History

of the

U.S. Food and Drug Administration

Interviewee: Janos T. Bacsanyi, M.D.

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

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TAPE 1, SIDE A

RT: This is another in the series of the FDA oral history interviews. Today, the interview is with Janos T. Bacsanyi, Medical Doctor. Dr. Bacsanyi is a Medical Officer in the Office of Drug Safety in the Center for Drug Evaluation and Research (CDER). The interview is being conducted at the Parklawn Building, and in addition to Dr. Bacsanyi, Dr. John Swann and Robert Tucker are conducting the interview for the History Office. The date is January 24, 2006.

Doctor, with that introduction, would you please give us some information regarding the early history of your education and professional experience.

JB: I was born in Hungary and grew up in Hungary, where I went to medical school at the age of 18 and graduated at the age of 24, in 1955. The following year, 1956, was a crucial year for Hungary. That was the year of the Hungarian uprising against the Soviet occupation. At that time, of course, the Hungarians were defeated and crushed by the Soviets, and I could see no future in Hungary, or reason for staying in Hungary. So I decided to leave the country in November 1956, with a good friend of mine. The two of us escaped to Austria.

RT: Doctor, before you go into that, could you mention where your pre-med and your

medical education was taken -- I think you began your medical education in Hungary.

JB: That's correct. The school system, of course, was different then than it is now, and after four years [recorder malfunctioned for a few minutes].

JS: Now we're recording.

RT: We're resuming recording now.

JB: After four years of elementary education, I was enrolled in a college preparatory school, which was called a gymnasium. Of course, the meaning of this term is different when we use it in the American context. This was eight years of preparatory school with a lot of courses, which later on you didn't really use it very much. But one thing was interesting. We had to take eight years of Latin, and this became very good when we went to Rome and we could read all the old Roman signs. Also, I could understand Julius Caesar's message to the Congress, which was, of course, the Roman Congress.

So that's, after eight years in the gymnasium, then, at age 18, I was enrolled in the medical school in Budapest, and the medical school duration was six years then.

RT: Was that the Semmelweiss?

JB: It's called Semmelweiss now. At that time they had a different name for it. But it's the same medical school except for change of name. But it's Semmelweiss right

now. It was named after the famous obstetrician who lived in Vienna most of his . . .

RT: Would that have been a state type education?

JB: Yes, it was a state type. There was no private medical school. It's all state supported, and there was no tuition. And if you were lucky, you could get a scholarship, and I was one of the lucky ones. There were only six or seven of us in the size of 240 in the medical school class, 240. And most of our schooling was in the local university hospitals. After two years of theoretical studies, chemistry, physics, and physiology. Actually, I graduated from medical school in 1955, and the following year, of course, I had to leave Hungary.

RT: When you graduated, were you in a particular department of the medical school?

JB: No. It was general. It was interesting that you had a general degree, which even included dentistry too, so you learned some element of the techniques like pulling teeth. Also, we learned how to fill teeth. And I remember I had to work on some children. I was amazed how well-behaved the children were. But the children's, the young children's teeth are not sensitive to pain. It comes, their [unclear] teeth, they don't have these nerve fibers, so you could use them pretty well. They have no pain.

JS: So you could drill without any anesthesia.

JB: There was no anesthesia.

Of course, when the children got older and they have their final teeth, they are sensitive.

RT: In Hungary, in the practices of medicine and dental science, are those sort of coexistent? In other words, are medical practitioners also dentists in practice there?

JB: Well, at that time they could do it. There was the general physician, and if you wanted -- most of us didn't go into dentistry, but you could. You were really authorized by doing it.

RT: So the medical training to become fully accredited was not necessarily a longer time period than dental school. Is that correct?

JB: Yes, that's correct. The dental schooling was part of the medical curriculum.

RT: I see.

JB: It's different now, but now it's completely separated.

JS: So you graduated with your medical degree in 1955. The uprising comes in 1956, and you said you left with a friend to Austria. I imagine that must have been quite frightening.

JB: Yes. The border crossings, the major roads were already supervised by the Russian troops, so you couldn't get through. You had to make your way through the woods. In order to do that, well, they recommended to do it at night, because at nighttime, most of the Russians didn't want to go in the woods. So at nighttime, you could go through. But you had to have somebody who knew the area, and we were lucky to find a local person who led us through the darkness. There's no lights or anything like that.

JS: And you have all of your belongings you can carry on your back, basically.

JB: That's right.

RT: You didn't have to pay or bribe somebody for help, did you?

JB: Well, what happened is that we had Hungarian money with us, and we said we won't be able to use it in Austria anyway, so we gave it to the person there.

JS: So you were in Austria just briefly, I gather.

JB: Yes. Well, in Austria, we spent just a couple of days in this village close to the border. Then we went to -- well, actually, we were transported to Vienna thanks to a local physician who took care of us. He came to the camp, and when he saw that we

were physicians there, he said, "Well, there's another place for you. You come with me." He took us to his house, and it was very, very generous of him. We stayed there a couple of days, and then he got transportation for us, and we went off to Vienna.

RT: Then did you go to Budapest? Where did you go when you went through the woods to escape?

JB: Well, there was a city fairly close to the border, which the Hungarian name was Sopron. The German name was Erdenberg because for quite a few years, Hungary and Austria were one country, so you find German names for a lot of the communities. From there, we had an ambulance that took us out to about two miles away from the border, and these ambulance drivers knew what we were about to do.

RT: Did you go as, shall we say, patients in the ambulance?

JB: Well, something like that. It was during the night, and they had very few ambulance calls at night, so they accommodated us. Actually, we were staying at the local hospital for two days, so we used the empty beds they had.

When we got out to Austria, of course, in Vienna, we had to make up our minds where we wanted to go. There were different countries making offers. For instance, Sweden, they were advertising for physicians who would practice in the Lapland. That's the northernmost part of Sweden where nobody wants to go. But they were very generous because they offered two years of education before they put us up there. We

had to learn the language that people used, and we had to learn the customs, and this would have been two years' education, then five years in service, and after five years, the Swedes said we could go anywhere in Sweden we wanted to. So I thought that was very generous of them.

And what was interesting is that the Swedes didn't discriminate; the Swedes would accept anybody, even a person who had some bad condition like tuberculosis and so on.

As far as the Americans were concerned, at that time, you know, it wasn't easy just to come over here and make a claim that I was escaping the Red Army or something like that. No. They would check you out, have a medical examination. Before you were taken over to an American camp, you would be taken and gone over.

So, well, of course, comparing the Lapland to New York, it wasn't a very difficult decision to make.

JS: How was your English at the time?

JB: Well, I had learned some in high school, so I was better off than most of them. And I knew a little bit of German too. Of course, my Swede wasn't good, so it would have been a struggle to learn a language like the Lapp language because of what that requires. It was easier really to go to the United States.

Well, we were accepted and flown out. On the way to the United States -- we arrived in New Jersey -- we stopped on the way in Newfoundland because of a storm. We had to land there, and we stayed there for a couple days till the storm blew over.

It was the McGuire Air Force Base in New Jersey where we landed. Outside New Brunswick, there was a camp, Camp Kilmer. It was named after the famous [unclear]. And we stayed there for about a couple of weeks or so. Then we were sort of segregated into different groups, like the physicians were separate, the scientists were separate, and then we received a very interesting course, introduction in American culture and education. We spent about four weeks at Rutgers University.

They invited quite a few well-known Hungarians, scientists like some of these famous atomic physicists that came to lecture.

JS: Was Szent-Gyorgyi still in Hungary?

JB: Szent-Gyorgyi. We didn't see him, but he was, I think, already up in New England.

But we saw Teller, the famous nuclear physicist. They called him father of nuclear.

We also went to Princeton, and there was a Hungarian physicist there who won the Nobel Prize. And we also met a well-known professor of chemistry.

We then went to Philadelphia, where Eugene Ormondy received us.

JS: Wow!

JB: Yes. There was a lot of prominent people. It wasn't a dull place! I would never dream I'm going to see Ormondy personally. When I was in Hungary, we knew about

him, but we never dreamed of meeting him.

RT: At this juncture, Doctor, was the medical education you had obtained at the university in Budapest accepted as adequate for practice in this country?

JB: Well, no. You had to pass an examination, which was for American graduates. At that time, I had no chance to do that. But I got an invitation to Duke University. There were some scientists there who were working on a project I had worked on back in Hungary. It was related to renal physiology. I guess they must have gotten my resume or something, so they said, "Well, you should join us because we are doing something which you have been doing back in Hungary."

RT: Did I understand that was renal, kidney?

JB: Renal, kidney physiology, yes.

RT: Fine, thank you.

JB: And these were actually two professors, husband and wife, at Duke University. The husband was Norwegian, the wife was Danish, quite a combination. They were very nice people. They really tested me before they would let me do things in the lab. They wanted to know that I'm not faking it, but that was done good-naturedly. I mean, they just wanted to be sure what I can do.

RT: Was Professor Nielsen at Duke University then?

JB: Yes. Well, the name of this professor was Schmidt Nielsen. He was the Norwegian. He was head of the Department of Biology. And his wife was the daughter of Danish Nobel Prize winner, Professor Krogh. Actually, her background was as a dentist in Denmark, but she couldn't practice in the United States. Her diploma wasn't accepted. She went into research with her husband, and it was quite interesting. The husband's interest was marine birds, and he was studying these birds who eat all the salty fish and how they got rid of the salt, which would kill them if they cannot get rid of it. So it was very interesting.

But these birds have a gland which will secrete the salts. It's very interesting that, though they eat the salty fish, they can't get to the salt.

JS: So, how long were you there working on their project?

JB: Well, at Duke University, I was there for a year and a half. Then I was studying to take this qualifying examination, but you have to know English to take the test. At the same time, I was looking for a medical school which would help me to prepare for this examination, and I got a job at the University of Florida in Gainesville, the Gators. That's the place for the Gators.

At that time, they had a live alligator in the center of the campus. Now, you cannot do that now because that's animal cruelty restrictions, but at that time there was a

live ‘gator.

What’s interesting is that Gatorade was developed at that time when I was there, and that’s why the name comes, Gator-Ade. That’s a product of Florida, where it was developed.

JS: I’m sure it’s made many, many millions of dollars for the university, hasn’t it.

JB: Yes. So that’s where Gatorade was created, right down there.

I spent a year there, and then I had a chance to take this qualifying examination, and I applied for an internship. I ended up at Rochester, New York, at St. Mary’s Hospital, which was my first real internship.

The system was different then. The requirement was that you have to rotate to different specialties as an intern. You have to go to surgery, obstetrics, internal medicine. And you could select another subject. That was a good introduction to the system. Of course, it’s changed now.

At that time, if you were an indigent person, you could go to the hospital clinic and you would be taken care of. You had no payment, nothing. The medical staff was taking care of me and, as an intern, I have to go to clinic twice a week. Actually, with some of the patients, you did not have quite a good relationship. They just came to you as you are a doctor.

RT: Was that a program unique to the state of New York for the care of the indigents?

JB: I can say that very likely it was a New York phenomenon, very likely.

Now, we weren't supposed to do everything there. As a staff member of the hospital, I had to be in there, but basically we had to do the work.

Of course, the other thing was that they had a nursing school next to the hospital, and we used their skills as nursing students. They were working nights quite often, covering parts of the hospital, and they also came to the clinic. They donated their services; it was free. There was no cost involved there.

This system I really liked because there was no questioning whether you were registered or anything. It wasn't like that. You just went in there, and nobody finds that you have to pay anything. You can buy medicine. They'll get it for you. So it did work out pretty well.

Of course, the nursing school didn't last forever because the idea that the nurses should have comparable education to the physicians, they should be college grads, that was a big change because the nurses didn't have the first-year exposure to patients, but they'd sit in a class and take theoretical subjects. And a lot of students didn't like that. They said, "We want to be nurses. We don't want to sit in a class. We want the contact with the patients. That's why we want to be nurses. We don't want to be scientists."

Anyway, that was very interesting.

RT: I suppose that was based on an accreditation program so graduate nurses would have status professionally.

JB: Yes. The major hospitals all had a nursing school attached to them, and the

hospitals were in charge of the nursing school. And you still see it. Sibley Hospital here in the District of Columbia. They put up a beautiful building for the nursing school, the nurses were housed there. I mean, they were a great source of help because you could always call on them. They were just next door. And when they were on call, they came. There was no pressure. It was an unlimited resource, practically. Well, that was the system then.

Then, for some reason, they thought that the physicians should specialize earlier than usual. They don't need this rotating system. They should start right away doing some specialty.

