

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER 19701 FAIRCHILD IRVINE, CA 92612 949-608-4492	DATE(S) OF INSPECTION 11/14, 16, 19-21, 26, 27, & 29/12 and 12/5, 6, & 13/12
Industry Information: <a href="http://www.fda.gov/oc/industry">www.fda.gov/oc/industry</a>	FEI NUMBER 3009855773

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED  
**TO: Paul R. Wheeler, Pharmacist In Charge/President**

FIRM NAME Custom Compounding Centers, LLC	STREET ADDRESS 10525 Humbolt Street
CITY, STATE AND ZIP CODE Los Alamitos, CA 90720	TYPE OF ESTABLISHMENT INSPECTED Compounding Pharmacy

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 (I) (WE) OBSERVED:

Observation 1: The following sterile injectable drug products were rejected and destroyed along with their batch records for failing sterility and fungal testing or having questionable results without conducting any investigation including determination of root cause or potential impact on other products. There is no detailed note and no investigation written about the out of specification or uncertain results. For example, the following notes were written on sterility or fungal testing log and lot number log 2012:

- A. Betamethasone Na Phos lot # 18859 – “batch was tossed”
- B. Wydase lot # 18827 – “batch was tossed”
- C. Morphine Sulfate 90mg/ml lot # 17961 – “batch was not used, unclear results – not dispensed”
- D. Omnipaque lot # 17959 – “tester was cloudy look, batch throw away – do not use”
- E. Ondasetron 2mg lot # 17847 – “unclear readings cloudy look. Do another sterility test & came out negative. Batch was thrown away. Did not use”
- F. Morphine sulfate 1mg/ml lot # 18183 – “positive” for fungi when tested in house. This lot was recalled and the firm sent the sample to an independent lab for testing which came up negative.

The firm did not write a written justification for why they released the lot below although one out of three sterility samples came back “unclear.” For example

- G. Promethazine 25mg/ml lot # 18148 – “unclear testing but sterility testing 1 & 2 came out good” – this lot was released although testing for sample # 3 was unclear

For all positive or unclear reading cases above, the firm did not identify the genus and species or the microorganisms found.

Observation 2: The firm does not conduct sterility and endotoxin testing at the end of drug products’ shelf lives in accordance with its procedure # PH103, date 07/09/09 titled “Clinical Policies & Procedures Beyond Use Dating/

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Expiration Dating (BUD)" which states "When considering the BUD product, the following factors need to be considered"... "Testing at the end of use date: sterility, endo, potency." Moreover, there's no requirement for storing vials various positions (i.e. upright, inverted, and sideways) to ensure that finished products come into contact with containers and closures.

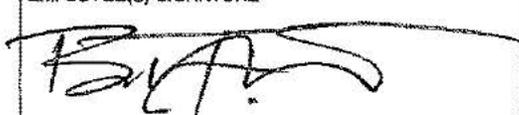
Observation 3: The firm allows employees to enter ISO 5 areas wearing street clothes underneath a non-sterile gown with exposed facial areas such as cheeks, eye brows, eye lashes, and forehead while performing aseptic filling of drug products. Movement of personnel in ISO 5 is not controlled to prevent particulate generation or shedding of microbes/particles from personnel. The firm has not established the maximum number of personnel that can be allowed in the clean rooms (ISO 5 and 7 areas) at any given time. Current gowning and movement in ISO 5 may introduce particulate matters and/or microbes into the ISO 5 area and drug products during filling.

Observation 4: the firm did not review, approved, reject, or comment on whether bacterial and fungal air results from viable air monitoring conducted by an independent company against USP <797> standards is acceptable or not. There is no statement of result conclusion such as passed, failed, meet USP <797>, and not meet USP <797> from the independent certification company. There was no evaluation of the air volume of (b) (4) collected in ISO 5 area is representative compared to a bio hood (smaller) with (b) (4) of air taken.

Observation 5: There was an accumulation of dust in the return vents underneath the table of ISO 5 observed during environmental sampling performed on 11/15/12. The daily, weekly, monthly cleaning log records do not require the firm to clean return vents. Note: ISO5 area only covers from the HEPA filter to the stainless steel counter top not the surface below the countertop.

