IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF TEXAS
DALLAS DIVISION

UNITED STATES OF AMERICA,	)	
	)	
Plaintiff,	)	
	)	
v.	)	Civil Action No. _____
	)	
DOWNING LABS, LLC,	)	
ASHLEY MICHELLE DOWNING,	)	**COMPLAINT FOR**
CHRISTOPHER VAN DOWNING, and	)	**PERMANENT INJUNCTION**
ROGER E. MANSFIELD,	)	**(21 U.S.C. § 332(a))**
	)	
Defendants.	)	
	)	

The United States of America, Plaintiff, by and through its undersigned counsel, and on behalf of the United States Food and Drug Administration ("FDA"), alleges and complains against defendants Downing Labs, LLC, Ashley Michelle Downing, Christopher Van Downing, and Roger E. Mansfield, (collectively, the "Defendants"), 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), to permanently enjoin the Defendants, Downing Labs LLC ("Downing Labs," the "firm" or "company"), a limited liability company, and individuals, Ashley Michelle Downing, Christopher Van Downing, and Roger E. Mansfield, 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, drugs that are adulterated within the meaning of 21 U.S.C. §

351(a)(2)(A) and/or (a)(2)(B); and (b) violating 21 U.S.C. § 331(k) by causing the adulteration of articles of drug within the meaning of 21 U.S.C. § 351(a)(2)(A) and/or 351(a)(2)(B), while the drugs are held for sale after shipment of one or more of their components in interstate commerce.

2. Downing Labs and its immediate predecessor company, NuVision Pharmacy, Inc., have a long history of manufacturing drug products under conditions that fall short of the minimum requirements to ensure safety and quality. Despite FDA's repeated attempts to obtain voluntary compliance with the Act, Downing Labs continues to demonstrate that it is 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 a permanent injunction 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. Downing Labs is a limited liability company formed in Texas in December 2013.

6. In January 2014, Downing Labs purchased NuVision Pharmacy, Inc. ("NuVision"), a Texas corporation that had received a pharmacy license from the Texas State Board of Pharmacy in 2011. Subsequent to its purchase of NuVision, Downing

Labs continued to operate under NuVision's name at NuVision's facility located at 4001 McEwen Road, Suite 110, Dallas, Texas (the "McEwen Road Facility"), within the jurisdiction of the Northern District of Texas. In June 2014, Downing Labs received a pharmacy license from the Texas State Board of Pharmacy and subsequently began operating solely as Downing Labs.

7. The McEwen Road Facility is adjacent to a suite once operated by Apothecure, Inc. ("Apothecure"). In 2012, Apothecure and its President pleaded guilty to misdemeanor criminal violations of the Act in Case Number 12-CR-047, in the Northern District of Texas, Dallas Division. The case related to the deaths of three people in the Pacific Northwest following Apothecure's shipment of a misbranded drug.

8. In June 2013, Apothecure informed the Texas State Board of Pharmacy that it had ceased operations and transferred its inventory to NuVision. Although Apothecure is no longer in operation, Downing Labs uses some of Apothecure's manufacturing equipment, and several Downing Labs employees, including Defendants Ashley Michelle Downing and Roger E. Mansfield, were previously employed by Apothecure.

9. Downing Labs manufactures, processes, packs, labels, holds, and/or distributes articles of drug within the meaning of 21 U.S.C. § 321(g)(1).

10. Ashley Michelle Downing, previously known as Ashley Michelle Sharp, co-owns Downing Labs with her husband, Christopher Van Downing. She also serves as the firm's Director and Vice-President/Secretary/Treasurer. She has held these positions since January 2014, when Downing Labs acquired NuVision, and is responsible for all operations. Downing Labs' Pharmacist-in-Charge, Roger E. Mansfield, reports directly

to Ashley Michelle Downing. Prior to Downing Labs' acquisition of NuVision in January 2014, Ashley Michelle Downing was employed by both NuVision and Apothecure, and held several positions at NuVision, including Director, Production Manager, and Quality Manager. She performs her duties in Downing Labs' McEwen Road Facility within the Northern District of Texas.

11. Christopher Van Downing co-owns Downing Labs with his wife, Ashley Michelle Downing. He also is the company's President, and has held this position since in or around January 2014, when Downing Labs acquired NuVision. His responsibilities include assisting in overall business management and compliance in Downing Labs' McEwen Road Facility.

12. Roger E. Mansfield is the current Pharmacist-in-Charge at Downing Labs and reports to Defendants Ashley Michele Downing and Christopher Van Downing. Mansfield was a staff pharmacist at the McEwen Road Facility in 2014 and became Pharmacist-in-Charge on or about December 30, 2014. As the Pharmacist-in-Charge, Mansfield is responsible for all pharmacy operations, including sterile drug production and oversight, supervision, and training of pharmacy staff. He is responsible for ensuring compliance with applicable state and federal regulations. He directs pharmacy staff engaged in the mixing, packaging, and labeling of sterile drugs, review of testing records, investigation of sterility test failures, cleaning of the sterile aseptic areas, and potency testing.

13. Downing Labs has been engaged in manufacturing drugs that, by virtue of their labeling and/or route of administration, purport to be or are intended to be sterile

("sterile drug products"), as well as non-sterile drug products. Downing Labs has manufactured and distributed its sterile drug products to physicians throughout the United States and internationally. Downing Labs' sterile drug products have included, among others, injectable vitamins and minerals, amino acids, hormones, and anesthetics.

