

History
of the
U.S. Food and Drug Administration

Interviewee: Frederick W. Blumenschein

Interviewer: John P. Swann, Ph.D.
Robert A. Tucker

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NAME: Frederick W. Blumenschein

NAME: John P. Swann, Ph.D.
Robert A. Tucker

ADDRESS: [REDACTED]

ADDRESS: Parklawn Building
5600 Fishers Lane
Rockville, MD 20857

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LAST FDA POSITION HELD: Chief, Case Management & Guidance Branch, Office of Compliance,
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Tape Page Subject

Interview with Frederick W. Blumenschein

June 24, 2008

TAPE 1, SIDE A

RT: This is another in the series of FDA oral history interviews. Today, June 24, 2008, the interview is with Frederick W. Blumenschein, who formerly was Chief of the Case Management & Guidance Branch in the Division of Manufacturing and Product Quality, in the Center for Drug Evaluation and Research.

Dr. John Swann and Robert Tucker are interviewing Mr. Blumenschein.

Fred, if you would give us a brief overview of your background, where you were born, educated, any prior experience to FDA's service. Then we'd like to pick up your FDA career and go through your achievements there.

FWB: Well, I was born and raised in Cincinnati, Ohio, for 16 years. My father was a government employee, and the gossip had it that after the election of 1960, the office that he worked in was, for political reasons, moved to Huntsville, Alabama, and so we were moved to Huntsville, Alabama in 1964.

RT: What agency was he with, Fred?

FWB: He was with the Department of Defense, procurement.

And so, we moved to Huntsville, Alabama, and that's where I completed the last two years of high school, and then, from there, I went to Vanderbilt University in Nashville.

As I was relating just a moment ago, although most investigators -- because I started with FDA as an investigator -- have a degree in science because they required so many hours of science, I may have been the only one, at least that I'm familiar with, whose degree was in history; my B.A. was in history.

As far as education goes, that was it until after I started working at the agency, and then I went to law school while I was working for the agency.

RT: When did you graduate from . . .

FWB: Vanderbilt?

RT: Yes, please.

FWB: Nineteen seventy, June of 1970.

JS: Did you have any interest in pursuing history as a profession?

FWB: You know, I think I would have. My father tended to be much more pragmatic than I am, and so he kept telling me, "What are you going to do with history? What are you going to do with history?" And I have to admit, although it's a shame in this

country, but teaching often does not pay well. I probably would have enjoyed teaching; you know, I enjoy giving presentations, etc., but it just didn't pay very well. But I loved history, I'd always loved history, especially European history, so that's what I finally decided to major in.

Along the way, I, like so many college students who don't know what they're doing and flounder around, said, "Gee, maybe I should consider medical school. So it was for that reason that I ended up taking a lot of science, because you did need to have a lot of science if you were to even consider medical school. And, fortunately, because I really did like my job with FDA, I'm glad that I did.

RT: Did you have any employment experience after graduation, before coming to FDA?

FWB: Well, I worked for the Army Topographic Command. My first job was with the Army Topographic Command in Washington, D.C. I worked there for about a year, and then was rified, reduction in force. The reason I was rified is because there were a number of different organizations -- Army Topographic Command, National Oceanographic -- I don't know what their whole title is [National Oceanographic and Atmospheric Administration] -- but there were several, and often their work product(s) were redundant. So they combined a lot of that in what's now called the Defense Mapping Agency, which still exists today, but a lot of us, especially non-veterans, lost their jobs.

Actually, I was prepared to go home at that point. I looked all over the place, including FDA, interestingly enough, and nothing was to be had. Because I could not find another job, I was prepared to go home and collect unemployment. This sounds terrible, but I wasn't that upset about it, because back in those days I used to play tournament bridge, and I said, "Well, this will be great. I'll collect unemployment and play as much bridge as I want."

The day before I was to fly home -- and this is not an exaggeration -- the phone rang. I was getting ready to walk out of the apartment. The phone rang, and I shouldn't have picked it up, but I did, and it turned out to be the head of the J. C. Breckenridge Library up at Quantico Marine Base. And he said, "You know, you're at the top of the hiring list," or whatever they call that. You know, if you're riffed, they have to put you at the top of the list before they can consider anybody else for a position.

"We have a position here that you qualify for, if you want to take it."

Well, I knew that if I turned it down, I wouldn't be able to collect unemployment, so I didn't have much choice in the matter, and I said, "Fine." And I said, "When do you want me to report?"

He said, "Tomorrow," or maybe that was Saturday and they wanted me to report on Monday. But it was the day before I was scheduled to leave.

I worked there for about five or six months, and I absolutely hated that job.

JS: It was working in the library at the Marine base.

FWB: Yes, yes.

JS: Acquisitions or cataloguing?

FWB: Well, I'll tell you what it was. You know, in the old days how updates to manuals worked -- you got these paper things and you'd tear them apart, and you'd take the old pages out and put the new pages in. My job was essentially updating every military manual in the place. It was the most boring, absolutely hideous thing you could imagine.

Well, what happened is a friend that I had gone to college with who I used to visit in New Jersey called me one night on the phone. He said, "You know, a guy I go to church with works for FDA"; (I had mentioned to him at one time that it sounded like FDA would be an interesting place to work).

"And he said here in New Jersey, FDA is hiring."

Well, the next day I was on the phone to the New Jersey office, saying, "I'd be interested," blah-blah-blah, and I think I talked to Ed Wilkens, actually, who was Director of Investigations Branch.

And he said, "Well, get an application to me right away."

Now, unbeknownst to me, interestingly enough, it turns out that FDA was hiring all across the country. This was Project Hire. But I just thought it was the New Jersey office. If I had known, I would have probably just started in Baltimore District or its Falls Church Resident Post, because I lived in Falls Church at that time, but I just thought they were only hiring in New Jersey. And I said, "Boy, I don't like the job I have. I want to go to FDA." And so that's how I ended up going to New Jersey District.

RT: You came into federal service at what level? As an investigator?

FWB: With FDA?

RT: Yes.

FWB: As an investigator; I was hired as a GS-5. But I was a Step 2 because I -- along with everybody else. I don't know, back in those days, if District investigators ever started out more than a GS-5. They did eventually, but I don't know if they did then. But I was a Step 2 because I had worked for a year in the Defense Department and received my in-step.

RT: You'd already qualified under the FES, federal exam.

FWB: Yes. In fact -- boy, I don't remember -- I actually had a couple of summer jobs with the government that I had used the FES exam for. That may have also been what I used when I applied with the Army Topographic Command. I'm not sure at this point.

RT: I assume that the first of your career, like most of our new personnel, you were in a training mode for a time. Was that in any special industry, or more focused in New Jersey since they have a lot of drug manufacturers?

FWB: No. I think back then, that the training program -- at least I was always under the impression that the training program they came up with was kind of a standardized thing nationally, because every office hired quite a few investigators. I don't know what the percentage increase the FDA was.

But they had a six-month training program, and it involved classrooms where they involved senior investigators teaching you, etc., and then combined that with on-the-job training. For example, they taught you how to collect the sample, then they'd take you out and have you actually collect a sample with someone who knew what they were doing. It really was a pretty good training program, actually, at least I thought so.

RT: In that area, you likely got into some import product surveillance.

FWB: Well, interestingly enough, the one thing at that time that New Jersey Inspections Branch never got involved in was imports. The two things that were unique about New Jersey District, or Newark District at that time, was, all the imports that did come into New Jersey were actually handled by the New York District Office. In fact, I think that's still true. The New York FDA office has a Resident Post in New Jersey that handles imports coming into New Jersey.

The other thing, of course, was that New Jersey did not have a laboratory, which I think nearly every other district did at that time. I could be slightly mistaken.

JS: Newark and Nashville I think were the first two districts established without a laboratory at that point; I believe they were.

FWB: Okay.

RT: When you did any import follow-ups, what was the nature of the work involved as an investigator?

FWB: Well, like I said, when I was in New Jersey as an investigator, I wouldn't have really been involved in imports.

JS: What was your primary concern, then, as a young investigator in . . .

FWB: Oh, I'm sorry, I failed to answer one question.

The training was not specialized back then. I think that's something that has kind of changed in the agency over time. Now, you're hired more with a certain background in mind, I think, than back then. Most people then really were kind of generalists, I think, back in '72. And so the training was broad -- and I'm glad for that.

You learned food work, you learned drug work, you learned a bit of everything. In fact, my first independent inspection was a toy manufacturer, because that was before the Consumer Product Safety Commission has been established and FDA then regulated toys. That's a story in itself.

RT: That was under the Federal Hazardous Substances Act?

FWB: I believe so.

