DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
300 River Place, Suite 5900 Detroit, MI 48207 (313) 393-8100 Fax:(313) 393-8139 Industry Information: www.fda.gov/oc/industry	03/04/2013 - 03/06/2013 FEI NUMBER 3002652326

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Lawrence D. Curtis, RPh., Vice President/Co-Owner

FIRM NAME	STREET ADDRESS
Portage Pharmacy Inc.	7966 Lovers Lane
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Portage, MI 49002	Producer of Sterile 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:

OBSERVATION 1

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

Specifically,

a-Sterilizing (b) (4) used in (b) (4) of injectable drugs formulated from non-sterile components (including Chorionic Gonadotropin Injectable, Morphine, and TriMix) were observed to have not been tested quantitatively, in determining the integrity of the sterilizing (b) post use (qualitative/tactile measure only). On 3/04/2013 we observed the use o (b) (4) (b) (4) during aseptic processing of injectable products including Chorionic Gonadotropin (HCG) 8000U/8ml lot 030413E.

b-The (b) (4) Sterilization cycle for Hydroxyprogesterone Caproate 250mg/ml (formulated from non-sterile components) was found inconsistent with routine processing instructions on the batch Worksheet. For example, as shown on the Hydroxyprogesterone Caproate 250mg/ml Injectable WorkSheet, the (b) (4) sterilization cycle instruction is (b) (4) (b) (4) which is less time then that performed in the last qualification (a verification). The last recorded (b) (4) (b) (b) (4) qualification (a verification) utilizing a Biological Indicator was dated 10/2011 with the following documented run parameters:

TIME	(b) (4)
Noon	
1:54 pm	
2:15 pm	
4:08 pm	
5 pm	

The Biological Indicator is a stand alone culture set that is not directly innoculated into product. Hydroxyprogesterone Caproate 250mg/ml Injectable lot 021313I processed in this same (b) (4) (b) (4) was recorded with the following cycle run parameter data:

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Time In: (b)(4) (b) (4)
Time Out

c- Written procedure SOP 8.020, Biological Indicators, Version 1.0 details the use of Biological Indicators (BI) in the (b) (4) loads. Written record supporting the use of the BI with each batch of formulated product sterilized within the (b) (4) was not always indicated. The results of the incubation of the same after the sterilization cycle are also not always recorded. For example, Hydroxyprogesterone Caproate 250mg/ml Injectable lot 021313I was processed in the (b) (4) (b) (4) on 2/13/13. No record supporting the use of a BI in this load, and the results of the incubation of the same, were provided.

d- The firm's ISO 5 smoke studies are deficient as follows:

i. The firm has no video recording of smoke studies having been performed on its (b) (4) ISO 5 hoods.

ii. The only evidence of a smoke study having been performed was a notation in a certification report provided by your cleanroom certification vendor and this notation only pertained to one of the (b) (4) ISO 5 hoods.

iii. The smoke studies were performed only in static conditions.

OBSERVATION 2

Batch production and control records do not include in-process results for each batch of drug product produced.

Specifically,

The documentation of the (b) (4) sterilization of Hydroxyprogesterone Caproate 250mg/ml Injectable consists only of handwritten start and stop times and the (b)(4) at those times. For example, lot 021313I.

OBSERVATION 3

Aseptic processing areas are deficient regarding the system for monitoring environmental conditions.

Specifically,

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Environmental monitoring of the ISO 5 hoods does not occur each time a sterile drug is formulated therein. For example, during processing of Chorionic Gonadotropin (HCG) 2000U/ml Injectable lot 030413D on 3/04/2013, no environmental monitoring was observed. In addition, personnel monitoring of aseptic processing employee was also not performed on this same day.

OBSERVATION 4

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

Specifically,

a-Observed gowning on personnel in the ISO 7 space working at the ISO 5 hood was found to include a non-sterile bouffant cap, a non-sterile face mask, and a non-sterile gown. The gloves donned for use in this same space were found labeled as sterile, however the stock supply in the gowning room was found to contain at least one unit that had expired 1/2013. Chorionic Gonadotropin (HCG) 2000U/ml Injectable lot 030413D was aseptically processed on 3/04/2013.

b-During cleaning of the ISO 7 area on the morning of 3/05/2013, an employee was observed wearing the specified clean room garb, however, was noted wearing shorts, exposing a portion of her lower legs. Chorionic Gonadotropin 5000U/5ml Injectable lot 030513F was aseptically processed at the ISO 5 hood within this ISO 7 space later on this same day.

OBSERVATION 5

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

Specifically,

Cephalosporin drug products are formulated in the same Cleanroom space used for processing other sterile drug products, and written procedures for the separation of operations for cephalosporin drug products from other human drug products were not provided. For example, on 3/01/2013 Cefazolin 50mg/ml Sterile Ophthalmic, was processed as lot # 030113E. That same day, Morphine PF 50mg/ml Injectable lot 030113J was also processed.

OBSERVATION 6

Each batch of drug product purporting to be sterile is not laboratory tested to determine conformance to such requirements.