14. The majority of Downing Labs' sterile injectable drug products have been aseptically processed, which involves filling drug products that have been rendered sterile via filtration into their final containers in a manner that maintains sterility. Some of Downing Labs' products have been subjected to a process for terminal sterilization using an autoclave that applies a predetermined amount of steam to products in their final sealed containers. Downing Labs also has used lyophilizing equipment to freeze-dry some of its aseptically filled sterile drug products into a powder form. A single production lot of a sterile drug product manufactured by the firm can be as large as 1,000 vials.

15. The McEwen Road Facility contains a "clean room" where the production of purportedly sterile drugs occurs. The clean room contains "ISO 5" and "ISO 7" processing areas (referring to International Standards Organization classifications for clean rooms). The ISO 5 processing area in the McEwen Road Facility purports to have sufficient protection from contamination during the aseptic processing of sterile drugs. Within the clean room, the ISO 5 area is separated from the ISO 7 area (which, by classification, has less protection from contamination) by vertical plastic panels that hang from the ceiling to approximately 14 inches above the work table upon which products are made.

16. In the past, FDA investigators identified that Downing Labs has filled both patient-specific orders and orders for "office stock" (i.e., drugs prepared and distributed not pursuant to a patient-specific prescription). Prior to the FDA's most recent inspection of Downing Labs, from September 14, 2015 to October 9, 2015 (the "September-October 2015 inspection"), Downing Labs informed FDA that it would be receiving patient-specific prescriptions for all drugs that it manufactures and distributes.

17. Downing Labs engages in manufacturing, processing, packing, labeling, holding, and distributing drugs in interstate commerce. For example, Downing Labs has distributed the sterile drugs it manufactured to physicians located outside of Texas, including, but not limited to, physicians in New York, Alaska, Indiana, Pennsylvania, and Hawaii.

18. Downing Labs manufactures drugs using components it receives in interstate commerce. For example, the firm receives components from California, Connecticut, and Alabama, including components originally manufactured in China and Germany, and has used those components to manufacture sterile drugs.

Requirements of the Act

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

20. The Act requires, subject to certain exceptions not applicable here, that drug manufacturers obtain FDA approval of a New Drug Application ("NDA") or

Abbreviated New Drug Application ("ANDA") with respect to any new drug they introduce into interstate commerce. 21 U.S.C. §§ 331(d) and 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).

21. 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).

22. The Act also requires that drugs be manufactured in accordance with current good manufacturing practice ("CGMP"). 21 U.S.C. § 351(a)(2)(B); *see also* 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 its 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. The FDA has promulgated CGMP regulations for drugs and finished pharmaceuticals. 21 C.F.R. Parts 210-211.

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

Exemptions in the Act for Compounded Drugs

24. 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 of a drug to create a medication. 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.

25. 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" in labeling (21 U.S.C. § 352(f)(1)); and approval of new drugs for humans (21 U.S.C. § 355). These exceptions are applicable to compounded drugs that 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 pharmacy 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).

26. In 2013, a new section of the Act was added under which a firm can register with the FDA as an "outsourcing facility." 21 U.S.C. § 353b. As with drug products compounded in accordance with 21 U.S.C. § 353a, drug products compounded in an outsourcing facility can qualify for certain exemptions from the Act, including the Act's requirements for "adequate directions for use" in labeling (21 U.S.C. § 352(f)(1)), and requirements pertaining to drug approval of new drugs for humans (21 U.S.C. § 355). Unlike drugs produced by firms under 21 U.S.C. § 353a, drug products compounded by outsourcing facilities are not exempt from the Act's CGMP requirements (21 U.S.C. § 351(a)(2)(B)). And 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)).

27. On June 23, 2015, Downing Labs registered with FDA as an outsourcing facility and its operations were thereafter subject to the requirements of 21 U.S.C. § 353b. As an outsourcing facility, all drugs that Downing Labs compounds, including any drugs that Downing Labs compounds pursuant to patient-specific prescriptions, are subject to the conditions of 21 U.S.C. § 353b and CGMP requirements in 21 U.S.C. § 351(a)(2)(B).

28. Furthermore, neither 21 U.S.C. § 353a nor 353b exempt 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.

FDA's Most Recent Inspections of Downing Labs' Facility

29. The FDA conducted inspections of Downing Labs or NuVision in 2013, 2014, and 2015, demonstrating multiple and ongoing violations of the Act.

30. During the most recent inspection, conducted in September-October 2015, FDA documented that Downing Labs manufactures drug products under insanitary conditions whereby they may have been contaminated with filth or rendered injurious to health and in a manner that does not conform to CGMP. The FDA's inspectional observations were listed in a Form FDA-483, Inspectional Observations ("FDA 483") that was provided to Ashley Michelle Downing at the conclusion of the inspection.

Insanitary Conditions in 2015

31. During the September-October 2015 inspection, the FDA observed numerous insanitary conditions at the McEwen Road Facility, including but not limited to the following:

A. Inadequate cleaning and sanitization of aseptic processing areas to reduce the risk

of microbial contamination. Specifically, the Defendants failed to ensure that the aseptic processing areas in their facility are adequately cleaned and sanitized to reduce the risk of microbial contamination during manufacturing. For example, the Defendants used a sterile disinfectant diluted with water from an inadequately qualified water system that was not demonstrated to be sterile, which could have contaminated the disinfectant. Furthermore, employees used a mop to clean a secondary surface (e.g., interior walls) in the firm's ISO 5 area before using the same mop on the most critical surfaces of the clean

ISO 5 area (e.g., work surfaces and equipment), which increased the risk of microbial contamination. There is no evidence to demonstrate that the Defendants' cleaning and sanitization are adequately performed to reduce the risk of microbial contamination to sterile drug products during manufacturing. The likelihood of microbial contamination of the compounding environment is supported by the firm's own environmental monitoring, which recovered spore forming microorganisms from the air in aseptic processing areas and personnel gloves worn there between July 2015 and August 2015.

