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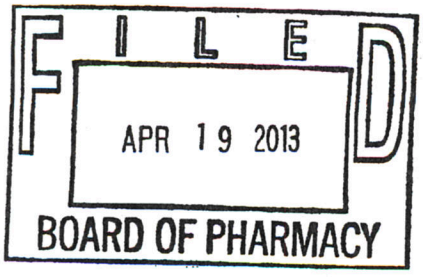

STATE BOARD OF NEW JERSEY
DEPARTMENT OF LAW & PUBLIC SAFETY
DIVISION OF CONSUMER AFFAIRS
STATE BOARD OF PHARMACY

IN THE MATTER OF THE PERMIT OF MedPrep Consulting Inc. Permit No.28RS00615400 TO OPERATE AS A PHARMACY IN THE STATE OF NEW JERSEY	Administrative Interim Order and Report of Hearing Committee to the Board

This matter was opened to the New Jersey State Board of Pharmacy (hereinafter the "Board") on April 2, 2013, upon receipt of the application of MedPrep Consulting Inc. (hereinafter "MedPrep") to discontinue the terms of Interim Consent Orders entered on March 15 and March 22, 2013 which required MedPrep to refrain from operation as a pharmacy. MedPrep's application to resume operation is based upon its assertion that operation would not pose a risk to the public health, safety and welfare. On April 9, 2013 the State filed opposition to MedPrep's application and a cross motion to extend the Interim Consent Order pending the Board's determination on an application it represented would be filed by April 19, 2013

seeking the immediate temporary suspension of MedPrep's permit to operate a pharmacy in New Jersey.

A hearing of nearly 18 hours (including deliberations) was held before a Committee of the Board on April 12 and April 15, 2013.[1] Deputy Attorneys General Kim Ringler and Jodi Krugman appeared on behalf of the State, Angelo Cifaldi, Esq. and Satish Poondi, Esq. of Wilentz Goldman and Spitzer appeared on behalf of MedPrep.

Summary of Evidence Presented

On March 15, 2013, MedPrep voluntarily recalled all magnesium sulfate products compounded at its facility. It subsequently expanded the recall to include all of its products. The recall resulted from MedPrep being notified by Yale New Haven Hospital that it observed visible particulate contaminants in 50 ml bags of magnesium sulfate intravenous solution belonging to unique and distinct lots compounded and dispensed by MedPrep only to Yale New Haven Hospital. (Exhibit S-Krugman-A, B & C).

The parties entered into a Voluntary Interim Consent Order filed March 15, 2013 in which MedPrep agreed to refrain from and stop all pharmacy operations through the close of business on Friday, March 22, 2013. The Order provided that upon voluntary

1 At the March 27, 2013 Board meeting, the Board authorized a Committee of the Board to conduct a hearing in this matter and to issue an Order having immediate effect, which the full Board may then ratify, modify or vacate at the next meeting at which such review can be scheduled.

consent or application of the Attorney General, the terms could be extended for an additional period of time. The Order was subsequently extended to April 5, 2013 and again to April 12, 2013 by voluntary consent of the parties. (Exhibit S-Krugman-A, B & C).

Prior to opening statements, and reserving the right to argue the weight to be given to the evidence, the parties stipulated that the authenticity of documents would not be questioned and all documents are considered entered into evidence without opposition. (See Appendix attached to this Order for a complete list of documents entered into evidence by both parties). The parties further agreed that the sole purpose of the hearing was to determine whether MedPrep could resume operation without posing a risk to the health, safety and welfare of the public and that the matter currently before the committee is not disciplinary in nature.[2]

In the Applicant's opening statement, Mr. Cifaldi asserted that MedPrep is a business committed to remaining in the State of New Jersey and is dedicated to producing a safe product and to complying with New Jersey laws. He asserted that MedPrep cooperated fully with all State and Federal investigations and recalled every product they manufactured, not just the suspect

2 As of the date of this Order, no formal Complaint has been filed by the State.

magnesium sulfate, as they are concerned about the health and welfare of their clients. Over 50,000 units[3] of drug product were visualized and a total of six bags were found to be contaminated. All the bags were associated with the Yale New Haven Hospital. Four weeks after the incident, there has not been any report of injury. The Applicant urged the Committee not to rush to judgment and to allow MedPrep to operate with any conditions thought necessary to go forward safely and to consider that with the serious drug shortages which exist, MedPrep provides a valuable service.

In its opening statement, the State argued that MedPrep's history of violations (of New Jersey law, the United States Pharmacopoeia standard [hereinafter "USP"] and its own policies) is such that there is insufficient comfort that history won't repeat itself. In particular, MedPrep's failure to correct deficiencies that they were aware of months prior to the Yale incident, use of Beyond Use Dates ("BUD") without valid justification, false audit trail records, and contamination of personnel and the facility, show that allowing MedPrep to resume operations at this time is premature and would pose significant risk to the public. Further, DAG Ringler argued that it cannot

3The terms "units" and "doses" were used interchangeably throughout the hearing, each referring to the mix of single dose bags, pumps and syringes produced by MedPrep.

be known whether patients have been harmed as a result of the contaminated drug product.

