

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER

U.S. FDA CBER Office of Compliance and Biologics Quality
10903 New Hampshire Ave W071-5128
Silver Spring, MD 20993-0002
TEL: 240-402-9159

DATE(S) OF INSPECTION

06/16/2022 - 06/23/2022

FEI NUMBER

3001417487

Industry Information: www.fda.gov/oc/industry

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Chiron GT. Howell, Site Director

FIRM NAME

Protherics UK Ltd.

STREET ADDRESS

Blaenwaun, Ffostrasol

CITY, STATE AND ZIP CODE

Llandysul, Ceredigion SA44 5JT, UK

TYPE OF 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 (I) (WE) OBSERVED:

1. QC testing procedures are deficient. Specifically,

A. There is a lack of study to support the (b)(4) of sample (b)(4) for endotoxin analysis per (b)(4) -13.160, v7, section 6.12.3.

B. (b)(4) media are not being compared to previously tested and approved batch of the same media type. Instead, they are being compared to (b)(4) obtained from (b)(4) per (b)(4) -13.015, v15, section 6.7.1.

C. There is a lack of (b)(4) under (b)(4) conditions despite (b)(4) qualification requires the assessment of (b)(4) recovery per (b)(4) -13.002, v7, section 2.

D. (b)(4) prepared (b)(4) cultures are not qualified prior to release for use. (b)(4) cultures are being used as (b)(4) for (b)(4) and (b)(4).

E. Drug samples are not (b)(4) in analytical sequences to verify (b)(4) control. A (b)(4) is analyzed (b)(4) sample and does not confirm that the (b)(4) instrument is in a calibrated state upon the completion of the analysis. As a result, drug product results were invalidated and retested, due to a (b)(4) calibration test failure. For example,

i). Quality Event 55795 - The (b)(4) calibration for the Quality Control (b)(4) was conducted per SOP (b)(4) entitled, "(b)(4)" on June 29, 2020, and failed the (b)(4) accuracy test during the calibration. Consequently, all CroFab and DigiFab (b)(4) drug product release tests that were performed (b)(4) were invalidated and retested. All sample retests had passing results.

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EMPLOYEE(S) SIGNATURE



EMPLOYEE(S) NAME AND TITLE (Print or Type)

Eileen A. Liu, Lead CSO
Burnell M. Henry, CSO

DATE ISSUED

06/23/2022

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

DISTRICT OFFICE ADDRESS AND PHONE NUMBER U.S. FDA CBER Office of Compliance and Biologics Quality 10903 New Hampshire Ave W071-5128 Silver Spring, MD 20993-0002 TEL: 240-402-9159 Industry Information: www.fda.gov/oc/industry	DATE(S) OF INSPECTION 06/16/2022 - 06/23/2022
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NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Chiron GT. Howell, Site Director

FIRM NAME Protherics UK Ltd.	STREET ADDRESS Blaenwaun, Ffostrasol
CITY, STATE AND ZIP CODE Llandysul, Ceredigion SA44 5JT, UK	TYPE OF ESTABLISHMENT INSPECTED Manufacturer

F. (b)(4) are not included at the end of analytical sequences to ensure (b)(4) control for the following (b)(4) analyzes.

- i. (b)(4) 13.059, entitled, "Determination of Drug Product Protein content by (b)(4)"
- ii. (b)(4) 13.0028, entitled, "Product speciation - (b)(4)"
- iii. (b)(4) 13.110, entitled, "Measurement of DigiFab biological activity (Potency) & specific content by (b)(4)"

2. (b)(4) testing (b)(4) conducted in -- Grade (b)(4) area in September 2021 as part of the facility qualification was deficient. Specifically,

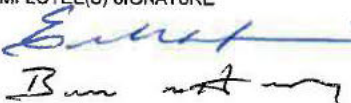
A. There was a lack of consistent supply of (b)(4) for an adequate assessment of (b)(4) HEPA (b)(4) or the absence of (b)(4) as required per (b)(4) -04.013, v1, section 6.2.

B. Aseptic operations carried out during routine processing including worst-case activities which cause the most potential for product contamination were not adequately simulated under dynamic conditions as required per (b)(4) -04.013, v1, section 6.4.

3. Classified (b)(4) areas are deficient regarding the system for monitoring environmental conditions. Specifically,

A. There is a lack of documented risk based assessments for identifying the environmental monitoring (EM) sample locations.

B. (b)(4) 13.009, entitled "Viable Environmental Monitoring Procedures", v27 is deficient in that the above procedures do not define specific EM sample locations when no processing is scheduled.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE 	EMPLOYEE(S) NAME AND TITLE (Print or Type) Eileen A. Liu, Lead CSO Burnell M. Henry, CSO	DATE ISSUED 06/23/2022

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Eileen A. Liu
Burnell M. Henry

EMPLOYEE(S) NAME AND TITLE (Print or Type)

Eileen A. Liu, Lead CSO
Burnell M. Henry, CSO

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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."