B. Microbial contamination of both finished drug products and media fill runs (i.e., a process simulation conducted to demonstrate that a firm's aseptic procedures are adequate to prevent contamination during actual sterile drug production). Specifically, testing results obtained from Downing Labs identified seven lots of aseptically filled injectable drug products manufactured from April 2014 to July 2014 that were contaminated with microorganisms, including *Afipia felis*, *Bacillus oleronius*, *Bacillus thermoamylovorans*, *Oceannobacillus caeni*, and *Micrococcus luteus*. These microorganisms, if introduced into the body, can cause septic shock, pneumonia, and urinary tract infections. In addition, testing revealed excessively high levels of endotoxins in two batches of the sterile drug products manufactured in May 2015 and June 2015. Endotoxins are substances found in certain bacteria that can cause a wide variety of serious reactions including high fever and shock. Furthermore, three lots prepared as media fills between May 2015 and August 2015 failed sterility tests due to the presence of microorganisms, including *Staphylococcus epidermidis*, *Brevibacillus parabrevis*, and an organism that was not identified. These microorganisms can cause

serious infections to the body, including but not limited to respiratory infections, pneumonia, bacteremia, and bloodstream infections, which are particularly dangerous to patients with immunocompromised systems.

C. Inadequate smoke studies and response to smoke studies conducted on the aseptic processing areas. Smoke studies are conducted under dynamic (i.e., operational) conditions in order to assess the airflow patterns necessary to maintain unidirectional flow 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 the sterile drug products during processing. On October 15, 2014, Downing Labs conducted a smoke study under dynamic processing conditions after modifications were made to the firm's cleanroom, including the installation of a Plexiglas panel to enclose the ISO 5 area on October 7, 2014. After the smoke study showed turbulent air flow within the ISO 5 area, the company continued producing sterile drug products while additional repairs were made. Although a subsequent smoke study on November 4, 2014 had a passing result, the company's records do not indicate that steps were taken to ensure the sterility of products manufactured before November 4, 2014. Furthermore, the next smoke study that Downing Labs conducted in March 2015 did not evaluate the potential for turbulent and reverse airflow from the ISO 7 area to the ISO 5 area. A video recording of the smoke study shows air flowing over the operator and onto the product. Downing Labs' smoke studies were also inadequate because they simulated only a single operator, whereas actual production frequently involves multiple operators in the ISO 5 and ISO 7 areas and an increase in personnel can affect the air flow.

D. Inadequate sterile aseptic practices. For example, while performing aseptic operations, a technician was observed blocking filtered air flow with gloved fingers over open vials of sterile drugs, picking up and inserting vial stoppers into vials without using any sterile tools, and resting a gowned arm on the ISO 5 work surface. These poor aseptic practices create a high risk for the introduction of microbial contamination into products purporting to be sterile.

32 The Defendants violate 21 U.S.C. § 331(a) by introducing or delivering for introduction into interstate commerce sterile drugs that 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 and/or rendered injurious to health. The Defendants also violate 21 U.S.C. § 331(k) by causing the adulteration, within the meaning of 21 U.S.C. § 351(a)(2)(A), of sterile drugs while such articles are held for sale after shipment of one or more of their components in interstate commerce.

Deviations from CGMP in 2015

33. During the September-October 2015 inspection, the FDA also observed significant deviations from CGMP requirements in Downing Labs' sterile drug manufacturing operation. Because Downing Labs was registered as an outsourcing facility on June 23, 2015, all drug products manufactured at the McEwen Road Facility after that date are subject to CGMP requirements. In addition, this inspection documented that Downing Labs manufactured and distributed drug products without receiving prescriptions for identified individual patients before registering as an

outsourcing facility. These drug products compounded and distributed without the receipt of prescriptions for identified individual patients did not qualify for the exemption under 21 U.S.C. § 353a from CGMP requirements. Therefore, drug products that Downing Labs manufactured both before and after registration as an outsourcing facility are adulterated within the meaning of 21 U.S.C. § 351(a)(2)(B). The deviations from CGMP included, but were not limited to, the following:

A. Failure to establish and follow appropriate written procedures, including the 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). Sterilization of drug products can be achieved by performing filter sterilization during aseptic processing, or by performing terminal sterilization of filled products after they are sealed in their final container. Validation of aseptic processing, or media fill, involves conducting a process simulation to demonstrate that the aseptic procedures are adequate to prevent contamination during actual sterile drug production. During media fills, all the conditions (e.g., an operator's technique, the facility/equipment performance, and the process steps) that a product would be exposed to during processing are simulated, allowing a manufacturer to assess risks to the sterility assurance of a drug product intended to be sterile. Validation of a terminal sterilization process includes documenting that the established procedure (e.g., steam sterilization using autoclave) consistently kills microorganisms with a high degree of sterility assurance of the finish product.

