IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF ARKANSAS
WESTERN DIVISION

| | | |
|---|---|---|
| UNITED STATES OF AMERICA, | ) | |
| Plaintiff, | ) | |
| v. | ) | Civil Action No. 4:18-cv-159 |
| CANTRELL DRUG COMPANY, a corporation, and JAMES L. McCARLEY, JR., an individual, | ) | |
| Defendants. | ) | |

**[PROPOSED] ORDER FOR PRELIMINARY INJUNCTION**

Plaintiff, the United States of America, by its undersigned attorneys, having filed a Complaint for Injunction against Cantrell Drug Company ("Cantrell"), a corporation, and James L. McCarley, Jr., an individual, (collectively, "Defendants"), a motion for preliminary injunction with supporting memorandum of law, and the declarations of (1) Brooke K. Higgins, Compliance Officer and Senior Policy Advisor, Center for Drug Evaluation and Research, United States Food and Drug Administration ("FDA"); (2) Latorie S. Jones, Investigator, Office of Pharmaceutical Quality Operations ("OPQO"), Division 2, FDA; (3) Lisa R. Whitt, Investigator, OPQO, Division 2, FDA; (4) Shelby N. Marler, Investigator, OPQO, Division 2, FDA; and (4) Monica R. Maxwell, Program Division Director, OPQO, Division 2, FDA, in support thereof, and this Court having considered such arguments and supporting evidence filed by Defendants, and it appearing that Defendants are violating the Federal Food, Drug, and

Cosmetic Act (the "Act"), 21 U.S.C. §§ 301 *et seq.*, and, unless restrained by order of this Court, will continue to violate the Act:

IT IS HEREBY ORDERED, ADJUDGED, AND DECREED as follows:

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

2. The Complaint for Injunction states a cause of action against Defendants under the Act.

3. The United States has a substantial likelihood of success on the merits of its claims that Defendants:

A. Violate the Act, 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), in that the drugs have been 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;

B. Violate the Act, 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)(B), in that the methods used in, or the facilities or controls used for, their manufacture, processing, packing, labeling, holding, and/or distributing do not conform to, or are not operated or administered in conformity with, current good manufacturing practice to assure that such drugs meet the requirements of the Act as to safety and have the identity and strength, and meet the quality and purity characteristics, which they purport or are represented to possess; and

C. Violate the Act, 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), while the drugs are held for sale after shipment of one or more of their components in interstate commerce.

4. For the purposes of this Order, the following definitions shall apply:

A. "Bulk drug substance" shall mean 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;

B. "CGMP" shall refer to the current good manufacturing practice requirements for drugs within the meaning of 21 U.S.C. § 351(a)(2)(B) and 21 C.F.R. Parts 210 and 211. In determining whether Defendants are compounding drugs at an outsourcing facility in compliance with CGMP, Defendants, their expert consultants, and FDA may consider any regulations and/or guidance that FDA has issued with respect to CGMP for outsourcing facilities;

C. "Compound" and "compounding" shall include the combining, admixing, mixing, diluting, pooling, reconstituting, or otherwise altering of a drug or bulk drug substances to create a drug;

D. The terms "manufacture," "manufactured," and "manufacturing" shall include manufacturing, compounding, processing, packing, repacking, labeling, and holding drugs;

E. "Distribution" and "distributing" shall mean to sell, trade, ship, or deliver and shall include, but not be limited to, delivery or shipment to a healthcare setting for administration and dispensing to a patient or to an agent of a patient;

F. "Drug" shall have the meaning given the term in 21 U.S.C. § 321(g)(1);

G. "Drug product" shall mean a finished dosage form (for example, tablet, capsule, or solution) that contains a drug substance, generally, but not necessarily, in association with one or more other ingredients;

H. "Sterile drug" shall have the meaning as set out in 21 U.S.C. § 353b(d)(5);

I. "Days" shall refer to calendar days unless otherwise stated;

J. "FDA" shall mean the United States Food and Drug Administration; and

K. "Defendants' facility" shall refer to the facility located at 7321 Cantrell Road, Little Rock, Arkansas, 72207, and any other location(s) (including any new locations) at or from which, at any time in the future, any Defendant, directly or indirectly, manufactures, processes, packs, labels, holds, and/or distributes drugs, whether or not any Defendant has an ownership interest in the business.

