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FDA Releases Guidance on COVID-19 CGMP Considerations for Drug Manufacturers

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Food, Drugs, and Devices

Drug manufacturers have responded to the COVID-19 pandemic by adopting critical measures to ensure continuity in their operations—continuity that is vital to safeguarding the global drug supply. In doing so, they have faced unprecedented challenges with regard to ensuring the health of their employees, preventing COVID-19 transmission at their facilities, and mitigating associated risks to product safety and quality. In light of these challenges, the U.S. Food and Drug Administration (FDA) released a guidance document on June 19, 2020, to advise manufacturers of human and animal drug and biological products on how to manage the unique risks associated with COVID-19 infection in employees.

The Guidance, titled "Good Manufacturing Practice Considerations for Responding to COVID-19 Infection in Employees in Drug and Biological Products Manufacturing," was published for immediate implementation, and focuses on three key topics: (I) the use of manufacturing controls to prevent product contamination by SARS-CoV-2, (II) the use of risk assessments to evaluate the risks to drug safety or quality posed by SARS-CoV-2, and (III) measures manufacturers should take to ensure continuity in the drug supply.

I. Manufacturing Controls to Prevent Contamination of Drugs

Under FDA's Current Good Manufacturing Practice (CGMP) requirements, manufacturers must implement certain controls to prevent or mitigate risks to product safety or quality during the manufacturing process. Given the heightened risks posed by the COVID-19 pandemic, FDA recommends that manufacturers review and assess whether their existing manufacturing controls are adequate to prevent product contamination by COVID-19-infected employees, and implement additional controls as needed to eliminate or minimize the risk of contamination.[1]

[1]Given the particular vulnerability of biological products to viral contamination, FDA recommends that manufacturers of such products evaluate their current viral control strategies, focusing on the following items:

- The potential for the production cell line to replicate SARS-CoV-2.
- Whether current cell bank and harvest testing for viruses would detect SAR-CoV-2.
- The effectiveness of viral clearance and inactivation steps for SARS-CoV-2.
- Controls in place for procedures taking place in open systems (e.g., buffer and media preparation areas).

FDA recommends that manufacturers take the following steps to prevent COVID-19 transmission among employees and mitigate the risk of product contamination:

- Excuse any employees who test positive for COVID-19 or who display the symptoms of COVID-19. Such employees must be excluded from drug manufacturing areas under CGMP, and FDA recommends that such employees should not return to work until CDC's criteria to discontinue home isolation are met.
- Ensure that employees practice good sanitation and health practices.
- Clean and sanitize nonproduction areas (such as offices, elevators, break rooms, changing rooms, and restrooms) 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.
- Properly clean, sanitize, and disinfect any affected areas when a potential or actual viral contamination event is identified.

FDA also states that manufacturers who encounter shortages of single-use masks or garb should prioritize supplies for use in sterile operations. Manufacturers who are required to re-sterilize or disinfect such products should do so in accordance with applicable FDA policies, many of which have already been posted on FDA's website.

II. Assessing the Risks to Drug Safety or Quality Posed by SARS-CoV-2

FDA notes that its CGMP regulations require manufacturers to assess whether novel pathogens—such as SARS-CoV-2—pose new risks to product safety or quality. As such, manufacturers should conduct a risk assessment to determine the potential impact of SARS-CoV-2 contamination on production materials, components, drug product containers and closures, in-process materials, and drugs. This risk assessment should be approved by the manufacturer's quality unit and documented within the manufacturer's quality management system.

III. Ensuring Continuity in the Drug Supply

Finally, FDA notes that high levels of absenteeism resulting from widespread COVID-19 infection among employees could meaningfully disrupt the manufacturing process. To prepare for this risk, FDA recommends that manufacturers implement contingency production plans, per FDA's 2011 guidance on "Planning for the Effects of High Absenteeism to Ensure Availability of

Medically Necessary Drug Products." FDA also recommends that manufacturers allow quarantined and recovering employees to perform their work remotely when appropriate.

Finally, FDA reminds manufacturers that, pursuant to section 506C of the Federal Food, Drug, and Cosmetic Act, they must notify FDA if they anticipate a meaningful disruption in the supply of certain drugs and biological products. FDA recently issued a guidance document summarizing manufacturers' obligations under section 506C during the COVID-19 pandemic.

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This guidance is effective immediately, but comments may still be submitted to the Agency for consideration. This version of the guidance will remain in effect for the duration of the public health emergency declared by the Secretary of Health and Human Services, but the Agency plans to revise and replace the guidance with a generally applicable version when the public health emergency is over. FDA may incorporate changes in the revised guidance, based on public comments received in response to this guidance.

If you have any questions concerning the material discussed in this client alert, please contact the following members of our Food, Drug, and Device Practice:

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