explored, identified, or addressed. Nonetheless, MPX distributed all affected lots.

d. Failure to perform adequate unidirectional airflow studies (also known as "smoke studies") under dynamic conditions to determine the movement of air and personnel during aseptic manufacturing operations, as required by 21 CFR § 211.113(b) (Sept. 29, 1978). Aseptic drug manufacturers must conduct smoke studies to assess the airflow patterns necessary to maintain air flow in one direction from areas of higher air quality to areas of lower air quality to prevent microbial contamination of sterile drug products during aseptic processing. Smoke studies must be conducted under "dynamic conditions," meaning that the aseptic processing area must contain all of the equipment and supplies, as well as

[3] Laminar flow hoods are ventilation devices used within the lab to provide an aseptic work area that helps protect both the laboratory personnel and the materials they are working with.

the maximum number of personnel allowed in the cleanroom, during simulations of all aseptic operations and manipulations. The presence of humans or equipment/supplies in an area that blocks the movement of air around an open container, whether before or after it is filled with sterile product, can create risk to product sterility. If unidirectional air over a critical surface is blocked, for example, by personnel, then contaminants on the personnel, particularly on exposed skin, could contaminate the drug products. Specifically, MPX failed to conduct adequate smoke studies under dynamic conditions, such as during the loading, unloading, and equipment opening used in their aseptic processing to reduce risks to product sterility.

e. Failure to maintain buildings used in the manufacturing, processing, and packing of a drug product in a good state of repair, as required by 21 CFR § 211.58 (Sept. 29, 1978). Specifically, a brown rust-like discoloration was observed on screws in the high-efficiency particulate air ("HEPA") filter framework in the ceiling directly above the sterile production line (vial turntable and the stopper hopper area) in the room used to fill sterile injectable drugs. Additionally, the HEPA filter housing in the ceiling directly above the production line appeared to have an empty screw hole.

f. Failure to establish laboratory controls that include the establishment of scientifically sound and appropriate sampling plans and test procedures designed to assure that components, drug product containers, closures, in-process materials, labeling, and drug products conform to appropriate standards of identity, strength, quality, and purity, as required by 21 C.F.R. § 211.160(b) (Sept. 29, 1978). Specifically, six out of seven of MPX's Rodac plates that measure bacteria living on the surface of a person's hands (also known as "bioburden") collected from the company's operators during aseptic production of its purportedly sterile injectable animal drug product Iron Dextran appeared not to have been contacted by the operators. The failure to contact the Rodac

plates means that MPX had an incomplete understanding of factors that may contribute to the bioburden of sterile injectable products. In addition, MPX's method of using vacuum filtration to inspect vials for particulate matter has not been evaluated to demonstrate it is capable of adequately detecting particulate matter. Moreover, MPX does not document the decontamination and sanitization of sterility samples and sterility sample totes that are transferred into the sterility testing room.

g. Failure to assure that the examination and testing of drug product samples and in-process material conformed to the drug product's specifications, as required by 21 C.F.R. § 211.110(b) (Sept. 29, 1978). Specifically, MPX's inspector qualification kits did not contain accurate simulations of defects in the product, including, among other things, simulated cosmetic or seal defects, and contaminants most likely to be found in a filled vial (e.g., construction material from the primary packaging components, such as rubber stoppers, glass vials, packaging fibers, and dried residual product).

h. Failure to have appropriate controls over computers or related systems to assure that changes in master production and control records or other records are instituted only by authorized personnel, as required by 21 C.F.R. § 211.68(b) (Sept. 29, 1978). Specifically, MPX had eight user accounts with "System Administrator" and "Permit User Administration" access; five of the accounts with "Enabled" status could access the highest level of system functions and security settings, but MPX did not have guidelines to establish authorization for system administrator access, security rights, and access controls.

14. At the close of the 2019 Inspection, the FDA investigators discussed their inspectional observations with Macedo and Rangnekar.

15. At the close of the 2019 Inspection, FDA investigators issued Macedo a detailed List of Inspectional Observations ("Form FDA-483").

16. On June 10, 2019, Defendants submitted a written response to FDA setting forth their purported strategy for addressing the issues raised in the Form FDA-483; Defendants updated this response in writing on January 10, 2020 and during an in-person meeting with FDA on March 3, 2020.[4] Defendants' written and in-person responses did not establish that Defendants have come into full compliance with the FDCA. For example, although Defendants asserted that they had conducted assessments, investigations and studies relating to some of the issues raised in the Form FDA-483, Defendants provided no evidence from such assessments, investigations, and studies.[5]

17. An animal drug is adulterated under the Act, 21 U.S.C. § 351(a)(2)(B), as a matter of law, 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 drug cGMP requirements.

