DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
1201 Harbor Bay Parkway Alameda, CA 94502-7070 (510)337-6700 Fax:(510)337-6702	12/2/2019-12/13/2019* FEI NUMBER 3006684882

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Tawnie L. McDonald, Quality Director

FIRM NAME	STREET ADDRESS
Hawaii Health Systems Corporation dba Kona Community Hospital Pharmacy	79-1019 Haukapila Street
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Kealakekua, HI 96750	Producer of Sterile Drugs

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

You did not make adequate product evaluation and take remedial action where actionable microbial contamination was found to be present in the ISO 5 classified aseptic processing area during aseptic production.

Specifically, actionable microbial contamination was discovered inside the ISO 5 aseptic processing environments during (b) (4) cleanroom certifications and no evaluation of product impact was made. For example:

a.) During the 12/11/18 (b) (4) recertification, the ISO 5 Hazardous Drug Room Biological Safety Cabinet (BSC) Surface Sample, ID (b) (4) had one mold colony isolated on the bacterial plate. The mold was not identified. The firm did not evaluate any products filled in the ISO 5 BSC on 12/11/18 for product impact, including but not limited to: Azacitidine 150mg.

b.) On the 01/24/19 retest, the ISO 5 Non-Hazardous Drug Room Laminar Airflow (LAF) Hood Viable Air Sample, ID (b) (4), had a calculated 4 colony forming units (cfu) /m^3, which was deemed acceptable in the report. The firm did not evaluate any products filled in the ISO 5 LAF Hood on 01/24/19 for product impact, including but not limited to: Octreocide 50mcg, Octreocide 500mcg, Pantoprazole 80mg, Clindamycin 61.161mg, Vancomycin 1000mg, Vancomycin 1250mg, Ampicillin 80mg, and Gentamicin 7.2mg.

OBSERVATION 2

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You did not make adequate product evaluation and take remedial action where actionable microbial contamination was found to be present in an area adjacent to the ISO 5 classified aseptic processing area during aseptic production.

Specifically, actionable microbial contamination was discovered inside (b) (4) rooms, where the ISO 5 Biological Safety Cabinet (BSC) and ISO 5 Laminar Airflow (LAF) Hood are located, during (b) (4) cleanroom certifications and periodic settling plate samples and no evaluation of product impact was made. For example:

a.) During the 12/11/18 (b) (4) recertification, the ISO 7 Non-Hazardous Drug Room Viable Air Sample, ID (b) (4) had a calculated 44 colony forming units (cfu) /m^3 identified as Coagulase-negative *Staphylococcus* species, *Dermabacter hominis*, and *Micrococcus luteus*, and the ISO 7 Hazardous Drug Room Viable Air Sample, ID (b) (4) had a calculated 18 cfu/m^3 identified as *Bacillus* species, *Micrococcus luteus*, *Micrococcus* species, and *Staphylococcus haemolyticus*. The firm did not evaluate any products filled in the ISO 5 LAF Hood and ISO 5 BSC on 12/11/18 for product impact, including but not limited to: Morphine 1mg/mL 50mL, Vancomycin 750mg, Vancomycin 1000mg, Vancomycin 1250mg, Vancomycin 1500mg, Acyclovir 600mg, Ertapenem 500mg, Ceftriaxone 473mg, Azithromycin 94.6mg, Ampicillin 473mg, Vasopressin 40 units, and Azacitidine 150mg.

b.) On the 01/24/19 retest from the December recertification, the ISO 7 Non-Hazardous Drug Room Viable Air Sample, ID (b) (4) had a calculated 27 cfu/m^3 identified as *Corynebacterium minutissimum, Corynebacterium* species, *Micrococcus* species, and *Staphylococcus haemolyticus*. The firm did not evaluate any products filled in the ISO 5 LAF Hood on 01/24/19 for product impact, including but not limited to: Octreocide 50mcg, Octreocide 500mcg, Pantoprazole 80mg, Clindamycin 61.161mg, Vancomycin 1000mg, Vancomycin 1250mg, Ampicillin 80mg, and Gentamicin 7.2mg.

c.) On 01/29/19, a settling plate located (b) (4) in the ISO 7 Non-Hazardous Drug Room had one colony of mold, which was not identified. The firm did not evaluate any products filled in the ISO 5 LAF Hood on 01/29/19 for product impact, which include: Hydromorphone 0.2mg/mL, Midazolam 1mg/mL, Fentanyl 550mcg/55mL, Vancomycin 750mg, Vancomycin 1250mg, Vancomycin 2000mg, and Ferric Carboxymaltose 750mg.

d.) On 03/27/19, a settling plate located (b) (4) of the ISO 7 Hazardous Drug Room had 2 cfu that were not identified. The firm did not evaluate any products filled in the ISO 5 BSC on 03/27/19

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for product impact, which include: Nivolumab 480mg, Pertuzumab 420mg, Trastuzumab 450mg, Obinutuzumab 1000mg, Bendamustine 125mg, Leucovorin 564mg, Oxaliplatin 120mg, Fluorouracil 564mg, Fluorouracil 3384mg, Irinotecan 212mg, and Carfilzomib 60mg.