5. On December 16, 2013, Defendants' facility located at 7321 Cantrell Road, Little Rock, Arkansas, 72207, was registered with FDA as an outsourcing facility pursuant to 21 U.S.C. § 353b. Cantrell re-registered as an outsourcing facility pursuant to 21 U.S.C. § 353b most recently on October 12, 2016.

6. Upon entry of this Order, Defendants and each and all of their directors, officers, agents, employees, representatives, successors, assigns, attorneys, and any and all persons in active concert or participation with any of them (including trusts, parent companies, holding companies, subsidiaries, affiliates, franchisees, "doing business as" entities, "consultants," "independent contractors," "independent business owners," and any other persons engaged in any part of the manufacture, processing, packing, labeling, holding, and/or distribution of

Defendants' drugs) who have received actual notice of this Order by personal service or otherwise, are preliminarily restrained and enjoined, under 21 U.S.C. § 332(a) and the inherent equitable authority of this Court, from directly or indirectly manufacturing, processing, packing, labeling, holding, and/or distributing any drugs manufactured at and/or from Defendants' facility, unless and until:

A. Defendants ensure that the facilities, methods, and controls used to manufacture, process, pack, label, hold, and/or distribute drugs are established, operated, and administered in conformity with this Order, the Act, and its implementing regulations, and are adequate to prevent Defendants' drugs from becoming adulterated within the meaning of 21 U.S.C. § 351(a)(2)(A) and 351(a)(2)(B);

B. Defendants ensure that each and every drug that Defendants intend to manufacture, process, pack, label, hold, and/or distribute at or from their facility satisfies all of the provisions of 21 U.S.C. § 353b, including but not limited to:

(1) Drug labeling at 21 U.S.C. § 353b(a)(10);

(2) Facility registration at 21 U.S.C. § 353b(b)(1);

(3) Use of bulk drug substances at 21 U.S.C. § 353b(a)(2);

(4) Drug reporting at 21 U.S.C. § 353b(b)(2); and

(5) Adverse event reporting at 21 U.S.C. § 353b(b)(5);

C. Defendants retain, at Defendants' expense, an independent person or persons (the "CGMP Expert") who: (1) is without any personal or financial ties (other than a retention agreement to satisfy the requirements of this provision) to Defendants, their officers or directors, or their families; and (2) by reason of background, training, education, or experience, is qualified to conduct inspections to determine whether Defendants' facility, methods, and

controls are established, operated, and administered in conformity with CGMP, and to recommend corrective actions and verify the implementation of corrective actions. Defendants shall notify FDA in writing of the identity and qualifications of the CGMP Expert within ten (10) days after retaining any such CGMP Expert;

D. Defendants submit a protocol that identifies the work plan for the CGMP Expert and the methodology that shall be used by the CGMP Expert (the "Work Plan") to: (1) conduct inspection(s) of Defendants' facility as described in paragraph 6.E.; (2) ensure that Defendants implement all recommended corrective actions; and (3) ensure that Defendants' manufacturing, processing, packing, labeling, holding, and/or distribution of drugs will be continuously administered in conformity with CGMP. Defendants shall not implement the Work Plan prior to receiving FDA's written approval of the Work Plan, and in no circumstances shall FDA's silence be construed as a substitute for written approval;

E. The CGMP Expert reviews all observations listed on Forms FDA-483 issued to Defendants in October 2016 and June 2017, and performs comprehensive inspection(s) of Defendants' facility and the methods and controls used to manufacture, process, pack, label, hold, and/or distribute drugs to determine whether Defendants' facility, methods, and controls are, at a minimum, in conformity with CGMP and are adequate to prevent Defendants' drug products from becoming adulterated within the meaning of 21 U.S.C. § 351(a)(2)(A) and 351(a)(2)(B). The CGMP Expert shall, at a minimum, evaluate whether:

(1) Defendants establish separate or defined areas for aseptic processing of drug products to prevent contamination;

(2) Defendants have cleaned, sanitized, and satisfactorily maintained the entire facility, including the equipment and utensils, as necessary to effectively address the

risks associated with aseptic processing, at appropriate intervals to ensure the safety, identity, strength, quality, and purity of Defendants' drugs;

(3) Defendants have established and implemented an adequate cleaning and disinfection program, which they have shown through valid scientific evidence is effective for cleaning and disinfecting equipment and facilities used to manufacture drugs;

(4) Defendants ensure that personnel engage in the manufacture, processing, packing, labeling, holding, and/or distributing of drug products wear clothing appropriate for the duties they perform, and that protective apparel, such as head, face, hand, and arm covering, are worn as necessary to protect drug products from contamination.