JS: There were a few acts, the Child Protection Act also. But you're absolutely right. We still had that authority in the early 1970s.

Was there much toy manufacturing in New Jersey.

FWB: Well, I don't know that I could answer that. I only did one toy manufacturer in my entire career, and it was my first independent inspection. I mean, I just find it somewhat ironic that your first independent inspection for FDA is a toy manufacturer. And it was an experience. I learned a lot from that inspection -- of what not to do.

RT: Inspecting toys, was primarily to evaluate hazards inherent in the product?

FWB: Yes, that's what I remember the thrust of the program was -- to look and see whether you thought anything was hazardous.

JS: But, still, something must stand out about that inspection . . .

FWB: Yes, what I learned about being an investigator. What happened was I thought I had found something that was or could be hazardous.

It was a toy fireplace for children. It was really just cardboard, etc. And then inside the hearth -- I guess you'd call it the hearth -- they had this wrinkled-up red paper and then it would have a light so it looked like flames, etc. And I noticed, when I was inspecting, that the paper was kept in place by this sharp-pronged thing, not a nail exactly, but a sharp device. And I said, "Gee, if a kid lost his balance and fell on there, he'd fall right on that sharp-pronged thing."

Now, we had an inspection program on this, on inspecting toys, like you have programs in FDA on everything. But, of course, I hadn't read the program; you know, being a new investigator, I thought I knew everything. So I collected one fireplace, saying to myself, "Let's take this into the lab and see if they agree that this is hazardous." I brought it back to the office to write up a collection report.

And my supervisor said, "What did you do?" and I explained it to him.

And he said, "And you collected a fireplace?"

I said, "Yes. I thought the lab could look at it."

He said, "You collected a fireplace?" He said, "What does the program say about that?"

So we looked up, I guess, it's Part 4 of the program, and it said, "If you're going to collect a sample, collect three, not one."

And I looked at him and I said, "But that doesn't make any sense. You only need to look at one."

He said, "The program says three."

So now I had to go back to the firm.

I mean, I think to a certain degree, he was doing this as a learning exercise.

I went back to the firm and, of course, being new, I was embarrassed. Thankfully, the guy in charge was very nice.

So I said, "I hate to bother you, but I shouldn't have collected just one, I should have collected three."

"Oh, that's not a problem at all." So I collected two more.

I got back to the office, we looked at them. The first one I had collected, the cardboard was like, the fireplace looked like beige brick. The two I came back with were red brick, otherwise identical.

The supervisor said, "What does the program say?" And the program said, "Three identical."

I had to go back again. Not only did I have to go back and return the two red, but I had to collect two beige fireplaces to replace them. And, of course, the upshot of all this is it went to the laboratory and they decided it wasn't really a hazard.

So I learned that as an investigator you had to read the program. It was a good lesson.

JS: But it still beat tearing apart Army manuals, right?

FWB: Oh, yes, absolutely, absolutely.

RT: As you continued there and got more experience, were you assigned to any area of specific interest to the agency?

FWB: Well, like I said, the training was pretty general. In other words, you were expected to do some food work as well as a little drug work, etc. But what I noticed was -- and I suppose for good reason, looking back on it now -- the more senior investigators in the office tended to do most of the drug work, and so the Project Hires ended up doing most of the food work.

And so I would say for about the first, oh, I'm going to say year, 10 months, or something like that, I did pretty much food work, actually. And I can't say that I liked it very well.

Now, there were some people in the office who preferred food work. Food work was usually sanitation issues, I mean counting rodent pellets and looking for insects, and I wasn't really thrilled with that.

So, at any rate, it just so happened that about 10 months or a year into the job, most of the senior people were not in the office one day; I can't remember the reason, but nearly all of them were gone. And my supervisor came up to me and said, "You know, we've got a little bit of an emergency here. We need a follow-up down at Squibb."

Am I allowed to talk about specific firms?

JS: Absolutely.

FWB: And he said, "Would you like to do it?"

I said, "Absolutely."

And so, if I say so myself (I can't remember all the details about what the investigation was about), I think I did a very thorough job and a good write-up, and I got actually, well, back in those days it was called a Supervisory Commendation, you know, something from your supervisor saying "well done." And from that time forward, I started getting more and more drug work.

JS: In the six or so years that you were in Newark, from '72 to '78, are there some cases, drug or otherwise -- obviously, the toy case you mentioned -- but are there some cases that stand out in your mind still as kind of a defining experience?

FWB: Well, I think during that period, there were a number of things that occurred that I will certainly never forget. One of the things I'll never forget -- and I guess that was right around the time I'd been there about a year was when they had the first mushroom recall. You don't remember the mushroom recalls?

JS: Go ahead and tell us about it.

FWB: Right. The first recall was Fred's Mushrooms, a company in -- I think it was Ohio. Most of the recalls I think were Pennsylvania companies, but this one was, I think, was in Ohio -- Fred's Mushrooms -- and I do remember that because my own name is Fred. The product was recalled because of improper processing resulting in the possibility of botulism. It all started like so often with Class I recalls, on a Friday afternoon, as I recall.

What then occurred, of course, is -- and being GS-5's or just beginning 7's, one or the other, nearly all of the Project Hires were interested in the overtime, especially living on the East Coast, and we certainly got our share of overtime, because there was one canned mushroom recall after another. We had the Fred's Mushrooms, and then just one after another. They immediately ran out to other mushroom companies and the Agency decided that a number of other canned mushrooms were under processed. Of course, they didn't have the low-acid canned food regulations at the time.

JS: About what year was this?

FWB: That would have been around '73, I think, when it actually started. I don't know how many Class I recalls they had, but there was quite a few.

So it just seemed to go on for weeks and weeks and weeks, and you kept going back to the same places, because back in those days, of course, foods, even low-acid canned foods, weren't required to have lot numbers. To trace distribution of the products, you had to go to the food distributor and just go through every record they had in the place and find out who all their customers were. And, of course, you were going to people who didn't even necessarily get mushrooms. I went to places like a prison once that I had a feeling never got canned mushrooms, especially the little sizes that they were talking about. And bars that wouldn't have had little canned mushrooms. But you inspected every single one if they were a potential customer because it was a Class I recall.

JS: Were there ever any cases that came out of this, where anybody actually died or were injured from botulism?

FWB: I don't think there were . . . I don't think there were actually any documented deaths from the mushrooms.

Now, what had caused the scare a little bit earlier was right before I joined the agency, and this was the Bon Vivant case, also out of New Jersey, by the way, the vichyssoise soup. And that, of course, had caused the interest in low-acid canned food manufacture, and I think eventually probably led to all the mushroom cases. In the Bon Vivant case, I know there were injuries; I don't know if there were any deaths.

JS: There were deaths; there was at least one death.

FWB: I wasn't sure. Like I said, it occurred right before I joined FDA.

JS: And so we certainly had a botulism mindset -- not that we didn't before, but having a case so close to this other one, we obviously were very aware of this sort of problem. So that was certainly a big case.

How about drug cases? Any stand out in your mind?

FWB: Well, the one that stands out in my mind, I suppose, this was very near the end of my career as an investigator.

What my district would do if you had been sent to an FDA school for training, was to get you out on an inspection requiring that expertise as soon as possible to reinforce what the investigator had just been taught.

Well, I and another investigator had just returned from radiopharmaceutical school. An inspection came up at Squibb, whose radiopharmaceutical facilities were in New Brunswick at that time. The two of us went out to do the inspection, and the agency was preparing an injunction against Squibb at that time based upon our inspection, when Squibb decided to close down and move their entire radiopharmaceuticals facility to Puerto Rico, and so staved off an injunction. In other words, the poor manufacturing conditions had been observed in New Brunswick; we had no inspectional findings for the new Puerto Rican facility.

A lot of the evidence at the New Jersey facility demonstrated that the facility and equipment were old and often “scotch-taped” together.

RT: Where did you move next assignment-wise from Newark?

FWB: I did something that hardly anybody else did. It was very common for New York District investigators to try to get a job in the New Jersey office because it was somewhat less expensive to live in New Jersey. It just so happened that, because I like opera and symphony, etc., I had moved to Manhattan while I was still in the New Jersey office.

I had thought for a couple of years that I might like to be a Compliance Officer, and what happened was a Compliance Officer position opened up in New York District. Well, I decided to apply for it, especially since I was already living in Manhattan.

I will tell you to this day, I think the reason I got the position, I honestly do, was the District Director in New York had a chance to get back for all the positions he had lost to New Jersey District, by taking somebody from New Jersey District. I am absolutely convinced of it. I mean, not that I wasn't qualified for the position, but there were probably one or two other people on the panel who were likely more experienced, and so I was always convinced that was the reason I got the position.