e.) On 05/28/19, a settling plate located (b) (4) in the ISO 7 Non-Hazardous Drug Room had one colony of yeast that was not identified. The firm did not evaluate any products filled in the ISO 5 LAF Hood on 05/28/19 for product impact, which include: Penicillin G 2.5 million Units/Saline 1000mL, Gentamicin 340mg, and Vancomycin 1250mg.

f.) During the 06/05/19 (b) (4) recertification, the ISO 7 Hazardous Drug Room Viable Air sample, ID (b) (4), had a calculated 56 cfu/m^3 identified as Coagulase-negative *Staphylococcus* species, *Corynebacterium minutissimum*, *Corynebacterium tuberculostearicum*, *Corynebacterium*-like bacteria, gram-positive cocci, *Micrococcus luteus*, and *Micrococcus* species, and the ISO 7 Hazardous Drug Room Surface Sample, ID (b) (4) had a calculated 9 cfu on the plate identified as *Cellumonas* species, Coagulase-negative *Staphylococcus* species, gram-positive rod, *Micrococcus luteus*, and *Staphylococcus saprophyticus*. The firm did not evaluate any products filled in the ISO 5 BSC on 06/05/19 for product impact, which include: Magnesium Sulfate 6g/Saline 162mL, Vancomycin 750mg, Vancomycin 1000mg, Vancomycin 1250mg, Vancomycin 1500mg, Ampicillin/Sulbactam 3000mg, Potassium Phosphate 15mmol, Acyclovir 715mg, Nivolumab 240mg, Nivolumab 480mg, Leucovorin 600mg, Leucovorin 664mg, Oxaliplatin 130mg, Oxaliplatin 141mg, Fluorouracil 600mg, Fluorouracil 664mg, Fluorouracil 3700mg, Bevacizumab 585mg, and Pembrolizumab 200mg.

OBSERVATION 3

Your facility design allowed the influx of poor quality air into a higher classified area.

Specifically, the air balance between rooms is not controlled to ensure cascading flow of air between areas of lesser classifications. For example:

a.) The (b) (4) area does not seal completely when the doors on either side of (b) (4). The ISO 7 Hazardous Drug Room is maintained at a negative pressure relative to adjacent spaces, allowing air from the unclassified area to continuously enter the room. The differential pressure between the ISO 7 Hazardous Drug Room and the unclassified office area is not monitored. Additionally, during the transfer of finished sterile hazardous drugs, we observed (b) (4) open at the same time. The ISO 7

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Hazardous Drug Room contains the ISO 5 Biosafety Cabinet, which is used in the production of sterile hazardous drug products, including but not limited to Leucovorin, Oxaliplatin, Fluorouracil, Gemcitabine, and Cisplatin.

b.) The air pressure differential between the ISO 8 Ante Room and the unclassified office area has been below the specified range of (b) (4) inches water column (" w.c.) on 39 of the 44 days between 10/09/19 and 12/05/19 for which data was recorded. Of the 39 instances, the pressure differential was measured as negative once on 11/13/19 at -0.003" w.c. allowing air from the ISO 8 Ante Room into the ISO 7 Non-Hazardous Drug Room. The ISO 8 Ante Room is used by operators performing production operations to don sterile garbing materials prior to entering one of the ISO 7 areas and the Ante Room is also used for storage of materials used for production operations.

c.) The air pressure differential between the ISO 7 Non-Hazardous Drug Room and the ISO 8 Ante Room has been below and above the specified range of (b) (4) " w.c. on 8 of the 44 days between 10/09/19 and 12/05/19 for which data was recorded. The ISO 7 Non-Hazardous Drug Room contains the ISO 5 Laminar Airflow Hood, which is used in the production of sterile non-hazardous drug products, including but not limited to Vancomycin, Phenylephrine, Penicillin, Ceftriaxone, and Fentanyl.

d.) The air pressure differential between the ISO 7 Hazardous Drug Room and the ISO 7 Non-Hazardous Drug Room has been below the specified range of negative (b) (4) " w.c. on 38 of the 44 days between 10/09/19 and 12/05/19 for which data was recorded.

e.) During the cleanroom certification performed on 12/11/18, the following air pressure differentials were out of specification: between the ISO 8 Ante Room and unclassified office area was measured at 0.138" w.c. using a calibrated instrument while the firm's wall gauge reading was 0.108" w.c., and between the ISO 7 Non-Hazardous Drug Room and ISO 8 Ante Room was measured at 0.00556" w.c. using a calibrated instrument while the firm's wall gauge reading was 0.044. The subsequent and most recent certification performed on 06/05/19 also had air pressure differentials out of specification: between the ISO 8 Ante Room and unclassified office area was measured at 0.145" w.c. (-0.132" w.c. wall gauge), between the ISO 7 Non-Hazardous Room and the ISO 8 Ante Room was measured at 0.00573" w.c. (0.01" w.c. wall gauge), and between the ISO 7 Hazardous Drug Room and ISO 7 Non-Hazardous Drug Room was measured at -0.0719" w.c. (-0.084" w.c.). The wall gauges used for daily readings have never been calibrated.

