DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
10 Waterview Blvd., 3rd Floor Parsippany, NJ 07054 (973) 331-4900 Fax:(973) 331-4969 Industry Information: www.fda.gov/oc/industry	03/15/2013 - 04/03/2013* FEI NUMBER 3002902471

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Gerry Tighe, President

FIRM NAME	STREET ADDRESS
MedPREP Consulting, Inc.	1540 W Park Ave Ste 5
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Tinton Falls, NJ 07712-3192	Processor of Injectable Drug Products

This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

For the aseptic processing of all injectable drug products in IV Bags and pre-filled syringes, such as:

- Magnesium Sulfate 2 grams in 50 mL 5% Dextrose, LOT: 0220138YNHMC, USE BY: 4/16/2013
- Heparin 5,000 units in 1000mL of 0.9% NaCL, LOT: 0312138YNHMC, USE BY 04/11/2013
- Oxytocin 20 units added to Lactated Ringer's 1000 mL, LOT: 0312137YHBH, USE BY: 4/26/2013
- Dexamethasone 20 mg in 50mL 0.9% Sodium Chloride, LOT: 0312139YNHMC, USE BY 04/02/2013
- Vancomycin HCL added to 250mL 0.9% Sodium Chloride, LOT: 03121314YNHMC, USE BY: 4/11/2013
- Phenylephrine 100 mcg per mL, LOT: 0313139STR, USE BY: 04/27/2013

QUALITY SYSTEM

OBSERVATION 1

There is a failure to thoroughly review any unexplained discrepancy and the failure of a batch or any of its components to meet any of its specifications whether or not the batch has been already distributed.

A. Your firm's complaint files indicate that within the last twenty-four months your firm incorrectly compounded, incorrectly labeled, or incorrectly packaged approximately 20 injectable drug products. You released and distributed those products and then needed to retrieve them from your customers for destruction or re-labeling. A thorough investigation was not conducted and corrective and preventative actions were not implemented or documented. Some examples from 2012 include:

1. A label control error resulted in a pre-filled syringe of Zosyn with 3.375 grams of active ingredient being incorrectly labeled to contain only 2.25 grams of the active ingredient (Lot 1002127CCH USE BY: 11/01/2012). The firm's customer noticed the volume difference in the syringe, and this super-potent drug product was returned and destroyed.

2. A label control error resulted in (b)(4) pre-filled syringes of Aztreonam with 2.0 grams of the active ingredient in 10 mL of Sterile Water For Injection being incorrectly labeled to contain only 1.0 gram of the active ingredient (LOT 0327121BCH, USE BY: 06/25/2012). The firm's customer noticed the difference in the purchase order and this super-potent drug product was returned, re-labeled with the correct dosage strength, and re-shipped.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Russell Glapion, Investigator James A. Liubicich, Investigator Barbara J. Wilimczyk-Macri, Investigator Jose M. Cayuela, Investigator	04/03/2013

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3. A label control error resulted in (b)(4) IV bags of Magnesium Sulfate Injection with 2.0 grams of the active ingredient being incorrectly labeled to contain only 1.0 gram of the active ingredient (LOT 03261211JS USE BY: 05/10/2012). The firm's customer noticed the purchase order discrepancy and this super-potent drug product was returned, re-labeled with the correct formulation, and re-shipped.

4. A label control error resulted in (b)(4) pre-filled syringes Zosyn 2.25 gram in sterile water being incorrectly labeled as Zosyn 2.25 gram in 5% Dextrose (LOT 0117129CCH USE: BY 02/16/2012). The firm's customer noticed the mistake and this drug product was returned, re-labeled with the correct formulation, and re-shipped.

5. A secondary packaging error resulted in a light sensitive drug product, (b)(4) IV bags of Bupivacine, 0.5% Epinephrine 1:200,000 Normal Saline, not being packaged is in the correct protective bags (LOT 1008127R USE BY: 10/28/2012). The firm's customer noticed the mistake and drug product was returned and destroyed.

6. (b)(4) IV bags of Gentamin, 80 mg in 25 mL of 0.9% NaCl, a frozen drug product, were shipped without temperature controls (LOT 06191210YNHMC, USE BY: 07/19/2012). This temperature abused drug product was returned and destroyed.

