IN brief

New self-reporting for GM crops

Aphis/USDA

APHIS regulates the introduction of GM crops.

Companies seeking approval for new biotech crops can now prepare their own environmental study or hire an outside contractor to do so. The new options, announced by the US Department of Agriculture's Animal and Plant Health Inspection Service (APHIS) in April, are part of a two-year voluntary pilot program designed to speed up document preparation, although critics argue such self-reporting is inevitably biased. Currently, genetically modified (GM) crops can take years to approve, as the agency faces a backlog of nearly two dozen petitions, according to APHIS deputy administrator Michael Gregoire. Before a crop can be deregulated, the law requires a preliminary environmental study, followed by a more comprehensive environmental assessment conducted by APHIS (the regulatory arm of the US Department of Agriculture (USDA). The environmental assessment costs the petitioner $75,000–$100,000, although the USDA may decide a crop warrants a more detailed environmental impact statement, which can cost over a million dollars. APHIS in most cases conducts the initial environmental reports, but in recent years it has paid contractors to handle that aspect of its growing workload, Gregoire says. The pilot program now allows petitioners to self-report or pay a contractor managed through APHIS. The drug industry follows a similar self-regulation system for managing the risks associated with drugs once they are on the market, known as Risk Evaluation and Mitigation Strategies (*Nat. Biotechnol.* **25**, 1189–1190, 2007). Still, Bill Freese of the Center for Food Safety in Washington, DC, says there is a possibility with self-reporting of introducing errors which have, in the past, led to environmental assessments being overturned in federal courts. "The emphasis here needs to be on quality environmental assessments," he says. "It's not a cost-cutting measure if they end up in court." But Greg Jaffe of the Center for Science in the Public Interest in Washington, DC, points out that "There are still enough checks and balances in the system." As in other federal processes, falsifying or omitting information from an environmental report would be a criminal act, so "you can't hide bad evidence" and like other agencies APHIS still must complete the environmental assessments itself, Jaffe says. "We'll have to see in the end how well it's done at this particular office." *Lucas Laursen*

absorbed from the GI tract (which once led the antibiotic to be abandoned) made it well-suited for treating CDAD. Broad-acting antibiotics help trigger CDAD in the first place, so targeted treatment would allow the ecological space to reestablish its microbial equilibrium, a process involving hundreds of species and billions of cells, says Schlaes.

In addition, the developers of Dificid were "spurred by the market for oral vancomycin," Schlaes continues. Annual sales for treating patients who develop CDAD with oral vancomycin are about $300 million, "which is a lot for a small company, but not much for large pharma." Those figures help to explain why many pharma companies exited antimicrobial development during the past decade or more, he says, viewing this sector market "as not large enough because they couldn't see their way to blockbuster drugs worth $1 billion or more per year." Only two large pharma, GlaxoSmithKline and AstraZeneca, both headquartered in London, are considered "committed" to pursuing the antimicrobial product spectrum, with several other companies, including Sanofi-aventis in Paris and Novartis in Basel, showing signs of renewed interest in this sector, he says.

"Regarding anti-infectives and biotech, the history is a good one because biotechs have been very successful and innovative," says Jason Kantor of RBC Capital Markets in San Francisco. In the case of Optimer, "the story is not so different from others," he continues. The company focused on an "emerging problem in the hospital," one on which "big pharma was not focused." Optimer then developed a "highly specific drug" and is "teaming up with a company—Cubist—that has fought and won these battles before."

This agreement, announced in April shortly before FDA approval, brings Optimer together with Cubist Pharmaceuticals, to market Dificid in the US later this year. Separately, Optimer, which is seeking approval for fidaxomicin from the European Medicines Agency, has also partnered with Astellas Pharma Europe near London for eventual marketing of the product in Europe and other countries outside the US.

Cubist is something of a role model in terms of realizing this updated, biotech-styled antibiotic development strategy. This Lexington, Massachusetts–based company used a similar strategy when it brought Cubicin (daptomycin) to market several years ago, reviving a Gram-positive antibiotic that was gathering dust in Eli Lilly's compound libraries. Cubist inlicensed the antibiotic from the big pharma, figured out how to overcome toxicity drawbacks and went on to receive FDA approval for treating complicated skin and skin structure infections caused by Gram-positive bacterial pathogens.

Other companies are developing candidate products for treating CDAD (**Table 1**). For instance, Cubist reports that its bacterial membrane–disrupting macrocyclic compound, CB-183,315, is in phase 2 clinical trials. Similarly, Actelion Pharmaceuticals, of Basel, is evaluating its antimicrobial drug candidate, ACT-179811, for treating CDAD in clinical trials. In addition, several companies, including Medarex of Princeton, New Jersey, and Progenics of Tarrytown, New York, are evaluating several versions of monoclonal antibodies that target toxins produced by *C. difficile*, including those from hypervirulent strains, as a way of quelling their physiologic effects while enabling the GI microbial equilibrium to become reestablished.

Yet other CDAD-targeted therapeutic approaches include development of probiotics, typically consisting of live microorganisms that are aimed at restoring the disrupted microbial balance in the GI tract during recurrent bouts of CDAD. At the extreme of this approach, some clinicians are experimenting with "fecal transplants," a procedure in which microbial populations from the GI tracts of healthy individuals are transferred into the GI tracts of CDAD patients. In part to reduce the yuck factor associated with this procedure but also to achieve better reliability, "there is a lot of energy going into developing synthetic fecal mixes," says Aronoff of the University of Michigan. Although far from conventional, the vision for such products is that they would be "more complex than probiotics" and would find their way into clinical use as commercial formulations.

Jeffrey L Fox, ***Washington DC***

Table 1 Selected antibacterial agents in late-stage development against *Clostridium difficile*[a]

Company (location)	Agent	Status
Merck (Whitehouse Station, New Jersey)	Fully human monoclonal antibody against *C. difficile* toxins (MK-3415A)	Phase 2b
Cubist	Oral lipopeptide against *C. difficile* (CB-183,315)	Phase 2
Nanotherapeutics (Alachua, Florida)	Glycolipodepsipeptide antibiotic ramoplanin against *C. difficile*	Phase 2
Actelion	Oral antibiotic ACT-179811 against *C. difficile*	Phase 2

[a]Does not include vaccine approaches to prevent recurrent *C. difficile* infection. Source: Biomedtracker/Sagient Research.