

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER 4040 North Central Expressway, Suite 300 Dallas, TX 75204 (214)253-5200 Fax:(214)253-5314	DATE(S) OF INSPECTION 4/17/2017-5/10/2017* FEI NUMBER 3011286349
--	---

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Shaun P. Riney , General Manager

FIRM NAME Qualgen, LLC	STREET ADDRESS 14844 Bristol Park Blvd
CITY, STATE, ZIP CODE, COUNTRY Edmond, OK 73013-1891	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility

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 OBSERVED:

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.

Specifically,

- a) Your firm has had five (5) sterility failures in 2016 (lot #B020 Testosterone 200mg pellets, lot #B054 Estradiol 25mg pellets, lot #B089 Estradiol 6mg pellets, lot #B120 Estradiol 25mg pellets and lot #B130 Estradiol 6mg pellets) and two (2) in 2017 (lot #C008 of Testosterone 200mg/20mg pellets and lot #C048 of Estradiol 18mg pellets). Your investigations do not always include a documented review of all potential items that may have contributed to these failures, for example environmental and personnel monitoring, engineering controls and the use of non-validated processes.

This is a repeat observation from the 8/24/15-9/17/15 inspection.

- b) From 6/21/16 through 9/19/16, your firm had eleven excursions for environmental monitoring (viable air, settle plates and/or surface samples). Ten excursions for the ISO 5 (b) (4) where the (b) (4) and one excursion in the ISO 5 (b) (4) where the (b) (4). Your investigations into these excursions did not identify a root cause and do not include a documented review of all potential items that may have contributed to these failures.
- c) The investigations into the HEPA filter leaks in the ISO 7 (b) (4) clean room do not state which HEPA filter was leaking, the size of the leak and also fail to perform a product impact

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Margaret M Annes, CSO	<input checked="" type="checkbox"/> Margaret M Annes Margaret M Annes CSO Signed by: Margaret M. Annes-S	DATE ISSUED 5/10/2017 5/10/2017

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER 4040 North Central Expressway, Suite 300 Dallas, TX 75204 (214)253-5200 Fax: (214)253-5314	DATE(S) OF INSPECTION 4/17/2017-5/10/2017* FEI NUMBER 3011286349
---	---

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Shaun P. Riney , General Manager

FIRM NAME Qualgen, LLC	STREET ADDRESS 14844 Bristol Park Blvd
CITY, STATE, ZIP CODE, COUNTRY Edmond, OK 73013-1891	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility

assessment. From 01/22/16 through the detection of the first HEPA filter failure on 06/09/16, there were approximately (b) (4) lots of testosterone pellets and one (b) (4) of (b) (4) made.

OBSERVATION 2

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile do not include validation of the sterilization process.

Specifically,

- a) Your firm lacks documentation to show that the process for the sterilization of all pellet products via (b) (4) has been validated. Specifically, the report for (b) (4) dated 5/19/15 for the (b) (4) sterilization validation from your 3rd party vendor that performs the (b) (4) sterilization process, was performed using (b) (4).

- b) The most recent smoke studies conducted on the ISO 5 (b) (4) located in (b) (4) ISO 7 cleanroom (b) (4) are not representative of your current operations. Specifically, on various dates throughout this inspection, your firm had (b) (4) (b) (4).
 Moreover, the following materials were observed in the hood while this process was ongoing: (b) (4) pans of depyrogenated vials (each pan contains approximately (b) (4) vials), (b) (4) piles of stoppers (each pile containing approximately (b) (4) stoppers), (b) (4) pairs of tweezers, (b) (4) trays to hold stoppered vials ((b) (4) vials per tray), small (b) (4) (b) (4) containing pellets, a Whirlpak bag with pellets, an (b) (4) or non-viable (b) (4) (b) (4) and a settle plate.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Margaret M Annes, CSO	<input checked="" type="checkbox"/> Margaret M Annes <small>Margaret M Annes CSO Signed by: Margaret M. Annes-S</small>	DATE ISSUED 5/10/2017

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER 4040 North Central Expressway, Suite 300 Dallas, TX 75204 (214)253-5200 Fax: (214)253-5314	DATE(S) OF INSPECTION 4/17/2017-5/10/2017* FEI NUMBER 3011286349
---	---

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Shaun P. Riney , General Manager

FIRM NAME Qualgen, LLC	STREET ADDRESS 14844 Bristol Park Blvd
CITY, STATE, ZIP CODE, COUNTRY Edmond, OK 73013-1891	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility

- c) On 4/17/17, during the production of lot #C075 of Testosterone 87.5mg pellets, the technician opened a bag of stoppers that had been (b) (4) and dumped them out directly onto the surface (deck) of the ISO 5 (b) (4) to be used in vialing the pellets.
- d) On 4/26/17, while placing the pellets from lot #C080 of Testosterone 200mg pellets into vials, one operator was seen placing (b) (6) gloved finger on top of the open vials before placing the pellets inside.

This is a repeat observation from the 8/24/15-9/17/15 inspection.

OBSERVATION 3

The separate or defined areas and control systems necessary to prevent contamination or mix-ups are deficient.