RT: When you were getting your degree both in Budapest and later at Gainesville, is the record correct that you were specializing in pathology?

JB: Yes. In Gainesville, I was a member of the Pathology Department. Again, I couldn't do clinical work because I hadn't yet passed my qualifying examination. And so that's as close as I could get to patients.

Of course, I did learn the system, that is, I learned the system of medical education. In the Pathology Department, you worked with some of the other departments, like surgery and others.

In those days, of course, the surgery of breast cancer was different, because the decision was made in the operating room whether we should take off the breast. They told the patient, "Well, what's going to happen, we have to take a sample out of your tumor and we have to examine it in the operating room, and you may wake up without a

breast," because at that time the surgery was removal of the breast. If it was cancer positive, that's it. I thought that was really a pretty hard thing to do, for somebody to wake her up and tell her, "Listen, this is positive; we have to go on."

RT: That was before the development of chemotherapy.

JB: That's right. There was no chemotherapy. It was all surgery. And the radical mastectomy meant they took off the breast plus the underlying muscle, so there was practically nothing over the bones here. That's not done anymore.

JS: No. The modified.

JB: Right. Today they would do a lumpectomy, and so they didn't do this, which really was unnecessary.

See, this radical-type surgery was developed in the age when women wouldn't go to the doctor until the cancer was far advanced and the cancer was deep in the tissue, and you really couldn't get rid of the cancer except for removal of the breast and the underlying muscle.

RT: At that period of time, a lot of individuals really didn't go for preventive exams.

JB: That's right.

RT: They only went when they had an acute condition.

JB: Yes. And a lot of women were modest. They wouldn't go to the doctor regularly or anything like that.

RT: That was at a time before there was much health insurance available.

JB: Yes.

TAPE 1, SIDE B

JB: So it was, you might say, a different world then.

And the therapies, they were promulgated on the basis of no clinical trial. It was just one person, a professor. He said something that this thing works, and everybody followed. And a few weeks later, they turn around and it doesn't work. That's too bad.

But I can tell you several therapies which were done then, and which were a failure, but nobody liked to talk about failure.

But I remember there was one therapy for ulcers, stomach ulcers, freezing the stomach, and this was proposed by a famous professor in Minnesota. And the procedure was to put a balloon down in the stomach, and you start cooling it. Then you go down below freezing, you freeze the lining of the stomach, and it did work. But at times it worked too well. You froze the stomach plus some other organs, like the pancreas, and I don't advise you to get a frozen pancreas because that kills the gland, thus all kinds of

complications.

JS: I have to ask, why would freezing the stomach not alter the way the lining and so on can work? Wouldn't that affect the . . .

JB: Well, that was the effect, that it would freeze those cells which secrete the acid. That was the idea behind it.

And, of course, much earlier, they used to just radiate, irradiate the stomach by x-ray. Again, what that was doing was killing off the cells which were lining the stomach, and it worked. But, again, what happened later on, you know, this radiational [sic] damage, it's more than the stomach. The other organs were irradiated, and, of course, radiation danger, especially when you look at later dates, you developed cancer and some other bad, bad outcomes. But these things were done, and it was done in the best of interests. Everybody thought it was great, people were just going forward.

There was no such thing as a controlled clinical trial, that, let's see, we're going to have two groups and we'll give the treatment to this group and the placebo to the other group and compare it. There was no such thing.

RT: That's what I was just going to ask you. At that juncture, no doubt, there really wasn't an adverse-reaction data system at all.

JB: No, no, not at all, not at all.

Actually, within FDA, it started in 1969. That's when the agency started to store

this information on adverse events.

RT: Now, you mentioned 1969. We're referring to drug adverse reactions being implemented at that time.

JB: Yes, that's right, that's right.

So when I joined the FDA, I joined the unit which was dealing with INDs. These were the Investigational New Drug applications. There was an IND Division, and there was an NDA, New Drug Application.

RT: We've moved forward to the Food and Drug Administration. Prior to your coming to FDA, I think you were in a postgraduate fellowship practice, weren't you?

JB: Yes. I had one year in surgery as a surgical resident, and I was here at Suburban Hospital in Bethesda, Maryland. After I left Suburban Hospital, of course, that was the time when FDA was trying to expand, and they were heavily recruiting physicians because the Kefauver-Harris Amendments passed in '62, and the drug companies had to do some testing. They had to show that whatever they approve is effective. So FDA needed physicians to develop this new system, the controlled clinical trial. And to do that, they needed additional physicians.

RT: You also, as I recall, Doctor, mentioned you were in practice at the Cleveland Clinic.

JB: Yes, that's correct. That was prior to coming to this area.

RT: What was the length of time you spent there?

JB: I had three years there. I was in internal medicine.

RT: Was that in any particular specialty area, or were you in general internal medicine practice?

JB: Well, I liked the system they had there, that every patient had practically two physicians: one surgeon and the other one was an internist. So either way, the surgeons were really under control. They just couldn't go out and operate. They had to agree with the internal medicine specialist. And that was a very interesting concept, to get second opinion.

JS: How did the two work together, the surgeon and the internist?

RT: Well, not always smoothly. There were some arguments, and there were some differences of opinion, that's for sure. But it was interesting to see those things.

RT: An interesting way of approaching the patients' care.

JB: Yes. That was a time when they started to develop the modern cardiology, like visualization of the coronary vessels. It was starting then. One of the pioneers was at Cleveland Clinic, where a pediatric cardiologist actually got the idea. They did a lot of injections of dyes in children with congenital cardiac abnormalities. It was found that when injecting the ventricles with this dye, the dye would go into the coronary vessels, and beautiful demonstrations of the coronaries were obtained. The researcher then started to do it in adults and developed a technique of seeing these, which was brand new then.

RT: In looking at your experience and that cited in your curriculum vitae, is it correct to conclude that you had a lot of experience specializing in surgery procedures?

JB: Well, yes, I did. Of course, when I was at Cleveland Clinic, I was in internal medicine. But we had access to the operating room and we saw some of the surgeons develop new techniques, like Dr. Crile, who did five operations one morning on the thyroid gland. He was a super specialist of the thyroid. He just went from one table to the next. The surgical residents made the opening, and when they opened up, they exposed the thyroid, he went there and did surgery, went over to the next patient. He could do five in the morning. It was quite interesting.

When I was going in there, I picked up things like where you have to put the incision in the neck when you want to work on the thyroid. Don't put the incision very low because there'll be a bad scar. Don't put it down. Put it up here. Little things.

RT: Patients would certainly appreciate that.

JB: Cleveland was part of the goiter belt.

JS: Goiter belt?

JB: Yes. That region of the country, a lot of people have goiters, and it was routine to examine the thyroid glands.

JS: Why there?

JB: Why? Because there was no iodine.

RT: The Midwest has been famous in years past for low iodine and lots of goiters.

JB: Lots of goiters because of this lack of iodine.

JS: And this is probably before the . . .

RT: Iodinzed salt.

JS: Right.

JB: Yes. You find iodine salt. But in that part of the country, there is little seafood in the diet. If you wanted to eat seafood, it wasn't easy. I know I used to go to Howard Johnson's. They used to have something. That was a hotel chain.

But that's why Cleveland developed -- the founder of it was Dr. Crile. He did an awful lot of surgery on the thyroid gland, on goiters.

JS: Who was the surgeon?

JB: Crile.

JS: Oh, Crile. George Washington.

JB: He was one of the founders of Cleveland Clinic. But he was so good that he used to travel. He went to Boston to do some surgery, and New York.

What was interesting is the way they did the surgery. They did the surgery in the patient's room, because the theory was that these people with overactive thyroids, they were very nervous and shaky, and if you shock them with the surgery, they can go into a crisis, thyroid crisis. I don't think that was, looking back on it, I'd say that was just a -- I don't believe in that. But they believed.

They used to come in, gave an injection, put the patient out, and then the surgeon came in with the lamps and everything else. Looked like a huge TV crew or something coming in there. And he did the surgery right there in the patient's room.

JS: That's a good way to avoid creating any anxiety, which would be a problem; that's a good way to avoid it.

JB: Well, that was the idea, and I don't think you could do it today. And, of course, when you operate like that, these are not the best conditions. You don't have proper lighting, and you may not have proper assistance; you may not have the instrument you want, that particular style.

So, yes, a tremendous success, but he did have some bad ones, too.

And the type of surgery, the crux of the matter is you have to be careful, not cut nerves which control the larynx, because if you cut one nerve, well, the patient is going to be hoarse for the rest of his or her life. I mean, for a woman, that's significant. And if you cut both nerves, you're dead; then the patient cannot breathe, and you have to do a tracheostomy, and you're going to have a tracheostomy for the rest of your life.

And I know we were treating some of these patients. The clinic was generous in the sense that they owned up for their mistakes. They gave free treatment for the rest of their lives.

JS: Hopefully, there weren't too many of these.

JB: There were no lawsuits then. That was interesting. There was nobody who thought, "Oh, can we sue Dr. Crile?" I mean, he's gone. You can't. That was a real thing [unclear].

JS: Well, you mentioned earlier when we were talking about the situation at FDA, and you said as an aftermath of the 1962 Kefauver-Harris Drug Amendments, the law changed drug clearance activities tremendously. Among other provisions, the manufacturers thereafter had to submit data to support effectiveness as well as safety to FDA.

JB: That's right.

JS: The agency is looking for physicians. So what is it that brings you to FDA then?

JB: Well, I had an interview when I was here.

JS: That's right. You were at Suburban Hospital at the time.

JB: So I was here in the Washington area, so it was easy to contact the agency, and somebody mentioned it to me that, why don't you look into working for FDA? I obtained an interview with Dr. Kelsey. Of course, she was famous. We were discussing my previous medical career, and she said, "You've done a lot of things, but what I really like is what you've done in the research line," like physiology. "This is the type of thinking I'd like to have in my department, people who understand the basics of physiology.

RT: I believe, based on the information you gave us, you had a research appointment

at Duke University in ’57 and ’58. Would that have been prior to Dr. Kelsey’s interview with you?

JB: Oh, yes, that was all before, yes.

RT: So you’d established yourself as a research person.

JB: Yes, yes, yes.

JS: Was the agency divided into this, I mean the Bureau at the time, divided into this section on INDs and NDAs, and Dr. Kelsey was in charge of INDs at the time?

JB: Yes. I suppose she was in charge of both. At least temporarily then, they had some other physicians coming in to take over the NDA part of it.

Well, of course, Dr. Kelsey’s great contribution was, while she was reviewing these drug applications, she picked up that this German tranquilizer seems to be causing some nerve damage, and so she wanted to get more information about that.

RT: Was that before the thalidomide episode?

JB: That was the thalidomide episode, yes.

Thalidomide was developed in Germany, and the German name was Contergan. This was a drug actually which was very well researched. They did pregnancy tests in

animals. They were all negative. But they didn't do one animal; it was the monkey. If they would have done the pregnancy test in the monkey, it would be positive. And they did it afterwards, after the whole thing mushroomed and thousands of babies were born without extremities. It was horrible side effect.

Canada approved, so only American women who had exposure to this picked it up in Canada.

JS: There were, I believe, 15-20 instances of children born with severe birth defects in this country.

JB: Yes.

JS: And certainly the firm, Merrill, had distributed this extremely widely in this country, 20,000 patients, over 600 pregnant woman.

JB: About that number.

JS: Apparently FDA didn't even know about this sort of wide distribution.

JB: Yes, it's true.

JS: And the law changes in substantial ways with respect to oversight of clinical investigations, and this I'm gathering is one of the things that the IND group was very

interested in. Right?

JB: Yes, right, correct.

JS: And how would you characterize the way the division worked with the sponsors of these INDs at the time?

JB: Well, the sponsors kept very quiet. They would submit an application and you wouldn't hear from them for months. They had this idea that you're the one to make those guys madder at you at FDA. You'd better stay out of their way. They don't tell them anything or let me call you. You just let them do their stuff. And that was how they treated us.

JS: Well, there were problems with Merrill, especially Merrill's attempt to influence the decision in FDA, and I don't remember if that was written into the regulations after the law, but perhaps that played into that sort of more acquiescent approach to the agency.

JB: Well, that's true, that is true. But the idea, like a blockbuster drug, that wasn't really well accepted then. I mean, Wall Street didn't follow the drug companies that closely, and you didn't read about things like this company is going to have a breakthrough or something like that. There was no talk like that.

RT: There was a little historical record prior to the 1962 amendments. I think you joined FDA in 1964?

JB: That's correct.

RT: Do you recall who was the head of the then called Bureau of Drugs and the kind of staff operating there at that period?