The Applicant began its presentation with testimony on behalf of MedPrep by Mr. Louis D'Orio who has over 20 years of experience in hospital, retail, homecare and sterile compounding. He is the principal of LDT Health Solutions, Inc. (hereinafter "LDT"), a medication safety and quality management consulting company. Mr. D'Orio lectures, consults and develops training and educational materials for State Boards of Pharmacy, Pharma companies, and other clients relevant to technical, regulatory and marketing topics, performance improvement, clean room design and construction. He was accepted as an expert in sterile compounding.

Mr. D'Orio testified that he went on-site at MedPrep in March 2013 following the recall and observed several areas of concern. However, the action plan proposed by MedPrep (Exhibit A-1) and constant vigilance would ensure the public safety were the Board to allow the company to resume operation. Mr. D'Orio testified that no more than 12 individuals should be allowed in the clean room until environmental testing done in a dynamic environment justifies an increase. All employees involved in the production of the contaminated product should be "brought to baseline and re-oriented" through the use of both ACPE accredited learning modules and one-on-one didactic training and

observation. (Exhibit A-P). MedPrep should initially compound only single use syringes to give the staff a chance to get up to speed without the challenge of multiple dosage units. Personnel and materials entering the clean room should be segregated and the anteroom limited to gowning to decrease the bioburden in the clean room. He recommended that a pharmacist within the clean room be dedicated to check inbound and outbound compounded sterile products and that MedPrep should implement a new audit trail to verify at least 8 touch points and checks (double the current checks). (Exhibits A-X, A-1 and A-2). Mr. D'Orio recommended USP General Chapters <797> and <71> compliant tests on samples of every batch of product produced.[4]

Mr. D'Orio discussed the environmental monitoring studies conducted by Gibralter Laboratories, Inc. (Exhibits A-B, A-C and A-D)[5] done on March 16, 17 and 22 after closure of the facility and prior to cleaning. The first two tests revealed the room to be under control and within limits. The March 22 test focused on more challenging locations and identified several out-of-limit variances, e.g. under one technician's chair in the clean room, and in the warehouse area. The March 22 test was done

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4 At MedPrep, each order is a separate batch, so every order would be tested for sterility.

5 Gibralter Laboratories, Inc. is a privately owned testing laboratory and contract research organization with a focus on quality control and testing in bacteriology, mycology, virology, chemistry and in vitro toxicology.

seven days after closure and after construction of a pass-through cabinet. (Exhibit A-D, page 5).

Mr. D'Orio provided an overview of MedPrep's actions to identify potentially contaminated drug product and ensure the facility meets USP standards of environmental control. MedPrep employees used black/white boxes to visualize 75,000 plus doses of recalled product. (Exhibit F). If sterility was in doubt, multiple pharmacists visualized the dose and it was sent out for testing. After extensive testing by Gibralter, a total of six bags, all associated with the Yale New Haven Hospital were found to be contaminated. (See also, Exhibit A-G). The clean room was recertified per CETA recommendations (as referenced by the USP) on March 18, 2013 by ENV services and again on March 26, 2013 by Energy Plus Scientific. (Exhibits A-H and A-J). MedPrep also replaced HEPA filters for the clean room (although not required to do so) and constructed a pass-through cabinet[6] at the recommendation of the FDA to eliminate the need for materials to pass through the anteroom. (Exhibits A-I and A-K).

Mr. D'Orio assisted MedPrep in developing a new policy and procedure manual which complies with USP <797> and New Jersey regulations (Exhibit A-R). He anticipates this manual will also be used as a teaching tool and reference document.

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6 Board approval has not yet been obtained for construction of the new pass-through cabinet.

Mr. D'Orio explained that MedPrep completed a self-assessment in November 2012 which identified several areas of needed improvement. (Exhibit S-Qi-B). Among other things: MedPrep was assigning BUD's beyond USP standards; personal sterility procedures needed improvement; no end product sterility testing was being done; and they could not identify all equipment maintenance logs. Ultimately, Mr. D'Orio opined that, assuming constant vigilance and compliance with the proposed action plan, patient safety would not be compromised by allowing MedPrep to resume operation.

On cross-examination, Mr. D'Orio noted that MedPrep focused on in-process sterility checks (often in excess of that required)and environmental controls, in lieu of testing the end product. Although process checks are considered sufficient by some, D'Orio again recommended that a sample from each batch of product be tested. He agreed that the use of non-sterile carts in the clean room was not good practice. He opined that the proposed action plan (Exhibit A-1) would ensure patient safety, even if the root cause of the Yale contamination was found at MedPrep.

The Applicant next presented Mr. Gerry Tighe, owner of MedPrep, who testified that MedPrep was granted a pharmacy permit in 2002 (Exhibit A-S) subsequent to submitting a detailed plan explaining its business model. (Exhibit A-T). MedPrep

engages only in non-patient specific compounding for in-office use and for hospitals with which they have a central fill or similar agreement. MedPrep currently holds permits to operate as an out-of-state pharmacy in 16 states (Exhibit A-U) and also ships into Pennsylvania where non-resident application is not available. Hospitals represent 75% of MedPrep's client base (70% of which are located in New Jersey). MedPrep has central fill agreements with all in-state hospital pharmacies and agrees not to resume shipments to out-of-state hospitals until central fill agreements are approved by the Board. The remainder of MedPrep product is shipped in small quantities to doctors for in-office use (50% NJ locations) and is not for resale. (Exhibit A-W). In most cases, the client orders the drugs from their distributor, MedPrep picks up the drugs, compounds them and sends them back to the client. MedPrep purchases everything except the drug.[7] In the case of the contaminated product dispensed to Yale New Haven Hospital, Yale provided the drugs and the bags. A drug is used only for the hospital that provided it. Currently, physicians also supply the drug and their product is limited to syringes.

