BLehrer LLC

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INTEGRATED BIOPHARMA
AND PHARMA SOLUTION

Handling of COVID-19 infection in employees – summary report

Based on FDA guidance on GMP considerations for Responding to COVID-19 infection in employees in Drug and Biological Products Manufacturing

Background

- In June 2020, FDA released a Guidance document titled “GMP considerations for Responding to COVID-19 infection in employees in Drug and Biological Products Manufacturing”
- The guidance gives details on controls to prevent contamination of drugs, Impact of COVID-19 on drug safety, quality and disposition and steps to be taken to maintain continuity of drug supply.

III. Manufacturing Controls to Prevent Contamination of Drugs

Guidance Requirement	Interpretation / Summary	Action Plan
Following are already part of GMP regulations: For Drugs: 21 CFR 211.28 – “Personnel Responsibilities”, For API: CCH Q7, Section III, Personnel For Biologics: 21CFR 600.10(c)(1) “restriction on Personnel – (1) Specific duties Does not allow persons with infectious diseases, open cuts / wounds, lesions to work in product exposure areas	These requirements are already part of the GMP regulations. All People (including Employees, contract workmen, external persons, etc.) entering the facility need to be checked for symptoms of COVID-19 (fever, dry cough, etc.) before allowing access to the facility. Any person/s experiencing or displaying COVID-19 like symptoms after entry to the facility need to immediately report to supervisor and move out of the facility.	• Procedure and documentation for daily check for all persons entering the facility for COVID-19 symptoms • Procedure and documentation to report signs of sickness after entry to workplace and take necessary action. • Monitoring of COVID-19 symptoms in employees who have been exposed to persons with suspected or confirmed COVID-19 • Mechanism to confirm home quarantine / hospitalization requirements have been fulfilled before allowing the person back to work.
To ensure compliance with CGMP requirements, drug product manufacturers must ensure that employees practice good sanitation and health habits	All employees and contract workmen need to follow Good sanitation and health practices	To provide training / awareness to employees and contract workmen on importance of good sanitation and health practices and how to follow it.

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Evaluate the adequacy of the CGMP controls already in place to protect materials, components, drug container closures, in-process materials, and/or drugs from sick employees in the context of this new coronavirus. For example, review cleanroom process controls such as air filtration, positive air pressure and movement of air to ensure proper function. Consider the likelihood of contamination or cross-contamination to other drugs in the facility. Current microbiological controls, if strictly implemented (e.g., employees only work in area with closed system processing), may be sufficient to protect the drugs and materials used to make them from SARS-CoV-2 contamination. If needed, implement additional controls to eliminate or minimize the risk of contamination.	An evaluation needs to be performed to confirm the adequacy of the existing controls related to product, process, people and material to prevent contamination from sick employees.	• Documented Risk assessment to evaluate the adequacy of current controls. • Action plan to address the gaps identified, if any. • Action plan for reviewing the cleanroom process controls in both DS and DP facilities.

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For biological products where manufacturing processes or materials are more susceptible to viral contamination, manufacturers should already have stringent viral control strategies in place. Potential risks from SARS-CoV-2 are likely to be mitigated by existing viral control strategies The potential for the production cell line to replicate SARS-CoV-2 Controls in place for procedures taking place in open systems (e.g., buffer and media preparation areas)	An evaluation needs to be performed to confirm the adequacy of the existing controls related to product, process, people and material to prevent viral contamination into the product / process.	• Documented Risk assessment with details of why the virus contamination and study is not applicable to yeast cell based processes • Details of controls in place processes happening in open systems and identification of gaps, if any • Action plan to address the gaps identified, if any.
During this COVID-19 public health emergency, drug manufacturers should review CGMP requirements and recommendations related to facility and equipment cleaning and sanitation and other controls that ensure materials, APIs, components, drug product containers and closures, in-process materials, and drug products are safe and meet their quality requirements	A review of existing cleaning and sanitation plan for area, equipment and components needs to be done to evaluate the effectiveness and identification of gaps, if any	• Documented review of the existing cleaning and sanitation plan for area, equipment and components along with controls in place. • Action plan to address the gaps, if any identified.

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• Clean and sanitize nonproduction areas more frequently. • Update existing procedures to institute more frequent cleaning, sanitization, and / or sterilization of surfaces in the production areas, particularly surfaces that are contacted frequently, such as door handles, equipment latches, bench / counter tops, and control panels. Special attention should be paid to sanitizing / sterilizing equipment and product-contact surfaces. • Consider expanding existing procedures to include using gloves, face masks, and/or gowning where such measures were not previously required. • Consider further restrictions on employee access to any manufacturing area, beyond that required by CGMP regulations and recommended by Agency guidance and normal practice, to limit the possibility of contamination.	Cleaning and sanitation of non production areas need to be done at a higher frequency (common areas like elevators, staircases, washrooms, change rooms, etc.) Focus on surfaces which are frequently touched by people (door handles, buttons, control panels, etc.) Evaluation of existing gowning requirements vis-à-vis areas and expanding to additional areas. Enhanced control on employee access to manufacturing area.	• Revision of cleaning and sanitation SOPs to increase frequency of sanitation of common areas with details of which surfaces to be considered. • Documented assessment to evaluate the need for expanding gowning, mask, glove requirement beyond existing system and implementation. • Evaluation of persons who are entering the manufacturing areas and determination whether the list of persons can be further reduced until the pandemic is controlled.

