FDA issued new guidance on June 19, 2020, advising manufacturers of drugs, biologics, and active pharmaceutical ingredients (APIs) on manufacturing controls to prevent contamination of drugs with SARS-CoV-2, including performing risk assessments to determine whether the virus poses new risks to drug products, or to the manufacturing facilities or processes that produce them. FDA is not aware of any drugs that have been contaminated with SARS-CoV-2, but the guidance provides the agency's expectations for limiting potential contamination. While the FDA has not yet resumed routine facility inspections, and therefore likely will not actively monitor implementation of the risk assessments (or other suggestions in the guidance), manufacturers should consider the recommendations in the guidance to protect the public health and health of their employees.

What Does the Guidance Cover?

The guidance covers human and animal drugs, biologics, and APIs. The Centers for Drug Evaluation and Research (CDER), Biologics Evaluation and Research (CBER) and Veterinary Medicine (CVM) jointly issued the guidance.

What Additional Manufacturing Controls are Suggested?

Vigilant Monitoring and Employee Exclusion. Drug manufacturers are expected 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. The current good manufacturing practice (cGMP) drug regulations, which apply to both drugs and biologics, already set forth requirements for limiting sick employees, or employees with open wounds, from direct contact with raw materials, drug products, and drug product containers. See, e.g., 21 C.F.R. § 211.28(d). The cGMP regulations also require employees to practice good sanitation and hygiene in order to prevent product contamination.

The guidance suggests vigilant monitoring of employees with confirmed or suspected COVID-19 symptoms or infection, and exclusion of such employees from manufacturing areas. Infected employees should only be allowed to return to work, in line with current CDC guidelines.

The guidance also asks manufacturers to evaluate the adequacy of their existing cGMP controls to protect raw materials, container closures, in-process materials, and finished drugs from sick employees in the context of the SARS-CoV-2. As an example, the guidance suggests—in the context of a cleanroom—to review existing air filtration and positive air pressure to ensure proper functioning.

More Frequent Cleaning, Sanitizing. The guidance suggests more frequent cleaning and sanitization of production areas and non-production areas (e.g., breakrooms, offices), and surfaces that are contacted frequently, such as door handles, benches, and countertops. If a potential or actual viral contamination event occurs, the guidance suggests promptly cleaning, disinfecting, and sanitizing any affected equipment, surfaces, or production areas before resuming manufacturing.

Further Access Restrictions. The guidance also recommends further restriction on employee access to product areas beyond the normal practice, to limit the possibility of contamination.

What Risk Assessment is Expected?

FDA expects drug manufacturers to evaluate whether SARS-CoV-2 poses new risks to their products, equipment, facilities or processes in a risk assessment. Drug manufacturers should determine if SARS-CoV-2 could adversely affect the safety or quality of their raw materials, components, drug product containers and closures, in-process materials, or drugs, if any were to become contaminated with the virus.

The risk assessment should consider the known characteristics of the coronavirus, as well as the drug products and their characteristics. For example, manufacturers should consider that the SARS-CoV-2 virus may be stable for several hours to days in aerosols and on surfaces. The product form—e.g., solid or liquid and product attributes (e.g., terminally sterilized, or non-sterile) may impact the viability of the virus.

For biological products where manufacturing processes or materials are more susceptible to viral contamination, manufacturers likely already have stringent viral control strategies in place. Potential risks from SARS-CoV-2, therefore, may be mitigated by existing controls. FDA recommends, however, that manufacturers perform a risk assessment of their current control strategies in light of SARS-CoV-2, and identify and implement, where necessary, mitigation strategies.
When Will FDA Resume Inspections?

FDA primarily enforces its guidance suggestions through facility inspections. Earlier this year, however, FDA suspended routine domestic and foreign inspections. The agency has not yet announced plans to resume inspections. An FAQ on FDA inspections during COVID-19 can be found [here](https://www.natlawreview.com/article/fda-issue-guidance-manufacturing-drugs-apis-during-covid-19).


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