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	5/15/2017-5/19/2017
	FEI NUMBER 3005949964

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Tedd M. Green , President

FIRM NAME	STREET ADDRESS
Cook Pharmica, LLC	1300 S Patterson Dr
CITY, STATE, ZIP CODE, COUNTRY Bloomington, IN 47403-4828	TYPE ESTABLISHMENT INSPECTED Manufacturer

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:
PHARMACEUTICAL

QUALITY SYSTEM

OBSERVATION 1

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

Specifically,

A. Changes to documents that include adjustments to protocol acceptance criteria or methodologies that affect validation protocol acceptance criteria do not include evaluation of the following:
- previously executed protocols to ensure results meet applicable updated criteria; and
- subsequent protocols that use criteria established in previous protocols.

For example, Change Request 1104-16, effective 15JAN16, to A-VCLN-00007-P (b) (4) (b) (4) Protocol – Process Residue, included a change to require the use of the lowest recovery (if between (b) (4)%) for establishing a recovery factor for use during cleaning validation and verification studies. However, no evaluation for impact to all previously executed product residue recovery studies was performed. For example, the original (b) (4) studies for (b) (4) excluded (b) (4) recoveries at (b) (4) and (b) (4) ppb and used a recovery of (b) (4)%. However, an evaluation against updated requirements would have required the use of a (b) (4)% recovery from (b) (4) . During execution of the Equipment Cleaning Performance Qualification for (b) (4) performed approximately 8/2016, a recovery of (b) (4)% was used to establish protocol acceptance criteria.

B. Deviation investigation PR 171911 into a potential HEPA leak failure in the (b) (4) of the (b) (4) line did not include a full evaluation of relevant data sources to support the conclusion of no product impact. For example, historical (b) (4) visual inspection trending for particulates was reviewed. However, no

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Emilie Kahn, Investigator Jeffrey D Meng, Investigator Sargum C Sood, Investigator Unverified X Emilie Kahn Emilie Kahn Investigator Signed by: Emilie E. Kahn -S	5/19/2017

documented review was performed of potentially impacting topics such as customer complaints, finished product testing, environmental monitoring data, and media fill results.

PRODUCTION SYSTEM

OBSERVATION 2

Written production and process control procedures are not followed in the execution of production and process control functions and documented at the time of performance.

Specifically,

- Document A-SOP-21-01-038, titled (b) (4) requires operators to identify a zone of breakage, inspect all parts for glass and damage, and to document both where the glass breakage occurred and all steps taken during clean up.

  Event Number 11 on the Filling Event Log for (b) (4) states: (b) (4)

  Your firm did not document any attempt to identify a zone of breakage, any inspection for glass or damage, nor any steps taken during cleaning.

  Additionally, this SOP does not provide instructions on investigating circumstances in which broken glass is observed but is not associated with a specific breakage event. For example, the operators documenting Event 11 only observed the glass while addressing a separate alarm for the (b) (4) . The operators assumed that the glass discovered in the (b) (4) was associated with previous rake alarm, but did not document any investigative activities confirming this assumption; your firm did not create a deviation investigation into when the breakage may have occurred, where the glass may have been on the line, or how the glass went undetected until the (b) (4) alarm sounded.

MEDICAL DEVICE

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OBSERVATION 3

Process control procedures that describe any process controls necessary to ensure conformance to specifications have not been adequately established.

Specifically, your firm's manufacturing and quality testing procedures for the Class II In Vitro Fertilization (IVF) Reproductive Media devices were not defined, documented, and/or implemented to ensure these devices conform to their specifications (e.g., sterility, stability, etc.). For example:

(A) Although section A.5.4 of your firm's procedure titled "Aseptic Filling" (A-SOP-23-05-003; Rev.15; Effective: 1/16/17) states to "***avoid touching parts of the item whose sterility is critical to the process***," sections C.13 to C.18 contradict this requirement by permitting handling of the (b) (4) (b) (4) by the operator during attachment to the (b) (4) . Notably, open vials are subsequently exposed to this (b) (4) as reproductive media is (b) (4) which requires placement (b) (4) (b) (4) to accomplish the filling process.

