Lonza

Risk Assessment on Coronavirus 2019 (COVID-19)

Cell culture media, buffer and supplement manufacturing

1. INTRODUCTION

In response to the recently declared pandemic of the novel (new) coronavirus, named “coronavirus disease 2019” and abbreviated “COVID-19”, our business has been tasked with taking the appropriate actions in order to limit the spread of the virus and to ensure safe supply of our finished products to the market. With the primary mode of transmission of the virus being established as being between person-to-person and the secondary mode being surface-to-person, all manufacturing operations are considered to be at risk for potential contamination if or when a colleague is confirmed to be infected with the COVID-19 virus.

Verviers site operates under EN ISO 13485 and partially under current Good Manufacturing Practices (cGMP). In this regard, heightened measures have been implemented regarding colleague hygiene. This includes proper gowning (hair, face, body, feet) and the reduction of human contact/interaction with raw materials, in-process materials, surfaces, and finished products to an absolute minimum based on adequate equipment design, set-up and procedures. Current guidelines for when a colleague becomes ill, poses a contamination risk, or requires medical intervention are clear and established and require the colleague to notify proper departments and remove themselves from the production environment. These practices and procedures are sufficient themselves to ensure safe products enter the marketplace and to ensure the health and wellbeing of the colleagues manufacturing them. However, in the exceptional event of a pandemic of a highly infectious disease, additional, temporary precautions are needed to strengthen our security, to lower the risk, and ensure a safe production environment.

The following risk assessment has taken into account several aspects specific to Verviers site including colleagues, visitors, manufacturing processes, environment, cleaning are addressed at a holistic level. The temporary controls are established using guidelines from the World Health Organization (WHO), local disease control agencies, and/or local authorities in light of the COVID-19 pandemic.

Specific information regarding the COVID-19 virus can be found by referencing the Food and Drug Administration (FDA), the Center for Disease Control (CDC), the World Health Organization (WHO), and other local or national agency websites.
Furthermore, on 22 June, USFDA issued an official guidance to industry, named “Good Manufacturing Practice Considerations for Responding to COVID-19 Infection in Employees in Drug and Biological Products Manufacturing”. This guidance is being issued to address the Coronavirus Disease 2019 (COVID-19) public health emergency. The guidance document is being implemented immediately.

2. RISK ASSESSMENT

Process or Source	Potential Failure	Potential Effects of Failure	S	Potential Causes of Failure	O	Controls
Colleagues	Infected colleague in production	Transfer of infection	5	Non-adherence to cGMP, company, and government guidelines	1	*See controls section*
Raw Materials Receipt/Sampling/dispensing	Infected raw material	Transfer of infection	5	Infected colleague in contact with the material or material was infected by the supplier	1	
Manufacturing Process	Infected in-process materials, surfaces, etc.	Transfer of infection	5	Infected colleague in contact with the material or surface, infected raw material used	1	
Equipment/High-Contact Surfaces	Infected surfaces	Transfer of infection	5	Infected colleague or raw material in contact with the equipment or surface	1	
Environmental Air	Infected air	Transfer of infection	5	Infected colleague within cGMP environment	1	

S = Severity; O = Occurrence; D = Detectability

Severity Scale		Occurrence Scale		Detectability Scale		RPN Score, R
1	Insignificant	1	Rare	1	Effective	25
						15
3	Moderate	3	Occasional	3	Not Effective	9
						5
5	Critical	5	Common	5	Not Aware	3
						1

3. CONTROLS:

Based on recommendations by competent health authorities (e.g. WHO, CDC, …) additional personal, sanitary environmental controls and practices where implemented to prevent transmission, exposure and persistence of the virus on site.

3.1 Colleagues

As COVID-19 is primarily spread person-to-person, the additional directives where implemented to minimize transmission and personnel exposure:

- Personnel who could work from home were directed to work from home.: +/- 70 people were working from home, +/- 80 people were on site supporting business critical activities.
- Additional hand sanitizers were provided at strategic location throughout the facility
- Published heightened hand-washing and disinfection guidelines
- Employees who were exposed to other employees suspected of being infected were quarantined,
- Gowning room occupancy was restricted to 1 or 2 people at a time.
- Mandatory temperature body monitoring upon arrival at the facilities for all personnel entering in production area
- Provision of face
- Recommendation to avoid unnecessary travel
- On-site social distancing practices:
  - remain ≥ 1.5 meters apart
  - Face to face meeting were cancelled, use of remote meetings (e.g. tele/web conference)
  - modified break and work schedules to minimize the number of colleagues in an area at one time
  - Seating in the cafeteria was limited to those who didn't have desk and the area was segregated to separate personnel (e.g. one colleague per table)
- Screening of visitors and contractors to reduce colleague interaction and/or potential spread of the virus

In addition, frequent communication is provided encouraging employees to maintain good hygiene, respiratory vigilance and limit time with colleagues wash hands, cover cough, and if any symptoms were present to stay at home.