RT: Who was Director of New York then?

FWB: George Gerstenberg.

RT: Thank you.

FWB: And so I became a Compliance Officer.

When I came back from an inspection one day in New Jersey, my supervisor said, "I've got to talk to you right away," and he took me aside and said, "They called and they want you for the position in New York." I was really flabbergasted. And he looked at me and he said, "Well, are you going to take it?"

And I said, "I wouldn't have applied for it if I wouldn't take it." And so I accepted the position.

But, boy, there were a lot of people in that New Jersey office that had been to New York who said, "You're going to get eaten alive!"

But I was a Compliance Officer in New York for about 11 years.

JS: From 1978 to 1989.

FWB: Eleven years. And I really enjoyed it; I really enjoyed being a Compliance Officer.

JS: What was it about it that really made it memorable?

FWB: Well, I think that's one of the reasons I eventually went to law school soon after, because I liked the legal aspect of it. I also liked reviewing other people's work and deciding if the evidence needed bolstering and whether the recommended legal action should go forward. I kind of liked that, and that's really what a Compliance Officer does.

As a Compliance Officer, I have often told investigators who got irritated at their Compliance Officers because the Compliance Officer had turned down or disapproved a regulatory action based upon the Investigator's work: "You've got to remember what a Compliance Officer is. A Compliance Officer is a Monday-morning quarterback."

That's exactly what they are. They're there to second-guess you, and assure that the evidence is sufficient and the case warrants going forward. And I can attest to that as an investigator who got cases turned down by my Compliance Officers. You didn't like it when you got turned down. But that's what a Compliance Officer sometimes has to do.

RT: As an ancillary interest, before you made this change, was the commute up there

in a very urbanized area from Manhattan over to Newark a problem, or was it an easy change?

FWB: Well, at the time, I was still working in the New Jersey office but living in Manhattan, I had given up my car. I didn't want a car living in Manhattan. And then when I got the job in Brooklyn, I just took the subway to work.

JS: When you were in the position in New York, were you involved at all in the Beech-Nut case, the Beech-Nut apple juice case?

FWB: No. But I can tell you a funny story about that. I can tell you why I wasn't involved. I probably would have been, but . . .

Okay. I went to law school.

JS: Well, I want to talk about the law school experience, but go ahead.

FWB: The Director of Compliance Branch in New York, Clarence Waltrous, was going to assign that case to me. Now, Clarence had also gone to law school when he was working for FDA. So, I mean, during the time I was in law school, going at night, you know, we kind of commiserated with one another, etc. And I walked up to him after he assigned me the Beech-Nut case, which we didn't know a great deal about since not all of the investigation had been completed, etc. But I told him, "You know, I hate to say anything, but I'm planning on taking at least a month off to study for the bar exam. I

don't know whether the case can sit waiting for me to return." So he reassigned the case and that is why I didn't do the Beech-Nut case.

JS: Oh, okay.

Just for the record, this was the case that involved a manufacturer, Beech-Nut Company, that was substituting flavored sugar water basically. Is that what it is?

FWB: Something like that, yes.

JS: Glucose solution or something like that.

FWB: Yes, glucose solution for real fruit juice.

JS: On a fairly massive scale.

FWB: Oh, yes.

JS: It was a major penalty that the firm had to take, if I remember right. Do you recall?

FWB: I don't remember. I think the convictions of the responsible individuals eventually were overturned, if I remember correctly, on appeal, but I don't remember about the fine. I'm not sure. I think they did probably get a heavy fine.

JS: I think those were in the millions, almost. It was a huge case.

RT: It was a substantial fine.

FWB: It was a very intensive investigation. A lot of good work was done by the investigative team and the Compliance Officer who handled the case.

TAPE 1, SIDE B

JS: I was just going to ask, while you were in the New York District, you were also attending, from 1979 to 1983, law school, which must have been a very difficult experience, doing full-time work in the district office as a Compliance Director and going to law school as well. Did the agency help out at all with the law school expenses, or was this footed on your own?

FWB: It was footed on my own.

I don't know what, after three years, the policies became with respect to FDA paying for schooling outside of work, but, no, I footed it on my own.

But back in those days, the criteria for getting what was called, I think federally subsidized student loans were nonexistent! I mean, it didn't matter who or what you were, you could qualify for a student loan. And the way the student loan worked, if I remember correctly, was you got the money, you didn't have to pay a cent until one year

after graduation, and at that point you would pay -- and the interest rate on it was something like, I think, 2 percent; it was unbelievable.

But, I mean, what was so surprising about it -- I didn't know it the first semester I was there, and one of the people I was going to law school with at the time said, "You know, you should get one of these student loans."

I said, "Well, I doubt if I'd qualify. I'm working full time at FDA. I probably make too much money."

So this person said, "It doesn't matter how much you make."

Now, of course, I think it does. I don't know that I'd qualify now. But then I did, even though I didn't really need the money. So I kept getting these student loans. And I probably shouldn't say this, but I eventually bought my house in Queens based upon being able to get the student loan. It was a pretty good deal.

Well, at any rate, FDA didn't pay for any of my law school.

JS: How did the background in law change your approach to your position in the agency? Did you look at things in a new light? It gave you perspective that obviously you didn't have before.

FWB: Well, you certainly don't need a law degree to be a Field Compliance Officer. I mean, you don't have to have a law degree.

I think if I were to read some of my memos approving or disapproving cases, they probably became more legalistic sounding, and I would probably do some more basic legal research than an average Compliance Officer would. I also felt like I was able to

establish, sometimes more easily, rapport with our own FDA attorneys as well as the U.S. Attorneys in the Southern District and Eastern District of New York simply because I was also a lawyer.

But, I mean, I really went to law school because I enjoyed reading legal cases. I also wanted an advanced degree.

Actually, what I first considered was to go to business school.

RT: You took that law education at Brooklyn Law School?

FWB: Yes, Brooklyn Law School.

RT: You also got into editing their *Brooklyn Law Review*. Was that after you graduated?

FWB: No, no, no, no. You had asked me how difficult it was, and it was. I've often said I'd probably never do anything academic again because it was very intense, going to school at night and working 40 hours a week.

The first year at law school, my classes were 6:00 to 10:00 p.m. Monday through Friday. And then, of course, the only time when you really might be able to get an hour of studying in was when you got home. But most of it was on the weekend. So I just had absolutely no time to do anything else.

I will never forget, during one of my first lectures at law school, this professor, Dr. Lightener -- I will never forget him -- got up, and he was looking out at about a

hundred of us in the classroom, and he said, “Now, look, folks, there’s a certain fact of life that you’ve got to accept.” He said, “Half of you in this classroom, I guarantee are going to be in the bottom 50 percent of your class.” And, of course, the entire time he was saying this, I thought he was staring right at me. I was just convinced of it. And he said, “I can also tell you that, without question, one of you is going to be at the very bottom of the class,” and I thought he was staring right at me. And I don’t know how to explain to you, but for that reason, I just really, really worked hard to assure I would not be at the bottom of the class.

Back in those days, at Brooklyn Law School, you got an invitation to try out for the *Law Review* if you were in the top three academic positions, and at the end of my first year I was in the top three, and so I got an invitation to try for *Brooklyn Law Review*. Being an invitee, you picked a topic on which to write an article over the summer. I happened to write what is called a Note on a subject called equitable estoppel of the government. And they thought the paper was relatively worthwhile, and so they made me a full-fledged member of the *Law Review*.

Now, I will tell you, during my second year, I was constantly working on and refining that Note. The editors wanted more information, more legal precedents, more footnotes.

Then, the third and fourth years, I was an editor in the *Law Review*. I will tell you that as hard as the first year was academically, it was even more difficult, I think, being an editor for law. It was just ridiculous.

I know as I was departing, I told the future editor-in-chief, I said, “Night students, if they’re working full time, should really not be an editor. It’s just too much!”

RT: You mentioned this term that may not be familiar with some of our researchers.

What is it, equitable estoppels?

FWB: Equitable estoppel.

RT: What does the estoppel term mean?

FWB: Well, it's kind of what it sounds like. It means if somebody, like a federal agent, misleads an individual, and that individual relying on that information does something or does not do something that later turns out to disqualify them for benefits, or something like that, can the government who now denies them the benefit be stopped from saying, "You don't qualify," despite the fact that one of their own agents had given them misinformation causing them to be disqualified. That's estoppel.

RT: Thank you. That's a term I hadn't heard before, but I suppose those in the law circles are very familiar with it.

