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Wayne Pines on the FDA and Crisis Management

By Norman M. Goldfarb

Wayne Pines joined the FDA in 1972 as director of consumer education and information, where he created the award-winning magazine, "FDA Consumer." He later served as associate commissioner for public affairs and chief media spokesman for the Agency for seven years. In 1983, he joined Burson-Marsteller as co-chair of its international healthcare practice. In 1993, he joined APCO Worldwide, a Washington DC-based public affairs firm, as president of health care and regulatory services. He currently advises pharmaceutical and medical device companies on regulatory strategy, crisis and media management, and advertising/promotion issues. He has written or edited a dozen books about FDA issues and crisis communications.

Why did you join the FDA?

I was an associate editor of "The Pink Sheet" in 1971 and was offered a job with the FDA Public Affairs Office. I was influenced by news reports of a couple in Connecticut who ate a can of soup contaminated with botulinum toxin. I felt there was no reason for an educated couple to have eaten soup from a swollen can. They should have known more about basic food safety. The FDA job gave me the opportunity to help educate the American public about food safety, about drug safety, and about the safety of other products.

When I joined the Agency in 1972, it was barely visible to the American public. But over the next decade, the FDA was on the front page all the time, and has been since. In the 1970s and into the 1980s, the FDA's efforts to ban saccharin, the controversy over Laetrile (the cancer treatment that didn't work), red dye #2, nitrites in food, the hazards of caffeine during pregnancy, and Rely tampons were all front-page stories for many, many days. As chief spokesman for FDA, I was right in the middle of all of that.

Was the problem with Laetrile that it didn't work or that there were never any controlled experiments to prove that it worked?

There was no evidence that it worked. But there was a lot of evidence that it was being sold by people who were not scientists, who had no interest in developing the science, but who were making a lot of money by selling Laetrile. It was a hoax on the American public that not only involved economic fraud but also jeopardized health because people were avoiding cancer therapy.

Laetrile is not a good example, but if a chemical is in the public domain, where is the incentive for pharmaceutical companies to do the research?

Even when a chemical is in the public domain, sometimes a new use of the chemical is patentable. Thalidomide is an excellent example. Thalidomide, as we all know, became the driving force behind the enactment of the 1962 Drug Amendments. It caused birth defects when it was sold overseas. It was not approved by the FDA at the time. Many decades later, an innovative drug company, Celgene, developed thalidomide as a treatment for leprosy and eventually for multiple myeloma. It is now the standard of care. So a creative and innovative company can often find opportunities in chemicals that are in the public domain.

I was very impressed with how your book, "FDA: A Century of Consumer Protection," included both highlights and lowlights.

Putting that book together took three years. It was the most important book project I have done. It was important to honestly characterize the FDA over the century since passage of the Pure Food and Drugs Act of 1906. FDA has been enormously successful in protecting the public health – it has established a worldwide standard. However, I did include criticisms of the Agency in the book. I put in case studies where the Agency had failed. I put in cartoons that were critical of the Agency; those were usually the funniest. It was important to present, for the current and also for future generations, an honest portrayal of the FDA.

The White House Press Secretary can't always be honest with the press. Given the sensitivity and the visibility of the issues the FDA had to deal with, were you ever put in that position at the FDA?

No. I was never put in the position where I was either asked to or felt the need to lie about something. That is not the culture of the FDA. Of course, the FDA has a lot of confidential information about financial data, trade secrets and ongoing investigations. There were times when I had to defer comment until an investigation was concluded. I've never heard any criticism that the Agency was not open and above-board during the time I was there. The government is supported by taxpayers, and taxpayers are entitled to information, certainly in the food and drug area. It is a matter of basic public health. That is always how I handled my responsibilities while I was at the FDA.

As the FDA became larger and more visible, how did the culture change?