JB: Yes. Well, the Director, Bureau of Medicine -- that's what they called the establishment for medicine, the Bureau of Medicine -- the director was Ralph Smith.

RT: I recall in that period, which is about the time I joined the agency, too, that it was a rather small group, and they were located in one of the Tempo buildings on Independence Avenue.

JB: Yes. It was right on the mall, actually. It was a temporary building. We were in Tempo S. And we liked it because they were old buildings from the Second World War, but they all had air conditioning.

JS: Were these Quonset huts?

JB: No, they weren't Quonset huts. They were temporary, like you see the schools now. You go by some of these schools, and they have an additional building with the

annex type of thing, more like, I think the best would be a barracks.

RT: Yes, they were somewhat like that.

JB: Like barracks.

RT: Self-contained, with their own air conditioning.

JB: Yes. But the air conditioning unit, you could turn it off and on, you know. And we were walking the steps of the National Gallery of Art, which is one of my favorite museums, enjoying -- I'd walk over at lunchtime. They had a cafeteria in the museum, so I could have lunch there and go back to work.

And as far as Dr. Kelsey's management style is concerned, she brought you the work to your office, and she would put it down and, "Let me know what you think about this." So there was no, "I want a report in two weeks," nothing like that. There was no time constraint. She left and said, "I'd like to know what you think about this."

RT: Now, later, I'm sure it was later when there was some allegation, by congressional members anyway, that we were slow and had a drug lag.

JB: Yes. Well, that's true.

RT: A drug-approval lag.

JB: Yes. Well, there was no time pressure, so . . .

RT: Was the industry evidently concerned about that, or were they too . . .

JB: The industry at that time, they were not, they still had the idea the best thing is not to offend FDA.

JS: And this is still in the ‘60s, and, I mean, the process, I think, is still so young that there’s . . .

JB: It was young.

JS: Right. I mean, there are many different things going on. There is certainly, under the Act, where the process of the DESI, the Drug Efficacy Study Implementation, and I wanted to ask you about that. I guess before I do, though, I wanted just to quickly -- what would you guess were the number of medical officers in the Bureau of Drugs at that time, when you came on board?

JB: When I came, there were 25.

JS: Twenty-five total.

JB: Total, yes. That covered everything.

JS: That's not a whole lot, especially when you have all this new data coming in.

JB: Yes. So you practically knew everybody at that time. You knew all the physicians.

JS: I know you worked primarily with your immediate supervisor, in your case Dr. Kelsey. But Dr. Ralph Smith, did you have much interaction with him?

JB: He would come around and ask us, "What are you doing?" "Why are you doing that?" things like that.

JS: Well, obviously, the drug-efficacy study was huge, and evaluation of all the new drug applications . . .

JB: Oh, it's still going on.

JS: Still going on, that's right, but it's evaluation of all the new drugs between 1938 and thereafter.

JB: That was a great project.

JS: How were the medical officers such as yourself involved in that?

JB: Well, there was a separate group who dealt with that, and I wasn't part of it. I knew very well who was in charge of it. Paul Bryant was the name of the physician, and he was a good friend of mine. And he had a group of . . .

There was a huge project because you have to go to all those previously marketed.

JS: And was Paul Bryant a liaison with all of the National Academy of Sciences panels that did the initial, I mean the evaluations based on the company-submitted data?

JB: Yes, that's right. Paul Bryant, he was the FDA representative.

JS: I see.

JB: So he was in touch with the National Academy of Sciences, since FDA didn't really have the manpower to do all of that.

JS: That was huge, a huge project.

JB: It had to be done. It was a great thing to look at some of those things which we used that were useless and physicians kept using them anyway. I mean, that was a great undertaking[unclear].

JS: And amazing that these stayed on the market, so many, 40 percent or so of which were less than effective.

JB: Yes. I mean, in Europe, this had a tremendous impact to the Europeans' practice, because with the European medications, what they did is they made extracts of everything. If you had liver disease, you received a liver extract. It didn't do anything really. It didn't do any harm, but it didn't do anything. If you had ulcers, then they gave you extract of modilidine, which is part of the stomach structure. So they had extracts of everything. And this was the idea.

So this was all untested. And when they saw it, they knew that what the Americans are doing. Then they started to look at, maybe we should do something similar. The drugs they use, 90 percent of them might not be effective.

JS: So there was an international impact.

JB: Oh, yes. I know FDA had tremendous respect from the established medical establishment in Europe. I was in Germany, in Italy, at an international meeting, and I remember I was sitting at a table with some professors, and they were really eager to hear me. Why am I going to talk to these professors? They're all luminaries and they all know that I'm a low medical officer. They're looking at me and questioning me, and, you know, what's the latest from FDA? And I remember they were using broad-spectrum antibiotics, tetracycline. They were using an injection form, [unclear] injecting in the muscle tissue, and that's a useless procedure, and we knew it in the United States

because of low absorption.

JS: What was the correct way to administer it?

JB: Intravenous. And the intramuscular use didn't work really, but they were doing it anyway.

Anyway, it started this idea of doing tests, comparisons, clinical trials, studies. And then the Europeans are Johnny-come-lately. They still had the idea of the professor knows everything. If you said it works, it works.

JS: I don't mean to jump around, but I have to ask one question. Do you remember your first NDA that you reviewed?

JB: Yes. The first NDA -- it was an IND, actually.

JS: Yeah, I'm sorry.

JB: The first IND was about a medication, which is still around even now. It was proposed by a professor from Romania, Professor Hauslaun, and the drug she called H3, and it's supposed to be a drug which would increase your energy, and in older people it would have an effect of rejuvenation. It was analyzed, and it showed nothing else, but a popular local anesthetic, procaine, which is not used that much now, but there's no way that could produce the effects the professor described.

But they had groups going to Romania to receive this treatment. They would go there . . .

TAPE 2, SIDE A

RT: Doctor, we had a break in the tape. Would you continue with what you were speaking of, please?

JB: Yes, sure.

So this Professor Hauslaun, she organized some of these 20, 30 people would go there and would receive this injection therapy, and it's basically nothing but procaine and maybe some contaminants, but there was nothing there which would explain all those wonderful effects. But a lot of people believed it. I mean, it was strange. People without any -- there was no proof for it that it works except for the professor was saying that it works. But that was typical European type of attitude; the professor knows the best. That was very prevalent in Germany and, of course, probably Italy, France.

But in this country, things were changing then, because the professor would know a lot, but there were associate professors who would know more in certain fields. So this was something different.

But, anyway, that was this famous vitamin. Actually, they had a name for it, vitamin H3, and they were talking about it like a vitamin. There was nothing to do with a vitamin. It was a good, catchy phrase.

Still, I see some advertising pops up about this thing once in a while.

JS: Did it go forward to NDA status?

JB: No. It was stopped.

JS: Interesting that your first NDA came from the system that you had grown up in, the system where the professor, as you said, is the . . .

JB: The professor said it works.

JS: If the professor said it works, it works. And here you are, your first NDA, you're reviewing this application, and that's that.

JB: They don't do any test. If the professor said it, then it works.

JS: Among the earliest years in your tenure in the agency, are there applications, either that you were directly involved in or others, that stand out in your mind as representing major changes, policy changes, or just interesting [unclear]?

JB: Well, it was interesting. I mean, the concept of this clinical trial, I mean, Dr. Robert Temple had a lot to do with it because they had to develop these things, and the idea was, one test is not enough; you have to do at least two groups, two trials.

And I remember I was in the Division of Cardiorenal Pulmonary Drugs. This was

in the ‘60s, in the late ‘60s, when the new drug was promoted from England, Alupent, which was . . .

JS: Can you spell that?

JB: Yes. A-l-u-p-e-n-t. This was a very important asthma drug because this drug could be administered by inhalation, and the idea was fairly new.

But what in England happened is that there were about 11 deaths reported. And so my responsibility was to be absolutely sure that this drug is safe. So I received about 120 volumes of information. I had to go through that, and there were journal articles in Germany, patient reports from England, and it actually turned out that this Alupent turned out to be one of the safest drugs. You still use it. But there are some newer ones developed.

Alupent has some cardiovascular side effects, such as giving you a rapid heartbeat, so the newer products tried to eliminate that. But the concern was that it caused this abnormal heartbeat. That’s why people died, because it had this effect on the heart and the heart just couldn’t keep up.

In Boston, we had some abnormal cardiac rhythms, too, but I couldn’t find any.

So this drug came on the market and has been on the market ever since. It’s probably the safest drug.

JS: When was this?

JB: With Alupent, it was 1968 or something like that.

JS: Sixty-eight or so?

JB: Yes.

Then, after the Alupent, there were two or three other drugs that came on the market, again for treatment of asthma, inhalation drugs for asthma. They may be a little bit better; I really don't know, but they seemed to be. But the Alupent was pretty safe, and it's still being prescribed today.

So this was my exposure to this new idea that two studies have to have the same results or similar results; they don't have to be the same, but similar results.

I remember during that, one group was young people and one group was older, and I found out that the older people didn't respond to this medication that well, as did the young people.

RT: The concept of so-called double-blind studies?

JB: Yes. At the same time it was being developed, double-blind studies.

RT: About this time, when it was necessary to really assess the drug-approval process, I think the agency recruited a lot of physicians to the Public Health Service Commissioned Corps.

JB: Yes, Commissioned Corps. That happened, yes indeed. Of course, that was during the war in Vietnam, which brought in a lot of physicians.

JS: But wasn't there an appointment? It seems either late under George Larrick's tenure or early under Dr. [James] Goddard's tenure, there . . .

JB: Dr. Goddard was the one who organized this.

JS: Yes. There was, I mean, a pretty substantial group, maybe two or three dozen, maybe more, of physicians who were in the Commissioned Corps who came in, but it was only on a temporary basis, I thought. Is that true?

JB: Yes. That's how it started.

JS: What was the reason for this, and what were these physicians doing? How did they interact with the permanent staff like yourself?

JB: Well, Goddard brought them in because he realized that we have increasing amount of workload, and he wanted to have especially younger physicians. We had quite a few older ones at that time. He wanted to have a younger group.

RT: A lot of the younger ones, because that was about the period of the Vietnam War?

JB: Yes.

RT: And that did qualify them for deferment from the regular military service.

JB: That's right, yes indeed. This was sort of like we were the military service when they came to the FDA. We called them yellow berets. There are not green berets.

JS: Did they get involved in drug evaluation [unclear]?

JB: Yes, they were. Well, they were young people, well trained. They were really ideal to do it. And, you know, the agency had problems attracting young people, partly because there weren't many female physicians. Right now, for the female physician, this is an attractive position because she doesn't have to work on the weekends and she doesn't have to work nights. If you are in practice, you just have to do those things. And even if your family wants you, you still have to attend to your patients.

RT: During that period, was there an increase in the number of female medical officers?

JB: Yes. Soon after that, yes. I think the medical school classes now are more than 50 percent female. I remember at Duke University, the class was 50; there were two girls in the class. There were just not enough females enrolled. It was a rarity. Now, of course, it is, even if a physician goes into medical practice, when they have a family, it's

very difficult. Usually if you are in pediatrics and you have young children at home, and you see sick young children outside the home, chances are you're going to take something home. That's why we have a lot of female physicians who come in from pediatrics.

RT: As a medical officer reviewing and so on, did you have a direct or indirect liaison with inspectors in the field doing investigational work?

JB: Well, we didn't have much of direct contact, but there was a time when there was a possibility to go with them on inspections. But for some reason, you don't hear much about that. But there was, I think, three or four years when you could sign up and go with the inspector and see what they do. It was very good, I think. Unfortunately, it's not done now.

RT: Would that co-inspection approach be helpful in the review of drug applications, or more in terms of orientation to the regulatory processes?

JB: Well, it's regulatory processes, and you also get the idea of what the inspector is looking for and how he does it, because you wouldn't know it otherwise. For example, how you inspect that production line. Well, to better learn it. You don't learn it in school, you know.

RT: Counter-wise, would the inspectors' exposure to the medical officer have trained

them some in what you're interested in?

JB: Yes. It's probably that is true, because the inspectors are pretty much concentrating on the process, whether it's done properly, whether everything is labeled properly so there's no possibility for confusion. And it's, in manufacturing of medical products, the purity, the cleanliness, is absolute, because you cannot say, "Well, we used some peanut butter in this thing last week. We cleaned this out. I think it's going to be ready to make some medicine." You cannot do that because people are very sensitive to a microscopic amount of material, and it's very important. This thing is very detailed.