III. Manufacturing Controls to Prevent Contamination of Drugs

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If a potential or actual viral contamination event is identified, drug manufacturers should promptly clean, disinfect, sanitize, and if necessary, sterilize affected equipment, surfaces, production areas, and facilities, before resuming manufacturing.	In case of any suspected or actual infection in the facility, the affected area, equipment, surfaces need to be clean, disinfect and where applicable, sterilized before restart of manufacture. Impact assessment needs to include fate of affected batch / batches.	• Create procedure / SOP for describing details of activities to be performed (cleaning, disinfection, sanitization, sterilization, etc.,) in the event any suspected or actual infection is observed. • Procedure for identification of the persons who have come in contact with the person with suspected or actual infection and actions to prevent further spreading.
If supplies of single-use masks and other garb used to control contamination during manufacturing are low, they should be prioritized for use in sterile manufacturing operations. To mitigate supply issues, drug manufacturers may need to re-sterilize or disinfect masks and garb, as appropriate, and reuse them during non-sterile drug operations.	Self explanatory	• Ensuring sufficient stock availability of single use PPEs like masks and other accessories in sterile / aseptic manufacturing. Single use garments are not used in any of the areas. Emphasis on effectiveness of the garment washing process.

III. Manufacturing Controls to Prevent Contamination of Drugs

Guidance Requirement	Interpretation / Summary	Action Plan
To ensure compliance with CGMP requirements, drug product manufacturers must ensure that all evaluations of the production controls (including risk assessments), follow-up, and changes are approved by the manufacturer's quality unit and documented within the manufacturer's quality management system	Any changes being proposed to increase control or mitigate identified / potential risks shall be reviewed and approved by the head of Quality before implementation	• All changes being proposed in light of this guidance need to be approved by the Head of Quality

IV. COVID-19 Impact on Drug Safety, Quality, and Disposition

Guidance Requirement	Interpretation / Summary	Action Plan
Drug manufacturers should determine if SARS-CoV-2 could adversely affect the safety or quality of their materials, components, drug product containers and closures, in-process materials, and drugs if they were to become contaminated with the virus. The risk assessment should consider the known characteristics and studies of this family of viruses as well as the drug types and their characteristics (e.g., drug product or API, sterile, non-sterile, solids, powders, liquids, large or small molecule).	Self explanatory	• Risk assessment shall be performed to evaluate the impact of a potential SARS-CoV-2 contamination on the safety or quality of material, component, product etc.
Lots or batches of components, drug product containers and closures, in-process materials, and/or drug products determined to be adversely affected in terms of safety and quality must not be released for further manufacturing or distribution.	Self explanatory	• No additional action is required. Procedures are in place to handle contaminated product / material.

IV. COVID-19 Impact on Drug Safety, Quality, and Disposition

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To ensure compliance with CGMP requirements, drug product manufacturer's must ensure that all evaluations (including risk assessments) to determine if drug safety or quality were adversely affected, as well as any follow-up and changes are approved by the manufacturer's quality unit and documented within the manufacturer's quality system	Self explanatory	• Any assessments, evaluations, changes, etc. being done in view of the COVID-19 pandemic shall be reviewed and approved by the Quality Head.

V. Maintaining the Drug Supply

Guidance Requirement	Interpretation / Summary	Action Plan
During this outbreak drug manufacturers may learn that an employee (s) has tested positive to COVID-19 or has been exposed to a person having the COVID-19 infection. Such an employee may or may not be symptomatic. TO ensure compliance with CGMP requirements, manufacturers should direct workers who have symptoms to notify their supervisors and stay at home. Manufacturers should also direct workers who have been exposed or potentially exposed to COVID-19 at work, home, or elsewhere to notify their supervisors	Self explanatory	• Reinforcing the reporting requirements by multiple training / discussion sessions. Employees should report about the symptoms, if any and stay at home.

Other considerations beyond the guidelines

Considerations	Action Plan
• Sanitization and handling of incoming material (raw material, packing material, accessories, consumables, etc.) • Control on vehicular movement within factory premises. • Control on entry of external personnel (drivers, helpers, manual labourers, etc.) into the factory premises. • Transportation of employees (pick up / drop) – social distancing, areas of pickup and drop (hotspots) • Employees using their own mode of transport	• Procedure for sanitation / disinfection and holding of incoming material for defined period of time before transfer into the main storage area. • Control on personnel transportation – social distancing, hand sanitization, masks, occupancy in bus, etc. • Control on number of persons in personal transport (car)