Specifically,

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According to SOP 9.120, all sterile products shall be tested for sterility. However, most lots of sterile injectable drug product that the firm produces are not tested for sterility. For example:

a. Human Chorionic Gonadotropin Injection 5000U/5ml lot 021113E, produced 2/11/2013, was released but was not tested for sterility.

b. TriMix (Papaverine/Phentolamine/Prostaglandin E1 Injection 30mg/0.5mg/20mcg/ml) lot 021113B, produced 2/11/2013, was released but was not tested for sterility.

c. Hydroxyprogesterone Injection 250mg/5ml lot 021313I, produced 2/13/2013, was released but was not tested for sterility.

OBSERVATION 7

Testing and release of drug product for distribution do not include appropriate laboratory determination of satisfactory conformance to the identity and strength of each active ingredient prior to release.

Specifically,

Most lots of sterile injectable drug product that the firm produces are not tested for potency. For example:

a. Human Chorionic Gonadotropin Injection 5000U/5ml lot 021113E, produced 2/11/2013, was released but was not tested for potency.

b. TriMix (Papaverine/Phentolamine/Prostaglandin E1 Injection 30mg/0.5mg/20mcg/ml) lot 021113B, produced 2/11/2013, was released but was not tested for potency.

c. Hydroxyprogesterone Injection 250mg/5ml lot 021313I, produced 2/13/2013, was released but was not tested for potency.

OBSERVATION 8

Acceptance criteria for the sampling and testing conducted by the quality control unit is not adequate to assure that batches of drug products meet each appropriate specification as a condition for their approval and release.

Specifically,

Most lots of sterile injectable drug product that the firm produces are not tested for endotoxins. For example:

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a. Human Chorionic Gonadotropin Injection 5000U/5ml lot 021113E, produced 2/11/2013, was released but was not tested for endotoxins.

b. TriMix (Papaverine/Phentolamine/Prostaglandin E1 Injection 30mg/0.5mg/20mcg/ml) lot 021113B, produced 2/11/2013, was released but was not tested for endotoxins.

c. Hydroxyprogesterone Injection 250mg/5ml lot 021313I, produced 2/13/2013, was released but was not tested for endotoxins.

OBSERVATION 9

The establishment of test procedures including any changes thereto, are not drafted by the appropriate organizational unit.

Specifically,

There is no procedure describing how to perform growth promotion testing on media used during media fills. For example, during a media fill conducted on 10/4/2011, growth promotion testing was performed by sterile (b) (4) into a vial and incubating it - no microorganisms were added. When the vial was clear after incubation, the growth promotion was marked as having passed.

OBSERVATION 10

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

Specifically,

The firm has not tested all of its products to assess their stability in support of their assigned expiration periods. For example, Methylcobalamin Preserved Injection 1mg/ml that the firm has produced has not been stability tested. Instead, the firm relies on a document published by a separate organization, however:

a. The document does not contain data; it simply describes how to produce the drug and estimates its expiration period.

b. The document only addresses potency; it does not address sterility or endotoxins.

c. The formula in the document is different than Portage Pharmacy's formula.

d. The concentration of the product in the document is different than Portage Pharmacy's product.

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OBSERVATION 11

Results of stability testing are not used in determining expiration dates.

Specifically,

Stability testing of the firm's products does not always support assigned expiration periods. For example,

a. The stability data for TriMix (Papaverine/Phentolamine/Prostaglandin E1 Injection 30mg/0.5mg/20mcg/ml) is deficient as follows:

i. Stability testing was performed on Prostaglandin 500mg/ml, which is (b) (4) than that which is in the TriMix product. Also, no Papaverine or Phentolamine was present in the product that was tested.

ii. Only potency was tested. Sterility, endotoxin, and preservative effectiveness were not tested.

iii. The stability data only covers 60 days, but the product's expiration period is 90 days.

b. The stability data for Human Chorionic Gonadotropin Injection 5000U/5ml only covers potency; there is no stability data for sterility or endotoxin.

OBSERVATION 12

Established test procedures are not followed.

Specifically,

Personnel producing sterile injectable drug products from non-sterile components do not conduct media fills every (b) (4) as required per procedure. For example, only two media fills for the main employee who produces such products (b) (6) have been conducted, one in the fall of 2011 and one in the fall of 2012.

OBSERVATION 13

The responsibilities and procedures applicable to the quality control unit are not fully followed.

Specifically,

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Written procedure, SOP 9.060, Product Quarantine, Storage and Release, Version 1.0, is not always followed in that section 9.3.1.7, visual inspection (b) (4) [redacted] is not performed (not documented). For example, there is no documentation supporting this visual inspection for Hydroxyprogesterone Caproate 250mg/ml Injectable lot 021313I, processed on 2/13/13.

OBSERVATION 14

Records associated with drug product production and control and within the retention period for such records, were not made readily available for authorized inspection.

Specifically,

The firm could not provide records of the most recent media fill, which purportedly occurred in the fall of 2012. Retention of such records is required per procedure.

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