JS: Well, we had a huge problem with cross-contamination of antibiotics in the 1960s, and hopefully we learned and the manufacturers learned from that.

JB: Yes, yes. You cannot just deal with it like the ordinary thing. I mean, I'm reading a paper sometimes, and these people are good-natured. You know, they are top-of-the-line manufacturers and managers, and they say, "Why do we have FDA? Why? Why don't we let the marketplace decide which is better, which drug is better?"

JS: Well, actually . . .

JB: That's what I'm saying. We saw mistakes being made and we had a few deaths, and we had to do something because things were out of control. It's not like making shoes, you know, that one brand is better than the other; let the marketplace decide; let

not the government decide which ones are better. And these people think that they have a case, that why do we waste all this money on the FDA? Why don't we just let the marketplace decide? We had that.

JS: We had that. It didn't quite work out.

JB: Yes, that's right.

RT: The time came when there was quite an extensive overhaul of the drug-approval process. Can you speak a little bit of your experience in that event?

JB: Well, in the drug approval process, of course, you have to prove that the drug is effective, which meant that, really, to be absolutely sure, you have to compare the product to a placebo, which has no effect and is not supposed to have any effect. Of course, later on, we found out that there is such a thing as a placebo effect, and that has a lot to do with the physician. I mean, if you recall the days when there were no effective medications, people didn't recover from their illnesses. And we thought, well, it's the physician or the potion. It was basically the personality, the personality which can project hope. That has a curing effect. Of course, this wasn't thought of. But we see more and more of that from the psychiatrist, and the placebo effect is like 30-40 percent. The drug effect is 45, but that's very little difference.

But what they used to do is, with regard to the psychiatrists, they used to have conferences with the patients two or three times a week, no pills, nothing, and they have

cure. They have people recover. And that was the placebo effect. That was looked down upon, that was like snake oil, that's not the real thing, but it is the real thing. We are coming around, seeing that there is a positive effect.

I believe in it, that if you have a choice of physicians and you feel like you can work with somebody better than the other one, I think that's important that you work with that person because you get a more beneficial effect.

But anyway, that was the placebo concept.

JS: About 1978 or 1979, there was a push to rewrite the law in terms of the drug regulation, and it didn't, obviously, pan out. But do you have any memories of that or any . . .

JB: No. Well, I can't say. At that time, I was more into the generic drugs I was working with, and generic drugs were very attractive to a lot of politicians because the price difference was tremendous then. It's not that much now, but then it was. I mean, in the budget perspective, with generic drugs, you save 50 or 60 percent or even more. And, of course, a lot of physicians, especially the older ones, they wouldn't believe that the generic drugs are as good as the brand names. They really had to develop tests to show this to be true, or do the bioequivalence testing. They had to do that to show this to the physicians, and we are comparing effects because the chemical analysis was very similar. There's more to it.

It was interesting when I made a trip once to Puerto Rico. The Puerto Rican government was ready to promote generics, and they invited a couple of us to talk to

them at a convention of the medical association. Then I realized that the word generics, as they used that word, they would say [henetic]. What that means is the product is inferior. So we had to change. They told us the physicians and the pharmacists in Puerto Rico don't use the word generic. They instead use bioactive, so that's what we have to say now.

JS: [Henetic] in Spanish means inferior.

JB: It's not as good, yes. It's inferior to a brand-name product. How it developed, I don't know. But the local pharmacists don't use the word generic; that's no good. You have to use . . .

JS: I haven't heard that before with the use of generics in Spanish. I've heard that with respect to products that people have tried to introduce in Spanish-speaking countries, and the brand name of a product means something horrible in the language, and no one anticipated this. I never had heard of this.

JB: Well, it was in Puerto Rico, so I don't know. Maybe Mexico is different. I thought that was sort of interesting.

JS: How were you working with generics at the time?

JB: That concerned adverse reactions due to generics. They have the same type of

adverse reaction as brand names. That's what we had to say. As far as the adverse effects of the generic or brand name, we saw the same type of adverse reactions. So I think right now, generics are pretty much accepted.

RT: Now, the drug industry itself, did they, or when did they, if so, begin to press for equality consideration of generics versus brand name?

JB: Well, what happened is that one of the brand-name companies bought up a generic company, so it's in the same pocket. And they were, of course, against the generics for quite a while, until Valium -- I guess Roche is the manufacturer of Valium. And they claimed that generic Valium is not as good as the brand name, and they actually formulated the tablet with a V on it, so when you have Valium, you've got the real thing, the brand name, see the V on it. That's the real thing. These other ones don't have it. But I don't think that that's true. But it's very interesting. Some people say, well, this doesn't have the V on it; that's not the real Valium.

JS: Well, if they could put a lowercase V on it, it would have the same effect.

RT: Well, it's perhaps ironic. You mentioned Puerto Rico. In later times, much of the pharmaceutical industry has developed production facilities there.

JB: Yes, that's right.

RT: I suppose by reason of better economic labor and so on.

JB: Yes. Well, the labor is cheaper, yes, yes. I don't know what it is now, but it's probably that generics are well accepted there too. And it's really, it's a good saving, especially certain products like antibiotics. I think you are on safe ground to buy the generics because often it's made by the same company who makes the brand name drug. Abbott makes it, and the generic is also made by them.

RT: When one considers drugs produced outside the continental United States, the issue of equality and export-import values arise. Do you have any comment on that phenomenon of the export and the import aspect of drug regulation?

JB: Well, the problem is, when you import drugs, you have to be careful because some of the manufacturing which is happening outside the United States, you really have to be very careful and you have to inspect them and check them that it's the real thing, that you are getting the real thing, not some inferior product.

RT: Concomitant with that is the issue of drugs produced here and shipped to Canada, and then the allegation in some places that they're available at lower cost re-imported than they were when, than they would be when sold in this country.

JB: Yes. Well, I think it's true that a lot of the drugs which come from Canada were made in the United States and shipped out to Canada, it's coming back, the same thing.

But the Canadians have this arrangement where the government negotiates the prices for the drugs. Since you buy volume, you should be able to negotiate that. Why it's not done in the United States, I don't know, but it could be done here too. It would make it so much simpler. I hear this is done under Medicare and so on, the rules are very confusing, and you are dealing with hundreds of companies.

RT: I guess one of the principal issues, isn't it, is the integrity of those drugs, being assured that you're not receiving back counterfeits or repackaged drugs or something like that.

JB: Yes. Well, it is true that -- I'm not that afraid of drugs from Canada, but I don't know, some may come from Asia. You really have to look and check and double-check.

RT: Would it be safe to assume that the drug-protective quality of regulation in this country is paramount, is the lead, or are other countries approaching similar effective controls over drug manufacture?

JB: Yes. Well, it's -- some of these countries, they don't have much. They have a couple of companies who make drugs; that's about it. But where we are in the United States, we have a huge, huge industry, and it's not easy. And some of the drug prices are very high, and you find people here who are cheats, like they have dishonest pharmacies in Georgia or somewhere who want to use the half strength of this cancer drug.

JS: Kansas City, I think.

JB: Yes, Kansas City. Instead of using the full strength of this product, the pharmacist watered it down so he could make money on it.

JS: I just wanted to ask a couple organizational questions, and if this strikes you in any way, comment; if not, that's fine.

A couple things on organization, one on sort of the way this Center did business.

One is, in, say, the late 1970s, early 1980s, when biologics and drugs were combined into one large center, it only lasted for a few years. But I was curious if, from the standpoint of where you were in the Center, if you saw any sort of unusual impact? Were the drugs people in any way less better off or better off, say, by this union, or did it seem to have any impact whatsoever from your standpoint?

JB: Yes. Well, of course, I just can speak for myself.

One thing is interesting, that the biological products, the adverse effects are different from the regular drugs. They look sort of unusual. And these biological products, they interact with the system differently than just ordinary chemicals, and there are different type of adverse reactions. Anybody who wants to study them should spend some time because they do cause different type of reactions. That's why biologics and some other complicated products, many times you cannot even show that what you have is exactly the same as in the previous batch, because you have these moieties of amino acids, and you look at the structure, it's like this, and something can get out of whack.

Maybe there are physical infirmities. In some ways it's difficult.

RT: In regulatory orientation, historical perspective, would you believe there was any difference between the drug-control people and that biologics was one more, shall we say, regulatory oriented in terms of regulatory action versus education?

TAPE 2, SIDE B

JB: Well, I think the industry has to educate them, the physician population, because very few of us learned anything about biologics in medical school. They were not just around. No. And I think that it's very important for physicians to continue medical education. You cannot just stop it after you finish school and say, "Well, I know everything now," because things do change. I mean, in just a few years, you have companies with new ideas, and it's very important for physicians to continue and learn.

RT: So the field of biologics or regulatory oversight is newer and less in time than drug control. Is that true?

JB: Yes, it's new; these things are all new. You just have to take a look at the chemical structure and you'll be amazed what they have. I mean, it's not just an ordinary chemical structure. It's all over. You can memorize it.

Well, actually, the manufacturer cannot be absolutely sure that what they produced is an exact copy because we can't tell the difference, really.

But we're going to have more and more biologics, and eventually treatment of cancer is going to come down to these products which will attack the cancer cells, not the body, and we have a lot of anticancer drugs which will attack the body just as well as they attack the cancer cells, and it's one of the worst things you see. As a pathologist, you see a woman about 40. She dies, and then you find no cancer at all. She died because of the therapy.

We have been using poisons, and that's not good enough, but I think with the biologicals, we'll be able to really go down to the cellular level, differentiating the cancer cells from the regular cell. I mean, that's the crucial thing that you have to do. Well, it's happening.

JS: In the area of drugs, within the last year in the area of drug safety, it's been an interesting year, with all the fallout from the COX-2 products and so on. Just your opinion here: Is there something that we can do better, or are we doing what we need to right now? Is there anything that we can do better as an agency when it comes to drug-safety issues?

JB: Well, I think it's been proposed before and it keeps coming back, that the Office of Drug Safety should be a separate group, not part of FDA. It should be outside, and so it would be completely independent as far as the post-marketing evaluation, because right now the people who approve the drugs, they're not going to, they're going to feel bad about condemning the drugs FDA approves. That just doesn't work right now.

JS: Do you have an opinion about the wisdom or lack of wisdom of situating that responsibility, not only outside the Center for Drugs, but outside of the FDA itself?

JB: Well, it depends how it's done, you know, the little details. But the point is, you have to have independence. We have no connection with the drug company and no connection with the group within FDA.

JS: With the approving officials.

Do you think it might be possible to do that, yet have the entity remain within the agency?

JB: Well, I don't know. That's a possible thing. It could be tried; it certainly could be tried. But I can see how the independent people would have no pressure from the colleagues at FDA.

JS: You've been here for quite a while, and I'm curious, looking back on things, on the relationship between those in the agency who approve the application, the INDs, NDAs, and those who are involved more in post-marketing surveillance, has there been historical tension between the two groups?

JB: There was some tension in the way that, when there were Advisory Committee meetings, they wouldn't allow the ODS group to testify.

JS: Which group is this?

JB: The Office of Drug Safety.

JS: Okay.

JB: Instead of somebody from Drug Safety, they have somebody else from the division who approved the drug to give a presentation and this type of thing. There was some disagreement there.

JS: Who would make that decision that ODS would not be present at the Advisory Committee meetings? Would that come from the Director's office or something?

JB: The director's office, sure.

JS: Okay.

JB: What I'm thinking is these are completely honest people, see. They think they are doing their best, so I'm not saying that anybody's a crook. No. Nobody's being paid off here. It's just that I personally think you work some of these officers, medical officers who have these drugs, they're working with them for six months. They practically live with the drug. And when they approve it, they feel that's the best they could do. But if something comes up later on, it's difficult to be completely unbiased, try to explain it in

another way.

So I see a little bit of tension there with the Office of Drug Safety. But I think FDA through the years, as it developed, has done its best. But not everything is a hundred percent.

But just like when you look at medical care as far as emergency care, it's outside FDA more or less, but you really have the blessing of these helicopter transports, which means that if you have an accident out somewhere in Hagerstown or somewhere, you can get the best medical care which is available. Before the establishment of a system, you had to wait an hour before somebody would show up, you know. They would take you to the local hospital, and the nurse might be on call. So she comes in and she says, "Well, this guy's in pretty bad shape. Better call for a doctor." So it takes hours before he gets there. That's the way it used to be.

Now you have -- I remember, you know, anybody can call a helicopter basically. My first helicopter case came from the western part of Maryland. He was in an accident and he had some blood on his face. The policeman called the helicopter. They brought him in. Turned out he had a broken tooth; that's all. But that's what happens when you let bystanders make the decision.