Mr. Tighe testified that until March 2013, MedPrep never received a citation or letter of concern from the Board and was

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7 MedPrep does purchase controlled substances directly from the wholesaler. CDS product represents less than 5% of their total production.

never sanctioned by the FDA. A 2009 five day inspection by the FDA spanning 5 days was closed out with a report advising they were in compliance with New Jersey law and making no "483" observations. The New Jersey Board of Pharmacy inspection in November 2012 identified only three items of concern: the pharmacist/technician ratio was over limit, two technician registrations were expired and the clean room had window sills with less than 45 degree angle. (Exhibit A-Y). MedPrep had requested a waiver of the pharmacist/technician ratio and the technician renewals had been submitted to the Board, but not processed yet. Tighe acknowledged Medprep did not intend to fix the window sill but indicated that the Board inspector advised they should await Board direction because environmental testing did not indicate the sill was creating an air quality problem.

Mr. Tighe noted that, following the NECC meningitis outbreak, MedPrep proactively hired LDT to do a gap analysis. This analysis, based on a self- assessment, was completed in late November 2012. Some recommendations were immediately acted on, others were not. They did reach out to Gibralter Laboratories, Inc. to begin negotiating a contract for end product testing.

Upon learning of the contamination of the Yale product, MedPrep immediately obtained the remaining bags, sent them to a lab for testing and reported the incident to the New Jersey

Board of Pharmacy. Without consulting with the FDA or the Board, MedPrep initiated an immediate recall of all magnesium sulfate product. They were fully compliant with the FDA and NJ Board of Pharmacy investigators and welcomed their assistance in isolating any potentially contaminated product. At the request of the FDA, MedPrep expanded the recall to all products compounded at the facility.

Mr. Tighe is proud of the "relationships of trust" MedPrep has built over a long time with licensed hospital pharmacies and drew the Committee's attention to testimonial letters from clients. (Exhibits A-Q and A-3). He noted that MedPrep provides millions of doses of medication for New Jersey hospitals.

Mr. Tighe explained that MedPrep has now been closed one month. Approximately 70 employees, more than half of whom have been with the company over ten years, have been furloughed or are on unemployment. If they are not able to resume operation within a week or so, Tighe claimed clients will be lost, employees will be gone and the company will have to "shut its doors." If allowed to re-open, Mr. Tighe envisions a slow start-up - with syringes only and about 15 drugs. The role of the pharmacist-in-charge will change to a management role rather than quality assurance and MedPrep will be in compliance with the 2:1 technician/pharmacist ratio. Mr. Tighe concluded by

stating that MedPrep is committed to do whatever the Board would like it to do to re-open and to get their good name back. "Please just tell us what we need to do."

Following Mr. Tighe's testimony, the applicant concluded its case and the State called Barbara Wilimczyk-Macri to testify.

Ms. Wilimczyk-Macri has been an investigator with the FDA for 4 years. She has a BA in molecular genetics and has been trained in inspection of manufacturers of sterile and non-sterile drug product. She was present during six days of the FDA inspection of MedPrep in March 2013. She was asked questions regarding the observations indicated on the FDA Form 483 (Exhibit S-Krugman-H). She had personal knowledge regarding only Observations 2, 5, 6, 7 and 12, and testified each inspector recorded their own observations of deficiencies of 21 C.F.R. 211 (Good Manufacturing Practice) based upon review of documents and interviews of employees. The FDA inspectors did not observe MedPrep in a dynamic environment. She confirmed that Form 483 observations are not final agency findings.

Ms. Wilimczyk-Macri testified that she is not familiar with New Jersey regulations regarding sterile compounding and although she "has read" USP <797> and USP <71> she was not willing to state she was familiar with them. She stated MedPrep fully cooperated with the FDA investigation. The Committee

observed the witness to look over to her supervisor, who was present in the room, prior to answering nearly every question posed to her. Although DAG Ringler represented that this was to confirm her ability to answer questions under FDA confidentiality standards, it was unclear to the committee whether at some points the witness was not also attempting to gain substantive assistance in answering questions. She also refused to answer multiple basic questions on cross-examination, leading to Mr. Cifaldi's motion to strike her testimony based upon his inability to effectively cross-examine her. This motion was denied by the Committee with the caveat that her testimony would be given appropriate weight.

The State's next witness, David William Newton, B.S. Pharm., Ph.D., PAPhA, who provided expert testimony via Skype, has been a professor of pharmacy at four universities since 1976, and a member of committees and panels for USP for 20 years. He was chair of the Sterile Compounding Committee of the USP Council of Experts for the 2000-2005 and 2005-2010 USP quinquennia. (Exhibit S-Krugman-E). He was accepted as an expert in the USP.