Specifically:

(1) Downing Labs failed to demonstrate through adequate controls in place and documentation that it maintained a robust validation process; for example:

(a) Downing Labs' Autoclave (identified as DWN-0294 (A6-5065)) failed a calibration test on September 16, 2015 because it did not achieve the appropriate set temperature. Downing Labs did not conduct any investigation into this failure nor had it undertaken corrective action at the time of the inspection. Because the last passing calibration check was September 3, 2014, all items placed in this autoclave between September 3, 2014, and September 16, 2015 are at risk for not having been sterilized.

(b) Downing Labs' ability to properly document each sterilization cycle is absent because its equipment lacks an adequate data recording mechanism. Because Downing Labs' equipment lacks adequate recording capability, there are no continuous documented temperature charts to demonstrate that the equipment has maintained the required temperature during the pre-established sterilization cycle to ensure proper sterilization.

(c) Downing Labs' weekly assessment of autoclave functionality with biological indicators ("BIs") is inadequate, as it is performed with the autoclave empty and does not simulate its actual use. BIs use heat resistant organisms to provide direct evidence of whether sterilizing conditions have been met.

(d) Water used to run Downing Labs' autoclaves comes from an inadequately qualified water system that was not demonstrated to be adequate and

suitable for product contact surfaces intended to be sterile. In addition, no endotoxin testing of this water is performed.

(e) Downing Labs' autoclaves are located and used in an unclassified area (i.e., an area that has not been certified according to ISO guidelines and is not considered a cleanroom). Because the firm's standard operating procedure requires the autoclave door to be partially opened during use to facilitate cooling and drying, materials in the autoclave are exposed to unclassified air (i.e., air that has not been certified to meet ISO standards for air cleanliness).

(f) Downing Labs has not validated autoclave cycles intended to sterilize the wipes used by the firm to clean the ISO-classified areas in its facility.

(2) Downing Labs did not perform adequate media fills. Specifically, the firm conducted media fills in a manner that failed to simulate actual aseptic processing operations or reflect worst case processing conditions. For example, the media fills do not simulate the use of additional processing equipment and manual aseptic techniques for the use of air sterilizing filters with nitrogen gas and a lyophilizer. Additionally, media fill procedures did not define the number of aseptic filters to be used for a particular batch size.

B. Failure to thoroughly review the failure of a batch or any of its components to meet any of its specifications, whether or not the batch has already been distributed. *See* 21 C.F.R. § 211.192. Specifically:

(1) Downing Labs failed to adequately investigate sterility test failures in seven lots of aseptically filled injectable drug products manufactured between April 2014 and July 2014.

(2) Downing Labs failed to adequately investigate sterility test failures in three lots produced as media fills between May 2015 and August 2015.

(3) Downing Labs failed to adequately investigate potency test failures in five lots of sterile drugs manufactured between April 2015 and September 2015. Potency refers to the amount of the active pharmaceutical ingredient(s) present in each dose. A potency failure occurs when the measured amount of the active pharmaceutical ingredient(s) present in the dose does not equal the intended amount to be present within a pre-determined range. In these cases, the measured amounts are either greater than the intended amount (super-potency) or less than the intended amount (sub-potency). Administration of super-potent drug to patients puts the patient at risk of receiving a toxic amount of the drug, while administration of sub-potent drugs puts the patient at risk of receiving a non-therapeutic amount of the drug.

(4) Downing Labs failed to adequately investigate the source and impact of at least 14 actionable and adverse environmental monitoring results identified in aseptic processing areas between June 2015 and August 2015.

(5) Downing Labs failed to adequately investigate the source and composition of particles identified by its contract laboratory during testing in April 2015, including particles found in two of the company's sterile drugs: Procaine 1% and L-Glutathione 50ml/200ml manufactured on March 24, 2015 and March 25, 2015, respectively.

(6) Downing Labs failed to adequately investigate three spore test failures associated with autoclave equipment used by the company for steam sterilization from September 2014 to March 2015. A spore test is used to verify whether the autoclave equipment is operating at the proper sterilization specifications to deactivate the most challenging microorganisms that might be present in a drug intended to be sterile. The Defendants also failed to investigate an autoclave that failed a temperature calibration in September 2015.

C. Failure to establish an adequate system for cleaning and disinfecting aseptic processing rooms and equipment. *See* 21 C.F.R. § 211.42(c)(10)(v). Specifically, Downing Labs has no data to demonstrate that the disinfectants it uses to clean work surfaces, floors, walls and ceilings in the ISO 5 and ISO 7 areas of its facility can sufficiently reduce the presence of microorganisms and the risk of microbial contamination of sterile drug products.

D. Failure to document at the time of performance the execution of the established written production, process control procedures, and process control functions for sterile drug products. *See* 21 C.F.R. § 211.100(b). Specifically, in June 2015, Downing Labs' consultant noted that the performance qualification of a lyophilizer used by the firm to freeze-dry aseptically filled sterile drug products into a powder form failed to reach expected temperature parameters. Therefore, no specific temperature parameters were successfully documented to ensure that the lyophilization process could be consistently and adequately conducted for each batch of manufactured sterile drug products. Furthermore, Downing Labs continued to use this equipment as part of the

manufacturing of sterile drug products, disregarding its consultant's recommendations to investigate and evaluate the cause of the temperature excursions of the lyophilizer before releasing the equipment for production.