(5) Defendants have established and implemented an adequate environmental monitoring program to: (a) ensure that all sterile and/or aseptic operations are properly monitored (including personnel, surfaces, and air quality); (b) include scientifically sound pre-established limits; and (c) ensure that Defendants identify, review, investigate, and address any results that exceed the pre-established limits and any adverse trends;

(6) Defendants have established and implemented adequate written procedures designed to prevent microbiological contamination of drug products purporting to be sterile and/or pyrogen free, including but not limited to, procedures for dynamic smoke studies, media fill simulations, and validation of all aseptic and sterilization processes;

(7) Defendants have established 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;

(8) Defendants have established and implemented adequate written standard operating procedures ("SOPs") for manufacturing, holding, and distributing sterile drugs;

(9) Defendants conform to written procedures for production and process control designed to assure that Defendants' drug products have the identity, strength, quality, and purity they purport or are represented to possess, and that any deviation from the written procedures are recorded and justified;

(10) Defendants have established and implemented a written program designed to ensure that any automatic, mechanical, or electronic equipment used in the manufacture, processing, packing, labeling, holding, and/or distribution 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;

(11) Defendants have established and implemented an adequate testing program designed to assess the stability characteristics of Defendants' drug products;

(12) Defendants have established and implemented written SOPs to ensure that an adequate number of batches of each drug product is tested to determine an appropriate expiration date;

(13) Defendants have, for each batch of drug product purporting to be sterile and/or pyrogen-free, appropriate and documented laboratory determination of satisfactory conformance to pre-established final specifications for the drug product, including the identity and strength of each active ingredient prior to release;

(14) Defendants have established and implemented written SOPs to ensure that Defendants: (a) thoroughly investigate and document in a timely manner, and retain

such documents, any unexplained discrepancy or the failure of a batch of drug product, whether or not the batch has already been distributed, or any of its components, to meet any of the product's or component's specifications, including the extension of such investigation to other batches of the same product and other products that may have been associated with the specific failure or discrepancy; and (b) take required and timely corrective actions for all products that fail to meet specifications, and create and maintain documentation of such corrective actions;

(15) Defendants have established and implemented written SOPs to ensure that the Defendants thoroughly investigate and document in a timely manner any drug complaints, returns, or adverse events, and any associated trends in these product quality deviations and/or problems, and take any needed corrective actions in a timely manner;

(16) Defendants' employee training and qualification practices are adequate including, but not limited to, employee training and qualification in CGMP, inspection techniques, aseptic techniques, media fill processes, and procedures for responding to product quality deviations;

(17) Defendants have established a quality control unit that has the responsibility and authority to approve or reject, among other things, drug products, and the authority to review production records to assure that no errors have occurred or, if errors have occurred, that they have been fully investigated; and

(18) Defendants' controls are adequate to ensure that data generated from the manufacturing operations, including laboratory testing, are maintained, including any changes to existing data that also capture information relating to the individuals making changes, the date, and the reason for changes.

F. The CGMP Expert certifies in writing to FDA and Defendants that:

(1) The CGMP Expert has inspected Defendants' facility, methods, and controls used to manufacture, process, pack, label, hold, and/or distribute drugs;

(2) All deviations from CGMP brought to Defendants' attention by FDA, the CGMP Expert, and any other source have been corrected;

(3) Defendants have undertaken corrective actions to ensure that their facility, methods, and controls are adequate to prevent drugs from becoming adulterated within the meaning of 21 U.S.C. § 351(a)(2)(A) and 351(a)(2)(B); and

(4) Defendants' facility, methods, and controls comply with CGMP. As part of this certification, the CGMP Expert shall include a detailed and complete report of the results of the inspection(s) conducted under paragraph 6.E.;

G. Defendants report to FDA in writing the actions they have taken to:

(1) Correct all the deviations brought to Defendants' attention by FDA, the CGMP Expert, or any other source; and

