

Clostridium difficile product labeling

September 22, 2008

Subject: *Clostridium difficile* product labeling

The Environmental Protection Agency (EPA) has determined all pesticide products that are registered for use against *Clostridium difficile* must demonstrate efficacious performance against the spore form of the organism. Further, the Agency believes claims of efficacy against the vegetative form of the organism are "false and misleading" because the vegetative form is not the organism of concern for infection control processes. *C. difficile* spores have the ability to remain viable for months on contaminated surfaces. These contaminated surfaces have been implicated in the spread of *C. difficile*-associated diarrhea. Efficacy testing performed on the vegetative form of the organism will not support a claim for *C. difficile* spores, and therefore cannot support registration of a product labeled as effective against *C. difficile*. In fact, using products registered and effective for only the vegetative form of the organism could potentially spread spore contamination thereby enlarging the potentially contaminated surface area that could trigger an infectious process.¹

Background:

C. difficile is a gram-positive, anaerobic, spore-forming bacillus. It is found in the gut of healthy individuals and in feces. *C. difficile* spores are heat resistant and can persist in the environment for years. Although *C. difficile* spores are persistent, they are fastidious *in vitro* and grow slowly.

Human infections can be acquired or spread by handling feces contaminated items or touching contaminated surfaces and then touching the mouth or a mucous membrane. Workers in hospitals, nursing homes, or other health care facilities can spread the bacterial spores through hand contact and contact with contaminated surfaces. Antibiotic use can suppress the normal micro flora found in the gut and allow *C. difficile* to proliferate.

Outbreaks of *C. difficile* diarrhea are not uncommon in hospitals and outpatient facilities where contamination with spores is prevalent; and the frequency of

these outbreaks appears to be increasing. The National Nosocomial Infections Surveillance System, developed by the Centers for Disease Control and Prevention, reports that as many as 3 million cases of diarrhea and colitis occur annually primarily among hospitalized patients.² *C. difficile* colitis is currently one of the most common nosocomial infections. The elderly, individuals with an underlying health condition, or individuals that require prolonged antibiotic treatment are most vulnerable to infection resulting from exposure to *C. difficile* spores. Conversely, healthy individuals are not at high risk of acquiring a *C. difficile* infection or associate diarrhea.

Regulatory Action:

The Agency is concerned that the currently registered antimicrobial products bearing specific claims for the vegetative form of *C. difficile* do not play a meaningful role in controlling *C. difficile* contamination or preventing its spread since the spore form is the appropriate target organism and no such products have demonstrated specific effectiveness against that form. Therefore, the Agency has determined that pesticide products that are efficacious only against the vegetative form of the organism may cause unreasonable adverse effects on health and the environment because the Agency believes they may increase rather than limit *C. difficile* spore contamination even if used in accordance with all label directions. (See 40 CFR § 156.10(a)(5)(vii).) Accordingly, in order to remain in compliance with FIFRA, it is the Agency's position that all registrants of pesticide products that bear a label claim of effectiveness against only the vegetative form of *C. difficile* and not against the spore form must amend their registration(s) to eliminate that label claim. Per 40 CFR § 152.130(c) the Agency will permit the sale and distribution under previously approved labeling bearing the *C. difficile* claim for a period of 18 months from the date of this posting.

The Agency is in the process of developing guidelines to address label claims for *C. difficile* spores. A letter Scientific Advisory Panel has reviewed information related to test methods and label claims. Once the Agency has completed its review of the recommendations, the guidelines will be posted for review. In the interim, applicants who intend to make label claims for *C. difficile* spores should consult with the Agency prior to generating any data.

If you have questions regarding this letter, please contact Dr. Tajah Blackburn at (703) 308-0372. Thank you in advance for your prompt attention to this serious matter.

Sincerely,

Frank Sanders, Director
Antimicrobials Division

Rutala WA, Gergen MF, Weber DJ. (1993) Inactivation of Clostridium difficile Spores by Disinfectants. Infect Contr Hosp Epidemiology 14, 36-9

Archibald LK, Banaerjee SN, Jarvis WR. (2004). Secular Trends in Hospital-Acquired Clostridium difficile Disease in the United States, 1987-2001. J Infect Dis, 189: 1585-1589