B. Investigations into product sterility and environmental monitoring test failures are not documented. Additionally, investigations into failing performance challenges do not include the evaluation of product impact.

1. You have your employees conduct a performance challenge of their aseptic technique on a (b)(4) basis by having them use media at the end of a processing run using the tailings of the drug product and the same container closure system that they just finished processing. Since 2011, there were at least 20 failed employee performance checks recorded after employees processed injectable drug products such as Heparin, Avastin, Oxytocin, and Norepinephrine. Contaminated aseptic performance check samples were analyzed and organisms such as bacteria (*Staphylococcus* sp. and *Bacillus* sp.) and mold (*Penicillium* spp) were identified. Your investigations into the failed performance checks did not evaluate the possible impact on the finished drug products.

2. Your microbiological testing identified at least seven drug products in the last 26 months that had either turbid broth or particle matter floating in injectable drug products such as Lidocaine, Bevacizumab, Heparin and Famotidine. Although re-test results are documented as passing in an environmental testing log, there is no investigation that explains the basis upon which the original failing test results were negated. In addition, you used an in-house re-test procedure that involves using (b)(4) [redacted] This procedure is not in writing, it is not a compendial method, and you have not validated it.

3. There are no investigations into the two non-viable room particle count excursions.
   a. During the environmental monitoring on 05/17/2012, particle counts of 275, 127, and 154 were noted at ISO 5 (Class 100) Laminar AirFlow Workbench 6, exceeding the specification of 1 (b)(4) Your environmental testing log noted that the root cause was that the HEPA was turned off to change a pre-filter. There is no formal

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investigation to assess the possible impact of this deviation on the injectable drug products processed at this workbench (Atropine Batch # 0516121YOP1, Atropine Batch # 0516121YOP2, Sodium Citrate Batch # 0517121NYPC, and Sodium Citrate Batch # 0517121NYPCO). No corrective or preventive action was implemented to reduce the chance of this type of deviation from occurring again.

b. On 01/20/2011, you recorded particle counts of 555, 1055, and 207 in the ISO 6 (Class 1,000) area referred to as Buffer Zone 1 (BZ1), near the cleanroom entrance and exit. You did not investigate the possible impact of this deviation on the injectable drug products processed near this area, or evaluate a possible root cause and implement a corrective or preventive action.

LABORATORY SYSTEM

OBSERVATION 2

Laboratory controls do not include the establishment of scientifically sound and appropriate sampling plans and test procedures designed to assure that drug products conform to appropriate standards of identity, strength, quality and purity.

Specifically, your firm produces approximately (b)(4) lots of injectable drug products per day and does not perform the following testing:

A. Assay or product identification testing for any sterile injectable drug product produced.

B. Sterility testing for all drug products produced is not performed. Less than 10% of the injectable drug products are tested for sterility per day (b) (4) lots, on average) and those drug products are tested using non-compendial methods that have not been validated to demonstrate that they are at least as good as the compendial methods. The written test method for the in-house sterility test does not include the quantity of drug product to be tested. In addition, there is no assurance the media, (b) (4) , is capable of detecting all growth.

C. Endotoxin testing data for any lot of sterile injectable drug product produced.

D. Antimicrobial effectiveness testing to support drug product "Use By" dates for sterile drug products containing preservatives. The firm processes approximately (b)(4) drug products with preservatives. For example, Oxytocin, which is labeled with a "Use By" date of 45 days after the date of preparation.

OBSERVATION 3

An adequate number of batches of each drug product are not tested to determine an appropriate expiration date.

Specifically, you produce approximately 113 injectable drug products, including the different packaging sizes and containers

(IV bags or pre-filled syringes.) For 94 of those drug products, you relied exclusively on literature searches to establish "Use By" dates for the drug product's. You have some stability data on the other 19 drug products, but the studies for those drug products were incomplete. For example, there was no stability study protocol or final report for Oxytocin 80 Units in 1000mL Dextrose 5% Lactated Ringers (D5LR) IV Bag, but there was testing data at two time points. That limited data was extrapolated to support all other Oxytocin/Diluent combination "Use By" dates.

OBSERVATION 4

Reserve drug product samples are not retained and stored under conditions consistent with product labeling.

Specifically, you do not collect or store retains for any of the injectable drug products that you produce. Upon receipt of a complaint on March 14, 2013 for visible contamination in Magnesium Sulfate IV bags, you could not visibly examine, nor perform any analytical testing of retains.

