

the farm-to-fork continuum and the impact of these conditions on *Salmonella* concentrations on tree nuts, including:

- Typical storage conditions (e.g., time, temperature, relative humidity) for different tree nuts, from the time of harvest until the application of treatments designed to reduce bacterial contamination, and whether those storage conditions change *Salmonella* contamination levels;

- The types of treatments designed to reduce bacterial contamination that are typically applied to different tree nuts before retail, the frequency with which these treatments are applied to different types of tree nuts, the exact processing conditions (e.g., time, temperature, relative humidity), and the efficacy of these treatments in reducing *Salmonella* contamination on different tree nuts;

- Typical storage conditions (e.g., time, temperature, relative humidity) for different tree nuts, from the time treatments designed to reduce bacterial contamination are applied to the time the tree nuts are consumed, including typical storage conditions at retail and in the consumer home.

- The types of handling practices that are typically applied to different tree nuts by the consumer before consumption that may change *Salmonella* contamination levels, and the typical conditions (e.g., time, temperature) that are applied during these practices.

5. Other comments, including the types of tree nuts that should be evaluated in this risk assessment and information about which types of tree nuts may enter the U.S. market without the application of treatments designed to reduce bacterial contamination.

### III. Comments

Interested persons may submit either electronic comments and scientific data and information to <http://www.regulations.gov> or written comments and scientific data and information to the Division of Dockets Management (see **ADDRESSES**). It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at <http://www.regulations.gov>.

### IV. References

The following references have been placed on display in the Division of Dockets Management (see **ADDRESSES**) and may be seen by interested persons

between 9 a.m. and 4 p.m., Monday through Friday. We have verified the Web site addresses in the References section, but we are not responsible for any subsequent changes to the Web sites after this document publishes in the **Federal Register**.

1. Isaacs, S., J. Aramini, B. Ciebin, J.A. Farrar, R. Ahmed, D. Middleton, A.U. Chandran, L.J. Harris, M. Whoes, E. Chan, A.S. Pichette, K. Campbell, A. Gupta, L.Y. Lior, M. Pearce, C. Clark, F. Rodgers, F. Jamieson, I. Brophy, A. Ellis, "Salmonella Enteritidis PT30 Outbreak Investigation Working Group. An international outbreak of salmonellosis associated with raw almonds contaminated with a rare phage type of *Salmonella enteritidis*." *Journal of Food Protection*, 68(1): pp. 191–198, 2005.

2. Outbreak of *Salmonella* serotype Enteritidis infections associated with raw almonds—United States and Canada, 2003–2004. *Morbidity and Mortality Weekly Report*, 53(22): pp. 484–487, 2004.

3. Ward, L., G. Duckworth, S. O'Brien, "Salmonella java phage type Dundee—rise in cases in England: update." *Eurosurveillance*, 3(12): p. 1435, 1999.

4. CDC (Centers for Disease Control and Prevention). Multistate Outbreak of Human *Salmonella* Enteritidis Infections Linked to Turkish Pine Nuts. Available at: <http://www.cdc.gov/salmonella/pinenuts-enteritidis/111711/index.html>. Last updated: 11/2011 [accessed 08/2012].

5. Danyluk, M.D., T.M. Jones, S.J. Abd, F. Schlitt-Dittrich, M. Jacobs, L.J. Harris. "Prevalence and amounts of *Salmonella* found on raw California almonds." *Journal of Food Protection*, 70(4): pp. 820–827, 2007.

6. Freire, F.D.O., L. Offord. "Bacterial and yeast counts in Brazilian commodities and spices." *Brazilian Journal of Microbiology*, 33(2): pp. 145–148, 2002.

7. StClair, V.J., M.M. Klenk. "Performance of 3 Methods for the Rapid Identification of *Salmonella* in Naturally Contaminated Foods and Feeds." *Journal of Food Protection*, 53(11): pp. 961–964, 1990.