JS: Well, you were in New York until 1989, and then you moved down to Washington to take a position on the Health Fraud staff in the Center for Drugs, and it sounds quite interesting, quite different. How did this change in position, change in location, come about, and what was it that interested you in the position?

FWB: Well, I guess I was just kind of looking for something different. I mean, I'd done the same thing for 11 years. It wasn't a promotion. In fact, it was essentially a Compliance Officer position, but at the Center level. But still, it was considered a Compliance Officer position. Most cases, once a District Compliance Officer writes it up and, let's say, approves it, it then goes to the Center, and the Center Compliance Officer looks at it and reviews it. That's what this position was, but in a very limited product area: fraudulent drugs.

In the field in New York, I could have handled any sort of legal case, whether it be foods, devices, or drugs, but once I got to the Center for Drugs, of course, the only thing I looked at, well, for the first three years, was health fraud cases, which at that time it was called.

JS: There's, of course, a very long history of FDA's concern with health fraud, and I'm sure you must have encountered some interesting cases that came along your desk while you were in that position, and interesting people too. I think this probably was the period of the height of maybe shark cartilage, the cancer cures like shark cartilage in the Brzezinski case.

FWB: The Brzezinski case. I think, actually, the case of Brzezinski was a little before I got there. But certainly we handled a lot with laetrile, which we also did in the District office.

Now, by the way, you had asked me earlier about imports. Let me just say, once I became a Compliance Officer in New York, I handled a lot of importation cases. I mean, every Compliance Officer in New York handled imports at that time. Eventually they split the District into imports and domestic. But I don't know how many thousands of import detentions I was responsible for. So, in New York, I got involved a lot in imports.

However, back to the Center Health Fraud staff.

The philosophy was a little bit different back in '89 and '92, I think, but the other products that I can remember we went after were wrinkle creams. And now, of course, they get away with more than I think we allowed them to in 1990-92.

JS: Well, the laws changed substantially since 1992, when you left there, with DSHEA [Dietary Supplement Health and Education Act] and supplements and waivers on supplement labeling and what manufacturers can and can't say. That wasn't the case necessarily at the time you were there. That had changed.

FWB: And the other thing that has changed, albeit a procedural matter, at one time nearly all those cases were handled by the Center for Drugs, because if you had claims, it was considered a drug. But now a lot of these cases are handled by the Center for Foods, including cases where they make drug-like claims.

This occurred after my time with the Health Fraud Staff. If it is a clear-cut medical "cure" type claim, the Center for Drugs still handles it, I believe. But I think most of the wrinkle-cream cases are now handled by the Center for Foods.

RT: As far as medical devices are concerned, are these a new area of interest in terms of the legal authorities? Did you get involved in that program area in CDER?

FWB: Not devices. The closest that we got involved with in terms of devices -- and that was really near the end of my career -- is the combination products. We had a couple of cases that involved products that were both a drug and a device, and so we didn't look at the device aspect per se. However, we looked at the drug aspect. The Center for Devices would review the device aspects.

RT: I believe it was in your next position where you got into things like the Interim Rule for Banked Human Tissue and so on. I don't know whether we're ready to get into that or not.

JS: Yes, I think so.

RT: Could you clarify what the Interim Rule for Banked Human Tissue required, and how it was put in place, since it's called an interim rule?

FBW: Well, if I remember correctly, it was '93, and this had to do with importation. I think it's what started the whole thing.

They got some imports of human tissue that had no pedigree (i.e., could not trace back to donor and donor's medical history). They had no pedigree and, of course, they

had no testing, or inadequate testing (e.g., for HIV and hepatitis). The senior management of the agency considered it a very serious situation, and they established the Interim Rule for Banked Human Tissue, and that was done -- oh, I should know the answer to this -- under Section 361 of the Public Health Service Act [PHS Act] where the Secretary can promulgate regulations to prevent the spread and transmission of communicable diseases. But it was an Interim Rule. But it was enforceable until such time as the Final Rule was finally published.

It established certain things in that rule, e.g., the tissue had to be tested. It had to be tested for hepatitis and it had to be tested for HIV. In addition, you had to have a pedigree on it so you knew its origin, etc. And if you didn't have a lot of those things, it was subject to -- what did we call that thing? It wasn't retention. It was an Administrative Order, you know, putting a hold on it, and eventually it probably would get destroyed.

RT: Right. It was denied entry if it was an import or . . .

FWB: Or even if it was not.

If it was already in domestic commerce, we could put the -- I can't think of what we called it -- Administrative Order on it.

I really can't remember if these cases were reviewed by General Counsel. I suppose they were but I don't remember, actually. These cases were processed very quickly because of the fear of transmission of HIV and hepatitis.

RT: No doubt General Counsel had a role in the decision for it.

FWB: They must have. I'm sure they did.

But who I worked with during that time . . .

Well, I mean, because it was a big area, a new area and a big area, and there was a lot of interest in Congress, etc., I know I was involved with a couple of briefings of the Commissioner and Mary Pendergast, who was an Associate Commissioner, I guess, who really honchoed the tissue, interim tissue rule.

JS: Well, there was another huge case at this time, when you were there, involving blood. Obviously, this was a Consent Decree with the American Red Cross in 1993. Could you tell us about that? Because this was a very, very key blood compliance issue at the time.

FWB: I really can't tell you much about that. No. And I can explain why. Let me see if I can explain it.

My position with Biologics was not on the compliance end except for banked human tissue. Who really handled the American Red Cross case was Biologics' Compliance Division. I wasn't in the Compliance Division. I was in the Inspections and Surveillance Division. So I really wasn't very intimately involved.

JS: Anything as far as leading up to what led to the decree, though, in terms of the blood bank inspections, issues we had that led to this?

FWB: No. In fact, you've got to understand that back in those days, probably a lot of those inspections were actually done by CBER [Center for Biologics Evaluation and Research] personnel. It depends. If they were licensed facilities, they would have been done by CBER personnel. Now, that's all changed. But at one time CBER did nearly all their own inspections, and that's kind of changed. So if they were licensed facilities; CBER inspected them. And in the case of the American Red Cross, a lot of their facilities were licensed. So I imagine that most of those inspections were done by CBER personnel.

Now, that wouldn't be true today. They now have something called Team Biologics. But back in those days, the field never got involved with inspecting therapeutics, vaccines; CBER did. And now, of course, that's kind of changed.

JS: Right.

RT: Now, in the Bioresearch Monitoring program, I think you had a supervisory role in conjunction with that too.

FWB: That was near the end of my tenure at CBER. When I was first hired at Biologics,

I was hired as a Branch Chief, and I can't for the life of me remember the name of the branch at that time.

I'm sure you all recall that at one time, the federal government decided that there wasn't a great enough ratio of supervisors to staff, and so they said there should be a minimum of eight people to a supervisor, etc. Well, typical bureaucracy, they wanted to come up with some means of meeting those criteria, and it just so happened that right at that time, there were three divisions, two branches in each division over where I was, in the Office of Compliance for Biologics. And it just so happened right at that time that one of the branches in each division was vacant. And so rather than rehire three Branch Chiefs, what they essentially did was reorganize and made the existing Branch Chief the Deputy Division Director. And therefore the Bioresearch Monitoring then came into our division.

RT: Fred, I think when you were in New York District, you were involved in a food-filth case that we might have overlooked earlier. Would you like to speak to that?

FWB: I was the Compliance Officer.

Back in those days -- you don't see this very often anymore -- it was not uncommon to bring misdemeanor prosecution cases, and a lot of those cases had to do with food filth. Now, I think we probably bring injunctions rather than do a prosecution, because if they are just misdemeanors as opposed to what FDA's OCI [Office of Criminal Investigations] works on, which are felonies. I think it is very rare nowadays that we do misdemeanor prosecutions because you just don't get the bang for the buck, so

to speak. Oftentimes, the sentences are suspended, the fines are very low, etc. You can probably accomplish more by just shutting them down.

But back in earlier days, we would bring misdemeanor cases, especially food-filth cases . . . We had this case in New York, and it actually started before I got there. The name of the company was Gel Spice. There were a number of inspections of this firm that were done over the course of time, starting in like '72, '73, long before I became a Compliance Officer, several years before I became a Compliance Officer. The inspections were violative, and they had held 305 hearings. Again, what has changed in the agency is they did 305 hearings back then, and, of course, we don't do that, or I haven't heard of anybody doing a 305 hearing in a long time. At a 305 hearing, the responsible individuals had the opportunity to present their views on why they should not be prosecuted. The district then recommended prosecution to the Bureau of Foods, I believe it was called at the time.

