WINSTON & STRAWN LLP

CLIENT ALERT

FDA Offers Good Manufacturing Practice Considerations to Drug/Biological Manufacturers Responding to COVID-19 Infections

JUNE 24, 2020

On June 19, 2020, in response to the ongoing COVID-19 public health emergency (PHE), the Food and Drug Administration (FDA or the Agency) issued new guidance (the Guidance) to provide recommendations to drug and biological product manufacturers,[1] including outsourcing facilities, regarding (1) manufacturing controls to prevent contamination of drugs and biologics, (2) risk assessment of SARS-CoV-2 as it relates to drug safety or quality and, (3) continuity of manufacturing operations.

While this policy is intended to remain in effect only for the duration of the COVID-19 PHE, FDA stated that the Guidance recommendations are expected to assist the Agency more broadly in its continued efforts to assure the safety and quality of drugs and maintain the drug supply beyond the termination of the PHE.

See Good Manufacturing Practice Considerations for Responding to COVID-19 Infection in Employees in Drug and Biological Products Manufacturing (June 2020), *available at* https://www.fda.gov/regulatory-information/search-fda-guidance-documents/good-manufacturing-practice-considerations-responding-covid-19-infection-employees-drug-and.

Manufacturing Controls to Prevent Contamination of Drugs and Biologics

FDA reminds and encourages drug manufacturers to review the following current good manufacturing practice (CGMP) regulations and recommendations regarding restriction of sick employees from production areas, as such recommendations are increasingly important to COVID-19 PHE responsiveness:

- Drug product manufacturers must ensure that employees practice good sanitation and health habits, in accordance with 21 C.F.R. 211.28(d), *"Personnel ."*
- Active pharmaceutical ingredients (API) manufacturers should ensure that employees practice good sanitation and health habits as described in the ICH guidance for industry *Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients (September 2016)*, section III.B., Personnel Hygiene (3.2).

- For positron emission tomography (PET) drugs, 21 C.F.R. 212.30 provides, *"What requirements must my facilities and equipment meet?"*
- For biological products, 21 C.F.R. 600.10(c)(1), *"Restrictions on personnel – (1) Specific duties."*

FDA recommends that drug manufacturers vigilantly monitor employees who perform drug manufacturing functions and have been exposed to others with confirmed or suspected COVID-19 for symptoms of COVID-19 infection. Manufacturers must exclude from drug manufacturing areas employees who test positive for COVID-19 (regardless of whether they have symptoms) or who have symptoms of COVID-19. FDA recommends that manufacturers not allow such employees to return to work in drug manufacturing areas until the CDC's criteria to discontinue home isolation are met, in consultation with healthcare providers.[2]

In accordance with quality risk management principles, drug manufacturers are expected to take the following steps to prevent or mitigate potential adverse effects on the safety and quality of drugs from an infected or potentially infected employee engaged in drug manufacturing:

- 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.[3]
- For biological products where manufacturing processes or materials are more susceptible to viral contamination, FDA recommends that manufacturers perform a risk assessment of their current viral control strategy and implement appropriate mitigation strategies responsive to SARS-CoV-2. These should include, but not be limited to, leveraging available information to assess:
  - The potential for the production cell line to replicate SARS-CoV-2;
  - Whether current cell bank and harvest testing for viruses[4] would detect SARS-CoV-2;
  - The effectiveness of viral clearance and inactivation steps for SARS-CoV-2;
  - Controls in place for procedures taking place in open systems (*g.*, buffer and media preparation areas).

FDA is encouraging drug manufacturers to 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. To help prevent transmission among employees and contamination of drugs/materials by a COVID-19-infected employee, FDA recommends that drug manufacturers:

- 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 to limit the possibility of contamination.

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

FDA clarifies that it is not aware of any drugs that have been contaminated with SARS-CoV-2 or of information indicating transmission of COVID-19 is associated with drugs. Nevertheless, there is an expectation that in order to maintain compliance with CGMP requirements, drug manufacturers must evaluate—as with any potential new risk—whether SARS-CoV-2 poses new risks in the context of their specific drugs, facilities, processes, and manufacturing

controls. To ensure compliance with CGMP requirements, drug product manufacturers 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 management system.

FDA recommends that risk assessments 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). Lots or batches of components, drug product containers and closures, in-process materials, and/or API and drug products determined to be adversely affected in terms of safety and quality must not be released for further manufacturing or for distribution. Moreover, such items must be properly dispositioned (*e.g.*, quarantined pending appropriate re-evaluation or reprocessing, or rejected).

Maintaining the Drug Supply

FDA declares that in order to ensure compliance with CGMP requirements, manufacturers should direct workers who have symptoms to notify their supervisors and stay 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. Regarding when employees may continue working following exposure or potential exposure, FDA is directing drug manufacturers to CDC guidance *Implementing Safety Practices for Critical Infrastructure Workers Who May Have Had Exposure to a Person with Suspected or Confirmed COVID-19*.[5]

Finally, FDA is recommending drug manufacturers of medically necessary human drugs implement contingency production plans if COVID-19 infections result in high absenteeism at drug manufacturing facilities during this public health crisis.[6] If the manufacturer's data and record management system supports it, drug manufacturers can consider permitting quarantined and recovering employees to work remotely on certain manufacturing functions that could be handled off-site (*e.g.*, batch record and analytical record review and investigations). If steps taken to prevent or mitigate adverse effects on safety and quality of drugs (*e.g.*, rejected lots or recalls) are likely to lead to a disruption in the drug supply, drug manufacturers should immediately contact FDA.

We note that government orders on the local, state, and federal level are changing every day, and the information contained herein is accurate only as of the date set forth above.

All entities should consult legal counsel for compliance issues and questions related to rapidly evolving COVID-19 legislation and policy.

View all of our COVID-19 perspectives here. Contact a member of our COVID-19 Legal Task Force here.

****

For further information or questions on the new Guidance or obligations under the Food, Drug and Cosmetic Act, please contact Amandeep S. Sidhu, T. Reed Stephens, Christopher Parker, or your Winston relationship attorney.

---

[1] For purposes of the Guidance, the term "drug manufacturer" is used to mean entities that make human or animal active pharmaceutical ingredients, prescription drugs, over-the-counter drugs, biological drug products, as well as drugs prepared by outsourcing facilities registered with FDA under section 503B of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. § 353b) or compounding pharmacies regulated under section 503A of the FD&C Act (21 U.S.C. § 353a).

[2] *See* https://www.cdc.gov/coronavirus/2019-ncov/hcp/disposition-in-home-patients.html.

[3] 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.

[4] *See* ICH guidance for industry *Q5A Viral Safety Evaluation of Biotechnology Products Derived From Cell Lines of Human or Animal Origin (September 1998).*

[5] *Available at* https://www.cdc.gov/coronavirus/2019-ncov/community/critical-workers/implementing-safety-practices.html.

[6] FDA directs manufacturers to the following guidance as a resource: *Planning for the Effects of High Absenteeism to Ensure Availability of Medically Necessary Drug Products (March 2011), available at* https://www.fda.gov/regulatory-information/search-fda-guidance-documents/planning-effects-high-absenteeism-ensure-availability-medically-necessary-drug-products-0.

7 Min Read

Related Locations

Charlotte | Chicago | Dallas | Houston | Los Angeles | New York | San Francisco | Silicon Valley | Washington, DC

Related Topics

COVID-19 | Health Care

Related Capabilities

Health Care

Related Regions

North America

Related Professionals

Amandeep S. Sidhu

T. Reed Stephens

Christopher M. Parker