But, actually, this works very well in a serious injury. This guy didn't need this transport, but he got it anyway.

JS: Had a nice helicopter ride.

RT: Well since probably the days of George Larrick, we have had as Commissioners,

for the most part, medical doctors or veterinarians, someone trained in the medical discipline. And that's, I guess, indicative of the fact we seem to be trying to provide more safety and efficacy in the drug control.

JB: Yes.

RT: In earlier times, that was maybe balanced more with food and other products that we regulated.

JB: Yes, yes.

RT: Do you have any particular suggestions? I know you're still active, so we're not trying to put you on the spot. But if you have any particular suggestions -- and John's kind of alluded at that -- for any policy changes in regard to this whole area?

JB: Well, I think the real thing, and that would be that tremendous improvement could be achieved in drug testing if one drug would be tested against another to see which is better, because right now what we are saying is, "Well, this drug has efficacy, it works, but we never say that's better than this other thing, and that would be a real step forward, when we can do that and say, "This drug is definitely better than this."

RT: Do you think that the pharmaceutical industry would be opposed to that?

JB: I'm sure they're averse to this because all of these me-too drugs wouldn't be developed.

JS: You look back at the Kefauver hearings and the possibility came up, they weren't too happy about that possibility.

JB: No. That's not . . .

JS: But that's a good point. That's what people, that's what practitioners . . .

JB: Yes, and it's better than this other thing? Well, we don't know for sure. All the things we say, it works.

RT: Doctor, if there's any other areas you'd like to cover, we'd welcome doing that. If not, we can close.

JB: Well, we can get together maybe later on.

RT: That would be great.

JB: We can discuss some other points.

JS: Absolutely.

Thank you so much for all the time you've spent with us this afternoon.

JB: Well, I enjoyed it because you have been a very good audience. Not everybody wants to know about these things.

JS: We were concerned that this might, us on one side of the table and you on the other, create some sort of tribunal appearance with this long table here, but I'm glad you obviously felt comfortable with the settings.

JB: Oh, yes.

RT: That's one of the riches of this oral history program. You get some of that. It's not in the written material necessarily.

JB: No, that's right. I don't mind coming back, you know.

RT: Great. We certainly appreciate that you've shared such a wealth of experience you've had, from a refugee to a very important role in this agency.

JB: Well, I mean, really, what makes me going and keeps me working is that I can see how things are developing continuously in the field of medicine, what improvements are occurring, especially with these new imaging modalities we have.

I remember when I was just a fellow in training, that we used to inject air, and we

used to put a needle in the spinal canal and inject air so it would bubble up into the brain and it would serve as a contrast area.

RT: We've come a long way.

JB: Yes, we've come a long way, really.

RT: Doctor, we'll have this transcribed and we will be in further touch with you. Thank you very much.

JB: Well, I enjoyed it, and you were pretty nice. It's always good when somebody listens to you.

END OF INTERVIEW

Interview with Janos T. Bacsanyi, M.D.

January 24, 2006

TAPE 1, SIDE A

RT: This is another in the series of the FDA oral history interviews. Today, the interview is with Janos T. Bacsanyi, Medical Doctor. Dr. Bacsanyi is a Medical Officer in the Office of Drug Safety in the Center for Drug Evaluation and Research (CDER). The interview is being conducted at the Parklawn Building, and in addition to Dr. Bacsanyi, Dr. John Swann and Robert Tucker are conducting the interview for the History Office. The date is January 24, 2006.

Doctor, with that introduction, would you please give us some information regarding the early history of your education and professional experience.

JB: I was born in Hungary and grew up in Hungary, where I went to medical school at the age of 18 and graduated at the age of 24, in 1955. The following year, 1956, was a crucial year for Hungary. That was the year of the Hungarian uprising against the Soviet occupation. At that time, of course, the Hungarians were defeated and crushed by the Soviets, and I could see no future in Hungary, or reason for staying in Hungary. So I decided to leave the country in November 1956, with a good friend of mine. The two of us escaped to Austria.

RT: Doctor, before you go into that, could you mention where your pre-med and your

medical education was taken -- I think you began your medical education in Hungary.

JB: That's correct. The school system, of course, was different then than it is now, and after four years [recorder malfunctioned for a few minutes].

JS: Now we're recording.

RT: We're resuming recording now.

JB: After four years of elementary education, I was enrolled in a college preparatory school, which was called a gymnasium. Of course, the meaning of this term is different when we use it in the American context. This was eight years of preparatory school with a lot of courses, which later on you didn't really use it very much. But one thing was interesting. We had to take eight years of Latin, and this became very good when we went to Rome and we could read all the old Roman signs. Also, I could understand Julius Caesar's message to the Congress, which was, of course, the Roman Congress.

So that's, after eight years in the gymnasium, then, at age 18, I was enrolled in the medical school in Budapest, and the medical school duration was six years then.

RT: Was that the Semmelweiss?

JB: It's called Semmelweiss now. At that time they had a different name for it. But it's the same medical school except for change of name. But it's Semmelweiss right

now. It was named after the famous obstetrician who lived in Vienna most of his . . .

RT: Would that have been a state type education?

JB: Yes, it was a state type. There was no private medical school. It's all state supported, and there was no tuition. And if you were lucky, you could get a scholarship, and I was one of the lucky ones. There were only six or seven of us in the size of 240 in the medical school class, 240. And most of our schooling was in the local university hospitals. After two years of theoretical studies, chemistry, physics, and physiology. Actually, I graduated from medical school in 1955, and the following year, of course, I had to leave Hungary.

RT: When you graduated, were you in a particular department of the medical school?

JB: No. It was general. It was interesting that you had a general degree, which even included dentistry too, so you learned some element of the techniques like pulling teeth. Also, we learned how to fill teeth. And I remember I had to work on some children. I was amazed how well-behaved the children were. But the children's, the young children's teeth are not sensitive to pain. It comes, their [unclear] teeth, they don't have these nerve fibers, so you could use them pretty well. They have no pain.

JS: So you could drill without any anesthesia.

JB: There was no anesthesia.

Of course, when the children got older and they have their final teeth, they are sensitive.

RT: In Hungary, in the practices of medicine and dental science, are those sort of coexistent? In other words, are medical practitioners also dentists in practice there?

JB: Well, at that time they could do it. There was the general physician, and if you wanted -- most of us didn't go into dentistry, but you could. You were really authorized by doing it.

RT: So the medical training to become fully accredited was not necessarily a longer time period than dental school. Is that correct?

JB: Yes, that's correct. The dental schooling was part of the medical curriculum.

RT: I see.

JB: It's different now, but now it's completely separated.

JS: So you graduated with your medical degree in 1955. The uprising comes in 1956, and you said you left with a friend to Austria. I imagine that must have been quite frightening.

JB: Yes. The border crossings, the major roads were already supervised by the Russian troops, so you couldn't get through. You had to make your way through the woods. In order to do that, well, they recommended to do it at night, because at nighttime, most of the Russians didn't want to go in the woods. So at nighttime, you could go through. But you had to have somebody who knew the area, and we were lucky to find a local person who led us through the darkness. There's no lights or anything like that.

JS: And you have all of your belongings you can carry on your back, basically.

JB: That's right.

RT: You didn't have to pay or bribe somebody for help, did you?

JB: Well, what happened is that we had Hungarian money with us, and we said we won't be able to use it in Austria anyway, so we gave it to the person there.

JS: So you were in Austria just briefly, I gather.

JB: Yes. Well, in Austria, we spent just a couple of days in this village close to the border. Then we went to -- well, actually, we were transported to Vienna thanks to a local physician who took care of us. He came to the camp, and when he saw that we

were physicians there, he said, "Well, there's another place for you. You come with me." He took us to his house, and it was very, very generous of him. We stayed there a couple of days, and then he got transportation for us, and we went off to Vienna.

RT: Then did you go to Budapest? Where did you go when you went through the woods to escape?

JB: Well, there was a city fairly close to the border, which the Hungarian name was Sopron. The German name was Erdenberg because for quite a few years, Hungary and Austria were one country, so you find German names for a lot of the communities. From there, we had an ambulance that took us out to about two miles away from the border, and these ambulance drivers knew what we were about to do.

RT: Did you go as, shall we say, patients in the ambulance?

JB: Well, something like that. It was during the night, and they had very few ambulance calls at night, so they accommodated us. Actually, we were staying at the local hospital for two days, so we used the empty beds they had.

When we got out to Austria, of course, in Vienna, we had to make up our minds where we wanted to go. There were different countries making offers. For instance, Sweden, they were advertising for physicians who would practice in the Lapland. That's the northernmost part of Sweden where nobody wants to go. But they were very generous because they offered two years of education before they put us up there. We

had to learn the language that people used, and we had to learn the customs, and this would have been two years' education, then five years in service, and after five years, the Swedes said we could go anywhere in Sweden we wanted to. So I thought that was very generous of them.

And what was interesting is that the Swedes didn't discriminate; the Swedes would accept anybody, even a person who had some bad condition like tuberculosis and so on.

As far as the Americans were concerned, at that time, you know, it wasn't easy just to come over here and make a claim that I was escaping the Red Army or something like that. No. They would check you out, have a medical examination. Before you were taken over to an American camp, you would be taken and gone over.

So, well, of course, comparing the Lapland to New York, it wasn't a very difficult decision to make.

JS: How was your English at the time?

JB: Well, I had learned some in high school, so I was better off than most of them. And I knew a little bit of German too. Of course, my Swede wasn't good, so it would have been a struggle to learn a language like the Lapp language because of what that requires. It was easier really to go to the United States.

Well, we were accepted and flown out. On the way to the United States -- we arrived in New Jersey -- we stopped on the way in Newfoundland because of a storm. We had to land there, and we stayed there for a couple days till the storm blew over.

It was the McGuire Air Force Base in New Jersey where we landed. Outside New Brunswick, there was a camp, Camp Kilmer. It was named after the famous [unclear]. And we stayed there for about a couple of weeks or so. Then we were sort of segregated into different groups, like the physicians were separate, the scientists were separate, and then we received a very interesting course, introduction in American culture and education. We spent about four weeks at Rutgers University.

They invited quite a few well-known Hungarians, scientists like some of these famous atomic physicists that came to lecture.

JS: Was Szent-Gyorgyi still in Hungary?

JB: Szent-Gyorgyi. We didn't see him, but he was, I think, already up in New England.

But we saw Teller, the famous nuclear physicist. They called him father of nuclear.

We also went to Princeton, and there was a Hungarian physicist there who won the Nobel Prize. And we also met a well-known professor of chemistry.

We then went to Philadelphia, where Eugene Ormondy received us.

JS: Wow!

JB: Yes. There was a lot of prominent people. It wasn't a dull place! I would never dream I'm going to see Ormondy personally. When I was in Hungary, we knew about

him, but we never dreamed of meeting him.

RT: At this juncture, Doctor, was the medical education you had obtained at the university in Budapest accepted as adequate for practice in this country?

JB: Well, no. You had to pass an examination, which was for American graduates. At that time, I had no chance to do that. But I got an invitation to Duke University. There were some scientists there who were working on a project I had worked on back in Hungary. It was related to renal physiology. I guess they must have gotten my resume or something, so they said, "Well, you should join us because we are doing something which you have been doing back in Hungary."

RT: Did I understand that was renal, kidney?

JB: Renal, kidney physiology, yes.

RT: Fine, thank you.

JB: And these were actually two professors, husband and wife, at Duke University. The husband was Norwegian, the wife was Danish, quite a combination. They were very nice people. They really tested me before they would let me do things in the lab. They wanted to know that I'm not faking it, but that was done good-naturedly. I mean, they just wanted to be sure what I can do.

RT: Was Professor Nielsen at Duke University then?

JB: Yes. Well, the name of this professor was Schmidt Nielsen. He was the Norwegian. He was head of the Department of Biology. And his wife was the daughter of Danish Nobel Prize winner, Professor Krogh. Actually, her background was as a dentist in Denmark, but she couldn't practice in the United States. Her diploma wasn't accepted. She went into research with her husband, and it was quite interesting. The husband's interest was marine birds, and he was studying these birds who eat all the salty fish and how they got rid of the salt, which would kill them if they cannot get rid of it. So it was very interesting.

But these birds have a gland which will secrete the salts. It's very interesting that, though they eat the salty fish, they can't get to the salt.

JS: So, how long were you there working on their project?

JB: Well, at Duke University, I was there for a year and a half. Then I was studying to take this qualifying examination, but you have to know English to take the test. At the same time, I was looking for a medical school which would help me to prepare for this examination, and I got a job at the University of Florida in Gainesville, the Gators. That's the place for the Gators.