Then what happened is the district, while they were waiting on the Bureau's decision, did another inspection in '73, and it was non-violative. And so the district recommended that the case be placed in temporary abeyance, with the intent that if we went back in future years and it was again violative, we could also bring those charges arising from the earlier inspections as well.

They went back in '76, I believe it was, and it was again violative. Okay? Then there were two inspections in '77 that were also violative. And what they did is they had another 305 hearing. They recommended a criminal prosecution on charges relating to the '76 and two '77 inspections to the Center or Bureau for Foods, which eventually got approved by the Bureau, went to General Counsel, and General Counsel forwarded the

case on to the Eastern District of New York. Before it was filed in court, the district, pursuant to its work plan, went back out to the firm in January of '79 and did another inspection. It was violative again. All right? So . . .

JS: I think I see a trend here.

FWB: So, we, of course, wanted to modify the criminal information at the Eastern District of New York because, actually, the '79 inspection was really, really horrendous. It was just really bad.

Also, for a lot of these inspections, we also did product seizures. Keep that in mind.

But we wanted to modify that criminal information by adding three or four counts to it, and so we had another 305 hearing. The district recommended that additional counts be added to the criminal information to the Center or Bureau, whichever it was at that time, and that eventually got approved. The Criminal Information was filed with the court.

The defense did something that you hardly ever see in FDA cases. The defense actually decided they were going to fight this, rather than plead out. Even after all these violative inspections and seizures, etc., they were going to fight this.

JS: Well, did they have a secret weapon or something?

FWB: The defendants argued that charges (or counts) from earlier inspections should be

thrown out because what FDA was doing was going back to the firm to bolster the evidence which supported the charges from earlier inspections. The most current charges from the 1979 inspection should be dropped because the Agency had already decided to prosecute but no search warrant was filed before doing the 1979 inspection. After the lower court ruled against the defendant's motions, they were convicted.

They appealed their conviction to the Second Circuit -- I don't know if it's still called the Second Circuit now or not, I know they've renumbered them -- the Second Circuit Court of Appeals, and the Second Circuit Court of Appeals wrote a written opinion, which is very important, and supported their convictions. Prior to discussing that opinion, I will tell you that they appealed to the U.S. Supreme Court after they lost at the Court of Appeals.

Our attorney team told me, they said, "Now, Fred, if it gets to the Supreme Court, we promise you we'll get you there so that you can listen to the oral argument," etc.

Well, I was actually hoping the Supreme Court would grant *certiorari*, but they didn't, they denied *certiorari*, and so I never got to attend oral arguments at the Supreme Court.

But the Second Circuit Court of Appeals' decision still stands, and it's still a very important FDA precedent-setting case. What essentially the Second Circuit said is that, first of all, there was no evidence whatsoever that we were going back for the sake of gathering evidence to support prior charges. That wasn't the reason. We were going back in the protection of public health according to an administrative scheme called Work Plans. Normally, we try to inspect firms every two years, but if they were violative, we owed it to the public to inspect them more often, and that's why we kept

going back to the firm and finding additional problems. And the Court said, “You can’t bind FDA from doing their job of protecting the public health.” First of all, no information had been filed with the Court. The agency had made a decision to go forward with it, but nothing had been filed with the Court on the first three inspections. And they had gone back on all those instances, according to an acceptable administrative scheme for the protection of the public, and so the firm’s arguments were dismissed on the first three inspections.

Now, the fourth inspection, January of ’79, the Court said we still are not going to agree with you, because even though the case had gone to the U.S. Attorney, it had not been filed with the Court, and the District was still inspecting the firm according to an administrative scheme for the protection of public health, so no search warrant was necessary, and you have not demonstrated that anything found in ’79 was being used to support charges from ’76 and ’77. So they dismissed their claims on the basis they were without merit.

And that’s become a pretty important actual FDA case. Of course, we don’t do food-filth cases very often anymore, but should we ever, the written opinion is there.

Now, the second thing that the defense raised was something called the impossibility defense. What the defense was arguing was that, although the Food, Drug and Cosmetic Act was a strict-liability statute, all right, and you don’t have to show intent, etc., there is something called an impossibility defense, that if the firm can establish that it was impossible for them to prevent the violation, then the burden shifts to the government to show that it was not impossible. All right? It doesn’t take them off

the hook; it just shifts the burden to the government if they establish the defense, to demonstrate that compliance was not impossible.

What happened was the District Court threw out the impossibility defense. They appealed to the Second Circuit. On appeal, the defense said the District Court used the wrong standard, and on appeal, the Court of Appeals upheld the District Court and said, “No, you really haven’t established the impossibility defense to shift the burden to the government. You haven’t really established that.” And one of the reasons the Court cited was the fact that in all those years of violative inspections, there were also several inspections that were non-violative. And so the Court said, if anything, that demonstrates that you were able, at different times of the year, whatever the case may be, to keep the place clean.

JS: I would guess that the impossibility defense would be that the courts would set a very high bar for a firm to really use that, because, if not, I imagine this would mean that firms would try to use it frequently.

FWB: I think the “bar” is that, despite extraordinary care, you were not able to prevent the violations. Now, that’s a pretty high standard. But what happens then is all it does is shift the burden to the government to show that beyond a reasonable doubt, the firm did have it in their power to prevent the violations.

JS: So this clearly was a precedent-setting case.

FWB: It really was.

JS: Interesting.

FWB: Not many go to the Court of Appeals.

JS: No.

FWB: With a written opinion, I might add.

TAPE 2, SIDE A

JS: Well, we're going to resume with your transition from the position in the health fraud staff in the Center for Drugs to your position in the Center for Biologics. And we talked a little bit about that already, but I wondered if you could characterize just generally what that experience was like and that transition was like, because you had been in field staff in the agency and then, obviously, in the Center for Drugs, and now you were in the Center for Biologics, which, of course, the function had just been transferred to FDA in the early 1970s from the National Institutes of Health. I wonder if you could talk a little bit about that experience.

FWB: Well, okay, I'll try.

I didn't have a lot of biologics experience when I applied for that position, and there's probably a reason for that. Certainly back in those days, Biologics did nearly all their own inspectional work, including the licensed blood banks, and the field rarely got involved. They might get invited to go along, but they were never in charge of, for example, inspections of therapeutic products facilities, vaccine facilities, licensed blood banks, licensed plasmaphoresis centers. Biologics did all of that, and Biologics also did, when a license was pending, all their pre-licensing inspections.

JS: If I may interrupt, could you just mention what the difference is between a licensed and an unlicensed blood bank?

FWB: It has to do with interstate commerce.

JS: Okay.

FWB: Essentially. In other words, if you're going to ship blood across state lines, you have to be licensed.

And as far as licensing therapeutic products, for example, although there are some differences, it's really kind of similar to an approved new drug application.

At any rate, when I applied for the position, I was interested in getting a promotion and getting a GS-14, and at that time, about the only way you could do it was either go into management or they had this kind of new thing called peer review. But

back in those days, peer review was a pretty rare thing; it wasn't very common then.

This management position came along, and I said, "Gee, I think I'll apply."

Like I said, I didn't have a biologics background. I never expected to really get the position. But lo and behold, to make a long story short, I did get the position, and I accepted it. And I guess the entire time I was at Biologics, because of what I just described to you, you know, I had very little Biologics background, so I always kind of felt a bit like a fish out of water, because most people at Biologics had biologics backgrounds.

For example, a lot of the people I worked with there had been blood bank supervisors, had been workers at plasmaphoresis centers, and so forth. I mean, they knew those regulations backwards and forwards, better than I could ever hope to know them. And so it was a bit uncomfortable for me, especially if I had to go to a meeting or something, and they would start tossing around regulations sometimes that I wasn't a bit familiar with.

Of course, I was used to a section of the agency that was very regulatory-minded. All right? And at first glance, when I got to Biologics, it did not seem that they were as regulatory-minded.

Now, I suppose what I perceived to be the problem at first was the fact that, instead of letting a regulatory field force do their inspections that possibly could remain more objective, they did their own inspections and they, I think, sometimes felt a collegial attitude toward fellow M.D.'s and Ph.D.'s in the industry, which I think sometimes creates a problem as opposed to letting an independent field force do it.

But one of the other things I learned when I was at Biologics -- and this helped me to understand the situation -- is they did also have a further problem in trying to bring legal cases, and that is, they had no generics industry. And so every single biologic, essentially, that was licensed was what we now call a medically necessary product, and so you couldn't very well seize the product. You couldn't very well enjoin the firm unless you did a very craftily worded injunction which allowed the enjoined firm to continue to produce. So Biologics always tried to work it out with industry as best they could before they got to the point of license suspension or license revocation, which are other things that they could do. I did come to understand that this was problematic, more so I think for Biologics than it was probably any of the other FDA Centers.