Dr. Newton testified that in preparation for the hearing, he was given the FDA Form 483, an FDA 2010 Warning Letter and exhibits A-A through A-N. He did not review all the materials he was given and did not receive Exhibits A-O through A-Z and A-

1 through A-3 submitted by MedPrep. He has not reviewed the revised policy manual, nor the action plan outlined in Exhibit A-1. He has not visited the MedPrep facility and has not spoken with any MedPrep employees. He is not familiar with New Jersey State Board of Pharmacy regulations.

Based on the material he reviewed, Dr. Newton opined MedPrep exhibited flaws in aseptic practices including cleaning and personnel. He indicated the evidence suggests a spore contamination that may have been resident in the facility or transported in by personnel on clothing or shoes. There were several reports of mislabeling such that the strength indicated on the label is either super potent or half the original strength, which he termed particularly dangerous for magnesium sulfate. He testified sterile isopropyl alcohol should be used to reduce the bioburden and USP <797> specifies that both sporacidal and microbacterialcidal cleaners must be used. Dr. Newton noted that Gibralter Laboratories, Inc. tested for mold and yeast and identified out-of-limit variances of Basillus bacteria, which reproduces by spores. He acknowledged that he did not know where the mold was found in relation to the clean room or that the testing was done subsequent to construction of a pass-through door.

Dr. Newton was unable to opine specifically on questions regarding the appropriate number of personnel in a 1,000 square

foot clean room and whether a window sill would compromise sterility in a clean room. Rather, he indicated that the more people and movement in a clean room, the more particulate shedding would occur and the more surfaces and 90 degree corners the more likely that contamination would occur.

When asked about changes which should be made at MedPrep prior to allowing them to resume operation, Dr. Newton testified no USP Chapter applies to low and medium risk compounding. He suggested that best practices for medium risk compounding would include: personnel training in aseptic technique, sequence of gowning, proper hand hygiene, and avoiding all direct contact with contamination.

Due to demonstrated visual contamination of product and to address spore contamination, Dr. Newton recommended MedPrep implement a logical plan of surveillance and investigation to include HEPA filters, floors, corners, ceiling and garments. A sporacidal cleaning agent should be applied to any area identified with possible contaminants. After cleansing, the area should be monitored with active air sampling and contact plates with media that would encourage spores to grow. MedPrep should test environmental sterility using the maximum number of personnel expected to be in the clean room under normal circumstances and using sterile culture media instead of drug product.

Dr. Newton noted that an "in control" process should result in all sterile product, and the USP does not generally require end product sterility testing for medium risk products. A "best practice" for a pharmacy engaged in high volume medium risk compounding would be to verify component products are from a trustworthy source. However, validation sterility testing would be required to utilize Beyond Use Dating to verify strength, purity and sterility and maintenance of bacterial endotoxins within the limit of USP for each drug product.

Dr. Newton testified that there is an expectation of some contamination due to personnel when a large volume of medium risk product is compounded. The statistical likelihood of contamination in a medium risk sterile compounding environment would be approximately 1%. He was unable to opine on cross-examination whether 20 instances of contamination out of 44,000 total batches (2.8 million doses) over a two year period would fall under 1%. With regard to whether MedPrep took proper steps following identification of contaminated personnel, Dr. Newton was unable to identify anything MedPrep should have done, but didn't, based on the record before him.

Dr. Newton acknowledged that in the event of a shortage of magnesium sulfate "an alternative source would need to be obtained. It is a medically necessary drug."

In conclusion, Dr. Newton opined that, assuming the factual observations in the FDA Form 483 are true, MedPrep was not compliant with USP <797>.

The State also presented testimony of Investigator Tony Qi who had six years of experience as a retail pharmacist, a regional clinical consultant for a Pharmacy Benefit Manager company for 8 years and a hospital IT pharmacist for 1 year. He holds a BA in pharmacy and will soon graduate with a Masters degree in Pharmacy. He is registered as a pharmacist in New Jersey and Pennsylvania.

Mr. Qi conducted a routine inspection of the MedPrep facility in November 2012 at which time he identified the three deficiencies noted on page 10, above. (Exhibit A-Y).

In March 2013 he returned to MedPrep to investigate the contamination of magnesium sulfate product dispensed to Yale New Haven Hospital. He testified that his main objective was to assist the CDC and Department of Health to contain the risk, and determine the root cause and scope of the contamination. MedPrep was very cooperative and timely produced everything requested. In response to Mr. Qi's request for lab reports to sustain 30 BUD dating, MedPrep provided a 2008 report issued by Eagle Analytical Services. (Exhibit S-1). MedPrep was unable to produce specific evidence to support a 45 day BUD.

Mr. Qi testified regarding the log sheets used at MedPrep to capture the preparation record at the work stations used to compound the contaminated magnesium sulfate on February 14, 21 and 28, 2013. (Exhibit S-2). The logs list only one technician and one pharmacist, yet employees indicated that when large batches of product were produced the drug might be compounded at two workstations and finished off at other work stations. Mr. Qi noted it is unclear whether anyone else may have worked on the contaminated drug product.

MedPrep relied on a random "real time" sterility testing program. They picked one unit from each type of product (syringe, bag, pump) from each product line per working day to be tested. Mr. Qi was aware of this practice during the November inspection but did not highlight it as a problem. As the November inspection was a routine inspection, not an investigation, he was not in possession of additional documents which may have indicated MedPrep was not utilizing sufficient overall testing procedures. Mr. Qi was aware the pharmacist/technician ratio exceeded the regulatory limit in November 2012, but did not know the ratio in March 2013.