Specifically,

- a) During re-certification of the clean rooms and ISO 5 (b) (4), a leak was detected in one of the HEPA filters in the (b) (4) (Lab^(U)(4)). The report from the 3rd party vendor does not mention the leak, identify which HEPA filter was leaking, the fact that the HEPA was changed, or the fact that they did not perform certification of the rooms or hoods on that date due to the leak. They returned on (b) (4) to certify the rooms and hoods after the HEPA filter was replaced. A (b) (4) HEPA filter was found to be leaking when they returned on (b) (4) to perform a cleanroom certification after (b) (4). The report does not mention the leak, identify which HEPA filter was leaking, or the fact that it was changed.
- b) Personnel performing fingertip sampling after working in the ISO 5 (b) (4) were observed lightly touching (b) (4) of their gloves to the plate during fingertip monitoring. The sampling does not include the pad of the finger.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Margaret M Annes, CSO	<input checked="" type="checkbox"/> Margaret M Annes Margaret M Annes CSO Signed by: Margaret M. Annes-G	DATE ISSUED 5/10/2017

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER 4040 North Central Expressway, Suite 300 Dallas, TX 75204 (214)253-5200 Fax:(214)253-5314	DATE(S) OF INSPECTION 4/17/2017-5/10/2017*
	FEI NUMBER 3011286349

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Shaun P. Riney , General Manager

FIRM NAME Qualgen, LLC	STREET ADDRESS 14844 Bristol Park Blvd
---------------------------	---

CITY, STATE, ZIP CODE, COUNTRY Edmond, OK 73013-1891	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility
---	--

- c) Operator (b) (6) had twelve (12) personnel monitoring excursions (fingertip sampling) from February 2016-September 2016.
- d) Your firm did not document pressure differential readings between classified areas i.e. ISO 7 cleanroom and the ISO 8 Ante Room where gowning occurs, for all days that production occurred. For example, there is no documentation of pressure differentials for all rooms on 7/1/16 (lot (b) (4) of Testosterone (b) (4) , 7/9/16 (lot #B066 of Testosterone 37.5mg pellets), 7/10/16 (lot #B067 of Testosterone 87.5mg pellets), 2/5/17 (lot # (b) (4) of Estradiol (b) (4) 3/4/17 (lot #C034 Testosterone 200mg/Anastrozole 20mg pellets), and 3/11/17 (lot #C042 of Testosterone 200mg pellets).
- e) On 4/21/17, I observed rust on the base of a chair being used inside of the ISO 7 (b) (4) (Lab (b) (4))

OBSERVATION 4

Written procedures are not established and followed that describe the in-process controls, tests and examinations to be conducted on appropriate samples of in-process materials of each batch.

Specifically,

- a. Your firm has no written justification for the sample sizes for in-process testing of (b) (4) and cannot demonstrate that they were established using suitable statistical procedures. Your firm (b) (4) for (b) (4) (b) (4). Theoretical batch sizes are (b) (4) pellets depending on the product.

This is a repeat observation from the 8/24/15-9/17/15 inspection.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Margaret M Annes, CSO	<input checked="" type="checkbox"/> Margaret M Annes <small>Margaret M Annes CSO Signed by: Margaret M. Annes -5</small>	DATE ISSUED 5/10/2017 5/10/2017

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER 4040 North Central Expressway, Suite 300 Dallas, TX 75204 (214)253-5200 Fax: (214)253-5314	DATE(S) OF INSPECTION 4/17/2017-5/10/2017* FEI NUMBER 3011286349
---	---

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Shaun P. Riney , General Manager

FIRM NAME Qualgen, LLC	STREET ADDRESS 14844 Bristol Park Blvd
CITY, STATE, ZIP CODE, COUNTRY Edmond, OK 73013-1891	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility

- b. Your firm has stopped documenting in the batch record for all Testosterone pellets the actual in-process individual pellet weight values obtained. For all testosterone drug products produced, the (b) (4) pellets that are determined by the operator (b) (4) and those results are not documented.

OBSERVATION 5

Each batch of drug product required to be free of objectionable microorganisms is not tested through appropriate laboratory testing.

Specifically,

- a. The sterility test method used by your current 3rd party vendor for release testing of finished drug products is not validated. The pieces of pellet that did not dissolve during the incubation period or dissolved late in the incubation period were not adequately incubated for the sterility test.
- b. The sterility test method used during the validation and (b) (4) for the (b) (4) sterilization process is not validated. The pieces of pellet that did not dissolve during the incubation period or dissolved late in the incubation period were not adequately incubated for the sterility test.
- c. The bioburden determination for validation of the sterilization process was not performed using product from your firm. With regards to the method used to determine bioburden, the (b) (4) (b) (4) may not recover the bioburden in the whole pellet.

***DATES OF INSPECTION**

4/17/2017(Mon),4/18/2017(Tue),4/19/2017(Wed),4/20/2017(Thu),4/21/2017(Fri),4/24/2017(Mon),4/25/2017(Tue),4/26/2017(Wed),4/27/2017(Thu),4/28/2017(Fri),5/02/2017(Tue),5/03/2017(Wed),5/04/2017(Thu),5/05/2017(Fri),5/10/2017(Wed)

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Margaret M Annes, CSO	<input checked="" type="checkbox"/> Margaret M Annes Margaret M Annes CSO Signed by: Margaret M. Annes-5	DATE ISSUED 5/10/2017