JS: Interesting insights into the different approaches of enforcement entities within the same organization.

FWB: Well, now, of course, I'm getting ahead of myself.

I do not remember this concept of "medically necessary" products ever coming up early in my career. In other words, I do not remember having a problem taking legal action against a drug firm or its products because they were "medically necessary." I don't remember that being an issue in the '70s and '80s, etc. But by the time I went back to the Center for Drugs (i.e., in the '90s), that had become a major issue even for drugs; that is, even the firm's product was "medically necessary," and if so, what restraints were on us in terms of legal actions.

JS: I recall when we had the issue with thyroid products, when their status with NDA's came into question across the board. I don't know if, the medically necessary status of these products was an issue then or not. I don't recall that coming up historically.

FWB: You mean this medically necessary concept?

JS: Yes.

FWB: Like I said, I don't know if Biologics even called it "medically necessary." Drugs call things medically necessary, and I can't tell you what year that policy came about. There is an administrative policy on what constitutes medically necessary. I don't know when that actually occurred. But certainly by the time I got back to the Center for Drugs, it was well in place.

JS: Well, you were in CBER, the Center for Biologics, until 1998, and then you had gone back to the Center for Drugs, the Center for Drug Evaluation and Research in 1998, which is the position you retired from.

FWB: That's right.

JS: In the Case Management Guidance Branch, among other things, you coauthored

the *Drug Manufacturing Inspections Programs*, introducing a systems-based approach. I wonder if you could talk a little bit about that and what that systems-based approach was in GMP's.

FWB: Well, the idea was to look -- and you've got to understand that what I was dealing with was Good Manufacturing Practices, not new-drug issues, not misbranding issues, but Good Manufacturing Practices, which are the rules governing the manufacture of drug products. Okay? This program that you're talking about now deals with inspecting drug manufacturers from the viewpoint of GMP's or Good Manufacturing Practices.

What had come about in the industry over the years was kind of a piecemeal approach to doing inspections, i.e., taking a "micro" approach and looking at the manufacture of individual products/processes, rather than a broader approach which examines a "system" used for all or most of a firm's products. In other words, determining compliance on the basis of a system(s) rather than an individual product or processes.

Now, how that came about, at least I think how it came about, was when FDA, back in, I believe it was '75, took over the Defense -- oh, what did they call it -- GWQAP, Government-Wide Quality Assurance Program, where we were responsible for contracts, like drug contracts for the military, reviewing the contracts, going out and doing the inspections, accepting the goods, etc. That all was inherited from the Defense Department by FDA. The Defense Department used to run it, and we inherited that work, and I believe it was '75.

When that came about, how they started reviewing things at drug firms was in terms of what they called the profile classes. A profile class, for example, would be small-volume parenterals, or another profile class would be immediate-release tablets or . . . All right. So, what would happen is it became, inspections became more compartmentalized.

Let's say a firm, just as an example, had 10 different profile classes; a drug firm had 10 different profile classes. An investigator might go out, for whatever reason, and look at three profile classes. And let's say they decided that those three profile classes were violative. Rather than saying, "Well, but if those three are violative, then the firm must be out of control," they would simply classify those three profile classes, as violative and leave the other profile classes that they didn't look at the same, because they haven't looked at them. All right?

What would happen is, then an assignment would come up regarding one of the other profile classes which had not been inspected during the most recent past inspection. For example, a defense contract would come up on one of the profile classes that hadn't been previously classified as violative; then they'd have to go back to the firm and look at it because they hadn't looked at it during the prior inspection. I mean, does that make any sense?

One of the ideas behind this drug program was to not compartmentalize it. In other words, if you could show that a profile class was out of control, then, and you could relate it to a system -- and we invented a classification of systems in that program, which I can go over with you. And you could relate it to a system, then the system was out of control. If any system was out of control, then the firm was judged to be out of control.

The importance of that is, even though you may have only looked at certain products (i.e., you can't look at all a firm's products, and if a firm has eight or nine profile classes, you can't look at all of the profile classes), all the profile classes would be regarded as violative even though you may have only looked at two.

JS: So the system in this case was a conduit that linked the different profile classes amongst one another?

FWB: Well, it didn't link . . . Well, in one sense you could look at it that way.

What the systems were -- I haven't done these for a while -- the systems were Materials, which is essentially raw materials. That was a system. Production. Packaging and Labeling. Laboratory. Facilities and equipment. And, finally, the overarching system was what was called Quality System.

The way the program is written is, although there were -- and I won't go into detail -- although there were ways of going about doing abbreviated inspections, as opposed to full inspections, you always had to cover the quality system. You then had options on which other systems of those six, you had other options as to which ones you could do. But you always had to do the quality system, because the quality system is the whole basis of the GMP's: i.e., you have to build quality into a product, you can't test quality into a product, and so that's the whole basis of Good Manufacturing Practices. The quality system is really the overarching system, so you always had to cover that. But the idea was, if any one of those systems was violative, then the firm was violative.

Now, any time you go to do an inspection, you don't just walk around and look at a "system." You do have to get down into the nitty-gritty. You have to say, "Well, I'm going to look at your thyroid tablets. I'm going to look at your thyroid tablet production. Let me see batch records for thyroid tablets," etc. You look at specific products, specific profile classes. All right? But what you find, i.e., deficiencies to GMP's relate to "systems." They may relate to the quality system, they may relate to the production system. Based upon those findings, i.e., deficiencies from GMP's, you can say that a system or systems are out of control.

Does that make sense?

JS: It's a new way of approaching GMP's, which had been . . .

FWB: Well, interestingly enough, when I first joined FDA, I think we took a non-systematic approach. A firm was either violative or not violative. It was because of that compartmentalizing that I think came about because of the Department of Defense function, when FDA started to separate everything into profile classes and looking at each profile class separately that the systemic approach began to unravel.

And what the problem was -- I'm sorry; I don't know that I made that clear. What was happening because of this compartmentalizing is there were some firms we were probably going to six or seven times a year, especially these larger firms. And other firms, although under the statute we were supposed to get to once every two years, we probably weren't going to for seven or eight years. I mean, that was one of the problems. Sure, if they had government contracts with a firm, we'd get out there all the time.

JS: How did this new approach affect the amount of time we could spend in an establishment?

FWB: Well, the new program had certain things built into it. I don't know, by the time I left, if they had any data showing its effectiveness. I mean, I'm not sure that they did. But, remember, I talked about how the program built into it what were called abbreviated inspections as opposed to full inspections. An abbreviated inspection, by definition, covered two or three systems, one of which had to be the Quality System, and a full inspection was four to six systems, one of which had to be Quality System.

One of the efficiencies we put in the program was in the regulatory section of the program. As you know, most of the time, before we take a legal action like a seizure or injunction against a firm, we, by agency policy, do something called prior warning. We establish prior warning. One of the ways we do that is through what nowadays is called Warning Letters. All right?

One of the things the program has built into it under the regulatory Part V of the program was, if you felt that you had a violative inspection, if a District felt that they had a violative inspection, even though it was an initial inspection for a firm, okay, they could stop after they had completed only two systems (the Quality plus one other) and proceed with a warning-letter recommendation to the Center for Drugs, rather than continue on and do the full inspection, because the idea was to establish the prior warning as quickly as possible. So that was one thing that was built into the program.

The second thing, of course, that was built into the program was the concept. This works in conjunction with new-drug approval. Okay, let's say a firm is ready to have a product approved (an NDA or ANDA). One of the things that the Review Division that reviews the applications will do is they will contact DMPQ [Division of Manufacturing and Product Quality] -- it wasn't my branch -- but they'll contact DMPQ and say, "We're ready to approve this drug. This is the drug product," and they would then look at the profile class of that drug product, and say, is this profile class violative or not violative? If it was not violative, let's say -- this gets very complicated, and I don't want to go into detail -- and if it was a recent inspection and it was not violative, all right, they might just be able to tell them, "Go ahead and approve it." If it was violative, on the other hand, all right, they would stop the approval of the product, or they would at least tell the reviewer, "You shouldn't approve this. It's currently violative." All right?

One of the things that this program was designed to do: let's say prior to the new program you have 10 profile classes at a firm, as an example, and you only classified three as violative during the most recent inspection. Then let's say a product application came up on one of the other seven that weren't classified as violative, based upon older inspections. We would be forced to go back to the firm to update this particular profile class of which the product awaiting approval was part. For a firm that had a lot of pending applications covering numerous profile classes, we'd be going back all the time. The idea in this new program was to classify all profile classes during one inspection. So if all profile classes were violative, we would not return to inspect until the firm claimed they were in compliance, even though new applications were pending approval. That's one of the ways it was supposed to be more efficient.