Observation 6: The firm does not perform environmental monitoring during filling (aseptically fill after (b) (4) (b) such as viable and non-viable monitoring. The firm does not perform personnel monitoring in the following areas: hand, chest, mask, and head areas as employees may walk back and forth between ISO 7 and ISO 5 areas. The firm only performs gloves monitoring of employees on every batch produced. Note: only the gloves and arm covers are sterile. Hair nets, face masks, and gowns are not sterile as those are worn in ISO 8 prior to entering ISO 7 and then ISO 5 areas without further gowning.

Observation 7: A training video using smoke to demonstrate air flow pattern in ISO 5 working areas under a static

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Compounding Pharmacy

condition (without production) performed in August of 2012 showed turbulent and upward airflow around the stainless steel working surfaces # 2 and 3 (over to the right of the room when viewing from outside) in ISO 5 area. These working surfaces # 2 and 3 are used for aseptic filling of sterile drug products. The firm did not take any action to correct the turbulent and upward airflow over working surfaces # 2 and 3. The firm has not conducted any dynamic smoke studies to verify the unidirectional airflow and air turbulence within the critical area where sterilized drug products, containers, and closures are exposed to environmental conditions.

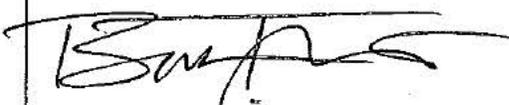
Observation 8: The firm does not use additives (i.e. lecithin and polysorbate 80 with media such as TSA) as neutralizing agents against disinfectants when testing for surface samples in clean rooms to assure that growth is not inhibited.

Observation 9: The firm does not conduct inhibitory/enhancement testing on all of their products to see if their products interfere with endotoxin testing. The firm uses (b) (4) to conduct endotoxin testing using products withdrawn directly from finished product vials. Results from the (b) (4) kits for all drug products are passed or not passed. There is no specification of endotoxin limit that is set for each of the finished drug product by the firm. There were some tests conducted by the independent contract lab in which no specifications were set for endotoxin limits. For example,

- A. Trypan Blue Ophthalmic Solution 0.06% Inj PF lot CC18361 (result: < 8.0 EU/ml, no endotoxin specification)
- B. Fentanyl Citrate 2mg/ml + Bupivacaine HCl 0.125% Injection in 0.9% NaCl 100ml (result: < 0.4EU/ml, no endotoxin specification)

Observation 10: the firm does not test for pyrogen for their closures (i.e. stoppers) used in the capping of their vials for all sterile drug products. The firm last performed pyrogen testing on their vials only in 2008 and 2006.

Observation 11: The firm does not assure on each of lot of biological indicators (BI's) received and used to determine the effectiveness of (b) (4) sterilization cycles. D-value (the decimal reduction time, the time required at a certain temperature to kill 90% of the organisms being studied) has not been determined for their (b) (4) cycles used to sterilize containers, closures, or bulk drug products. The firm has not conducted a sterilization study for a small (b) (4) and (b) (4) used in the sterilization of small glass vials.

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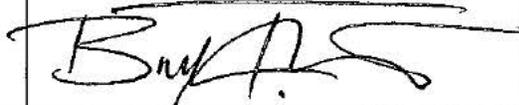
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Observation 12: The firm does not conduct any growth promotion testing on purchased media. For example, purchased (b) (4) media tubes, (b) (4) and (b) (4) media tubes used for environmental monitoring and fungal testing of products are not growth promotion tested to ensure that these media are able to support growth.

Observation 13: The firm makes all of their high-risk level sterile solutions subjected to (b) (4) sterilization without using any (b) (4) preceding or during filling into their final containers to remove particulate matter.

Observation 14: The firm has not verified/certified that the purchased (b) (4) are able to retain at least 10 to the 7th microorganisms of a strain of Brevundimonas (Pseudomonas) diminuta on each square centimeter of final filter prior to filling into finished product vials.

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The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or
2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration.

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgement, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."