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FDA Fiddles With Remote Drug Inspections While Pharma Burns

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Nearly a year into the pandemic, the Food and Drug Administration, unlike its foreign counterparts, has yet to advance alternatives to on-site facility inspections. Mark I. Schwartz, a director at Hyman, Phelps & McNamara P.C. and former deputy director for the FDA's Office of Compliance and Biologics Quality, says the FDA must address this to cure shortages of front-line drugs for treating Covid-19 patients and other lifesaving medications.

The Food and Drug Administration remains under heightened public scrutiny due to the White House's politicization of the Covid-19 vaccine review process.

A more immediate concern, however, is the agency's failure to develop an alternative to on-site drug facility inspections during the pandemic. Without these inspections, new, cutting-edge therapies are being deferred or rejected, and drug shortages are worsening, including for front-line drugs in the treatment of Covid-19 patients.

As a recent example, on Nov. 16 the FDA deferred action on a novel cancer therapy application by Bristol Myers Squibb (BMS) for Liso-cel, a CAR T-cell therapy for the treatment of adults with large B-cell lymphoma. BMS said the pandemic prevented agency investigators from traveling to a facility in Houston involved in the manufacture of the drug.

The FDA should have been able to determine the facility's compliance status by other means, particularly since the agency had tacitly acknowledged that the facility met its definition of a "mission critical" inspection, suggesting that the FDA needed to perform the inspection despite the pandemic.

What Does 'Mission Critical' Mean?

Liso-cel had received both what is referred to as breakthrough therapy (BT) designation and regenerative medicine advanced therapy (RMAT) designation from the FDA. These designations are granted when the agency believes that a drug "may demonstrate substantial improvement over available therapies" and that it "has the potential to address unmet medical needs." The agency has suggested in guidance that products so designated would be deemed "mission critical."

By any objective standard, a BT and RMAT-designated product under review should receive the highest possible agency attention. Yet the Houston facility was not inspected, and the agency used this as a basis for punting on whether to approve the novel, potentially life-extending cancer treatment. This leaves one to wonder what "mission critical" could possibly mean.

Back in August, the FDA had issued guidance emphasizing that it intended to use "other tools" to determine the compliance status of drug facilities that could not be inspected on-site. However, none of these other tools appears to have been used to determine the compliance status of the Liso-cel Houston facility, nor of the many other facilities that are in a similar dilemma as BMS.

One option that the agency could have used is a remote inspection, where audio and visual equipment attached either to a mobile device, or to a person, tours the facility at the instruction of agency officials, who pose questions and provide direction in real time regarding issues that require particular scrutiny.

Numerous pharmaceutical companies have pleaded with agency officials to conduct such inspections over the past several months in order to resolve manufacturing compliance issues and get critical new drugs approved, and have even offered to obtain the requisite technology, but the FDA has rebuffed such requests.

The agency has not made public any plans for the adoption of this remote method of inspecting, despite multiple requests from the pharmaceutical industry to do so.

Foreign Agencies Utilizing Remote Assessments

By contrast, several foreign regulatory bodies, such as the European Medicines Agency (EMA) allow drug facilities to be evaluated by remote assessments, including new facilities that previously never have been inspected by the EMA.

The same is the case for Australia's Therapeutic Goods Administration (TGA), which instructs drug manufacturers to "have pre-recorded videos of the site and operations so that the inspectors can be presented with a virtual tour of GMP [good manufacturing practice] relevant areas."

Likewise, Health Canada has stated that "to ensure compliance, we are implementing other ways of conducting inspections, such as using remote GMP evaluations." Remarkably, the U.K.'s Medicines and Healthcare products Regulatory Agency (MHRA), has relied on remote inspections since a few weeks after the pandemic hit.

The FDA is now more than nine months into this pandemic and they still haven't implemented a plan to inspect drug facilities by remote means, seemingly content to wait it out. When asked recently about a timeline for implementation, FDA officials declined to comment.

In the meantime, the backlog of uninspected facilities grows, as do the list of drug product applications that remain unapproved, together with the list of drugs that are in shortage.

FDA Has Authority to Amend Inspection Methods

The agency has the statutory authority to replace on-site inspections with a combination of remote inspections, review of the facility's records, and review of the facility's recent foreign regulatory reports and supplier/customer reports.

The FDA needs to do so immediately. Nothing short of that would be acceptable from a public health perspective.

Whether by reason of bureaucratic paralysis or otherwise, FDA drug inspections have slowed to a crawl since the start of the pandemic, with no end in sight. The agency seems incapable of implementing a means of remotely determining the compliance status of facilities whose critical products are needed for treating Covid-19 patients and cancer patients alike.

The agency used to be viewed as the world's gold standard for drug oversight. That designation is currently in doubt.

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