JS: Was this approach then applied to any other commodities, the systems approach?

FWB: Well, interestingly enough, when we were writing -- when the other person who coauthored this, his name is Nick Buhay -- and when Nick and I were writing this, one of the things we looked at was the device program. And it did have kind of a system. They had put their device industry into eight systems -- I think it's eight systems, if I remember correctly, and one of the differences -- and we didn't care for that approach -- was they had major systems and minor systems, and we didn't want to make that distinction. We felt, in the drug industry, all systems were pretty much equal. So we modified that. But they did have a systems kind of basic approach with devices. And then, since we did ours, I think Biologics has modified their program and included a systems-based approach.

I can't speak with authority about the other Centers.

RT: Now, in the GMP area, you, of course, published human drug GMP notes. Are those notes sort of advisories or summaries of the requirements promulgated?

FWB: They were This has an interesting story to it, too.

They were a publication answering questions from industry concerning compliance with GMP's, e.g., was something required as part of the stability program, whatever it is. We would have one of the GMP experts on the staff -- in that case, probably a person who was an expert on stability -- write an answer to the question, and

then we would publish the answer. Each time we published, there would be four or more questions and answers, I don't know what was the maximum . But CDER published quarterly, every three months, starting in '92, I believe. They were basically questions that had been raised by industry, so that the answers were like, if you will, advisories, they were like guidance, you know, *informal* guidance. It hadn't been "vetted" as guidance. And that's where the issue really came up.

What eventually happened is that *Human Drug GMP Notes* were not only published, they were also mailed out. And I might add, industry loved it. Then what happened was, part of the arm of the Center eventually questioned whether these "answers" were being vetted properly in terms of good guidance practices, and they said it wasn't.

So they said, "You can't publish it publicly. You can continue doing it, but it can only go to the FDA field offices." Okay? So, for a while, several years, we continued *Human Drug GMP Notes*, but they were only available internally on the Intranet.

Now, I haven't been on the Internet to look this up in a long time, at least since I've retired. But what you used to have on the Internet was *Human GMP Notes* from something like '95 to 2000. All right? Then, when we got handed this ruling, *Human GMP Notes* continued for a couple of years, but they were only on the Intranet. Then we worked together with the Office of Regulatory Policy and came up with what we thought would be a system that would meet GGP [Good Guidance Practice] Level 2. So, starting around 2004, the questions and answers have been posted on the Internet again. However, it is no longer called *Human Drug GMP Notes*; it is called something like *GMPQ&A*.

RT: Years ago, the agency used to have what was called a PC [Precedent Correspondence] file staffed by two full-time employees who were librarians or curators of that information. So, when staff people had an inquiry dealing with foods or drugs, they could always draw that information out from this PC file source, so you would have a standard approach or a standard reply to the issue in question, which, of course, preceded the later development of a more efficient historical data retrieval system which was much more sophisticated. So the agency had pioneered that kind of reference system back in the '50s.

JS: Well, even for historical background farther back, we started using answers to industry questions and promulgated these. Now, I'm not sure how widely we did, but these were under the guise of what we called trade correspondence, and these started right after the 1938 Act was passed. Now, the Federal Register, of course, had started in the mid-'30s, right before the 1938 Act was passed. But we issued these, which pretty much carried the practical effect of regulation because this is how we started, essentially, prescription requirements for drugs under the 1938 Act, through this trade correspondence identifying what we called dangerous drugs. And this applied not just to drugs, but to all commodities we regulated, and these continued for several years. So they did have the practical effect of regulatory policy.

FWB: Well, I mean, this gets into interesting legal questions about, you know, guidance as opposed to regulation, and enforcing guidance, etc. And, of course, technically, if it's

not a regulation, you can't enforce it. But what guidance is really saying is, if you meet this guidance, we will consider you meeting the applicable part of the regulations. If you don't meet it, you may not be outside the regulation if you can show us that your system is as good or better. But otherwise, you know, we're probably going to rely on our guidances. So it's a very fine legal distinction, actually.

JS: During this time, there were some pretty major drug GMP cases that were prosecuted, and major fines, if I remember, were there not?

FWB: Oh, there were a couple.

The one I, of course, probably remember the most distinctly what the Schering case, horrendous GMP's violations at three different facilities. We really brought a nearly corporate-wide injunction -- it was against three facilities -- of Schering. If I remember correctly, the consent decree that we finally hammered out was something like 60 pages long of legal-size paper. It was nearly impossible to understand.

That was an interesting case for, among other reasons, Schering happened to manufacture a lot of what was called medically necessary drugs. So we had special provisions in the Decree which would enable the firm to continue making these medically necessary products. But with regard to many of the drugs they manufactured, the manufacture of these just had to be stopped until substantial compliance was achieved. But if they were medically necessary, the firm was permitted to continue manufacturing them but under very close scrutiny. They had to do batch-by-batch review by on-site consultants.

JS: This decree was enforced for several years?

FWB: Actually, you know, I think they finally requested that the Decree be lifted. I'm trying to remember the year the decree went into effect. I'm going to have to guess, but we'll say 2002, 2003, something like that. I think it was right before I left that the firm asked to be released from the provisions of the decree. I think we agreed just right before I left, so that would have been like 2007. And that was a major case.

At the time, I think the fine against the firm -- now, I can't quote the figure, but it was the largest in FDA history at the time, I think, because they also had something in the Decree that is kind of controversial called . . . It'll come to me. This is -- oh, what do they call that. It's to fine the company for past retributions and what they did to the public. It is called disgorgement.

JS: This was in the order of hundreds of millions of dollars, wasn't it?

FWB: Oh, yes. I think it was \$500 million. That's what I want to say. I'm just not absolutely certain. I think it was \$500 million.

Another major case, of course, more recent, was the GlaxoSmithKline case, involving two products that we ended up seizing all across the country, all over the place, at all of their facilities.

JS: Do you recall which product?

FWB: One was a diabetes medication, Roglitazone and metformin. It was a combination of metformin -- metformin isn't a brand name -- and Roglitazone or something like that. The idea was that Roglitazone was supposed to enhance the effects of the metformin.

The other product was Paxil CR, an antidepressant.

TAPE 2, SIDE B

JS: There were two products, and we seized both in this action, correct?

FWB: Yes, absolutely. And, again, it was, they were worth a lot of money. They eventually were destroyed.

JS: Major fines.

FWB: Well, it was really just the value of the goods. I don't know that there were separate fines. It was just the value of the goods that they eventually had to absorb. But, I mean, that cost them quite a bit of money.

Then, of course, the third case that comes to mind, but it never resulted in a legal action -- I think there was a warning letter, but it never resulted in an injunction, was the Eli Lilly case, which gained some notoriety. Very horrendous GMP deficiencies at Eli Lilly, at their sterile manufacturing plant. Again, a lot of people have questioned why we didn't go forward with the injunction, and I think one of the reasons was the concept of

insulin being medically necessary, and they had such a large share of the insulin market. It would have been very difficult to either seize product or enjoin the firm without running the risk of shortages or consumer panic.

Now, I think the second factor involved in this was the fact that, when the company came in for meetings, they really did a very good job in establishing their concern, how they were going to overhaul the system, etc., and so we decided to try to work with them rather than do an injunction. That was a big case. There were many, many other cases, but those are the three that readily come to mind.

JS: I wonder if you could say just a little bit about, in pursuing actions, how things changed: the way we handled issues, warning letters, what-have-you, in this time period. How the Department would be involved, how the General Counsel's office would be involved in these actions. Is there anything that stands out in your mind about that?

FWB: Well, actually, there's a couple of things that changed. We're talking about GMP's now, not new drug or misbranding charges, but GMP's, or adulterations, i.e., a drug adulteration. That's an adulteration charge. At one time, the field offices had direct-reference authority for warning letters for drug GMP's. All right?

I was the head of the committee that revoked that authority. Well, it was part of the GMP's for the 21st Century, and they had a bunch of subcommittees. One of the subcommittees was to look at warning letters and consider whether that should be revoked, and it was decided that this authority should be revoked. And, you know, there's a lot of common sense behind that.

Industry had complained about an inconsistency between various district offices because they weren't being vetted by one office, the Center. And so what one district would consider violative, another district might not consider violative, and so industry did some complaining about, you know, "We don't know which end is up at this point." And it makes sense if you stop and think about it. If you've got 20 or 21 different offices trying to make decisions on the same issue, GMP's, you're going to have 20 or 21 different opinions on whether we should go forward or not go forward.

JS: Were we working from the same playbook on decisions like this?