8. Riyaz-Ul-Hassan, S., V. Verma, A. Malik, G.N. Qazi. "Microbiological quality of walnut kernels and apple juice concentrate." *World Journal of Microbiology and Biotechnology*, 19(8): pp. 845–850, 2003.

9. CDC (Centers for Disease Control and Prevention). *Salmonella* in Pistachio Nuts, 2009. Available at <http://www.cdc.gov/salmonella/pistachios/update.html>. Last updated: 2009 (Accessed 08/2012).

10. FDA (Food and Drug Administration). Recalls, Market Withdrawals, & Safety Alerts. Available at <http://www.fda.gov/Safety/Recalls/default.htm>. (Accessed 04/2013).

11. FDA (Food and Drug Administration). Enforcement Reports. Available at <http://www.fda.gov/Safety/Recalls/EnforcementReports/default.htm>.

12. National Research Council. Committee on Food Protection. 1975. Nuts, macaroni, and noodle products and dry blended foods in prevention of microbial and parasitic hazards associated with processed foods. A guide for the food processor, pp. 68–76. In: National Academies of Sciences (ed.). Prevention of Microbial and Parasitic

Hazards associated with Processed Foods—A Guide for the Food Processor. National Academy of Science Publishing Office, Washington, DC.

13. Uesugi, A.R., M.D. Danyluk, R.E. Mandrell, L.J. Harris. "Isolation of *Salmonella* Enteritidis phage type 30 from a single almond orchard over a 5-year period." *Journal of Food Protection*, 70(8): pp. 1784–1789, 2007.

Dated: July 9, 2013.

**Leslie Kux,**

*Assistant Commissioner for Policy.*

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**BILLING CODE 4160–01–P**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

[Docket No. FDA–2013–D–0811]

#### Guidance for Industry: Enforcement Policy Regarding Investigational New Drug Requirements for Use of Fecal Microbiota for Transplantation To Treat *Clostridium difficile* Infection Not Responsive to Standard Therapies; Availability

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice.

**SUMMARY:** The Food and Drug Administration (FDA or Agency) is announcing the availability of a guidance for industry entitled "Enforcement Policy Regarding IND Requirements for Use of Fecal Microbiota for Transplantation to Treat *Clostridium difficile* Infection Not Responsive to Standard Therapies," dated July 2013. This guidance informs members of the medical and scientific community and other interested persons that we intend to exercise enforcement discretion regarding the investigational new drug (IND) requirements for the use of fecal microbiota for transplantation (FMT) to treat *C. difficile* infection not responding to standard therapies. FDA intends to exercise this discretion provided that the treating physician obtains adequate informed consent from the patient or his or her legally authorized representative for the use of FMT products. Informed consent should include, at a minimum, a statement that the use of FMT products to treat *C. difficile* is investigational and a discussion of its potential risks. This policy does not extend to other uses of FMT. FDA intends to exercise this discretion on an interim basis while we further consider the matter. This guidance has an immediate implementation date because FDA has

determined that prior public participation is not feasible or appropriate.

**DATES:** Submit either electronic or written comments on Agency guidances at any time.

**ADDRESSES:** Submit written requests for single copies of the guidance to the Office of Communication, Outreach and Development (HFM-40), Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, 1401 Rockville Pike, suite 200N, Rockville, MD 20852-1448. Send one self-addressed adhesive label to assist that office in processing your requests. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the guidance document.

Submit electronic comments on the guidance to <http://www.regulations.gov>. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

**FOR FURTHER INFORMATION CONTACT:** Paul E. Levine, Jr., Center for Biologics Evaluation and Research (HFM-17), Food and Drug Administration, 1401 Rockville Pike, suite 200N, Rockville, MD 20852-1448, 301-827-6210.