During the March 2013 investigation, Qi observed that a rolling cart was stored in the warehouse area until drug product was transported from the warehouse to the clean room. The cart would then be cleaned, sprayed with non-sterile isopropyl

alcohol and transported to the clean room via the anteroom. Mr. Qi opined that this process would increase risk of contamination.

In Mr. Qi's opinion there are multiple factors that might have led to the contamination of the magnesium sulfate that was dispensed to Yale New Haven Hospital and the root cause may never be found. He noted that the volume of magnesium sulfate compounded by MedPrep increased from 4,000 units in January to 7,000 units in February, but there was no increase in sterility testing. The warehouse contains the same species of mold that was found in the contaminated bags. The rolling cart and/or bags could have contracted spores in the warehouse and carried them to the clean room. The bags were not wiped prior to entry to the clean room because paper labels affixed to the bags could "smear." The non-sterile isopropyl alcohol used does not kill spores. Vents in front of the two working stations implicated in the Yale contamination were obstructed by boxes. Smoke tests showed the vents were working, but air flow may have been compromised. Finally, bags may have been transferred to other work stations to be completed.

Mr. Qi does not believe that additional time is necessary to adequately investigate this matter. All recalled bags have been visually inspected over three different time frames by the

FDA, CDC and the Board and there have been no additional reported incidents.

Finally, enforcement bureau investigator Leida Martinez testified on behalf of the State. Ms. Martinez assisted in the March 2013 investigation with Mr. Qi. She spoke to employees who indicated that MedPrep's audit trail and "batch record" don't include a space to record all employees who assist in the compounding process or to reflect that product was moved to another work station. At least one employee indicated she signs batch records even when she doesn't work on the batch. (Exhibits S-Martinez-A and B). Although staff were cooperative with Ms. Martinez, some could not recall if they worked on the contaminated batches.

At the conclusion of testimony, the parties gave closing arguments. The Applicant argued that MedPrep has been a responsible and valuable member of the New Jersey healthcare system for many years, they are committed to full compliance with Federal and State law and that allowing them to resume business subject to the proposed action plan will not place the public at risk of harm. The State argued that MedPrep has demonstrated a systemic failure to comply with State and Federal regulations and failure to act on known deficiencies such that it would be premature and imprudent to allow them to resume operation until the State has had a chance to review thousands

of documents to determine if suspension or revocation is appropriate.

Discussion

MedPrep appears to have been fully cooperative with State and Federal investigations following contamination of product compounded by MedPrep and dispensed to Yale New Haven Hospital. Following recall of all MedPrep product (in excess of 40,000 units[8]) only six[9] bags were found to be contaminated, and all these bags were associated with the Yale facility. As of the date of hearing, no injuries or illness attributable to the contamination have been reported and MedPrep has voluntarily refrained from practice for more than four weeks.

The investigation following the Yale contamination has revealed multiple deficiencies which are possible violations of State and Federal law. Of particular concern are MedPrep's lack of an adequate audit trail; use of BUDs that are not compliant with USP standards; and labeling deficiencies.[10] However, the Committee is keenly aware we are charged solely with determining whether MedPrep can resume business without unnecessary risk to the public health, safety and welfare.

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8 Testimony varied between in excess of 40,000 and in excess of 75,000 units.
9 At the conclusion of deliberations and following the announcement of the Committee's decision, DAG Ringler advised the Committee that she was advised within the prior hour that the FDA had found one additional bag had grown mold.
10 The Committee notes that although an inspection was done by enforcement bureau investigators in November 2012, these violations were not brought to the attention of MedPrep at that time.

These proceedings are not disciplinary in nature, indeed no action seeking discipline has been filed as of this time.

The experts for both the State and MedPrep agreed on key points including that prior to resuming operation, MedPrep would need a logical plan of surveillance and investigation encompassing: appropriate environmental and personnel controls, re-training of staff, implementation of sterility testing to validate beyond use dating, and limiting the number of people in the clean room pending appropriate environmental testing. Indeed, the State's Expert acknowledged in his testifimony that several recommendations made by Mr. D'Orio were "highly desirable."

A compounding pharmacy is a dynamic atmosphere where any number of things can increase bioburden and introduce risk of contamination. It is telling that neither expert opined that the violations observed by inspectors were so egregious that the public would be put at risk if MedPrep were allowed to resume business with a corrective action plan in place. Similarly, neither expert testified that it is possible to eliminate all risk of contamination from a compounding environment. Although present[11] for Mr. D'Orio's testimony regarding MedPrep's proposed plan of action to lower the risk of environmental and personal

11 Dr. Newton was able to view and hear the proceedings on April 12, 2013 via a Skype connection.

contamination, the State's expert never indicated that he disagreed with Mr. D'Orio's testimony or that the plan of action suggested by MedPrep and endorsed by Mr. D'Orio were insufficient to protect the public health. The Committee has incorporated all of the recommendations of the State's expert into the resolution recommended by the Committee herein.

There was considerable testimony regarding end product sterility testing. Significantly, the State's expert acknowledged that end product testing is required by Federal good manufacturing practice, but not USP <797> for products with Use-by Dates within the USP guidelines. Yet, MedPrep has volunteered to test end product of every batch of product compounded, which exceeds even USP validation testing requirements for beyond use dating.