(2) Ensure that Defendants' facility, methods, and controls used to manufacture, process, pack, label, hold, and/or distribute drugs will be continuously administered and operated in conformity with this Order, the Act, and its implementing regulations, and are adequate to prevent Defendants' drugs from becoming adulterated within the meaning of 21 U.S.C. § 351(a)(2)(A) and 351(a)(2)(B);

H. Defendants establish and maintain a system to report to FDA through the MedWatch reporting system all adverse drug experiences (in the manner described in 21 C.F.R. § 310.305 and/or 21 C.F.R. § 314.80) associated or potentially associated with any and all of

Defendants' drugs as soon as possible, but no later than fifteen (15) days after initial receipt of the adverse event information triggering a MedWatch report;

I. Defendants establish and maintain a system to submit to FDA, at the address specified in paragraph 13, Field Alert Reports (in the manner and as described in 21 C.F.R. § 314.81(b)(1)) for all of Defendants' distributed drugs within three (3) working days after initial receipt of information triggering the Field Alert Report;

J. FDA representatives, without prior notice and when FDA deems necessary, inspect Defendants' facility to determine whether Defendants are in compliance with the requirements of this Order, the Act, and its implementing regulations, and whether Defendants' facility, methods, and controls are adequate to prevent Defendants' drugs from becoming adulterated within the meaning of 21 U.S.C. § 351(a)(2)(A) and 351(a)(2)(B); and

K. Following FDA's inspection(s), FDA notifies Defendants in writing that Defendants appear to be in compliance with all of the requirements set forth in paragraphs 6.A.–6.I. of this Order. In no circumstance, shall FDA's silence be construed as a substitute for written notification.

7. Defendants shall recall and destroy, in accordance with the procedures provided in this paragraph, all non-expired drugs manufactured, held, and/or distributed by Defendants. The recall shall be initiated within twenty-four (24) hours after entry of this Order. Within thirty (30) days after entry of this Order, Defendants shall, under FDA supervision, destroy all finished and/or in-process drugs and components that are in Defendants' possession, custody, or control. With respect to any additional recalled drug products that subsequently come into the Defendants' possession, custody, or control, the Defendants shall quarantine any such products, promptly notify FDA of their receipt, and destroy any such products, under FDA's supervision,

no later than thirty (30) days after their receipt. Defendants shall bear the costs of destruction and the costs of FDA's supervision at the rates specified in paragraph 9. Defendants shall be responsible for ensuring that the destruction is carried out in a manner that complies with all applicable federal and state environmental laws, and any other applicable federal or state laws.

8. Representatives of FDA shall be permitted, without prior notice and as and when FDA deems necessary, to make inspections of Defendants' facility, collect samples, and, without prior notice, take any other measures necessary to monitor and ensure continuing compliance with the terms of this Order. During such inspections, FDA representatives shall be permitted access to Defendants' facility including, but not limited to, all buildings, equipment, in-process or unfinished and finished materials and products, containers, labeling, and other promotional material therein; to take photographs and make video recordings; to take samples, without charge to FDA, of finished and unfinished materials and products, containers and packaging material therein, labeling, and other promotional material; and to examine and copy all records relating to the receipt, manufacturing, processing, packing, labeling, holding, and distribution of any and all drugs and their components. The inspections shall be permitted upon presentation of a copy of this Order and appropriate credentials. The inspection authority granted by this Order is separate from, and in addition to, the authority to conduct inspections under the Act, 21 U.S.C. § 374.

9. Defendants shall pay all costs of FDA's supervision, inspections, investigations, analyses, examinations, and reviews that FDA deems necessary to evaluate Defendants' compliance with this Order, including the travel incurred by specialized investigatory and expert personnel, at the standard rates prevailing at the time the costs are incurred. As of the date that this Order is signed by the parties, these rates are: $93.26 per hour and fraction thereof per representative for inspection work; $111.77 per hour or fraction thereof per representative for

analytical or review work; $0.535 per mile for travel by automobile; government rate or the equivalent for travel by air or other means; and the published government per diem rate or the equivalent for the areas in which the inspections are performed per representative and per day for subsistence expenses, where necessary. In the event that the standard rates applicable to FDA supervision of court-ordered compliance are modified, these rates shall be increased or decreased without further order of the Court.