The Agency, at that time and still today, attracts people who could be making a lot more money doing other things but who are dedicated to the public health. When I joined the FDA, the vast majority of the people were lifetime employees, especially the field force. People would join the Agency right out of college in their early twenties and plan to stay there until they retired at the age of 55 or 60. When they retired, they went fishing, so to speak. They didn't turn into industry consultants. Now, people tend to stay for shorter periods and then go out and work as consultants to the industry. There is nothing the matter with that; I did it myself. This trend isn't just a characteristic of the FDA; it is true generally of American society. But it has changed the FDA.

Nevertheless, underlying the Agency is a great consistency – its sense of mission. You can disagree with the Agency's scientific decisions; you can disagree with and be frustrated by the length of time it sometimes takes for FDA to reach a decision, but, for the most part, the people are very well-intentioned in protecting the public health.

For example, the FDA is always accused of either going too quickly or too slowly in approving new drugs. The Prescription Drug User Fee Act (PDUFA), which was originally passed in 1992 and was just renewed this year for the fourth time, established deadlines for FDA reviews of new products. Before PDUFA, many drugs were not reviewed in a timely way. Not because of laziness, not because of incompetence, but simply because of a lack of staff. To this day, the FDA is not adequately funded or adequately staffed to do all of the things that the public and Congress and the media and all of the FDA's other constituencies expect it to do.

Has PDUFA shifted the FDA's mission from protecting America's health to getting timely approvals of drugs that will protect America's health?

I was instrumental in developing and articulating the view that FDA is both a science agency as well as a legal agency. Its mission is to assure that drugs and medical devices in the marketplace are safe and effective, and that unsafe and ineffective products are not in the marketplace. Part of that mission has always been to assure that drugs and devices that can cure symptoms, that can extend lives, that can cure disease, are made available to the public as expeditiously as possible. It is not just a matter of protecting the public from unsafe products; it's a matter of assuring that products that are safe and effective are made available as rapidly as possible so people with diseases can be helped.

Is the current balance between quality and timeliness of review correct?

PDUFA was beneficial in establishing deadlines for review because it provided FDA with the resources it needed to conduct new drug reviews more efficiently. However, where the Agency draws the line between benefits and risks has shifted over the years. The line swings back and forth like a pendulum; sometimes there is a greater emphasis on the risk side; sometimes there is a greater emphasis on the benefit side. Over the past few years, largely because of the highly publicized phen-fen and Vioxx issues, plus other drug withdrawals, the pendulum has swung a little bit towards more caution in approving new drugs, in requiring more data from companies. There will come a time when the pendulum will swing a bit in the opposite direction. These are not big swings, just a few degrees on the benefit/risk spectrum. But clearly we are now seeing a cautious FDA.

How much tension is there between the front-line medical officers and management at FDA?

There is always that tension. FDA has highly professional, highly trained people. They have their own views about the balance between benefits and risks. Some of them have their own clinical and research experience. There has always been a lively debate within the Agency. Any important decision that the FDA makes today is based on a consensus. It's not a decision by an individual.

Before I started with the Agency, in the late 1960s and early 1970s, there was more opportunity for individuals with their own personal views to make judgments that were not subject to consensus or review. Since the 1970s, the Agency has made a significant effort to make its decisions on a consensus basis. So the tension that we are talking about is a natural and healthy tension among professionals. But, once a decision is made, whether you agree with it or not, you should support it unless you think it is contrary to good ethics, in which case you have to deal with that on an individual basis.

There have been stories in the media about certain decisions that allegedly were made for political reasons or were unduly influenced by individuals rather than by consensus. I don't know whether those concerns are accurate, but if they are, that would be unfortunate.

How has the relationship between industry and the FDA changed over the years?

When I was at the Agency, it was a much less formal relationship. Representatives of the drug industry could visit with reviewers without making an appointment. There were times when people from drug companies knew more about what was happening with the progress of their product than I did, and I was in the Agency. I don't think any organization like the FDA, or a drug company for that matter, can operate effectively these days with open access like that.

Now the relationship is much more formal. The only opinions and guidances that count are what is in writing. That can be frustrating. Having to set up formal meetings and run them in a very specific way slows down communications. There needs to be a better balance between informality and the great, time-consuming formality that exists now.