It is also noteworthy that the FDA has not yet taken any action to attempt to sanction or close the facility and that the "observations" in the FDA Form 483 are not final findings of violations of law.

Mr. Tighe's testimony, which we found credible and sincere, demonstrated that he is committed to ensuring that MedPrep not only is in compliance with State and Federal regulations regarding the operation of compounding pharmacies, but that he is eager to go above and beyond these requirements to regain the good name of the company and ensure patient safety. Mr. Tighe

indicated a strong commitment to initially reduce production volume and the number of employees in the clean room, retrain all employees, improve the audit trail and contract with a third party monitor to oversee operations and ensure compliance with New Jersey Board of Pharmacy regulations and USP <797>. Indeed, MedPrep has already taken significant steps to implement many of these tasks.

The record thus far does not convince the Committee that MedPrep cannot be trusted to implement improvements and safeguards to ensure safe practices. Indeed, the Committee is assured that the public would not be placed at risk of harm if MedPrep resumes operation pursuant to a controlled plan as outlined below, including among other things: extensive staff retraining; environmental testing and sporacidal cleaning; third party monitoring; validation of environmental monitoring with dynamic air testing; and a simulated four day production week to afford an appropriate platform for observation of aseptic technique and dynamic air testing prior to fulfillment of customer orders. Whether MedPrep was the root cause of the Yale contamination or not, compliance with the steps outlined herein would alleviate any concerns that might exist.

The Committee had concerns that the pharmacist-in-charge was not available to provide testimony regarding MedPrep's operations, as the deficiencies noted on the record thus far are

virtually all within the responsibility of the pharmacist-in-charge. However, any lack of professional judgment or oversight that might have existed due to possible inadequacies of the pharmacist-in-charge or other staff can be addressed by the removal of the pharmacist-in-charge from that position and placement of a third party monitor.

The Committee is aware that recent events regarding the compounding of medication, such as the meningitis outbreak tragedy, have led to more intense scrutiny of compounding pharmacies. As noted by both experts, compounding pharmacies fill an important role in the health care community, assisting hospitals with pharmaceutical needs and compounding product when there are shortages of necessary medications. While we believe that increased scrutiny is desirable, and recognizing, as does the State's expert, that there will always exist a small measure of risk, we are seeking to take a measured, careful approach to the issues presented, permitting practice only after a demonstration of remediation consistent with safe medium risk compounding.

After hearing the testimony presented in this case[12] and reviewing all documents available to us, we find it consistent

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12 Following the reading of the oral order on the record, the State made a motion requesting the Committee to reconsider its decision, based upon new information, which was conveyed in a phone call to counsel that the FDA had an additional bag of magnesium sulfate that tested positive for fungal growth. The magnesium sulfate was compounded and dispensed by MedPrep in a

with the public health and safety to allow MedPrep to preliminarily resume operations subject to the controls and restrictions outlined in this Order and to begin dispensing to the public only following approval of reports required to be submitted by a third party monitor.

ACCORDINGLY, IT IS, on this 19th day of April, 2013,

ORDERED, as announced orally on the record and effective April 15, 2013:

1. MedPrep shall contract with a third party monitor ("the Monitor") pre-approved by the Board to fulfill the monitoring and reporting requirements outlined in this Order for a minimum period of six months and until further Order of the Board. For the purposes of this Order, LDT Health Solutions, Inc. is Board-approved. All costs associated with the

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bag manufactured by Hospira and provided to MedPrep by Yale New Haven Hospital. Counsel for the State argued that this new information shows the MedPrep situation continues to evolve and it is premature to allow the pharmacy to reopen. Counsel for MedPrep objected based upon the last minute nature of this information, lack of documentary evidence, lack of chain of custody proofs and inability to cross-examine. Counsel for MedPrep also argued that the lot identified by the State as being contaminated had been tested previously with negative results as illustrated by Exhibit A-Z in evidence.

The Committee deliberated regarding the State's motion, and unanimously voted to pass a motion which clarified its previous ruling and included a modification including that: the Order previously read into the record requires that MedPrep engage in training of staff prior to beginning a minimum of 4 days of simulated production, with observed validation testing of aseptic technique. This period was to be followed with a report to the Board President and subject to his approval prior to opening for business and prior to any product being dispensed to the public. Based upon the new material brought to the committee's attention, the Committee will request consideration of any such monitoring report, which we anticipate will not arrive until the beginning of next week in any event, to be considered by the full Board rather than by the Board President at its meeting on Wednesday April 24, 2013, if the report is available by that time.

monitoring outlined in this Order shall be the responsibility of, and paid directly by, MedPrep.

2. Prior to commencement of a simulated production week as described in this Order and prior to commencement of fulfillment of customer orders, all compounding, packaging and labeling employees shall perform three core training modules provided by LDT and complete the first two modules (18 CEU) of the Critical Point Internet-based USP <797> training program. Each employee shall certify in writing that they have completed the training and the certifications will be provided to the Board by the Monitor.

3. Prior to commencement of fulfillment of customer orders MedPrep must submit written evidence to the Board showing they have conducted sporacidal inspection and cleansing which is acceptable to the Board. MedPrep must also submit a proposed standard operating procedure for ensuring routine cleansing of the pharmacy to include but not be limited to sporacides and consistent with the USP and Board of Pharmacy regulations.