10. Within three (3) days after becoming aware of any of the following information about any drugs manufactured, processed, packed, labeled, held and/or distributed at or from Defendants' facility, Defendants shall submit to FDA at the address specified in paragraph 13, a product quality report describing all information pertaining to any:

A. Product and/or manufacturing defects that could result in adverse drug experiences;

B. Mislabeling or mix-ups, including incident(s) that causes any drug or its labeling to be mistaken for, or applied to, another article; and/or

C. Contamination, including any bacteriological or fungal contamination, or any significant chemical, physical, or other change or deterioration, or lack of stability or incorrect potency, in any drug.

11. Defendants shall provide notice of this Order in the following manner.

A. Within seven (7) days after entry of this Order, Defendants shall:

(1) Provide a copy of this Order, personally or, when necessary, by certified mail, return receipt requested, to each and all of their directors, officers, agents, employees, representatives, successors, assigns, attorneys, and any and all persons in active concert or participation with any of them (including trusts, parent companies, holding companies,

subsidiaries, affiliates, franchisees, "doing business as" entities, "consultants," "independent contractors," "independent business owners," and any other persons engaged in any part of the manufacture, processing, packing, labeling, holding, and/or distribution of Defendants' drugs) (collectively referred to as "Associated Persons");

(2) Post a copy of this Order on a bulletin board in the employee common areas at Defendants' facility and publish the Order on any internal and/or publicly-available website maintained and/or controlled by Defendants for as long as the Order remains in effect; and

(3) Hold a general meeting or series of smaller meetings for all Associated Persons, at which Defendants shall describe the terms and obligations of this Order, either in person or via video conference or webinar.

B. Within thirty (30) days after entry of this Order, Defendants shall provide to FDA an affidavit of compliance, signed by a person with personal knowledge of the facts, stating the fact and manner of compliance with the provisions of this paragraph, identifying the names, addresses, and positions of all persons who have received a copy of this Order pursuant subparagraph A.(1) along with a copy of the executed certified mail return receipts, and attaching a copy of the agenda, list of attendees, meeting minutes from the meeting(s) held pursuant to subparagraph A.(3). Within seven (7) days after receiving a request from FDA for any information or documentation that FDA deems necessary to evaluate Defendants' compliance with this subparagraph, Defendants shall provide such information or documentation to FDA.

C. In the event that Defendants becomes associated with any additional Associated Person(s) at any time after entry of this Order, Defendants immediately shall provide a copy of this Order, by personal service or certified mail (restricted delivery, return receipt

requested), to such Associated Person(s). Within thirty (30) days after each time Defendant becomes associated with any such additional Associated Person(s), Defendants shall provide to FDA an affidavit stating the fact and manner of their compliance with this paragraph, identifying the names, addresses, and positions of all Associated Persons who received a copy of this Order pursuant to this paragraph, and attaching a copy of the executed certified mail return receipts. Within seven (7) days after receiving a request from FDA for any information or documentation that FDA deems necessary to evaluate Defendants' compliance with this subparagraph, Defendants shall provide such information or documentation to FDA.

12. Defendants shall abide by the decisions of FDA, and FDA's decisions shall be final. All decisions conferred upon FDA in this Order shall be vested in FDA's discretion and, to the extent that these decisions are subject to review, shall be reviewed by this Court under the arbitrary and capricious standard set forth in 5 U.S.C. § 706(2)(A). Review by the Court of any FDA decision rendered pursuant to this Order shall be based exclusively on the written record before FDA at the time of the decision. No discovery shall be taken by either party.

13. All notifications, certifications, reports, correspondence, and other communications to FDA required by the terms of this Order shall be prominently marked "Order Correspondence," and shall be addressed to the Program Division Director, FDA Dallas District Office, Office of Pharmaceutical Quality Operations, 4040 North Central Expressway, Suite 300, Dallas, Texas 75204.

14. Except as provided in the foregoing provisions of this Order, the parties shall bear their own costs and attorneys' fees in this action.

15. This Court retains jurisdiction of this action and the parties thereto for the purpose of enforcing or modifying this Order and for the purpose of granting such additional relief as may be necessary or appropriate.

IT IS SO ORDERED, this _____ day of _____, 2018.

_____
UNITED STATES DISTRICT JUDGE