Industry has much less influence on the FDA than the public thinks. Drugs are not approved because of political influence. The Agency bases its decisions on good science and good judgment, not on the economic needs of drug companies or statements made by the industry.

The industry never used to challenge the FDA in court. Now it does, sometimes simply out of frustration. If you think there is a cozy relationship, just ask any drug company that has recently had its drugs rejected.

Given all the physicians and scientists who have financial arrangements with industry, how should FDA staff its advisory committees?

People who have a direct financial interest in a particular product or company should not be advising FDA what to do. An investigator on a study clearly should not be judging that study. On the other hand, just because individuals have consulted with a drug company or spoken on behalf of a drug company, does not mean that they cannot render objective recommendations. My view is that advisors must fully disclose any relationships that might influence their decision-making. But we can't go to the other extreme and preclude people just because they have consulted with industry; they are often the best experts in the field. If we preclude people from serving just because they have received money from a company, we are going to wind up with people without the right expertise. If they are the best in the field, then the drug companies would have reached out to them and asked them to consult or speak on their behalf. Of course, not every physician accepts their invitation.

Advisory committees are not juries. The jury in a courtroom basically has the final decision; FDA advisory committees are only advisory. In a courtroom, there is a jury of ordinary people looking at criminal behavior. FDA advisory committees are made up of highly trained experts who can evaluate the nuances of clinical trials and other medical matters.

Do pharmaceutical companies run ads expecting objections from the FDA and then just run other ads when they hear from the FDA?

Absolutely not. There is too much at stake now for companies to take that kind of risk. FDA requirements, while they stay fundamentally unchanged, do shift in nuance, so companies need to be constantly on top of that. There can be legitimate disagreements about the data and what kind of information can be communicated, and about the takeaway messages of certain statements. In some cases, violations result from just plain sloppiness or oversight on the part of the company. But companies need to be and are ultra-responsible because the consequences of not being responsible are to open themselves up not only for an FDA enforcement letter but also for a whistleblower suit under the False Claims Act or an inquiry from a U.S. Attorney's Office, or a Lanham Act case, where one company is suing another, or even for product liability.

There have been many major settlements where drug and device companies paid the government tens of millions of dollars for promoting off-label uses. The illegal activity was documented in marketing plans and there were a lot of witnesses. What were those people thinking?

This is a complex question. The rules affecting the advertising and promotion of drugs have evolved considerably. Sometimes company officials have not understood the current rules – or the government's interpretation of them. The Washington Legal Foundation case in the 1990s caused a lot of confusion as to what could be communicated and what could not. I don't think government prosecutors always take into account the environment that existed at the time the promotional or educational activities were taking place, and do not always make a medical assessment as to whether patients were actually helped by the communication of information not in the FDA-approved labeling.

But we now have much more educated marketing groups. We have more oversight by regulatory affairs and legal affairs departments. We have larger consequences for off-label promotion. The situation is better than it was, but still more clarity from the FDA would help improve compliance.

U.S. Attorneys across the country are prosecuting the False Claims Act cases you mentioned. Each of them approaches it from their own perspective. They continue to expand the personal liability aspects; for example, in the Purdue Pharma case, three senior executives personally pleaded guilty. I think, in some cases, the U.S. Attorneys would like to see more punishment of individuals to send a message. I think the Purdue case may be just the first example.

I really enjoyed your book on how to work with the FDA. How important is etiquette when working with the FDA?

You have to deal with the FDA on its own terms. You have to understand FDA's rules, its own limitations in what it can do, why certain interactions are formal. For example, going two levels above an individual to appeal a decision is not going to turn out right. People sometimes go outside the system and try to ride roughshod over the FDA. For a company that wants to have a long-term relationship, going to Capitol Hill to influence the FDA on a specific decision generally is not a good idea.

What impact do you expect from the recently-passed Food and Drug Administration Revitalization Act?