E Failure to establish a written testing program designed to assess the stability characteristics of the drug products. *See* 21 C.F.R. § 211.166. Specifically, Downing Labs failed to conduct product stability studies to ensure expiration dates of 180 days for six lots of sterile drugs manufactured and distributed in July 2015 and August 2015. Product stability studies are required to confirm whether the sterile drugs can maintain the proper potency and sterility in appropriate storage conditions.

F. Failure to prevent unauthorized access or changes to data and to provide adequate controls to prevent omission of data. *See* 21 C.F.R. § 211.68(b). Specifically, during the inspection Ashley Michelle Downing admitted that two media fill records were deleted from computerized production logs. Although these records were initially seen by the FDA investigator while reviewing the logs, they were no longer in the system when the FDA investigator requested copies.

34. The 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), in that the methods used in, or the facilities or controls used for, their preparation do not comply with CGMP requirements. These requirements are meant to assure that the drugs 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. The Defendants also

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

FDA's June-July 2014 Inspection

35. FDA previously inspected Downing Labs' McEwen Road Facility from June 3, 2014 to July 16, 2014. Much like the FDA's most recent September-October 2015 inspection, the June-July 2014 inspection documented that Downing Labs manufactured drug products under insanitary conditions whereby they may have been contaminated with filth or rendered injurious to health, and in a manner that does not conform to CGMP. The Form FDA 483 that was provided to Downing Labs at the conclusion of the inspection identified numerous unacceptable practices and conditions. Many of these practices and conditions were the same as those FDA observed in the September-October 2015 inspection.

Insanitary Conditions in 2014

36. During the June-July 2014 inspection, the FDA observed numerous insanitary conditions at the McEwen Road Facility, including but not limited to the following:

A. A total of 19 lots of drug products intended to be sterile produced by Downing Labs or NuVision between June 2013 and June 2014, tested positive for microbial contamination. Fourteen different microorganisms typically present on human skin or in the environment, including *Staphylococcus haemolyticus*, which could cause septicemia, peritonitis, and infections of the urinary tract, wounds, bone, and joints, and

Nocardia nova, which causes skin infections, sinusitis, and pneumonia, were identified in the company's products. Additionally, three lots of drug products intended to be sterile were found to contain excessive amounts of endotoxins, which are substances found in certain bacteria that can cause a wide variety of serious reactions including high fever and shock. While the company did not distribute these lots after receiving the test results, the rate of contamination in purportedly sterile product was extremely serious and was indicative of insanitary conditions existing during this time.

B. Although major repairs and renovations were made to the company's cleanroom between June 2013 and May 2014, there was no evidence that adequate cleaning and sanitization was performed during and after the construction and prior to resuming production to ensure that aseptically filled injectable drug products made during this timeframe were not contaminated. Recertification of the ISO 5 area was inadequate because it did not include sufficient evidence of controlled air flow (i.e., unidirectional and non-turbulent) through dynamic smoke studies.

C. On June 2, 2014, Downing Labs temporarily removed the ends of a plastic curtain that separated the ISO 5 production area from the less protected ISO 7 production area while making additional renovations to their cleanroom. No recertification or smoke studies were completed after this modification. However, the firm continued to compound sterile drug products in the non-certified cleanroom while the curtain was removed.

D. Downing Labs failed to adequately monitor the environmental conditions in aseptic processing areas. The monitoring performed by the firm appeared to be

ineffective to mitigate microbial contamination risk, as evidenced by excessive levels and types of microbial contamination identified in their purportedly sterile drug products.

E. Downing Labs failed to ensure that the aseptic processing areas in the McEwen Road Facility were adequately cleaned and sanitized to reduce the risk of microbial contamination during manufacturing. For example, the firm used non-sterile wipes to clean critical surfaces in the ISO 5 area, which increased the risk of microbial contamination. There was also insufficient evidence to demonstrate that the plastic curtains surrounding the firm's ISO 5 area were adequately cleaned to reduce the risk of microbial contamination. In addition, the firm rinsed glass beakers used to manufacture aseptically filled injectable drug products with substandard water (i.e., water that has not been shown to meet United States Pharmacopoeia ("USP") standards for purified water intended for injection), which increased the risk of endotoxins in finished drug products.

Deviations from CGMP in 2014

37. During the June-July 2014 inspection, FDA determined that Downing Labs compounded and distributed drug products without receiving patient-specific prescriptions for approximately 24% of their sterile drug sales. These drug products did not qualify for the exemption from CGMP requirements under 21 U.S.C. § 353a. FDA observed multiple deviations from CGMP requirements in the company's sterile drug manufacturing. The CGMP violations included, but were not limited to, the following:

A. Failure to thoroughly review the failure of a batch or any of its components to meet any of its specifications, whether or not the batch has already been distributed. *See* 21 C.F.R. § 211.192. For example, Downing Labs or NuVision either

completely failed to investigate or failed to adequately investigate 19 lots of aseptically filled injectable drug products made between June 2013 and May 2014 that failed sterility testing due to the presence of microorganisms. Additionally, after learning of three endotoxin failures between January 2014 and May 2014, Downing Labs failed to adequately investigate the source of the endotoxin contamination, including a lot of L-Carnitine Injection which contained an extraordinary amount of endotoxins. Finally, the firm failed to investigate the source or composition of fibers identified in at least 185 lots of aseptically filled injectable drug products between April 6, 2013 and June 23, 2014. In one instance, although particles were visible in approximately 43% of the vials from a single lot, the firm only held back the affected vials. The remaining vials from each lot were released, and no investigation was performed to determine the cause of the contamination.