FWB: Well, yes, the regulations obviously are the playbook, but how you interpret those regulations, what weight you give in this particular scenario, whether it's the manufacturer of a parenteral as opposed to a medicated cough drop, depending on how much weight you give those regulations and whether it's worth the government's resources and time to do an injunction against, for example, the medicated cough drop manufacturer where there's absolutely no risk involved to the human public, as opposed to a parenteral manufacturer that could kill hundreds of thousands of people from contaminated vials of product. I mean, you've got to understand that not all the districts were looking at it that way. Something that came about from this massive undertaking of GMP's for the 21st Century was the utilization of risk in our decision-making. That was a very important prong to GMP's for the 21st Century.

JS: The program you mentioned was a major endeavor during the time you're in this office, when you worked GMP's for the 21st Century.

FWB: Right.

JS: And that was . . .

FWB: It came about -- in 2003 it was announced, I believe.

JS: What prompted this was, among other things, the concern that the issue of risk being applied to GMP's was not being applied in an even way?

FWB: Well, actually, that was part. I think the three underlying pillars, if I can remember them, of GMP's for the 21st Century is risk, science-based decision-making, and quality assurance. Those are the three pillars of the GMP's for the 21st Century. Risk management. Science, and making sure that all our decisions were very science-based. All right? And that actually goes further than just GMP's. Finally, to quality assurance, both external and internal. While we were expecting firms to develop adequate quality assurance and quality systems, FDA also needed internally to develop its own quality systems. To me, these were the three underlying pillars for the GMP's for the 21st century initiative. As far as I know, that endeavor continues today. It is being

headed out of the Commissioner's office now as opposed to Director of the Center for Drugs' office.

RT: I think that you had a harmonization subgroup which worked to harmonize GMP's internally and externally.

FWB: Yes. One of the things that the GMP Harmonization Group did is to examine and compare all the various manufacturing practice regulations. In other words, the various types of manufacturing regulations that FDA has, whether they're drugs, whether they're devices, whether they're human food, and compare all those, as well as compare the drug GMP's to other foreign requirements, such as the European Union manufacturing of products, and look at those and see where, if at all, we should modify our own regulations. The purpose of the Harmonization Group, was to study and compare and contrast all those various GMP's or manufacturing requirements and say what revisions to the drug GMP were needed and then propose such revisions. That group is in the process of doing this.

It's no longer called the Harmonization Group. It's now called something like the GMP Regulation Group.

One of the things the GMP Harmonization Group, through the Steering Committee of the GMP's for the 21st Century, decided is that any changes to GMP should be incremental in nature.

Now, you have to go back to what this is all about. There was a massive proposed regulation in 1996 to the GMP. It would have modified the GMP's pretty

substantially, and it was proposed in 1996. A lot of that came about from a very famous case called the Barr decision. You know, the judge actually said in the *Barr* decision, if I remember correctly, “Why don’t you codify some of this? You need to get some of this on record, that firms need to do all this,” etc., and so that was what the part of the proposed Rule of ’96 was about, to codify a lot of this business about process validation.

JS: The Barr decision stemmed from what?

FWB: It was, I think, both a New Jersey and New York case. It wasn’t my case, but a drug GMP case from the ‘90s. The firm, if I remember correctly, didn’t, for example, do proper sampling. The firm was what we call testing into compliance and hadn’t properly validated their manufacturing processes. So if you look at the proposed ’96 regulation, it was trying to codify a lot of what came out of the Barr case.

What happened, if I can put this in a nutshell, once the GMP’s for the 21st Century was initiated, the proposed rule never got finalized. You know, we kept writing a preamble. I actually was one of the team trying to write a preamble to the ’96 proposed rule. When we ceased working on it, I think the preamble we were preparing was like up to 287 pages.

JS: The preamble?

FWB: Well, because of all the comments. It was just unbelievable, hundreds of comments, and they all have to be addressed in a preamble to a Final Rule. I don’t know

if you've ever been involved in regulation writing. It's not the easiest thing in the world because everybody has their opinion.

At any rate, the proposed rule was not finalized by 2003. And then, under the auspices of the GMP's for the 21st Century, they started debating this concept of validation: i.e., what really validation is and what it should be defined as. The steering committee decided that we needed to make that decision, because one of the sections in the proposed rule had to do with validation. There was a whole new section on validation in the proposed rule. Since that had not yet been finalized, the committee said, "Well, since we're still debating about the concept of validation, let's make sure we are in agreement before we go final with what is in the proposed rule."

So one of the things the Harmonization Group did is they not only said any changes to the GMP should be incremental in nature; they also said we probably should withdraw the '96 proposed rule. They were announced, for all intents and purposes, at the same time: i.e., both the withdrawal of the '96 proposed rule and the first set of incremental changes.

So we recommended to the Steering Committee, withdraw the '96 rule and take an incremental approach to revising the GMP's. And the incremental approach was to try to take the least-controversial, least-difficult things and go forward with those first. So the first set of changes we came forward with -- I think it was just published back in November or December of 2007, right before I left; I'm pretty sure I'm right on that -- it was a direct final rule. We thought that the changes were so noncontroversial, the first increment was so noncontroversial -- some of them were just wordsmithing -- that we could do a direct final rule.

Now, when you do a direct final rule, you also publish a sister proposed rule so that in case you do get significant comment, you simply treat the changes as “proposed.” You don’t have to start the whole process all over again.

I think the comment period was up like in March of this past year. Of course, I was gone by then. And they are currently working on doing revisions, and the committee, which eventually I became co-chair of before I retired, is now working on the next incremental changes to the GMP’s.

JS: How far out will these increments be incorporated into rules? Does anyone have any idea?

FWB: Although it can be very rewarding and very exciting to work on guidance -- now, I don’t mean the GMP notes, I mean guidance, formal guidance documents and regulations -- it can be very frustrating because it has to be vetted through so many people, and every time it gets vetted, it comes back, and it gets wordsmithed again, and so it takes a long time to get any of this done, a long time. It is one of the frustrating things about it.

If I can express an opinion, it’s unfortunate that it takes so long for FDA to publish Final guidances. In other words, you would think that FDA would be leading the way in terms of getting GMP guidance out there, but I think because of this vetting process, oftentimes the trade associations get “guidance” out before FDA does. Now, sometimes we work with the trade associations on their guidance documents, but it would be nice if FDA could get more finalized GMP guidance published.

JS: Is this vetting we are talking about strictly within the agency?

FWB: No.

JS: Well, within the agency and the Department, or are you talking about stakeholder interests too? I mean, are they having input?

FWB: They have input, certainly, once it's published as a proposal. Then, of course, they can comment.

I don't think, as a rule, the public usually gets involved. It probably would depend on the set of circumstances, but they don't always get involved with, like guidance documents.

JS: As someone who's been closely involved in this, can you imagine ways to streamline it so it's not so long and drawn-out?

FWB: Well, one of the things that I think would help -- yes, I will tell you one of the things I feel strongly about -- one of the things that I think the agency tends to do is not think that they can get something perfect as a proposal. I think they need to get that out of their mind and say, "Look, it's just going to be a proposal. Let's get it out there and get comments. Then we'll take time refining it based upon the comments." But I think oftentimes it takes so much time just getting the proposal out, and I don't know that it has

to be that perfect for the proposal. Does that make sense? I think you could save a little time there and go ahead and let the public and the industry, etc., comment on the proposal. Even if some of the comments are kind of insulting to the agency, at least we can get it out there and get people's comments on it, rather than thinking we're going to ever put out something that doesn't get comments.

I mean, I will tell you right now that what we thought was going to be so noncontroversial that we published it as a direct final rule, still got comments. Things that you would never have dreamed would receive comments, did. So, I mean, it's just kind of interesting.

RT: Sometimes the agency is criticized for lethargy in this process, but it's probably a lack of understanding on the part of consumers, in particular as to the intricacies of promulgating things like this.

FWB: Well, I suppose so. I mean, I doubt if they have any idea the line of approvals it has to go through, just unbelievable.

RT: Well, you know, this recent imported tomato-peppers incident about which one of the CNN commentators was criticizing the agency as though we should not have let any of those products in. It showed on his part, I believe, a lack of understanding of the complexities of such investigations.

FWB: I remember.

JS: Well, I don't know if we have left things out that you think need attention, whether it's in this time period or any of the others, but I think this has been enlightening and covered many areas that we have really little record on in our oral history program, so we certainly appreciate the time that you spent with us here.

FWB: Well, I've enjoyed it.

RT: We do, indeed, appreciate your input, and we will get a draft for your review as soon as we can.

FWB: That should be fun.

END OF INTERVIEW