4. Prior to commencement of fulfillment of customer orders the Monitor shall validate, in writing, to the Board that all employees have been visually observed by the Monitor to have proper aseptic techniques and gowning, garbing and gloving processes for a minimum of 4 production simulation days. The simulation shall include observation of all processes conducted

in a normal production week including but not limited to orders of large batch quantities to simulate expected order volume and type (such as syringes and bags). Media may be used.

5. During the simulated production week, there shall be validation of environmental monitoring with dynamic air testing conducted with twelve people in the clean room. Results shall be reported in writing by the Monitor to the Board.

6. Prior to commencement of fulfillment of customer orders, a new pharmacist-in-charge shall be in place. The pharmacist-in-charge and the pharmacist supervising the clean room may not be the same person. Neither position can be filled by the current pharmacist-in-charge. The names of the individuals assigned each title shall be reported in writing by the Monitor to the Board.

7. Upon approval by the Board of the reports required to be submitted by the Monitor, MedPrep may commence production of fulfillment of customer orders subject to the following:

A. Staffing

i. MedPrep shall abide by a 2:1 pharmacy technician to pharmacist ratio as set forth in N.J.A.C. 13:39-6.15 until such time that MedPrep submits and the Board approves a modification of that ratio;

ii. MedPrep shall limit the number of personnel within the clean room to 12 until the completion of environmental testing

under dynamic conditions that supports an increase in that number; and

iii. MedPrep shall implement an additional layer of inspections through the creation of a dedicated supervisory pharmacist position within the cleanroom.

iv. MedPrep shall temporarily reassign those staff members directly involved in the compounding of the contaminated bags in question.

B. Operations

i. MedPrep shall cease use of all Baxter Viaflex bags until further Board Order;

ii. MedPrep shall compound continuous infusion bags no earlier than 2 weeks following reopening;

iii. MedPrep shall dedicate a specific work station for the compounding of penicillin and beta-lactam drugs;

iv. The dedicated supervisory pharmacist position within the cleanroom will be responsible for the following activities: secondary check of batch kit upon introduction to cleanroom; confirmation of compounding components prior to beginning of compounding; primary inspection of completed batch including visual inspection of final containers, confirmation of components used, accuracy of labels, proper completion of batch record/audit trail;

v. All compounding staff will be required to don sterile gowns;

vi. All staff will be required to maintain dedicated scrubs and shoes for the workplace. No street clothes will be permitted in the cleanroom or the area immediately outside the cleanroom;

vii. All staff performing wipe down of supplies immediately before introduction to the cleanroom will be required to wear a hairnet, mask, smock and sterile gloves;

viii. All staff performing labeling, packaging and inspection of final containers will be required to wear hairnet and smock; and

ix. MedPrep shall implement the following measures with respect to cleaning and disinfection:

a. Policy and Procedures clearly describing routine cleaning schedules.

b. Preparation of cleaning solutions will be reviewed and updated to clearly describe acceptable detergents and disinfectants (to include sporacidal cleansers), including proper preparation.

c. Sterile 70% Isopropyl Alcohol will be used for all disinfection of critical work surfaces, critical injection sites, gloved hands and all supplies that are introduced into the cleanroom.

d. Only disposable cleaning supplies will be used.

C. Labeling

i. Labeling accompanying the compounded product will follow the product throughout the process in a sealable plastic bag;

ii. The label accompanying the compounded product will state the date and time that the product was prepared; and

iii. MedPrep shall utilize a process by which the label and the compounded product will be checked at least six times, in the manner described below:

a. There will be a pre-compounding inspection of the compounding batch kit by a pharmacist.

b. The Clean Room Supervising Pharmacist will perform the same check, as in section a above, but in the clean room;

c. The registered pharmacy technician in the clean room at the compounding station will perform an identical check as in section a above.

d. The Clean Room Supervising Pharmacist will perform an in-process check of the drug and diluent prior to compounding;

e. The Clean Room Supervising Pharmacist will inspect the completed batch for appropriateness and accuracy. This check will include, but is not limited

to the clarity of the compound, dose, label, and spent vials.

f. After labeling, the pharmacist outside the clean room will perform a final check of each dose for integrity, clarity, label accuracy, and the proper recordation of information. The audit trail shall identify each person involved in any way with the production of compounded sterile product from beginning to end.

D. Monitoring

i. The Monitor will have at least one individual physically present at MedPrep during all production to witness all aspects of the operation and monitor MedPrep's implementation of the corrective action plan, implementation of new policy and procedures, documentation procedures, including the documentation of information pursuant to the audit trail, and the laboratory testing agreed to by MedPrep. The Monitor will submit weekly reports to the Board for the first month of operations, followed by bi-weekly reports during the second and third months of operations, followed by monthly reports thereafter;

ii. The Monitor will assist MedPrep in the training and/or recruitment of a permanent Quality Manager; and

iii. MedPrep will implement a formalized Variance Reporting procedure by which there will be immediate notification of MedPrep's President, as well as the Monitor, of any incident. The Monitor will notify the Board of Pharmacy in writing and via telephone within 48 hours of any out-of-limit variances.