At that time, they had a live alligator in the center of the campus. Now, you cannot do that now because that's animal cruelty restrictions, but at that time there was a

live ‘gator.

What’s interesting is that Gatorade was developed at that time when I was there, and that’s why the name comes, Gator-Ade. That’s a product of Florida, where it was developed.

JS: I’m sure it’s made many, many millions of dollars for the university, hasn’t it.

JB: Yes. So that’s where Gatorade was created, right down there.

I spent a year there, and then I had a chance to take this qualifying examination, and I applied for an internship. I ended up at Rochester, New York, at St. Mary’s Hospital, which was my first real internship.

The system was different then. The requirement was that you have to rotate to different specialties as an intern. You have to go to surgery, obstetrics, internal medicine. And you could select another subject. That was a good introduction to the system. Of course, it’s changed now.

At that time, if you were an indigent person, you could go to the hospital clinic and you would be taken care of. You had no payment, nothing. The medical staff was taking care of me and, as an intern, I have to go to clinic twice a week. Actually, with some of the patients, you did not have quite a good relationship. They just came to you as you are a doctor.

RT: Was that a program unique to the state of New York for the care of the indigents?

JB: I can say that very likely it was a New York phenomenon, very likely.

Now, we weren't supposed to do everything there. As a staff member of the hospital, I had to be in there, but basically we had to do the work.

Of course, the other thing was that they had a nursing school next to the hospital, and we used their skills as nursing students. They were working nights quite often, covering parts of the hospital, and they also came to the clinic. They donated their services; it was free. There was no cost involved there.

This system I really liked because there was no questioning whether you were registered or anything. It wasn't like that. You just went in there, and nobody finds that you have to pay anything. You can buy medicine. They'll get it for you. So it did work out pretty well.

Of course, the nursing school didn't last forever because the idea that the nurses should have comparable education to the physicians, they should be college grads, that was a big change because the nurses didn't have the first-year exposure to patients, but they'd sit in a class and take theoretical subjects. And a lot of students didn't like that. They said, "We want to be nurses. We don't want to sit in a class. We want the contact with the patients. That's why we want to be nurses. We don't want to be scientists."

Anyway, that was very interesting.

RT: I suppose that was based on an accreditation program so graduate nurses would have status professionally.

JB: Yes. The major hospitals all had a nursing school attached to them, and the

hospitals were in charge of the nursing school. And you still see it. Sibley Hospital here in the District of Columbia. They put up a beautiful building for the nursing school, the nurses were housed there. I mean, they were a great source of help because you could always call on them. They were just next door. And when they were on call, they came. There was no pressure. It was an unlimited resource, practically. Well, that was the system then.

Then, for some reason, they thought that the physicians should specialize earlier than usual. They don't need this rotating system. They should start right away doing some specialty.

RT: When you were getting your degree both in Budapest and later at Gainesville, is the record correct that you were specializing in pathology?

JB: Yes. In Gainesville, I was a member of the Pathology Department. Again, I couldn't do clinical work because I hadn't yet passed my qualifying examination. And so that's as close as I could get to patients.

Of course, I did learn the system, that is, I learned the system of medical education. In the Pathology Department, you worked with some of the other departments, like surgery and others.

In those days, of course, the surgery of breast cancer was different, because the decision was made in the operating room whether we should take off the breast. They told the patient, "Well, what's going to happen, we have to take a sample out of your tumor and we have to examine it in the operating room, and you may wake up without a

breast," because at that time the surgery was removal of the breast. If it was cancer positive, that's it. I thought that was really a pretty hard thing to do, for somebody to wake her up and tell her, "Listen, this is positive; we have to go on."

RT: That was before the development of chemotherapy.

JB: That's right. There was no chemotherapy. It was all surgery. And the radical mastectomy meant they took off the breast plus the underlying muscle, so there was practically nothing over the bones here. That's not done anymore.

JS: No. The modified.

JB: Right. Today they would do a lumpectomy, and so they didn't do this, which really was unnecessary.

See, this radical-type surgery was developed in the age when women wouldn't go to the doctor until the cancer was far advanced and the cancer was deep in the tissue, and you really couldn't get rid of the cancer except for removal of the breast and the underlying muscle.

RT: At that period of time, a lot of individuals really didn't go for preventive exams.

JB: That's right.

RT: They only went when they had an acute condition.

JB: Yes. And a lot of women were modest. They wouldn't go to the doctor regularly or anything like that.

RT: That was at a time before there was much health insurance available.

JB: Yes.

TAPE 1, SIDE B

JB: So it was, you might say, a different world then.

And the therapies, they were promulgated on the basis of no clinical trial. It was just one person, a professor. He said something that this thing works, and everybody followed. And a few weeks later, they turn around and it doesn't work. That's too bad.

But I can tell you several therapies which were done then, and which were a failure, but nobody liked to talk about failure.

But I remember there was one therapy for ulcers, stomach ulcers, freezing the stomach, and this was proposed by a famous professor in Minnesota. And the procedure was to put a balloon down in the stomach, and you start cooling it. Then you go down below freezing, you freeze the lining of the stomach, and it did work. But at times it worked too well. You froze the stomach plus some other organs, like the pancreas, and I don't advise you to get a frozen pancreas because that kills the gland, thus all kinds of

complications.

JS: I have to ask, why would freezing the stomach not alter the way the lining and so on can work? Wouldn't that affect the . . .

JB: Well, that was the effect, that it would freeze those cells which secrete the acid. That was the idea behind it.

And, of course, much earlier, they used to just radiate, irradiate the stomach by x-ray. Again, what that was doing was killing off the cells which were lining the stomach, and it worked. But, again, what happened later on, you know, this radiational [sic] damage, it's more than the stomach. The other organs were irradiated, and, of course, radiation danger, especially when you look at later dates, you developed cancer and some other bad, bad outcomes. But these things were done, and it was done in the best of interests. Everybody thought it was great, people were just going forward.

There was no such thing as a controlled clinical trial, that, let's see, we're going to have two groups and we'll give the treatment to this group and the placebo to the other group and compare it. There was no such thing.

RT: That's what I was just going to ask you. At that juncture, no doubt, there really wasn't an adverse-reaction data system at all.

JB: No, no, not at all, not at all.

Actually, within FDA, it started in 1969. That's when the agency started to store

this information on adverse events.

RT: Now, you mentioned 1969. We're referring to drug adverse reactions being implemented at that time.

JB: Yes, that's right, that's right.

So when I joined the FDA, I joined the unit which was dealing with INDs. These were the Investigational New Drug applications. There was an IND Division, and there was an NDA, New Drug Application.

RT: We've moved forward to the Food and Drug Administration. Prior to your coming to FDA, I think you were in a postgraduate fellowship practice, weren't you?

JB: Yes. I had one year in surgery as a surgical resident, and I was here at Suburban Hospital in Bethesda, Maryland. After I left Suburban Hospital, of course, that was the time when FDA was trying to expand, and they were heavily recruiting physicians because the Kefauver-Harris Amendments passed in '62, and the drug companies had to do some testing. They had to show that whatever they approve is effective. So FDA needed physicians to develop this new system, the controlled clinical trial. And to do that, they needed additional physicians.

RT: You also, as I recall, Doctor, mentioned you were in practice at the Cleveland Clinic.

JB: Yes, that's correct. That was prior to coming to this area.

RT: What was the length of time you spent there?

JB: I had three years there. I was in internal medicine.

RT: Was that in any particular specialty area, or were you in general internal medicine practice?

JB: Well, I liked the system they had there, that every patient had practically two physicians: one surgeon and the other one was an internist. So either way, the surgeons were really under control. They just couldn't go out and operate. They had to agree with the internal medicine specialist. And that was a very interesting concept, to get second opinion.

JS: How did the two work together, the surgeon and the internist?

RT: Well, not always smoothly. There were some arguments, and there were some differences of opinion, that's for sure. But it was interesting to see those things.

RT: An interesting way of approaching the patients' care.

JB: Yes. That was a time when they started to develop the modern cardiology, like visualization of the coronary vessels. It was starting then. One of the pioneers was at Cleveland Clinic, where a pediatric cardiologist actually got the idea. They did a lot of injections of dyes in children with congenital cardiac abnormalities. It was found that when injecting the ventricles with this dye, the dye would go into the coronary vessels, and beautiful demonstrations of the coronaries were obtained. The researcher then started to do it in adults and developed a technique of seeing these, which was brand new then.

RT: In looking at your experience and that cited in your curriculum vitae, is it correct to conclude that you had a lot of experience specializing in surgery procedures?

JB: Well, yes, I did. Of course, when I was at Cleveland Clinic, I was in internal medicine. But we had access to the operating room and we saw some of the surgeons develop new techniques, like Dr. Crile, who did five operations one morning on the thyroid gland. He was a super specialist of the thyroid. He just went from one table to the next. The surgical residents made the opening, and when they opened up, they exposed the thyroid, he went there and did surgery, went over to the next patient. He could do five in the morning. It was quite interesting.

When I was going in there, I picked up things like where you have to put the incision in the neck when you want to work on the thyroid. Don't put the incision very low because there'll be a bad scar. Don't put it down. Put it up here. Little things.

RT: Patients would certainly appreciate that.

JB: Cleveland was part of the goiter belt.

JS: Goiter belt?

JB: Yes. That region of the country, a lot of people have goiters, and it was routine to examine the thyroid glands.

JS: Why there?

JB: Why? Because there was no iodine.

RT: The Midwest has been famous in years past for low iodine and lots of goiters.

JB: Lots of goiters because of this lack of iodine.

JS: And this is probably before the . . .

RT: Iodinzed salt.

JS: Right.

JB: Yes. You find iodine salt. But in that part of the country, there is little seafood in the diet. If you wanted to eat seafood, it wasn't easy. I know I used to go to Howard Johnson's. They used to have something. That was a hotel chain.

But that's why Cleveland developed -- the founder of it was Dr. Crile. He did an awful lot of surgery on the thyroid gland, on goiters.

JS: Who was the surgeon?

JB: Crile.

JS: Oh, Crile. George Washington.

JB: He was one of the founders of Cleveland Clinic. But he was so good that he used to travel. He went to Boston to do some surgery, and New York.

What was interesting is the way they did the surgery. They did the surgery in the patient's room, because the theory was that these people with overactive thyroids, they were very nervous and shaky, and if you shock them with the surgery, they can go into a crisis, thyroid crisis. I don't think that was, looking back on it, I'd say that was just a -- I don't believe in that. But they believed.

They used to come in, gave an injection, put the patient out, and then the surgeon came in with the lamps and everything else. Looked like a huge TV crew or something coming in there. And he did the surgery right there in the patient's room.

JS: That's a good way to avoid creating any anxiety, which would be a problem; that's a good way to avoid it.

JB: Well, that was the idea, and I don't think you could do it today. And, of course, when you operate like that, these are not the best conditions. You don't have proper lighting, and you may not have proper assistance; you may not have the instrument you want, that particular style.

So, yes, a tremendous success, but he did have some bad ones, too.

And the type of surgery, the crux of the matter is you have to be careful, not cut nerves which control the larynx, because if you cut one nerve, well, the patient is going to be hoarse for the rest of his or her life. I mean, for a woman, that's significant. And if you cut both nerves, you're dead; then the patient cannot breathe, and you have to do a tracheostomy, and you're going to have a tracheostomy for the rest of your life.

And I know we were treating some of these patients. The clinic was generous in the sense that they owned up for their mistakes. They gave free treatment for the rest of their lives.

JS: Hopefully, there weren't too many of these.

JB: There were no lawsuits then. That was interesting. There was nobody who thought, "Oh, can we sue Dr. Crile?" I mean, he's gone. You can't. That was a real thing [unclear].

JS: Well, you mentioned earlier when we were talking about the situation at FDA, and you said as an aftermath of the 1962 Kefauver-Harris Drug Amendments, the law changed drug clearance activities tremendously. Among other provisions, the manufacturers thereafter had to submit data to support effectiveness as well as safety to FDA.

JB: That's right.

JS: The agency is looking for physicians. So what is it that brings you to FDA then?

JB: Well, I had an interview when I was here.

JS: That's right. You were at Suburban Hospital at the time.

JB: So I was here in the Washington area, so it was easy to contact the agency, and somebody mentioned it to me that, why don't you look into working for FDA? I obtained an interview with Dr. Kelsey. Of course, she was famous. We were discussing my previous medical career, and she said, "You've done a lot of things, but what I really like is what you've done in the research line," like physiology. "This is the type of thinking I'd like to have in my department, people who understand the basics of physiology.