OBSERVATION 4

Your facility was designed and/or operated in a way that permits poor flow of personnel and materials.

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Specifically, the design of the cleanrooms was deficient in the following ways:

a.) Smoke studies performed in the ISO 5 Biological Safety Cabinet used to produce sterile hazardous drug products were not conducted under dynamic conditions to show unidirectional airflow during routine production operations.

b.) HEPA filtered air supply vents and air returns are all located on the ceilings of the ISO 7 Hazardous Drug Room, ISO 7 Non-Hazardous Drug Room, and ISO 8 Ante Room. The metal air vents are not designed to provide unidirectional air to the rooms with air dispersing in two to four different directions from each vent. The firm has not evaluated the air patterns in each room.

c.) The ISO 7 Hazardous Drug Room, ISO 7 Non-Hazardous Drug Room, and ISO 8 Ante Room share air handling units ((b) (4)) and a common final HEPA filter with the unclassified office area of the pharmacy. There are no HEPA filters located directly at the air supply vents to each ISO-classified room.

d.) Operators entering the ISO 7 Hazardous Drug Room must first enter the ISO 8 Ante Room to perform initial gowning and pass through the ISO 7 Non-Hazardous Drug Room to enter the ISO 7 Hazardous Drug Room, where additional gowning and gloves are donned. On 12/03/19, we observed the operator go back and forth between the ISO 7 Hazardous Drug Room and ISO 8 Ante Room on at least two occasions to obtain more supplies needed for production and cleaning. Upon exiting the ISO 7 Hazardous Drug Room, the secondary gowning was removed and redonned upon reentry; however, there are no restrictions of products being made in both rooms simultaneously and there has been no evaluation of the air patterns created by the movement between rooms.

e.) Room light fixtures located in the ISO 7 Hazardous Drug Room, ISO 7 Non-Hazardous Drug Room, and ISO 8 Ante Room protrude from the ceiling and are not completely sealed around the edges. Gaps of approximately 1/8" in width were observed along the length of each side of the various light fixtures in each room.

OBSERVATION 5

The segregated production areas surrounding the ISO 5 classified aseptic processing area contained dust-collecting overhangs without adequate and frequent cleaning.

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Specifically, apparent dust-like residue was observed on a sterile wipe after wiping the crevices of the metal HEPA-filtered air supply vents in the ISO 7 Non-Hazardous Drug Room and ISO 8 Ante Room. These rooms share the same HEPA-filtered air supply that also goes to the ISO 7 Hazardous Drug Room and unclassified office area. The metal vent located closest to the ISO-classified areas located in the unclassified office area also showed apparent dust-like residue after wiping the crevices with a sterile wipe.

OBSERVATION 6

HEPA filters were not sealed around each perimeter to the support frame.

Specifically, the firm's cleanroom certification reports indicate the room supply HEPA filters are not leak tested in the ISO 7 Hazardous Drug Room, ISO 7 Non-Hazardous Drug Room, and ISO 8 Ante Room because the filters in the housing are not clamped down. On 12/04/19, the Pharmacy Director indicated she did not believe the HEPA filters have ever been leak tested. The ISO 7 Hazardous Drug Room contains the ISO 5 BSC, which is used in the production of sterile hazardous drug products. The ISO 7 Non-Hazardous Drug Room contains the ISO 5 LAF Hood, which is used in the production of sterile non-hazardous drug products. The ISO 8 Ante Room is used by operators performing production operations to don sterile garbing materials prior to entering one of the ISO 7 areas and the Ante Room is also used for storage of materials used for production operations.

The edges of the air inlet metal vents installed in the ceilings of the ISO 7 Hazardous Drug Room, ISO 7 Non-Hazardous Drug Room, and ISO 8 Ante Room are not sealed to the ceilings of the rooms.

OBSERVATION 7

Personnel donned gowning apparel improperly, in a way that may have caused the gowning apparel to become contaminated.

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Specifically, on 12/03/19, after producing the hazardous drugs Gemcitabine and CISplatin in the ISO 7 Hazardous Drug Room, we observed an operator hanging a used gown on the shelf in the ISO 8 Ante Room. When asked about the gown, the operator indicated the gown is reused throughout the day and replaced daily. Although a separate "Chemo Gown" is donned upon entry in the ISO 7 Hazardous Drug Room, there are no controls in place to prevent reuse of the gown that was contacted with bare hands.

OBSERVATION 8

Disinfecting agents and cleaning wipes used in the ISO 5 classified aseptic processing areas were not sterile.

Specifically, non-sterile (b) (4) is a disinfectant used for daily cleaning of the ISO 5 Laminar Airflow (LAF) Hood and ISO 5 Biological Safety Cabinet (BSC) surfaces, which the firm uses in the production of sterile injectable drug products.

*DATES OF INSPECTION

12/02/2019(Mon), 12/03/2019(Tue), 12/04/2019(Wed), 12/05/2019(Thu), 12/09/2019(Mon), 12/10/2019(Tue), 12/12/2019(Thu), 12/13/2019(Fri)

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