**SUPPLEMENTARY INFORMATION:**

**I. Background**

FDA is announcing the availability of a guidance for industry entitled "Enforcement Policy Regarding IND Requirements for Use of Fecal Microbiota for Transplantation to Treat *Clostridium difficile* Infection Not Responsive to Standard Therapies," dated July 2013. This guidance is being issued consistent with FDA's good guidance practices (GGP) regulation § 10.115 (21 CFR 10.115). This guidance is being implemented without prior public comment because the Agency has determined that prior public participation is not feasible or appropriate (§ 10.115(g)(2)). The Agency made this determination because the guidance requires immediate implementation for public health reasons. This guidance deals with an urgent issue affecting patients with life-threatening infections with *C. difficile*. Although this guidance document is immediately in effect, it remains subject to comment in accordance with the Agency's GGP's regulation.

Fecal microbiota collected from healthy individuals are being investigated for use in the treatment of *C. difficile* infection. Published data suggest that the use of fecal microbiota to restore intestinal flora may be an effective therapy in the management of

refractory *C. difficile* infection. However, the efficacy and safety profile of this intervention have not yet been fully evaluated in controlled clinical trials.

In the **Federal Register** of February 25, 2013 (78 FR 12763), FDA announced a public workshop, entitled "Fecal Microbiota for Transplantation," which was held on May 2 and 3, 2013. The purpose of the workshop was to provide a forum for the exchange of information, knowledge, and experience among the medical and scientific community about the regulatory and scientific issues associated with FMT. During that workshop, and in subsequent communications, physicians and scientists expressed concern to FDA that FMT is not appropriate for study under the Agency's IND regulations (21 CFR part 312). Some health care providers stated that applying IND requirements will make FMT unavailable and suggested that an alternative regulatory approach is needed to ensure the widespread availability of FMT for individuals with *C. difficile* infection unresponsive to standard therapies.

FDA acknowledges these concerns. The Agency intends to exercise enforcement discretion regarding the IND requirements for the use of FMT to treat *C. difficile* infection not responding to standard therapies, provided that the treating physician obtains adequate informed consent from the patient or his or her legally authorized representative for the use of FMT products. Informed consent should include, at a minimum, a statement that the use of FMT products to treat *C. difficile* is investigational and a discussion of its potential risks. FDA intends to exercise this discretion on an interim basis while the Agency further considers the matter.

This policy does not extend to other uses of FMT. Data related to the use and study of FMT to treat diseases or conditions other than *C. difficile* infection are limited, and study of FMT for these other uses is not included in this enforcement policy.

This guidance represents the Agency's current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

**II. Comments**

Interested persons may submit either electronic comments regarding this document to <http://www.regulations.gov> or written comments to the Division of Dockets Management (see **ADDRESSES**). It

is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at <http://www.regulations.gov>.

**III. Electronic Access**

Persons with access to the Internet may obtain the guidance at either <http://www.fda.gov/RegulatoryInformation/Guidances/default.htm> or <http://www.regulations.gov>.

Dated: July 12, 2013.

**Leslie Kux,**

*Assistant Commissioner for Policy.*

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**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Food and Drug Administration**

[Docket No. FDA-2013-N-0001]

**Advisory Committee for Pharmaceutical Science and Clinical Pharmacology; Notice of Meeting**

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice.

This notice announces a forthcoming meeting of a public advisory committee of the Food and Drug Administration (FDA). The meeting will be open to the public.

*Name of Committee:* Advisory Committee for Pharmaceutical Science and Clinical Pharmacology.

*General Function of the Committee:* To provide advice and recommendations to the Agency on FDA's regulatory issues.

*Date and Time:* The meeting will be held on September 25, 2013, from 8 a.m. to 5 p.m.

*Location:* Bethesda North Marriott Hotel and Conference Center, White Oak Room, 5701 Marinelli Rd., Bethesda, MD. The hotel phone number is 301-822-9200.

*Contact Person:* Yvette Waples, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 31, rm. 2417, Silver Spring, MD 20993-0002, 301-796-9001, Fax: 301-847-8533, email: [ACPS-CP@fda.hhs.gov](mailto:ACPS-CP@fda.hhs.gov), or FDA Advisory Committee Information Line, 1-800-741-8138 (301-443-0572 in the Washington, DC area). A notice in the **Federal Register** about last minute modifications that impact a previously