FACILITIES AND EQUIPMENT SYSTEM

OBSERVATION 5

Equipment used in the manufacture, processing, packing or holding of drug products is not of appropriate design to facilitate operations for its intended use and cleaning and maintenance.

Specifically, your firm lacks adequate environmental monitoring data to support that the process capabilities of its cleanroom can maintain ISO 5 (Class 100) conditions at the (b) (4) work stations, the ISO 6 (Class 1000) conditions in the surrounding area, and the ISO 7 (Class 10,000) conditions in the gowning room (anteroom) given the following design limitations and practices.

A. The ISO 7 gowning room serves as the entrance and exit for all personnel, sterile drug products, containers and closures, and non-sterile, non-sanitized processing equipment such as carts and totes that are brought in and out of the cleanroom numerous times during the work day.

B. (b) (4) cleanroom HEPA filters have operated with leaks for at least one year without being repaired or replaced.

C. There is a sink, an electric hand blow drier, mops and other cleaning equipment stored in the ISO 7 gowning room.

D. Several cleanroom exhaust vents are blocked on either the inside or the outside of the cleanroom by shelves, bins, and totes.

E. There is an excess of particle generating non-sterile material in the cleanroom such as clipboards with papers, adhesive notes attached to equipment, a radio, and a telephone.

F. (b) (4) is used as the final sanitizing agent in the cleanroom.

G. Approximately (b) (4) inadequately gowned employees with exposed skin and exposed street clothes (see observation 6) work in a (b) (4) square foot cleanroom.

H. Smoke studies were not performed under dynamic conditions to verify that operators and processing equipment do not alter or impede the cascade of air from the HEPA filters to the ISO 5 workbenches where injectable drug product is opened and manipulated, and to the rest of the ISO 6 cleanroom.

OBSERVATION 6

Clothing of personnel engaged in the manufacturing and processing of drug products is not appropriate for the duties they perform.

Specifically, the gowning worn by employees entering the ISO 6 cleanroom includes an individually wrapped, non-sterile laundered smock that is approximately knee-length. The smock can be reused during an operational day by hanging it within the ISO 7 gowning room and spraying the smock with (b) (4) before re-donning.

OBSERVATION 7

Written procedures for cleaning and maintenance fail to include maintenance and cleaning schedules, description in sufficient detail of methods, equipment and materials used, instructions for protection of clean equipment from contamination prior to use, and parameters relevant to the operation.

Specifically, the cleaning agent, (b) (4) used within your cleanroom is not documented as an approved cleaning agent as per Procedure 4.00, Med Prep I.V. Specialty Pharmacy Facility Cleaning, Rev. 09/08/06 which only lists (b) (4) (b) (4). Additionally, there is no documentation to support that the dilution of (b) (4) (b) (4) is adequate as a sanitization solution.

OBSERVATION 8

The operations relating to the processing and packing of penicillin are not performed in facilities separate from those used for other drug products for human use.

Specifically, your firm is processing Penicillin, and penicillin-type injectable drug products such as Oxacillin, in the same cleanroom with your non-penicillin products. The absence of a structurally isolated area creates the potential that accidental breakage of vials of penicillin could contaminate your other drug products. Additionally, the lack of separation creates the

risk that a penicillin product could be mislabeled as a non-penicillin product. A number of problems with your product and label control were noted during the inspection. Patients allergic to Penicillin could be adversely effected (Observation 1A).

OBSERVATION 9

Separate or defined areas to prevent contamination or mix-ups are deficient regarding the manufacturing and processing operations.

Specifically, your firm is processing beta-Lactam injectable drug products such as Cefazolin and Cefepime from glass vials to IV bags and syringes in the same cleanroom with the rest of your non-Beta-Lactam drug products. The absence of a structurally isolated area creates the potential that accidental breakage of vials of Beta-Lactam drug products could contaminate your other drug products. Patients allergic to Beta-Lactam drug products could be adversely effected. Additionally, the lack of separation creates the risk that a beta-Lactam drug product could be mislabeled as a non-Beta-Lactam drug product. A number of problems with your product and label control were noted during this inspection (Observation 1A).

MATERIALS SYSTEM

OBSERVATION 10

Written procedures are lacking which describe in sufficient detail the receipt, identification, storage, handling, sampling, testing, approval, and rejection of components, drug product containers, and closures.