18. Defendants violate the FDCA, 21 U.S.C. § 331(a), by introducing or delivering for introduction, or causing the introduction or delivery for introduction, into interstate commerce articles of animal drugs, as defined by 21 U.S.C. § 321(g)(1), that are adulterated within the meaning of 21 U.S.C. § 351(a)(2)(B).

19. Defendants violate the FDCA, 21 U.S.C. § 331(k), by causing animal drugs 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.

PRIOR WARNINGS

20. Defendants have a history of failing to comply with the FDCA and the drug cGMP regulations. Many of the drug cGMP deficiencies present at the 2019 Inspection are the same as, or similar to, prior violations observed by FDA during

[4] Macedo and Rangnekar attended the March 2020 meeting.

[5] *See, e.g.*, Med-Pharmex, Inc.'s FDA 483 Response Action Matrix (Jan. 2020) at 2, 4, 5, 7, 11, 12.

inspections conducted between December 4, 2017, and January 11, 2018 ("2018 Inspection"); January 17, 2017, and February 1, 2017 ("2017 Inspection"); and between February 8 and 17, 2016 ("2016 Inspection").

21. Defendants' failure to comply with the drug cGMP regulations has continued in the face of repeated warnings from FDA. At the close of each inspection, FDA investigators issued Macedo and/or Rangnekar a Form FDA-483. The FDA investigators discussed the violations listed in the Forms FDA-483 with MPX's management, including Macedo and Rangnekar.

22. At the close of the 2018 Inspection, FDA investigators issued Macedo a Form FDA-483 that identified many of the same violations observed during the 2019 Inspection. Several of the violations observed by FDA investigators during the 2019 Inspection were repeated violations from the 2018 Inspection, including: failing to investigate complaints; failing to investigate unexplained discrepancies to identify a root cause of particulate matter events reported during aseptic filling of sterile drug product; failing to perform adequate smoke studies under dynamic conditions; failing to maintain buildings used in the manufacturing, processing, and packing of a drug product in a good state of repair; failing to establish laboratory controls that include the establishment of scientifically sound and appropriate sampling plans and test procedures; failing to assure that the examination and testing of drug product samples and in-process material conformed to the specifications; and failing to have appropriate controls over computers or related systems to assure that changes in master production and control records or other records are instituted only by authorized personnel.

23. At the close of the 2017 Inspection, FDA investigators issued Rangnekar a Form FDA-483 that addressed several of the same violations observed during the 2019 Inspection, including: failing to clean and disinfect aseptic processing areas; failing to conduct smoke studies under dynamic conditions; and failing to have appropriate controls over computers or related systems.

24. Due to the significant cGMP violations observed during the 2017 Inspection, FDA issued a Warning Letter to Defendants on May 17, 2017.[6] Following the issuance of the Warning Letter, FDA held a meeting with Macedo and Rangnekar on July 27, 2017, to discuss Defendants' failure to correct their violations.

25. At the close of the 2016 Inspection, FDA investigators issued Rangnekar a Form FDA-483 that addressed several of the same violations observed during the 2019 Inspection, including: failing to investigate unexplained discrepancies and failing to establish the specifications of non-viable particulates in its aseptic processing area.

26. Plaintiff is informed and believes that, unless restrained by the Court, Defendants will continue to violate the FDCA in the manner set forth herein.

WHEREFORE, Plaintiff respectfully requests that the 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 (including individuals, directors, corporations, subsidiaries, affiliates, and partnerships), cease manufacturing, processing, packing, holding, or distributing articles of drug, at or from the MPX facility or at any other current or future location, unless and until Defendants' methods, facilities, and controls used to manufacture, process, pack, hold, and distribute articles of drugs are established, operated, and administered in conformity with the FDCA and the applicable drug cGMP regulations, in a manner that has been found acceptable to FDA;

II. Permanently restrain and enjoin, under 21 U.S.C. § 332(a), 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 (including individuals, directors, corporations,

[6] Available at https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/med-pharmex-inc-522676-05172017 (last accessed Sept. 24, 2020).

subsidiaries, affiliates, and partnerships), from directly or indirectly violating 21 U.S.C. § 331(a), by introducing or causing the introduction or delivery for introduction into interstate commerce drugs that are adulterated within the meaning of 21 U.S.C. § 351(a)(2)(B);

III. Permanently restrain and enjoin, under 21 U.S.C. § 332(a), 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 (including individuals, directors, corporations, subsidiaries, affiliates, and partnerships), from directly or indirectly violating 21 U.S.C. § 331(k), by causing drugs 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; and

IV. Order that FDA be authorized pursuant to this injunction to inspect Defendants' place(s) of business and all records relating to the manufacturing, processing, packing, labeling, and distribution of drugs to ensure continuing compliance with the terms of the injunction, the costs of such inspections to be borne by Defendants at the rates prevailing at the time the inspections are accomplished.

DATED this 27 day of October, 2020.

Respectfully submitted,

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