

# Safety Alert Regarding Use of Fecal Microbiota for Transplantation and Additional Safety Protections Pertaining to Monkeypox Virus

**August 22, 2022**

Since May 2022, an outbreak of monkeypox disease has been ongoing in multiple countries, including the United States. In the United States, monkeypox is thought to be spreading primarily through close contact with an infected, symptomatic individual. Whether, and the extent to which, monkeypox virus can be transmitted through feces or from asymptomatic infected individuals is not known.

The Food and Drug Administration (FDA) is informing health care providers and patients of the potential risk of transmission of monkeypox virus through fecal microbiota for transplantation (FMT) products and that FDA has determined that additional safety protections are needed.

## **Summary of the Issue**

Recent studies have documented the presence of monkeypox virus DNA in rectal swabs and/or stool samples from infected individuals.<sup>1-2,3</sup> One study reports detection of monkeypox virus DNA in rectal swabs from three individuals who reported no symptoms of monkeypox disease, including two individuals who had viable monkeypox virus isolated from rectal swabs.<sup>2</sup> This information suggests that monkeypox virus may be transmitted through FMT products, although the risk of such transmission is unknown.

Although there is an available test for detection of monkeypox virus DNA from swab samples taken directly from a lesion, at this time, there is limited information on the availability and sensitivity of direct testing of stool for monkeypox virus.

## **Additional Protections for the Use of FMT**

FDA is advising that clinical use of FMT has the potential to transmit monkeypox virus. Due to the potential for serious adverse events to occur, FDA has determined that additional protections are needed for any investigational use of FMT, whether used as part of a study under an Investigational New Drug Application (IND) on file with the FDA or otherwise, if it involves stool donated on or after March 15, 2022. These additional protections are as follows:

- Donor screening with questions directed at identifying donors who are at high risk for monkeypox, may be currently infected with monkeypox virus, or may have been recently infected with monkeypox virus;
  - Donor screening includes retrospective screening for the use of FMT prepared from stool donated between March 15, 2022, and the date of prospective implementation of updated donor screening for monkeypox
- Development of criteria for exclusion of donors and donor stool based on donor screening; and
- Informed consent that includes information about the potential for transmission of monkeypox virus via FMT, including FMT prepared from stool from donors who are asymptomatic for monkeypox.

## **Actions**

FDA is notifying Investigational New Drug Application (IND) holders of the potential risk of transmission of monkeypox virus via FMT and of FDA's determination that they need to develop and implement additional safety protections.

FDA is communicating this information with this statement to all other stakeholders to ensure that everyone is fully informed.

FDA will provide further information, as warranted, including on any additional protections pertaining to monkeypox that may be needed for use of FMT.


### **Information for Health Care Providers and Patients About Enforcement Discretion**


In July 2013, FDA [issued a guidance \(/media/86440/download\)](/media/86440/download) document explaining that the Agency intends to exercise enforcement discretion under limited circumstances regarding the IND requirements for the use of FMT products to treat *C. difficile* infection in patients who have not responded to standard therapies. The guidance states that FDA intends to exercise enforcement discretion provided that the treating physician obtains adequate consent for the use of FMT from the patient or his or her legally authorized representative. The consent should include, at a minimum, a statement that the use of FMT to treat *C. difficile* is investigational and a discussion of its potential risks.


### **Reporting Adverse Events**

FDA encourages all health care providers and patients to report any suspected adverse events or side effects related to the administration of FMT products to the FDA at 1-800-FDA-1088 or [http://www.fda.gov/medwatch \(/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program\)](http://www.fda.gov/medwatch (/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program)).

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<sup>1</sup>Peiró-Mestres Aida, Fuertes Irene, Camprubí-Ferrer Daniel, et al, on behalf of the Hospital Clinic de Barcelona Monkeypox Study Group. Frequent detection of monkeypox virus DNA in saliva, semen, and other clinical samples from 12 patients, Barcelona, Spain, May to June 2022. *Euro Surveill.* 2022;27(28):pii=2200503. <https://doi.org/10.2807/1560-7917.ES.2022.27.28.2200503> (<https://doi.org/10.2807/1560-7917.ES.2022.27.28.2200503>).  (<http://www.fda.gov/about-fda/website-policies/website-disclaimer>)

<sup>2</sup> Irith De Baetselier, Christophe Van Dijck, Chris Kenyon, et al. Retrospective detection of asymptomatic monkeypox virus infections among male sexual health clinic attendees in Belgium. *Nature Medicine.* 2022. <https://doi.org/10.1038/s41591-022-02004-w> (<https://doi.org/10.1038/s41591-022-02004-w>).  (<http://www.fda.gov/about-fda/website-policies/website-disclaimer>)

<sup>3</sup> Antinori Andrea, Mazzotta Valentina, Vita Serena, et al, INMI Monkeypox Group. Epidemiological, clinical and virological characteristics of four cases of monkeypox support transmission through sexual contact, Italy, May 2022. *Euro Surveill.* 2022;27(22):pii=2200421. <https://doi.org/10.2807/1560-7917.ES.2022.27.22.2200421> (<https://doi.org/10.2807/1560-7917.ES.2022.27.22.2200421>).  (<http://www.fda.gov/about-fda/website-policies/website-disclaimer>)