DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
CDER/OPQ/OPMA/DBM, Attn: Zhihao Peter Qiu, Ph.D., Director 10903 New Hampshire Avenue; White Oak Building 22, Room 5112 Silver Spring, MD 20993 E-mail: OPFBLAInspection483Responses@fda.hhs.gov	08/12/2021-08/20/2021
	FEI NUMBER 3012163998

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Sangjun Cho, Head of Quality

FIRM NAME	STREET ADDRESS
Hugel, Inc.	23, Geodudanji 1-gil, Dongnae-myeon
CITY, STATE, ZIP CODE, COUNTRY Chuncheon, Gangwon, Korea 24398	TYPE ESTABLISHMENT INSPECTED Drug Substance and Drug Product manufacturing

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:

1. *Clostridium botulinum* spore containment in the drug substance manufacturing areas is inadequate to mitigate spore cross contamination risk of other manufacturing areas. The (b) (4) drug substance and drug product are manufactured in the same Geodu building.
   a. (b) (4) where *Clostridium botulinum* (b) (4) teps are d at a (b) (4) compared to the adjacent manufacturing areas. The (b) (4) (b) (4) than the (b) (4) room and (b) (4) lower than (b) (4) (b) (4) (b) (4) maintains (b) (4) and thus, spores are not contained in the (b) (4)
   b. There is no procedure control to prevent personnel entering the drug product manufacturing area after exiting the drug substance area.

2. Decontamination of *Clostridium botulinum* spores and toxin in the drug substance manufacturing areas is inadequate.
   a. In room (b) (4) *Clostridium botulinum* (b) (4) (b) (4) (b) (4) (b) (4) (b) (4) (b) (4) (b) (4) (b) (4) pose a risk of contaminating the spectrometer and adjacent areas with *Clostridium* spores.

	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE *(Print or Type)*	DATE ISSUED
SEE REVERSE OF THIS PAGE	Madushini N. Dharmasena -S Digitally signed by Madushini N Dharmasena -S DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=2001406605, cn=Madushini N Dharmasena -S Date: 2021.08.19 22:59:06 -04'00' Mekonnen Lemmadechassa -S Digitally signed by Mekonnen Lemmadechassa -S DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=2001897504, cn=Mekonnen Lemmadechassa -S Date: 2021.08.19 23:10:48 -04'00'	Madushini Dharmasena, Ph.D., SR PHARMA. QUALITY ASSESSOR Mekonnen Lemma Dechassa, Ph.D., BIOLOGIST	08/20/2021

b. The disinfectant qualification study did not demonstrate that the disinfectants used in the manufacturing facility can effectively decontaminate *Clostridium* spores and toxin (ALC15011-P-01 and ALC15011-R).

3. Environmental monitoring is insufficient to ensure that the drug product manufacturing areas are not contaminated with *Clostridium botulinum* spores as *Clostridium* spores are not monitored as part of environmental monitoring (AWLS-FE-039-29).

4. Investigation of out-of-specification (OOS) DV19-019 for identification and purity by SDS-PAGE is inadequate. The OOS report concluded that the root cause for level of impurity exceeding the acceptance criteria was because of the physical stress on the protein by (b) (4) (b) (4) during the extra sampling. Re-test of the sample was not conducted to confirm the presumed root cause, and the lot was rejected.

5. The SOP for logbooks preparation and management (SOP # AWLS-QA-015:F05) was not updated in a timely manner to include adequate controls to prevent the loss of logbooks (DV19-035). Specifically, in November 22, 2019 the firm discovered that twelve logbooks that document the use of incubators went missing in 2016 and 2017 and as a result, SOP # AWLS-QA-015:F05 was not revised until January 29, 2020 to mitigate the problem.

6. The working cell bank (WCB) lot # (b) (4) used to manufacture the drug substance lots and submitted in (b) (4) s different from a WCB lot # (b) (4) used to manufacture (b) (4) drug substance during inspection. In addition, comparability data are not available to demonstrate that the critical product quality attributes of drug substance manufactured using new WCB lot # (b) (4) is comparable to the drug substance manufactured using WBC lot # (b) (4)

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
CDER/OPQ/OPMA/DBM, Attn: Zhihao Peter Qiu, Ph.D., Director 10903 New Hampshire Avenue; White Oak Building 22, Room 5112 Silver Spring, MD 20993 E-mail: OPFBLAInspection483Responses@fda.hhs.gov	08/12/2021-08/20/2021 FEI NUMBER 3012163998

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Sangjun Cho, Head of Quality	
FIRM NAME Hugel, Inc.	STREET ADDRESS 23, Geodudanji 1-gil, Dongnae-myeon
CITY, STATE, ZIP CODE, COUNTRY Chuncheon, Gangwon, Korea 24398	TYPE ESTABLISHMENT INSPECTED Drug Substance and Drug Product manufacturing

7. (b) (4) for (b) (4) drug product batch (b) (4) manufactured on (b) (4) exceeded the specified filling time (b) (4) (b) (4) and the time validated by the media fill (b) (4) leading to batch failure. The delay in (b) (4) stopper supply, damaged vials and operators taking breaks were identified as initial root cause for this deviation (DV21-066).

	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE *(Print or Type)*	DATE ISSUED
SEE REVERSE OF THIS PAGE	Madushini N. Dharmasena -S Mekonnen Lemmadechassa -S Digitally signed by Mekonnen Lemmadechassa S DN: c US o U.S. Government ou HHS ou FDA ou People 0.9.2342.19200300.100.1.1 2001897504 cn Mekonnen Lemmadechassa S Date: 2021.08.19 23:15:22 04'00'	Madushini Dharmasena, Ph.D., SR PHARMA. QUALITY ASSESSOR Mekonnen Lemma Dechassa, Ph.D., BIOLOGIST	08/20/2021