RT: I believe, based on the information you gave us, you had a research appointment

at Duke University in ’57 and ’58. Would that have been prior to Dr. Kelsey’s interview with you?

JB: Oh, yes, that was all before, yes.

RT: So you’d established yourself as a research person.

JB: Yes, yes, yes.

JS: Was the agency divided into this, I mean the Bureau at the time, divided into this section on INDs and NDAs, and Dr. Kelsey was in charge of INDs at the time?

JB: Yes. I suppose she was in charge of both. At least temporarily then, they had some other physicians coming in to take over the NDA part of it.

Well, of course, Dr. Kelsey’s great contribution was, while she was reviewing these drug applications, she picked up that this German tranquilizer seems to be causing some nerve damage, and so she wanted to get more information about that.

RT: Was that before the thalidomide episode?

JB: That was the thalidomide episode, yes.

Thalidomide was developed in Germany, and the German name was Contergan. This was a drug actually which was very well researched. They did pregnancy tests in

animals. They were all negative. But they didn't do one animal; it was the monkey. If they would have done the pregnancy test in the monkey, it would be positive. And they did it afterwards, after the whole thing mushroomed and thousands of babies were born without extremities. It was horrible side effect.

Canada approved, so only American women who had exposure to this picked it up in Canada.

JS: There were, I believe, 15-20 instances of children born with severe birth defects in this country.

JB: Yes.

JS: And certainly the firm, Merrill, had distributed this extremely widely in this country, 20,000 patients, over 600 pregnant woman.

JB: About that number.

JS: Apparently FDA didn't even know about this sort of wide distribution.

JB: Yes, it's true.

JS: And the law changes in substantial ways with respect to oversight of clinical investigations, and this I'm gathering is one of the things that the IND group was very

interested in. Right?

JB: Yes, right, correct.

JS: And how would you characterize the way the division worked with the sponsors of these INDs at the time?

JB: Well, the sponsors kept very quiet. They would submit an application and you wouldn't hear from them for months. They had this idea that you're the one to make those guys madder at you at FDA. You'd better stay out of their way. They don't tell them anything or let me call you. You just let them do their stuff. And that was how they treated us.

JS: Well, there were problems with Merrill, especially Merrill's attempt to influence the decision in FDA, and I don't remember if that was written into the regulations after the law, but perhaps that played into that sort of more acquiescent approach to the agency.

JB: Well, that's true, that is true. But the idea, like a blockbuster drug, that wasn't really well accepted then. I mean, Wall Street didn't follow the drug companies that closely, and you didn't read about things like this company is going to have a breakthrough or something like that. There was no talk like that.

RT: There was a little historical record prior to the 1962 amendments. I think you joined FDA in 1964?

JB: That's correct.

RT: Do you recall who was the head of the then called Bureau of Drugs and the kind of staff operating there at that period?

JB: Yes. Well, the Director, Bureau of Medicine -- that's what they called the establishment for medicine, the Bureau of Medicine -- the director was Ralph Smith.

RT: I recall in that period, which is about the time I joined the agency, too, that it was a rather small group, and they were located in one of the Tempo buildings on Independence Avenue.

JB: Yes. It was right on the mall, actually. It was a temporary building. We were in Tempo S. And we liked it because they were old buildings from the Second World War, but they all had air conditioning.

JS: Were these Quonset huts?

JB: No, they weren't Quonset huts. They were temporary, like you see the schools now. You go by some of these schools, and they have an additional building with the

annex type of thing, more like, I think the best would be a barracks.

RT: Yes, they were somewhat like that.

JB: Like barracks.

RT: Self-contained, with their own air conditioning.

JB: Yes. But the air conditioning unit, you could turn it off and on, you know. And we were walking the steps of the National Gallery of Art, which is one of my favorite museums, enjoying -- I'd walk over at lunchtime. They had a cafeteria in the museum, so I could have lunch there and go back to work.

And as far as Dr. Kelsey's management style is concerned, she brought you the work to your office, and she would put it down and, "Let me know what you think about this." So there was no, "I want a report in two weeks," nothing like that. There was no time constraint. She left and said, "I'd like to know what you think about this."

RT: Now, later, I'm sure it was later when there was some allegation, by congressional members anyway, that we were slow and had a drug lag.

JB: Yes. Well, that's true.

RT: A drug-approval lag.

JB: Yes. Well, there was no time pressure, so . . .

RT: Was the industry evidently concerned about that, or were they too . . .

JB: The industry at that time, they were not, they still had the idea the best thing is not to offend FDA.

JS: And this is still in the ‘60s, and, I mean, the process, I think, is still so young that there’s . . .

JB: It was young.

JS: Right. I mean, there are many different things going on. There is certainly, under the Act, where the process of the DESI, the Drug Efficacy Study Implementation, and I wanted to ask you about that. I guess before I do, though, I wanted just to quickly -- what would you guess were the number of medical officers in the Bureau of Drugs at that time, when you came on board?

JB: When I came, there were 25.

JS: Twenty-five total.

JB: Total, yes. That covered everything.

JS: That's not a whole lot, especially when you have all this new data coming in.

JB: Yes. So you practically knew everybody at that time. You knew all the physicians.

JS: I know you worked primarily with your immediate supervisor, in your case Dr. Kelsey. But Dr. Ralph Smith, did you have much interaction with him?

JB: He would come around and ask us, "What are you doing?" "Why are you doing that?" things like that.

JS: Well, obviously, the drug-efficacy study was huge, and evaluation of all the new drug applications . . .

JB: Oh, it's still going on.

JS: Still going on, that's right, but it's evaluation of all the new drugs between 1938 and thereafter.

JB: That was a great project.

JS: How were the medical officers such as yourself involved in that?

JB: Well, there was a separate group who dealt with that, and I wasn't part of it. I knew very well who was in charge of it. Paul Bryant was the name of the physician, and he was a good friend of mine. And he had a group of . . .

There was a huge project because you have to go to all those previously marketed.

JS: And was Paul Bryant a liaison with all of the National Academy of Sciences panels that did the initial, I mean the evaluations based on the company-submitted data?

JB: Yes, that's right. Paul Bryant, he was the FDA representative.

JS: I see.

JB: So he was in touch with the National Academy of Sciences, since FDA didn't really have the manpower to do all of that.

JS: That was huge, a huge project.

JB: It had to be done. It was a great thing to look at some of those things which we used that were useless and physicians kept using them anyway. I mean, that was a great undertaking[unclear].

JS: And amazing that these stayed on the market, so many, 40 percent or so of which were less than effective.

JB: Yes. I mean, in Europe, this had a tremendous impact to the Europeans' practice, because with the European medications, what they did is they made extracts of everything. If you had liver disease, you received a liver extract. It didn't do anything really. It didn't do any harm, but it didn't do anything. If you had ulcers, then they gave you extract of modilidine, which is part of the stomach structure. So they had extracts of everything. And this was the idea.

So this was all untested. And when they saw it, they knew that what the Americans are doing. Then they started to look at, maybe we should do something similar. The drugs they use, 90 percent of them might not be effective.

JS: So there was an international impact.

JB: Oh, yes. I know FDA had tremendous respect from the established medical establishment in Europe. I was in Germany, in Italy, at an international meeting, and I remember I was sitting at a table with some professors, and they were really eager to hear me. Why am I going to talk to these professors? They're all luminaries and they all know that I'm a low medical officer. They're looking at me and questioning me, and, you know, what's the latest from FDA? And I remember they were using broad-spectrum antibiotics, tetracycline. They were using an injection form, [unclear] injecting in the muscle tissue, and that's a useless procedure, and we knew it in the United States

because of low absorption.

JS: What was the correct way to administer it?

JB: Intravenous. And the intramuscular use didn't work really, but they were doing it anyway.

Anyway, it started this idea of doing tests, comparisons, clinical trials, studies. And then the Europeans are Johnny-come-lately. They still had the idea of the professor knows everything. If you said it works, it works.

JS: I don't mean to jump around, but I have to ask one question. Do you remember your first NDA that you reviewed?

JB: Yes. The first NDA -- it was an IND, actually.

JS: Yeah, I'm sorry.

JB: The first IND was about a medication, which is still around even now. It was proposed by a professor from Romania, Professor Hauslaun, and the drug she called H3, and it's supposed to be a drug which would increase your energy, and in older people it would have an effect of rejuvenation. It was analyzed, and it showed nothing else, but a popular local anesthetic, procaine, which is not used that much now, but there's no way that could produce the effects the professor described.

But they had groups going to Romania to receive this treatment. They would go there . . .

TAPE 2, SIDE A

RT: Doctor, we had a break in the tape. Would you continue with what you were speaking of, please?

JB: Yes, sure.

So this Professor Hauslaun, she organized some of these 20, 30 people would go there and would receive this injection therapy, and it's basically nothing but procaine and maybe some contaminants, but there was nothing there which would explain all those wonderful effects. But a lot of people believed it. I mean, it was strange. People without any -- there was no proof for it that it works except for the professor was saying that it works. But that was typical European type of attitude; the professor knows the best. That was very prevalent in Germany and, of course, probably Italy, France.

But in this country, things were changing then, because the professor would know a lot, but there were associate professors who would know more in certain fields. So this was something different.

But, anyway, that was this famous vitamin. Actually, they had a name for it, vitamin H3, and they were talking about it like a vitamin. There was nothing to do with a vitamin. It was a good, catchy phrase.

Still, I see some advertising pops up about this thing once in a while.

JS: Did it go forward to NDA status?

JB: No. It was stopped.

JS: Interesting that your first NDA came from the system that you had grown up in, the system where the professor, as you said, is the . . .

JB: The professor said it works.

JS: If the professor said it works, it works. And here you are, your first NDA, you're reviewing this application, and that's that.

JB: They don't do any test. If the professor said it, then it works.

JS: Among the earliest years in your tenure in the agency, are there applications, either that you were directly involved in or others, that stand out in your mind as representing major changes, policy changes, or just interesting [unclear]?

JB: Well, it was interesting. I mean, the concept of this clinical trial, I mean, Dr. Robert Temple had a lot to do with it because they had to develop these things, and the idea was, one test is not enough; you have to do at least two groups, two trials.

And I remember I was in the Division of Cardiorenal Pulmonary Drugs. This was

in the ‘60s, in the late ‘60s, when the new drug was promoted from England, Alupent, which was . . .

JS: Can you spell that?

JB: Yes. A-l-u-p-e-n-t. This was a very important asthma drug because this drug could be administered by inhalation, and the idea was fairly new.

But what in England happened is that there were about 11 deaths reported. And so my responsibility was to be absolutely sure that this drug is safe. So I received about 120 volumes of information. I had to go through that, and there were journal articles in Germany, patient reports from England, and it actually turned out that this Alupent turned out to be one of the safest drugs. You still use it. But there are some newer ones developed.

Alupent has some cardiovascular side effects, such as giving you a rapid heartbeat, so the newer products tried to eliminate that. But the concern was that it caused this abnormal heartbeat. That’s why people died, because it had this effect on the heart and the heart just couldn’t keep up.

In Boston, we had some abnormal cardiac rhythms, too, but I couldn’t find any.

So this drug came on the market and has been on the market ever since. It’s probably the safest drug.

JS: When was this?

JB: With Alupent, it was 1968 or something like that.

JS: Sixty-eight or so?

JB: Yes.

Then, after the Alupent, there were two or three other drugs that came on the market, again for treatment of asthma, inhalation drugs for asthma. They may be a little bit better; I really don't know, but they seemed to be. But the Alupent was pretty safe, and it's still being prescribed today.

So this was my exposure to this new idea that two studies have to have the same results or similar results; they don't have to be the same, but similar results.

I remember during that, one group was young people and one group was older, and I found out that the older people didn't respond to this medication that well, as did the young people.

RT: The concept of so-called double-blind studies?

JB: Yes. At the same time it was being developed, double-blind studies.

RT: About this time, when it was necessary to really assess the drug-approval process, I think the agency recruited a lot of physicians to the Public Health Service Commissioned Corps.

JB: Yes, Commissioned Corps. That happened, yes indeed. Of course, that was during the war in Vietnam, which brought in a lot of physicians.

JS: But wasn't there an appointment? It seems either late under George Larrick's tenure or early under Dr. [James] Goddard's tenure, there . . .

JB: Dr. Goddard was the one who organized this.

JS: Yes. There was, I mean, a pretty substantial group, maybe two or three dozen, maybe more, of physicians who were in the Commissioned Corps who came in, but it was only on a temporary basis, I thought. Is that true?