When a colleague is suspected or confirmed of being infected with the COVID-19 virus, the Lonza corporate guidance is followed to ensure proper notification, contact tracing, and disinfection of areas/surfaces is conducted.

3.2 Raw Material Receipt/Dispensing

The receipt of raw materials and processing aids contaminated with COVID-19 by the supplier is very unlikely to occur. Suppliers' quality systems are in line with good manufacturing practices per either regulatory or voluntary (ISO, EXCIPACT, FSSC, etc.) agency requirements and are carrying out the same risk assessments and mitigation strategies in response to the COVID-19 pandemic as per recent correspondence.

The raw materials used by Verviers site are either of non-animal origin or derived exclusively from

animals recognized as TSE/BSE free and safe for human consumption following ante and post mortem inspections by official veterinarians. Raw materials are required to meet compendial and regulatory requirements for quality and safety as established via purchasing specifications. Additionally, the manufacturing processes for most raw materials include treatments steps using pH, temperature (e.g. high heat, pasteurization, sterilizing), or filtration designed to reduce or eliminate microbiological or virologic risks.

Receiving raw material packaging, primarily of plastic and cardboard materials, contaminated with COVID-19 is also very unlikely. While it is not certain how long the virus that causes COVID-19 survives on surfaces, it seems to behave like other coronaviruses. Studies suggest that coronaviruses (including preliminary information on the COVID-19 virus) may persist on surfaces for a few hours or up to several days. This include plastics for as long as 72 hours and cardboard for as long as 24 hours. Taking into account the transport lead times from our suppliers to our site, the likelihood for a contamination is extremely low.

The virus that causes COVID-19 has not been detected in drinking water. Conventional water treatment methods that use filtration and disinfection, such as those in most municipal drinking water systems and at Verviers site, should remove or inactivate the virus that causes COVID-19[1]

Contamination of the raw material or colleague during receipt, sampling, transportation, and utilization by a colleague is very unlikely due to the mitigation activities being taken under the Colleagues section.

3.3 Manufacturing Processes

Primary source for contamination of the manufacturing process is via colleague interaction. The mitigations taken between colleagues and Equipment/High-Contact Surfaces are adequate in reducing this risk. Manufacturing processes are controlled under strict cGMP conditions and direct contact with raw materials, in-process materials, and finished products has been reduced to the absolute minimum based on adequate equipment design, process set-up, and procedures. Additionally, Aseptic Process Simulation (APS) is performed for every manufacturing process (Bottles, bags and vials). The APS challenges and evaluates the aseptic processing operation capability using media to demonstrate aseptic manufacturing. Successful completion demonstrate that a process can be performed without introducing microbial contaminants and quality operators to perform aseptic process.

3.4 Equipment/High-Contact Surfaces

The frequency of cleaning has not be increased but in the other hand we increase the awareness and adherence to BEVE-437 “Nettoyage et désinfection des zones à atmosphere contrôlée”, procedure for cleaning and sanitization of manufacturing area.

3.5 Environmental Air

All premises of the production area are designed to meet minimum class D up to class A. Material and personnel entry should go into production via specific personal or material channel.

[1] US Center for Disease Control and Prevention, website: https://www.cdc.gov/coronavirus/2019-ncov/php/water.html

Ambient air within the manufacturing area along with air directly blown on in-process products is passed through high efficiency filtration. The filters are on a routine preventive maintenance schedule to ensure proper operation. The appropriate pressure cascade is maintained to avoid product contamination and environmental contamination. The environment is also monitored on regular frequency for viable and non-viable particles.

4. DISPOSITION OF FINISHED PRODUCTS

The likelihood of colleagues contaminating finished product is low due to the direct contact with finished products being reduced to an absolute minimum based on adequate equipment design, process set-up, and procedures, including those under Colleagues section.

Per the US FDA, there is currently no evidence to support that COVID-19 can be transmitted to humans through food or food packaging materials. When necessary hygiene measures are put in place, the FDA does not anticipate the need for products to be held, recalled, or withdrawn from the market due to possible exposure to COVID-19 through a person that has been confirmed to be infected working at a facility.[2]

That position is confirmed by the European Commission in a Q&A on COVID-19 and Food Safety.[3]

5. CONCLUSION

Overall, the product quality risk was determined to be low.
The risk of spreading COVID-19 through the products manufactured by Verviers site has been reduced to an acceptable level by implementing additional, and temporary mitigation steps detailed above.

[2] US Food and Drug Administration, Food Safety and the Coronavirus Disease 2019 (COVID-19), website: https://www.fda.gov/food/food-safety-during-emergencies/food-safety-and-coronavirus-disease-2019-covid-19, April 14, 2020

[3] European Commission Directorate-General for Health and Food Safety, COVID-19 and Food Safety - Questions and Answers, April 8, 2020