B. Failure to establish and follow appropriate written procedures, including the 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). Specifically,

(1) Downing Labs did not perform adequate media fills. The company performed media fills in a manner that failed to simulate aseptic processing operations or reflect worst case processing conditions. For example, the company's media fills did not simulate the filling of all vial sizes used by the firm in routine fill operations or the volume of production.

(2) Downing Labs also failed to perform adequate integrity testing on the 0.2 micron filters that they use during aseptic processing of sterile drug products. Post-use integrity testing of these filters is necessary to identify whether filters used have been damaged during processing, thus allowing contaminants to enter finished drug products. Despite these risks, from April 2013 to June 2014, Downing Labs or NuVision only performed integrity testing on approximately 17% of the 0.2 micron filters used to sterilize injectable drug products, while all filters used should have been tested.

C. Failure to establish an adequate system for cleaning and disinfecting aseptic processing rooms and equipment. *See* 21 C.F.R. § 211.42(c)(10)(v). Specifically, Downing Labs had no data or effectiveness studies demonstrating that the disinfectants that they used to clean work surfaces, floors, walls and ceilings in the ISO 5 and ISO 7 areas could sufficiently reduce the risk of microorganisms, particles, and cross-contamination between lots.

D. 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). Specifically, no potency testing was performed to identify whether their finished drug products were sub-potent or super-potent. At the time of a previous inspection in March and April 2013, the company was performing potency testing on approximately 29% of drug product lots, and identified 110 potency failures. Shortly thereafter, the firm ceased potency testing, thus eliminating their ability to identify

potency deviations, despite the high number of failing drugs revealed by their earlier testing.

FDA's March 18-April 18, 2013 Inspection

38. The FDA first inspected the McEwen Road Facility from March 18 to April 18, 2013. At the time of this inspection, the firm was still operating as NuVision. Between March 2012 and March 2013, 35% of NuVision's sterile drugs were not compounded and distributed pursuant to patient-specific prescriptions. Defendant Ashley Michele Downing served as NuVision's Pharmacy Technician and Quality Manager.

39. The FDA 483 issued at the conclusion of the March-April 2013 inspection cited, among others, the following insanitary conditions and deviations from CGMP requirements: (1) failure to establish an adequate system for cleaning and disinfecting the room and equipment in aseptic processing areas; (2) failure to establish and follow appropriate written procedures, including the validation of all aseptic and sterilization processes, designed to prevent microbiological contamination of drug products purporting to be sterile; (3) personnel engaged in drug manufacturing did not wear clean clothing appropriate for the duties they perform, and did not wear apparel, such as head, face, hand, and arm coverings, necessary to protect drug products from contamination; (4) failure to establish an adequate air supply filtered through high-efficiency particulate air filters under positive pressure in the aseptic processing area; (5) failure to establish an adequate system for monitoring environmental conditions in aseptic processing areas; and (6) failure to thoroughly review the failure of a batch or any of its components to meet any of its specifications, whether or not the batch has already been distributed.

40. At the close of the March-April 2013 inspection, the FDA issued a Form FDA 483, setting forth the FDA's inspectional observations and discussed the findings with the company's then Pharmacist-In-Charge. Defendant Ashley Michelle Downing was also present during the inspection close-out discussion.

Prior Unapproved New Drugs Violations

41. During the June-July 2014 and March-April 2013 inspections, the FDA observed that Downing Labs or NuVision marketed numerous drug products that lacked an approved NDA or approved ANDA, as required by 21 U.S.C. § 355, and were not exempt from approval. These products were new drugs within the meaning of 21 U.S.C. § 321(p) because they were not generally recognized as safe and effective. At the time of the June-July 2014 inspection, Downing Labs had not yet registered its facility with FDA as an outsourcing facility under 21 U.S.C. § 353b. In addition, the March-April 2013 inspection occurred before enactment of 21 U.S.C. § 353b concerning outsourcing facilities. Thus, at the time of both of these earlier inspections, for their compounded drugs to be exempt from the Act's new drug approval requirements (21 U.S.C. § 355), Downing Labs or NuVision was required to comply with the conditions set forth in 21 U.S.C. § 353a (which include, among other things, that the compounded drugs be prepared pursuant to patient-specific prescriptions). Nevertheless, the company did not satisfy all of these conditions.

42. Downing Labs or NuVision thus violated 21 U.S.C. § 331(d) by introducing or delivering for introduction into interstate commerce unapproved new

drugs that were neither approved, pursuant to 21 U.S.C. § 355(a), nor exempt from approval.

Prior Violations Concerning Misbranded Drugs

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

44. "Adequate directions for use" means directions under which a layperson could use a drug safely and effectively for the purposes for which the drug was 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). Although the FDA, by regulation, has established certain exemptions from the requirement that labeling bear adequate directions for use *(see, e.g.*, 21 C.F.R. § 201.115), Downing Labs' drug products are unapproved new drugs and do not satisfy the conditions for any of these exemptions.

45. At the time of the June-July 2014 and March-April 2013 inspections, Downing Labs or NuVision was required to comply with the conditions set forth in 21 U.S.C. § 353a for its drugs to be exempt from certain provisions of the Act, including U.S.C. § 352(f)(1) (the requirement that labeling of drug products bear adequate directions for use). The company did not satisfy all of these conditions because it did not obtain patient-specific prescriptions for all of their drug products.