(B) Section D.12 of A-SOP-23-05-003 (nor any other procedure) does not define and document the sequence in which the Stoppering Operator shall place stoppers over the vials filled by the Filling Operator. On 5/16/17, we observed your Stoppering Operator use sterile (b) (4) to place stoppers in a (b) (4) filled vials located in the (b) (4) during the aseptic filling process of the Sydney IVF Blastocyst Media devices (Part #: 103-K-SIBM, Lot #: M0517019). Notably, section A.1.10 of A-SOP-23-05-003 specifically states to (b) (4) "

(C) Although section D.1 of your firm's procedure titled "Gowning for Entry into Small Scale Form/Fill/Finish" (A-SOP-23-01-015; Rev.13; Effective: 4/10/17), which instructs operators on how to put on sterile gloves, states to "***touch only the outside, sterile, surface***" of the (b) (4) , we observed your Assistant touch the inside, non-sterile surface of the (b) (4) during the aseptic filling process of the Sydney IVF Blastocyst Media devices (Part #: 103-K-SIBM, Lot #: M0517019) on 5/16/17.

(D) The procedure titled "Sydney IVF Follicle Flush Buffer" (103-K-SIFB; Rev.12; Effective: 1/14/17) (nor any other procedure) does not require documentation of the time from the end of aseptic filling to cold storage at (b) (4) °C of the Sydney IVF Follicle Washing Buffer Media devices (Part #: SIFB) to ensure the elapsed time remains below the hours established during the stability study.

(E) The procedure titled "(b) (4) " (A-SOP-23-03-004; Rev.9; Effective: 2/4/16) (nor any other procedure) does not require documentation of the beginning and end time of the (b) (4) step to ensure the (b) (4) although this step was instituted under change control # 139429 (1/25/16) to prevent invalid integrity testing results. Furthermore, there are no instructions on the settings to use for velocity (b) (4) rpm) and acceleration (b) (4)) on the pump to ensure proper (b) (4) (b) (4) .

Note the Sydney IVF Follicle Flush Buffer is intended for use during in vitro fertilization procedures for follicle flushing and oocyte collection and Sydney IVF Blastocyst Medium is intended for use during in vitro fertilization procedures for extended culture and transfer of embryos.

OBSERVATION 4

A process whose results cannot be fully verified by subsequent inspection and test has not been validated according to established procedures.

Although section 4.6 of your procedure titled "Aseptic Process Simulation Policy" (A-POL-06-01-001; Rev.13; Effective: 2/20/17) requires inclusion of routine interventions during the manual aseptic media fill process validations, the repetitive standard activity of the operator selecting the desired velocity (b) (4) rpm), acceleration (b) (4))), and delay (b) (4) seconds) settings on the pump to dispense media into vials during routine manufacturing of Class II In Vitro Fertilization Reproductive Media devices (excluding K-SICO and K-SIPV) was not included as an intervention in the following aseptic media filling process validations:

- Requalification (JAN 2017) Room (b) (4) Small Scale Form/Fill/Finish Aseptic Media Fill (b) (4) mL, (b) (4) mL, & (b) (4) mL Vials Validation (A-VPPQ-00089; Approved 3/8/17)
- Requalification (JAN 2017) Room (b) (4) Small Scale Form/Fill/Finish Aseptic Media Fill (b) (4) mL, (b) (4), & (b) (4) mL Vials Validation (A-VPPQ-00090; Approved 2/27/17)
- Requalification (JAN 2017) Room (b) (4) Small Scale Form/Fill/Finish Aseptic Media Fill (b) (4) mL, (b) (4) mL, & (b) (4) mL Vials Validation (A-VPPQ-00091; Approved 3/8/17)

OBSERVATION 5

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Procedures to ensure that all purchased or otherwise received product and services conform to specified requirements have not been established.

Although section 3.7 of your procedure titled "Vendor Complaint" (A-SOP-12-01-036; Rev.4; Effective: 9/22/14) requires initiation of vendor complaints when deviation report(s) exist for the respective supplier, no vendor complaint was initiated for your (b) (4)) service supplier investigated under CAPA # 120866 (3/31/15) for out of specification(b) (4) results. As such, the "Vendor Reassessment" (Approved 7/24/15) for this (b) (4) service supplier did not reference any vendor complaints since the last (re)assessment.

OBSERVATION 6

Procedures for corrective and preventive action have not been adequately established.

Specifically, your firm's procedure titled "Corrective and Preventive Action" (A-SOP-03-01-006; Rev.15; Effective: 11/21/16) does not require verifying or validating the corrective and preventive action to ensure that such action is effective and does not adversely affect the finished device.

Annotations to Observations

Observation 1: Annotation Intentionally Left Blank
Observation 2: Annotation Intentionally Left Blank
Observation 3: Promised to correct
Observation 4: Promised to correct
Observation 5: Promised to correct
Observation 6: Promised to correct

Unverified

X Jeffrey D Meng
Jeffrey D Meng
Investigator
Signed by: Jeffrey D. Meng -S

Unverified

X Sargum C Sood
Sargum C Sood
Investigator
Signed by: Sargum C. Sood -S

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 judgment, 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."