

NEWS ANALYSIS

FDA nears approval of Calgene's Flavr Savr

WASHINGTON, D.C.—During a sometimes tumultuous three-day meeting last month, members of the Food and Drug Administration's (FDA, Rockville, MD) Food Advisory Committee (FAC) agreed with FDA officials that Calgene's (Davis, CA) Flavr Savr tomato is safe for consumers and the environment. FDA approval to market the product—which is genetically engineered to ripen on the vine longer and so be tastier than currently available fresh tomatoes—will likely come within 90 days, according to FDA Commissioner David Kessler. Although some biotech critics are promising boycotts and lawsuits to block distribution of Flavr Savr tomatoes, the main focus of these critics is what they view as shortcomings in the FDA's oversight procedures for biotech foods, rather than any perceived problems with the Flavr Savr.

The Flavr Savr is the first genetically engineered, whole food to receive premarket scrutiny from the FDA, which ordinarily evaluates food additives, rather than whole foods. Yet recognizing that the public might insist on some form of regulatory review of the Flavr Savr, Calgene first approached the FDA for guidance about five years ago. By mid-1991, Calgene submitted a formal request for a voluntary "consultation" with the FDA on the tomato. That course of action was subsequently replaced with a still more-formal food-additive petition to the FDA for the Flavr Savr.

The change to a food-additive petition reflected a shift in the FDA's safety concerns to the second component of the two-part gene construct used by Calgene to modify tomatoes, namely, the kanamycin-resistance (kan-r) gene. Calgene used resistance to the antibiotic, kanamycin, as a marker while selecting modified plant cells during the early stages of engineering the Flavr Savr tomato. The kan-r gene, though, plays no further role in the intact, engineered plant or in its tomatoes.

The business end of the two-part

gene construct in the Flavr Savr tomato is an antisense gene targeting the gene encoding polygalacturonase (PG), an enzyme produced in ripening tomatoes. Since this antisense gene blocks production of PG, it prevents PG's catalytic activity. When active, PG helps to dissolve pectin, a polysaccharide that imparts firmness to tomatoes. Because the antisense gene halts PG production, Flavr Savr tomatoes remain firm, instead of becoming soft, as they ripen.

Since ordinary tomatoes produce plenty of PG, they are picked when still hard and long before they ripen naturally. In this hardened, but not so tasty, state, ordinary tomatoes better survive transport and handling on the way to distant markets. By contrast, because the Flavr Savr tomato lacks PG and softens much less readily, it can stay on the vine until ripe and flavorful and still survive transport and handling. According to Calgene, the Flavr Savr is not so tasty as "backyard tomatoes" but is far more tasty than tomatoes currently available in most U.S. supermarkets.

Yet matters of taste were not a major concern during last month's FAC meeting. Instead, FDA officials presented FAC, whose membership was nearly doubled for the meeting, with a somewhat confusing task that involved splitting their focus between Flavr Savr specifics and the more general question of how the FDA deals with biotech foods. Thus, although committee members were invited to reexamine the FDA's review of the Flavr Savr, they were also asked to consider the more general issue of how the FDA currently evaluates genetically engineered foods.

In the end, however, the FDA's Kessler personally insisted that the FAC consider the safety of the Flavr Savr. "It's very important to stay focused on the safety questions. That's the prime order," says Kessler.

Yet not all FAC members are satisfied with that narrow mandate of safety. Joan Gussow of Columbia University (New York), who represents consumer interests on the FAC,

and several other FAC members say that they are frustrated by a debate that, to them, ignores other key issues that affect consumers' preferences for foods, such as religious, ethical, or aesthetic criteria. They also join with other critics of the FDA who say that the agency's approach to biotech foods is flawed in several crucial ways. They urge the FDA to require reviews, or at least mandatory notification, for genetically engineered foods. They also say that such foods should carry labels for consumers.

Nonetheless, FDA scientists and legal staff, as well as the dominant group of scientists on the FAC, reserved most of their attention for Flavr Savr safety issues. "I did not hear any dissent on the safety evaluation of the Flavr Savr tomato," says Kessler.

The consensus view is that use of an antisense gene to block PG production poses no conceivable risk to consumers. And although speculative concerns were raised regarding the kan-r gene's potential for spreading antibiotic resistance, which is a public health problem, neither FDA officials nor FAC members argue that putting the kan-r gene in the Flavr Savr poses a significant risk. Moreover, traditional toxicology experiments in which rats were administered high doses of Flavr Savr puree also indicate that the tomato is safe.

On more general grounds, FAC members urge the FDA to scrutinize other biotech-food scenarios that could pose more serious risks and that could necessitate labeling such foods. For example, the transfer of genes from allergenic sources or the use of other antibiotic-resistance markers or herbicide-resistance markers in whole foods could pose safety concerns.

For its part, Calgene "complied with the strictest standards that we could set," says the FDA's Kessler. Indeed, even critics urge the FDA not to subject other companies to the cumbersome process to which Calgene was subjected during the five-year voluntary review of its Flavr Savr tomato.

—Jeffrey L. Fox

An FDA advisory committee agreed with the FDA that Calgene's Flavr Savr tomato is safe for consumers and the environment. Approval will likely come within 90 days.