46. Because Downing Labs' drug products were not exempt from the requirement to have labeling with adequate directions for use under either 21 U.S.C. § 353a or FDA regulations, the company's drugs were misbranded within the meaning of 21 U.S.C. § 352(f)(1). Downing Labs violated 21 U.S.C. § 331(a) by introducing or delivering for introduction into interstate commerce articles of drug that were misbranded within the meaning of 21 U.S.C. § 352(f)(1), in that the labeling of the drugs failed to bear adequate directions for use. Downing Labs or NuVision also violated 21 U.S.C. § 331(k) by causing the misbranding, within the meaning of 21 U.S.C. § 352(f)(1), of drugs while such drugs were held for sale after shipment of one or more of their components in interstate commerce, in that the labeling of the drugs failed to bear adequate directions for use and they were not exempt from that requirement.

Previous Efforts to Obtain Voluntary Compliance

47. On April 15, 2013, following FDA's recommendation, NuVision agreed to voluntarily recall unexpired lots of the lyophilized compounds HCG 5000IU/5mL and Sermorelin/GHRH6/5mL due to sterility assurance concerns for lyophilized products that FDA identified during the March-April 2013 inspection.

48. On May 13, 2013, FDA participated in a conference call with NuVision representatives and its counsel during which the FDA explained its sterility concerns about all of the company's sterile drug products on the market because of the poor aseptic practices documented during the March-April 2013 inspection. The FDA recommended that NuVision recall all sterile drug products from the market and cease production of sterile drug products until corrections were made. Although NuVision, through counsel,

indicated it would get back to the FDA, no follow-up discussions occurred about FDA's recommendation for a recall.

49. On May 14, 2013, the FDA received NuVision's response to the Form FDA 483 issued at the conclusion of the March-April 2013 inspection. NuVision's response indicated, among other things, that it had contracted with a consulting firm and corrections would be made. NuVision's response also asserted that it was not required to comply with the CGMP regulations, 21 C.F.R. Parts 210 and 211. NuVision claimed that there was no evidence to suggest that its sterile drug products were prepared under insanitary conditions or contaminated. Despite FDA's recommendations that it recall and cease production of its sterile drug products, NuVision did not agree to do either.

50. On May 18, 2013, the FDA issued a "Safety Alert" to health care providers that highlighted the FDA's concerns about "a lack of sterility assurance of all sterile drug products made and distributed by NuVision . . . ." NuVision then modified its website to claim that it was a compounding pharmacy, as opposed to a manufacturer, and thus was not required to meet the CGMP standards set forth at 21 C.F.R. Parts 210 and 211, and was not recalling sterile injectable products. NuVision did not further respond to the FDA's concerns about the sterility of its products.

51. On July 26, 2013, FDA formally requested in a letter that NuVision "immediately initiate a recall of all lots of sterile products produced by NuVision that are within expiry." The FDA's letter explained that FDA observed poor sterile production practices during the March-April 2013 inspection and detailed nine of the most objectionable conditions observed. The letter stated the FDA's determination that "due

to the lack of sterility assurance of NuVision sterile products, the sterile drugs distributed by NuVision present a risk of illness or injury to consumers." The letter also explained that all sterile products produced at NuVision are adulterated under 21 U.S.C. § 351(a)(2)(A) and that those products produced and distributed by NuVision without patient-specific prescriptions are also adulterated within the meaning of 21 U.S.C. § 351(a)(2)(B). The letter further explained that the corrective actions described in the firm's FDA 483 response were inadequate.

52. By letter dated August 6, 2013, NuVision informed the FDA that it disagreed with the FDA's observations and conclusions and, despite the FDA's public health concerns, would not agree to a recall. NuVision's letter to the FDA addressed the observations discussed in FDA's July 26, 2013 letter and asserted that NuVision was not required to follow 21 C.F.R. Parts 210 and 211. It also claimed that NuVision had "never had a sterility failure from a distributed lot" and that a "complete recall of all sterile products [would] put us out of business."

53. On August 16, 2013, the FDA updated its May 18, 2013 Safety Alert to remind healthcare providers about "safety concerns with all sterile drug products made and distributed by NuVision . . . ." The alert recommended that health care providers should not administer any NuVision sterile products to patients because the products' sterility was not assured.

54. On July 18, 2014, following the FDA's June-July 2014 inspection of the McEwen Road Facility, FDA participated in a conference call with Ashley Michelle Downing and Christopher Van Downing. During the call, the FDA informed them that

based on the inspectional findings noted during the June-July 2014 inspection, the FDA had serious concerns about the company's products. FDA highlighted, among other things, Downing Lab's poor aseptic practices, test results that showed microbial contamination, and inadequate investigations. Although the FDA recommended that Downing Labs voluntarily cease sterile production and recall any sterile products that were still on the market in light of the risks to public health, Downing Labs declined to recall their sterile products and did not cease sterile operations.

55. On July 18, 2014, the FDA issued a Safety Alert that informed health care professionals and consumers that, based on observations made by FDA during the June-July 2014 inspection, Downing Labs' sterile products may be contaminated. On July 24, 2014, Downing Labs posted a response on its website that claimed that all lots of compounded sterile products were held until sterility and endotoxin test results were received, and any products that failed such testing were investigated and destroyed.