Specifically, you purchase or receive from customers, sterile articles including: drug products, diluents in IV bags, syringes, and sterile processing equipment. You use these items to produce injectable drug products without assurance of sterility by either qualifying the vendor and reviewing certificates of sterility, or conducting your own quality assurance testing on those articles.

PRODUCTION SYSTEM

OBSERVATION 11

Master production and control records lack complete manufacturing and control instructions and sampling and testing procedures.

Specifically,

A. Your firm's Master Batch Records do not include copies of the starting component label, so that individuals can verify that the correct product components are being used. In the last 24 months, approximately 20 finished

injectable drug products were distributed after they were incorrectly compounded, incorrectly labeled, or incorrectly packaged (See Observation 1A).

B. Your firm's Master Batch Records only require that the primary technician and the primary pharmacist sign or initial the production record. When other technicians or pharmacists assist, and/or work with part of the lot at another workstation, that information is not recorded. This does not allow for a complete review of the manufacturing process prior to finished product release or during any subsequent investigation. For example, environmental monitoring data cannot be completely correlated to the all personnel and applicable equipment.

OBSERVATION 12

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not established, written, and followed.

Specifically,

A. Procedure 6.02, Microbiological and Environmental Testing/Alert and Action Thresholds and Retest Requirements, does not require immediate corrective actions for action limit excursions. The area or employee is retested an additional (b) (4) and the location is only taken out of service if it fails the retest. There have been at least 55 action reports since 2011, finding bacteria and mold from monitoring of personnel gloves and gowns, and viable air samples. Examples include:
   1. *Bacillus pumilus* and *Paecilomyces* spp. (mold) from an employee glove, sampled on 05/24/11 (action level is (b) or more colony forming units), result was 3 cfu; retested again on 05/31/11 with no additional action taken.
   2. *Staphylococcus hominis* and *Phialophora* spp. (mold) from viable air sample collected at Laminar AirFlow Workbench 10 (ISO 5) on 12/29/11 (action level is (b) cfu per m^3), result was 6 cfu per m^3; retested again on 01/05/2012 with no additional action taken.
   3. *Bacillus cereus*, *Brevibacillus laterosporus*, and *Aspergillus* spp. (mold) from an employee's gloves and non-sterile gown, respectively, on 06/20/2012 (action level is (b) or more and (b) or more, respectively); results were 6 and 5 cfu (gloves), and 16 cfu (non-sterile gown); the employee was retested again on 06/27/12 and 06/28/12, with no additional action taken.

B. Environmental monitoring testing conducted by your firm is inappropriate in that employees sanitize their gloves and non-sterile smock with (b) (4) before collecting personnel agar test plates.

C. The incubation of the environmental monitoring surface contact and personnel agar test plates are incubated incorrectly. All contact plates were observed incubated with the agar side down and not inverted, thereby allowing the condensation formed during incubation to possibly interfere with microbial growth.

D. Environmental monitoring is not performed on a frequent basis or during dynamic conditions.
   1. Each ISO-5 workstation is not tested for contact, viable, and non-viable environmental monitoring on a frequent basis. Environmental monitoring of each workstation is performed every (b) (4), at the conclusion of

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compounding of the last operational day of that week, after most compounding operations have been completed.

2. Environmental monitoring of personnel is not performed each day of production. The testing is performed every (b) (4) . Additionally, Procedure, 6.02, Microbiological and Environmental Testing, Implemented 07/29/2002, does not reflect current practice because it lists (b) (4) surface samples to be collected instead of the three surface plates currently collected.

3. Environmental monitoring has not been performed during operations representing the maximum number of personnel to demonstrate that the ISO-6 classification of the cleanroom can be maintained.

OBSERVATION 13

Written procedures are not drafted, reviewed and approved by the appropriate organizational units.

Specifically, your firm does not have a system in place to track or assess the impact of changes made to processes, equipment, or procedures. There is no change control system available for investigations into process deviations or failures.

*** DATES OF INSPECTION:**
03/15/2013(Fri), 03/18/2013(Mon), 03/19/2013(Tue), 03/20/2013(Wed), 03/21/2013(Thu), 03/26/2013(Tue), 03/28/2013(Thu), 04/03/2013(Wed)

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