E. Beyond-Use Dating

i. MedPrep shall adhere to the guidelines set forth by N.J.A.C. 13:39-11.11(as they currently appear or subject to modification of the regulation), USP General Chapter <797>, and Med Prep Policy # 06-02.01 - Sterile Formula Stability and Beyond-Use Dating (BUD) Guidelines to determine the Use-by Date for all compounded sterile preparations (CSPs) compounded by Med Prep as follows:

a. Absent sterility testing, MedPrep shall assign a maximum Use-by Date of 9 days from the date the product was compounded for medium risk products in cold temperature storage and a maximum Use-by Date of 45 days from the date the product was compounded for medium risk products in a frozen state.

b. Additionally, MedPrep shall assign a maximum Use-by Date pursuant to the protocols described below, based on samples obtained by Gibraltar Laboratories of Fairfield, NJ (Gibraltar Laboratories) up through March 22, 2013:

1. Gibraltar Laboratories has or will conduct method suitability testing of all USP <71> sterility tests conducted by Gibraltar for CSPs compounded by the Pharmacy;
2. Following these method suitability tests, a USP <71> Sterility test will be conducted to assure that MedPrep can compound the CSP under sterile conditions;
3. The final step in determining a valid Beyond-Use Date will be for MedPrep to request that the contracted laboratory conduct a container closure integrity test, as described by the USP; or
4. alternatively by conducting three consecutive USP <71> compliant sterility tests on day(s) 1,15, and 30.

8. This Order is subject to adoption, modification or rejection by the full Board of Pharmacy after consideration of the written record at its next meeting, currently scheduled for April 24, 2013.[13]

NEW JERSEY STATE BOARD OF PHARMACY

By: Edward G. McGinley RPh

Edward G. McGinley, R.P.
Board President/Committee Chair
For the Committee

13 The Committee notes that MedPrep agreed to run sterility tests on a sample of every batch of drug produced and agreed to refrain from shipping to out-of-state pharmacies until they have valid central fill agreements approved by the Board. These terms were inadvertently left out of the verbal order read into the record on April 15, 2013, and the Committee recommends that the full Board modify the Order to incorporate these requirements.

APPENDIX

Applicant's Exhibits in Evidence

A-A	Expert Report and Curriculum Vitae of Louis S. Diorio, R.Ph.
A-B	Environmental Monitoring Study, March 16, 2013
A-C	Environmental Monitoring Study, March 17, 2013
A-D	Environmental Monitoring Study, March 22, 2013
A-E	Maps of the MedPrep Facility
A-F	Visual Inspection Reports
A-G	Laboratory Tests of Source Products
A-H	Clean Room Certification, ENV Services
A-I	Energy Plus Scientific Report
A-J	Clean Room Certification, Energy Plus Scientific
A-K	Photographs of Pass-Through Cabinets
A-L	(Product Flow Diagram- replaced by Exhibit A-X)
A-M	Interim and Final Reports by Gibralter Laboratories, Inc.
A-N	(Updated MedPrep Policies and Procedure Manual – replaced by Exhibit A-R)
A-O	(Work Flow Audit Trail Form – replaced by Exhibit A-2)
A-P	Continuing Education Coursework Manual
A-Q	Customer Testimonials
A-R	Revised Policy and Procedure Manuary
A-S	Pharmacy Permit Approval
A-T	March 2002 Letter to Board
A-U	Out of State Pharmacy Licenses
A-V	Central Fill Approvals
A-W	Exemplar Contract
A-X	Product Flow Diagram
A-Y	New Jersey Pharmacy Inspection Reports
A-Z	Gibralter Laboratories, Inc. Report, April 11, 2013
A-1	Action Plan proposed by MedPrep
A-2	Work Flow Audit Trail Form
A-3	Reference Letter, Pamela Allen, RP

State's Exhibits in Evidence

S-Krugman	Certification of Jodi Krugman, DAG
S-Krugman-A	Third Voluntary Consent Order Extending Time, Filed April 5, 2013
S-Krugman-B	Second Voluntary Consent Order Extending Time, Filed March 22, 2013
S-Krugman-C	Voluntary Interim Consent Order, Filed March 15
S-Krugman-D	MedPrep Recall Notices
S-Krugman-E	Curriculum Vitae of David William Newton, B.S. Pharm., Ph.D., PAPhA
S-Krugman-F	Email dated April 3, 2013 from Stephen Kalinowski
S-Krugman-G	Copy of printout from MedPrep's website, dated April 4, 2013
S-Krugman-H	Report of Inspection of the United States Department of Health and Human Services, Food and Drug Administration, dated April 3, 2013.
S-Martinez	Certification of Leida Martinez, Investigator, Enforcement Bureau
S-Martinez-A	Signed Statements from pharmacy technicians Marilyn Rible; Patricia Sanford; Christina Mordaunt; Patricia Chandley; and Lori Coplan
S-Martinez-B	Statement from Nancy E. McIlvaine, R.P.
S-Qi	Certification of Tony Qi, Investigator, Enforcement Bureau
S-Qi-A	Selected documents provided by MedPrep to the FDA
S-Qi-B	USP<797> Survey Analysis, prepared by LDT Health Solutions, Inc. dated November 27, 2012
S-Rubinaccio	Certification of Executive Director Anthony Rubinaccio
S-1	2008 Eagle report(30 day BUD testing)
S-2	MedPrep Log Sheet used to capture preparation record at workstations