"Scientific Proof"—An Elusive Goal

Every two to three years since 1965, we have witnessed the appointment and installation of a new Commissioner to head the U.S. Food and Drug Administration. And, although their respective interests, expertise, and styles of operation have varied, we can honestly say that each performed capably and with distinction. Each of them was a credit to the Agency, to the health care professions, and to the nation.

We have often used the occasion of a new Commissioner's appointment to devote our editorial to welcoming him to Washington and to his new position. But the "welcome" was only an incidental message packaged in with some other key point that appeared to us to be pertinent and timely.

For example, when Commissioner Arthur Hull Hayes assumed office we noted the prevailing change in the national regulatory climate ("FDA Takes a Turn in the Road"). With Commissioner Jere Goyan we addressed his philosophic approach to education *versus* regulation ("FDA: Policeman or Teacher?"). The Alexander M. Schmidt to Donald Kennedy transition prompted us to comment on how each Commissioner has left his own individual imprint on the Agency ("Passing the Baton at FDA"). And, in addition to welcoming the new Commissioner, we have also expressed concern that the frequent rate of turn-over in that office has had a damaging effect on the FDA and the morale of its staff ("A Plea for FDA Stability").

The opening two paragraphs from that latter editorial, in July 1979, are again all too relevant and seem to merit repeating:

"Kings, popes, and presidents come and go with the passing of time. It should not be strange, therefore, that the same is true of Food and Drug Commissioners.

"Nevertheless, the departure of the last several FDA Commissioners has seemed to have come too soon, too abruptly, and all too unexpectedly. Indeed, each of them seems to have little more than arrived, got settled in office, established an operating style, developed a rapport with the health professions and the regulated industry, when 'poof!'—they were gone from office!"

With that lamentation regarding all-too-brief tenure now aside, it is our pleasure to welcome the latest resident to the "hot seat" of the Parklawn Building where FDA is headquartered.

Frank E. Young, M.D., Ph.D., comes to the Agency with little previous FDA or regulatory background, but with a solid reputation as a microbiological scientist. He is noted for his work in genetics and recombinant DNA—an area that is soon going to require some landmark FDA attention and regulation. Consequently, we may again see a fortuitous situation at FDA in that the right person was in the job at just the right time to handle the chief problem or problems of the period.

But the key observation that we would like to bring out in this editorial relates to the increasing complexity of the decisions that the FDA Commissioner is required to make as technology advances and life in general becomes more and more complicated.

Consider, for example, one of the items that Commissioner Young found near the top of his "in box" when he assumed office: namely, the Pandora's Box of artificial sweeteners.

At various times, FDA has approved three artificial sweetening agents: saccharin, cyclamate, and aspartame. Subsequently, it rescinded its approval of cyclamate and that agent is currently off the market in the U.S. (but continues to be available in Canada and some other countries). Later, it acted to rescind its approval of saccharin, but Congress stepped in and, *via* legislation, applied a year-by-year staying action on that ban. And, although it has yet to respond officially (as of this writing), FDA is now the object of a request to Congress by the consumer-oriented lobbying group Common Cause to investigate the merit and justification for FDA's approval of aspartame. Common Cause has been joined by a second organization, the Community Nutrition Institute, which has also mounted a legal challenge to the approval of aspartame.

The basic problem common to all three of these regulatory actions dealing with the artificial sweeteners is the Delany Amendment to the Federal Food, Drug, and Cosmetic Act. That clause prohibits the marketing of any food additive that, under virtually any conditions of use or testing, has been shown to cause cancer. The specific wording reads: "no (food) additive shall be deemed to be safe if it is found to induce cancer when ingested by man or animal."

Deceptively simple sounding, this provision leads to incredible complications. In animal studies, for example, animals have been tested for their full life-time with daily dose-levels at thousands of times what would normally be ingested; then perhaps only a few animals developed tumors—but at just slightly higher levels than the control group. Under these circumstances, how does a scientist make a judgment that the agent induced cancer or not?

Dr. Young will soon find that even the legendary wisdom of Solomon would be sorely tested in deciding upon the artificial sweetner question. Specifically, in addition to the above mentioned brouhaha over aspartame, the Congressional stay on the saccharin ban will expire in April 1985 and, if the stay is not extended, FDA will need to take some action. But perhaps even more significant is the reconsideration now being given to cyclamate.

The FDA's cancer assessment committee concluded in April that cyclamate is not a carcinogen after all, and the National Research Council (NRC) has been commissioned to issue an independent judgment.

The NRC's Commission on Life Sciences reported on its acceptance of this study assignment in that organization's Summer 1984 *newsletter*. In the lead article, entitled "Cyclamates Revisited," the NRC reporter begins with a quote from the September 16, 1980, issue of the *Federal Register:* "Cyclamate has not been shown not to cause cancer; and . . . cyclamate has not been shown not to cause heritable genetic damage." The reader is literally tied in knots by the double negatives!

The difficult position of the FDA Commissioner was further emphasized to us recently in a private conversation with a past Commissioner in which he told us that he saw no proof that saccharin was carcinogenic; but he also saw no absolute proof that it wasn't carcinogenic either. Hence, he felt that the law obligated him to recommend it be banned—demonstration of safety being a prerequisite of marketing approval.

But how can safety be proven? Especially absolute safety, and proven in terms that satisfy scientists, the public, and the Congress?

Commissioner Young will probably be forced "to bite the bullet" in this issue, to a far greater degree than any of his predecessors. It will be a most difficult decision. For his own sake, as well as that of science, the FDA, and the public at large, we hope that he has the scientific wisdom—as well as the scientific knowledge—to make the right choice.

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Editor's Note: Dr. Feldmann's editorials are an expression of personal opinion and do not necessarily reflect views or policies of APhA. The editorials are intended to be provocative and to stimulate thinking. Readers having reactions, either pro or con, are invited to submit them for publication in the *Open Forum* section.

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