It is going to change a lot of things. The most significant part is REMS: Risk Evaluation and Mitigation Strategies. It will give FDA the legislative authority to require risk management programs, which it did not believe it had before. There will be a lot of changes in how the industry and FDA look at risk. Companies will need to prepare earlier in the drug development process to make sure that all the risks are taken into account. Once a drug is on the market, they will have to make sure that the risks are more aggressively monitored.

Companies are going to have to pay a lot more attention to explaining risks when they market products. In addition to REMS, the Office of Inspector General has penalized companies for alleged off-label promotion, and the companies have gotten the message very clearly. Also, drug labels now include a half-page or three-quarters-page summary that sets forth the risks associated with the product.

We don't have a good post-marketing surveillance system today. We need more Phase IV studies, more voluntary reporting on the part of physicians, more reporting by the patients, and more resources to FDA to evaluate adverse drug reactions. The number of adverse drug

reaction reports that FDA receives has increased very, very significantly in recent years and the Agency does not have even a fraction of the resources it needs to do a proper evaluation of those adverse drug reactions.

A recent opinion piece in *The Wall Street Journal* expressed the view that comparative trials need to focus more on which drugs can be used in combination with each other, which is how drugs are prescribed, rather than comparing one chemical directly against another, as if medicine were practiced that way. There needs to be a debate about such matters.

In your book on crisis management, you point out that every crisis had its own peculiarities. When your clients hit a public relations rough spot, do you advise them to go very visible like Johnson & Johnson did with Tylenol, or just keep their heads down and wait for the storm to pass?

Every crisis is different. You have to use your judgment. There are times when you make public statements. There are times when you keep your head down. There is no set formula.

Certainly, if the situation involves a safety issue that the public needs to know about, or there is a lot of media coverage, then I generally advise getting out front, trying to make sure that the coverage is accurate and the public learns what it needs to do. If a matter doesn't have that level of public interest, and if it is being managed properly, and it doesn't pose any immediate public health threat that people need to do something about, then it might be handled more quietly. It is always easier to deal with a crisis when it doesn't become public. You don't have to deal with the media; you don't have to deal with the various constituencies.

Jesse Gelsinger's death in a clinical trial at the University of Pennsylvania had no general public health ramifications but the news coverage rapidly spun out of control. In a case like this, is the best strategy to watch how much visibility it gets and then quickly react?

That was a tragic, unnecessary, unfortunate death. But the reason it got all of the visibility was not only because an individual in a clinical trial died, which, as you know, does happen because sometimes clinical trial patients are very sick to start with, but because (a) it was a very young man; (b) there was a question as to whether he should have been in the clinical trial to begin with; (c) it involved a new technology – gene therapy; (d) the University of Pennsylvania arguably could have handled it better; and (e) there was a government investigation. Because of all of these factors, it became a very prominent case and deservedly so.

The story probably would not have gotten so out of control if the University and the people involved had acted more quickly to lay out all the facts and take responsibility. Usually, if an individual or an institution makes a mistake, the best way to handle it from a public relations perspective is to deal with the situation quickly and honestly. Take responsibility, explain what has been learned, and move on. Unfortunately, sometimes our litigious environment makes it difficult to take that full measure of responsibility, but from a public relations standpoint, it is terribly important.

Increasingly, we see stories in the media about companies discontinuing trials of drugs because of adverse outcomes. The companies not only seem to be making those decisions more quickly, but also more publicly. The industry is learning that if there are unexpected and unacceptable adverse effects in a clinical trial, they need to move quickly. We've seen Pfizer and Merck make such announcements in recent months.

If the clinical research industry were to hire you to put together a campaign to improve the image of clinical research in the public's eye, what advice would you give it?

The first thing to do is engage the public in basic education about how clinical research works, why it is important, what the challenges are, and how consumers can get the most out of a clinical trial. The public needs to understand not only how clinical research works, but also the benefits to the community and for the people in a clinical trial. Other than efforts such as CISCRP and your community outreach speakers bureau, the industry has not engaged in that kind of education.