56. On August 6, 2014, and August 20, 2014, the FDA received the firm's responses to the Form FDA 483 that was issued to the firm at the conclusion of the June-July 2014 inspection. The company's August 6, 2014 response indicated, among other things, that as of August 4, 2014, the firm was only dispensing drug products pursuant to patient-specific prescriptions and that corrections would be made in response to observations noted in the FDA 483. The August 6, 2014 response continued to assert that the firm was not required to comply with the CGMP regulations, 21 C.F.R. Parts 210 and 211. In its August 20, 2014 response, Downing Labs revised its proposed timetable for completing corrective actions.

57. On September 9, 2014, FDA again formally requested that Downing Labs "immediately initiate a recall of all lots of sterile products produced at Downing Labs LLC dba NuVision Pharmacy . . . within expiry." FDA's letter noted that Downing Labs' own testing had found microbial contamination and endotoxins in their purportedly sterile drug products and explained that "products made at the facility present a risk of illness or injury to consumers." The FDA's letter reiterated several of the significant observations that FDA made during the June-July 2014 inspection, and noted that, as a result of these deficiencies, purportedly sterile products produced at the McEwen Road Facility are adulterated under 21 U.S.C. § 351(a)(2)(A) and (a)(2)(B). The letter further explained that the corrective actions described in Downing Lab's FDA 483 response were inadequate.

58. On September 11, 2014, Downing Labs informed the FDA that it "did not agree" to initiate a recall of its sterile products, noting that all lots of compounded products that had failed sterility or endotoxin results were destroyed. Although the response noted that Downing Labs was taking steps to address deficiencies and had met with a third-party consultant who would be advising the firm, the response provided no indication that Downing Labs had limited its production of sterile products.

59. On November 24, 2014 – over four months after the conclusion of the June-July 2014 inspection – Downing Labs sent FDA a document entitled "Assessment of FDA Form 483 Issued July 16, 2014." The assessment, prepared by an independent consulting firm, discussed the FDA's observations and recommended numerous systemic proposals to address the deficiencies observed. Although the assessment identified a list

of "Deliverables" to be completed, Downing Labs' correspondence did not specify if or when any specific corrective actions were or would be taken in response to the assessment, nor did it specify any interim actions to be taken by the firm to ensure the quality of drugs processed prior to the implementation of corrective actions. Moreover, it failed to indicate any plans for recalling any product manufactured by the firm since the June-July 2014 inspection.

60. On April 10, June 5, and July 4, 2015, Downing Labs sent FDA a series of additional responses to the FDA Form 483 that it received in July 2014. The responses purported to describe Downing Labs' efforts to correct deficiencies and improve processes. On June 23, 2015, Downing Labs registered with FDA as an outsourcing facility pursuant to 21 U.S.C. § 353b.

61. On October 15, 2015, following the FDA's September-October 2015 inspection of the McEwen Road Facility, FDA participated in a conference call with the counsel for Downing Labs, Ashley Michelle Downing, and Christopher Van Downing. FDA informed counsel that, based on the inspectional findings noted during the September-October 2015 inspection, the FDA had serious concerns about the lack of sterility assurance of Downing Labs' sterile drug products. These concerns were based on deviations including but not limited to poor aseptic practices, lack of cleaning of the aseptic processing areas, lack of sterilization validation, and inadequate investigations. FDA recommended that Downing Labs voluntarily recall all lots of sterile drug products on the market within expiry, cease sterile production until implementing adequate corrective actions, and notify FDA before resuming sterile production. On October 16,

2015, counsel for Downing Labs, Ashley Michelle Downing, and Christopher Van Downing reported that the Downings and Downing Labs agreed to initiate a recall and to temporarily cease sterile production. The Downings and Downing Labs did not agree to notify FDA before resuming sterile drug product production.

62. Despite limited promises to correct some prior deficiencies, Downing Labs' serious and repeat violations have persisted, as evidenced by the violations observed during the FDA's September-October 2015, June-July 2014, and March-April 2013 inspections, as well as the numerous lots of the company's sterile drug products that have tested positive for contaminants. The Plaintiff is informed and believes that, unless restrained by this Court, the Defendants will continue to violate 21 U.S.C. § 331(a) and (k), in the manner alleged herein, and continue to pose a risk to the public health.

WHEREFORE, Plaintiff respectfully requests that this Court:

I. Permanently restrain and enjoin the 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 from manufacturing, repackaging, processing, packing, labeling, holding, or distributing any article of drug, unless and until Defendants bring their manufacturing, repackaging, processing, packing, labeling, holding, and distribution operations into compliance with the Act and its implementing regulations to the satisfaction of FDA;

II. Permanently restrain and enjoin the Defendants Downing Labs, LLC, Ashley Michelle Downing, Christopher Van Downing, and Roger E. Mansfield and each and all of their officers, agents, employees, successors or assigns, representatives, and

attorneys, and any and all persons in active concert or participation with any of them, pursuant to 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 or delivering, or causing to be introduced or delivered, into interstate commerce drugs that are adulterated within the meaning of 21 U.S.C. § 351(a)(2)(A) and/or 351(a)(2)(B).

B. Violating 21 U.S.C. § 331(k) by causing drugs that the Defendants hold for sale after shipment of one or more of their components in interstate commerce to become adulterated within the meaning of 21 U.S.C. §§ 351(a)(2)(A) and/or 351(a)(2)(B).

III. Authorize the FDA pursuant to this injunction to inspect the Defendants' places of business and all records relating to the receipt, manufacture, repackaging, processing, packing, labeling, holding, and distribution of any drug to ensure continuing compliance with the terms of the injunction and the Act, 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 4th day of January, 2016.

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