A lot of companies falsely believe that the public understands their industry and will give them the benefit of the doubt when they get into trouble. I learned that lesson three decades ago. The FDA announced that it was banning saccharin based on animal studies. The Agency was ridiculed because the public did not understand what a high-dose animal study meant. You can't presume that the public knows very much about scientific or regulatory processes. You need to educate the public, not in a moment of crisis, but in the moment when there is no crisis, and on an ongoing basis.

In addition to your advisory work, chairing of educational meetings, and book-writing, are you working on anything else?

I serve on the board of a specialty drug company, Scolr Pharma, and also as chair of the board of the Medstar Research Institute, which oversees research at seven hospitals in the Washington-Baltimore area. In both capacities, I have the ability to help advance medical research and the development of beneficial new medical products; that's very important to me.

I also am the president of the FDA Alliance, a coalition of more than 100 organizations, companies and individuals seeking to increase appropriated funds for FDA. Our position is that the FDA doesn't have nearly enough resources to do what is expected of it. We are advocating for more resources for the FDA.

The drug approval area is well-funded because of user fees. The rest of the drug area, whether it's post-marketing surveillance, evaluation of adverse drug reactions, or compliance, is severely under-funded. The entire food area is under-funded by far. The food officials at FDA often are doing two and three jobs. I don't think anybody who is familiar with the Agency believes that the FDA has the resources it needs is to do the job that needs to be done in the food area.

The cosmetics area has always been an orphan for FDA. The Agency has ultra-limited resources to devote to cosmetics. The law limits the Agency to deal with safety issues only after a problem occurs; there is no premarketing review. The industry has done a very good job of self-regulating itself, but the FDA has very limited resources.

The FDA's role in the Critical Path Initiative is not well understood outside the Agency. It has the potential to help the Agency focus on what is truly important from a therapeutic standpoint. That is another area that needs better funding.

The Agency has a very active bioterrorism group, but it doesn't have the resources that it needs to protect us from deliberately adulterated food or drugs. People don't want to talk about it, but one of the easiest ways to undermine the security of this country is by contaminating the food and the drug supply. FDA does not have the resources, either at the import level or even at the inspection level, to assure fully the integrity of those supplies.

The industries regulated by FDA support the need for a well-funded Agency because FDA's ability to assure the integrity and safety of the marketplace is central to business interests.

An underfunded FDA cannot approve new products efficiently or remove unsafe products quickly.

The FDA Alliance has held more than 80 briefings on Capitol Hill. Across the board, there has been a positive response. Congress understands better than before that FDA is under-funded. However, the current level of partisan distrust makes it hard to get legislators from both parties to work together. Nevertheless, I am optimistic that FDA will eventually get the funding it needs. Not this year, perhaps not next, but eventually.

Aside from more funding, what else can make the FDA more effective?

There is room for improvement in many areas. For example, FDA is trying very hard to be transparent, but it could still be more transparent about some of its decisions. Sometimes FDA provides too much direction to its advisory committees, rather than letting them make their own judgments. FDA isn't doing enough to educate the public about what the Agency does, why it does it that way, and how the public benefits. There should be more consumer education about taking drugs properly; that could make a big difference in the incidence of adverse reactions.

What does the future hold for us?

The most remarkable thing that happened in the 20th century was not the advent of the automobile or the airplane or the computer. It was that the average life expectancy increased from 47 years in 1890 to 74 years in 2000, and it is still increasing. That progress is due to many factors, but at the top of the list are better sanitation and all of the new drugs and other new medical technology. Everybody has ancestors who died of infections that would not even be thought twice about today.

Medical technology is advancing at a very rapid pace. Products are coming along for personalized medicine, for implants, for building autologous organs. I hope the FDA has the capacity to keep pace with advances involving such innovative technologies; companies need FDA support and direction so their research can continue to move quickly and efficiently. I am optimistic that FDA will be able to provide that support and direction simply because that is the tradition of the Agency and because the people at the FDA remain basically sound and committed. I think the future will be just fine.

Interviewer

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