JB: Yes. That's how it started.

JS: What was the reason for this, and what were these physicians doing? How did they interact with the permanent staff like yourself?

JB: Well, Goddard brought them in because he realized that we have increasing amount of workload, and he wanted to have especially younger physicians. We had quite a few older ones at that time. He wanted to have a younger group.

RT: A lot of the younger ones, because that was about the period of the Vietnam War?

JB: Yes.

RT: And that did qualify them for deferment from the regular military service.

JB: That's right, yes indeed. This was sort of like we were the military service when they came to the FDA. We called them yellow berets. There are not green berets.

JS: Did they get involved in drug evaluation [unclear]?

JB: Yes, they were. Well, they were young people, well trained. They were really ideal to do it. And, you know, the agency had problems attracting young people, partly because there weren't many female physicians. Right now, for the female physician, this is an attractive position because she doesn't have to work on the weekends and she doesn't have to work nights. If you are in practice, you just have to do those things. And even if your family wants you, you still have to attend to your patients.

RT: During that period, was there an increase in the number of female medical officers?

JB: Yes. Soon after that, yes. I think the medical school classes now are more than 50 percent female. I remember at Duke University, the class was 50; there were two girls in the class. There were just not enough females enrolled. It was a rarity. Now, of course, it is, even if a physician goes into medical practice, when they have a family, it's

very difficult. Usually if you are in pediatrics and you have young children at home, and you see sick young children outside the home, chances are you're going to take something home. That's why we have a lot of female physicians who come in from pediatrics.

RT: As a medical officer reviewing and so on, did you have a direct or indirect liaison with inspectors in the field doing investigational work?

JB: Well, we didn't have much of direct contact, but there was a time when there was a possibility to go with them on inspections. But for some reason, you don't hear much about that. But there was, I think, three or four years when you could sign up and go with the inspector and see what they do. It was very good, I think. Unfortunately, it's not done now.

RT: Would that co-inspection approach be helpful in the review of drug applications, or more in terms of orientation to the regulatory processes?

JB: Well, it's regulatory processes, and you also get the idea of what the inspector is looking for and how he does it, because you wouldn't know it otherwise. For example, how you inspect that production line. Well, to better learn it. You don't learn it in school, you know.

RT: Counter-wise, would the inspectors' exposure to the medical officer have trained

them some in what you're interested in?

JB: Yes. It's probably that is true, because the inspectors are pretty much concentrating on the process, whether it's done properly, whether everything is labeled properly so there's no possibility for confusion. And it's, in manufacturing of medical products, the purity, the cleanliness, is absolute, because you cannot say, "Well, we used some peanut butter in this thing last week. We cleaned this out. I think it's going to be ready to make some medicine." You cannot do that because people are very sensitive to a microscopic amount of material, and it's very important. This thing is very detailed.

JS: Well, we had a huge problem with cross-contamination of antibiotics in the 1960s, and hopefully we learned and the manufacturers learned from that.

JB: Yes, yes. You cannot just deal with it like the ordinary thing. I mean, I'm reading a paper sometimes, and these people are good-natured. You know, they are top-of-the-line manufacturers and managers, and they say, "Why do we have FDA? Why? Why don't we let the marketplace decide which is better, which drug is better?"

JS: Well, actually . . .

JB: That's what I'm saying. We saw mistakes being made and we had a few deaths, and we had to do something because things were out of control. It's not like making shoes, you know, that one brand is better than the other; let the marketplace decide; let

not the government decide which ones are better. And these people think that they have a case, that why do we waste all this money on the FDA? Why don't we just let the marketplace decide? We had that.

JS: We had that. It didn't quite work out.

JB: Yes, that's right.

RT: The time came when there was quite an extensive overhaul of the drug-approval process. Can you speak a little bit of your experience in that event?

JB: Well, in the drug approval process, of course, you have to prove that the drug is effective, which meant that, really, to be absolutely sure, you have to compare the product to a placebo, which has no effect and is not supposed to have any effect. Of course, later on, we found out that there is such a thing as a placebo effect, and that has a lot to do with the physician. I mean, if you recall the days when there were no effective medications, people didn't recover from their illnesses. And we thought, well, it's the physician or the potion. It was basically the personality, the personality which can project hope. That has a curing effect. Of course, this wasn't thought of. But we see more and more of that from the psychiatrist, and the placebo effect is like 30-40 percent. The drug effect is 45, but that's very little difference.

But what they used to do is, with regard to the psychiatrists, they used to have conferences with the patients two or three times a week, no pills, nothing, and they have

cure. They have people recover. And that was the placebo effect. That was looked down upon, that was like snake oil, that's not the real thing, but it is the real thing. We are coming around, seeing that there is a positive effect.

I believe in it, that if you have a choice of physicians and you feel like you can work with somebody better than the other one, I think that's important that you work with that person because you get a more beneficial effect.

But anyway, that was the placebo concept.

JS: About 1978 or 1979, there was a push to rewrite the law in terms of the drug regulation, and it didn't, obviously, pan out. But do you have any memories of that or any . . .

JB: No. Well, I can't say. At that time, I was more into the generic drugs I was working with, and generic drugs were very attractive to a lot of politicians because the price difference was tremendous then. It's not that much now, but then it was. I mean, in the budget perspective, with generic drugs, you save 50 or 60 percent or even more. And, of course, a lot of physicians, especially the older ones, they wouldn't believe that the generic drugs are as good as the brand names. They really had to develop tests to show this to be true, or do the bioequivalence testing. They had to do that to show this to the physicians, and we are comparing effects because the chemical analysis was very similar. There's more to it.

It was interesting when I made a trip once to Puerto Rico. The Puerto Rican government was ready to promote generics, and they invited a couple of us to talk to

them at a convention of the medical association. Then I realized that the word generics, as they used that word, they would say [henetic]. What that means is the product is inferior. So we had to change. They told us the physicians and the pharmacists in Puerto Rico don't use the word generic. They instead use bioactive, so that's what we have to say now.

JS: [Henetic] in Spanish means inferior.

JB: It's not as good, yes. It's inferior to a brand-name product. How it developed, I don't know. But the local pharmacists don't use the word generic; that's no good. You have to use . . .

JS: I haven't heard that before with the use of generics in Spanish. I've heard that with respect to products that people have tried to introduce in Spanish-speaking countries, and the brand name of a product means something horrible in the language, and no one anticipated this. I never had heard of this.

JB: Well, it was in Puerto Rico, so I don't know. Maybe Mexico is different. I thought that was sort of interesting.

JS: How were you working with generics at the time?

JB: That concerned adverse reactions due to generics. They have the same type of

adverse reaction as brand names. That's what we had to say. As far as the adverse effects of the generic or brand name, we saw the same type of adverse reactions. So I think right now, generics are pretty much accepted.

RT: Now, the drug industry itself, did they, or when did they, if so, begin to press for equality consideration of generics versus brand name?

JB: Well, what happened is that one of the brand-name companies bought up a generic company, so it's in the same pocket. And they were, of course, against the generics for quite a while, until Valium -- I guess Roche is the manufacturer of Valium. And they claimed that generic Valium is not as good as the brand name, and they actually formulated the tablet with a V on it, so when you have Valium, you've got the real thing, the brand name, see the V on it. That's the real thing. These other ones don't have it. But I don't think that that's true. But it's very interesting. Some people say, well, this doesn't have the V on it; that's not the real Valium.

JS: Well, if they could put a lowercase V on it, it would have the same effect.

RT: Well, it's perhaps ironic. You mentioned Puerto Rico. In later times, much of the pharmaceutical industry has developed production facilities there.

JB: Yes, that's right.

RT: I suppose by reason of better economic labor and so on.

JB: Yes. Well, the labor is cheaper, yes, yes. I don't know what it is now, but it's probably that generics are well accepted there too. And it's really, it's a good saving, especially certain products like antibiotics. I think you are on safe ground to buy the generics because often it's made by the same company who makes the brand name drug. Abbott makes it, and the generic is also made by them.

RT: When one considers drugs produced outside the continental United States, the issue of equality and export-import values arise. Do you have any comment on that phenomenon of the export and the import aspect of drug regulation?

JB: Well, the problem is, when you import drugs, you have to be careful because some of the manufacturing which is happening outside the United States, you really have to be very careful and you have to inspect them and check them that it's the real thing, that you are getting the real thing, not some inferior product.

RT: Concomitant with that is the issue of drugs produced here and shipped to Canada, and then the allegation in some places that they're available at lower cost re-imported than they were when, than they would be when sold in this country.

JB: Yes. Well, I think it's true that a lot of the drugs which come from Canada were made in the United States and shipped out to Canada, it's coming back, the same thing.

But the Canadians have this arrangement where the government negotiates the prices for the drugs. Since you buy volume, you should be able to negotiate that. Why it's not done in the United States, I don't know, but it could be done here too. It would make it so much simpler. I hear this is done under Medicare and so on, the rules are very confusing, and you are dealing with hundreds of companies.

RT: I guess one of the principal issues, isn't it, is the integrity of those drugs, being assured that you're not receiving back counterfeits or repackaged drugs or something like that.

JB: Yes. Well, it is true that -- I'm not that afraid of drugs from Canada, but I don't know, some may come from Asia. You really have to look and check and double-check.

RT: Would it be safe to assume that the drug-protective quality of regulation in this country is paramount, is the lead, or are other countries approaching similar effective controls over drug manufacture?

JB: Yes. Well, it's -- some of these countries, they don't have much. They have a couple of companies who make drugs; that's about it. But where we are in the United States, we have a huge, huge industry, and it's not easy. And some of the drug prices are very high, and you find people here who are cheats, like they have dishonest pharmacies in Georgia or somewhere who want to use the half strength of this cancer drug.

JS: Kansas City, I think.

JB: Yes, Kansas City. Instead of using the full strength of this product, the pharmacist watered it down so he could make money on it.

JS: I just wanted to ask a couple organizational questions, and if this strikes you in any way, comment; if not, that's fine.

A couple things on organization, one on sort of the way this Center did business.

One is, in, say, the late 1970s, early 1980s, when biologics and drugs were combined into one large center, it only lasted for a few years. But I was curious if, from the standpoint of where you were in the Center, if you saw any sort of unusual impact? Were the drugs people in any way less better off or better off, say, by this union, or did it seem to have any impact whatsoever from your standpoint?

JB: Yes. Well, of course, I just can speak for myself.

One thing is interesting, that the biological products, the adverse effects are different from the regular drugs. They look sort of unusual. And these biological products, they interact with the system differently than just ordinary chemicals, and there are different type of adverse reactions. Anybody who wants to study them should spend some time because they do cause different type of reactions. That's why biologics and some other complicated products, many times you cannot even show that what you have is exactly the same as in the previous batch, because you have these moieties of amino acids, and you look at the structure, it's like this, and something can get out of whack.

Maybe there are physical infirmities. In some ways it's difficult.

RT: In regulatory orientation, historical perspective, would you believe there was any difference between the drug-control people and that biologics was one more, shall we say, regulatory oriented in terms of regulatory action versus education?

TAPE 2, SIDE B

JB: Well, I think the industry has to educate them, the physician population, because very few of us learned anything about biologics in medical school. They were not just around. No. And I think that it's very important for physicians to continue medical education. You cannot just stop it after you finish school and say, "Well, I know everything now," because things do change. I mean, in just a few years, you have companies with new ideas, and it's very important for physicians to continue and learn.

RT: So the field of biologics or regulatory oversight is newer and less in time than drug control. Is that true?

JB: Yes, it's new; these things are all new. You just have to take a look at the chemical structure and you'll be amazed what they have. I mean, it's not just an ordinary chemical structure. It's all over. You can memorize it.

Well, actually, the manufacturer cannot be absolutely sure that what they produced is an exact copy because we can't tell the difference, really.

But we're going to have more and more biologics, and eventually treatment of cancer is going to come down to these products which will attack the cancer cells, not the body, and we have a lot of anticancer drugs which will attack the body just as well as they attack the cancer cells, and it's one of the worst things you see. As a pathologist, you see a woman about 40. She dies, and then you find no cancer at all. She died because of the therapy.

We have been using poisons, and that's not good enough, but I think with the biologicals, we'll be able to really go down to the cellular level, differentiating the cancer cells from the regular cell. I mean, that's the crucial thing that you have to do. Well, it's happening.

JS: In the area of drugs, within the last year in the area of drug safety, it's been an interesting year, with all the fallout from the COX-2 products and so on. Just your opinion here: Is there something that we can do better, or are we doing what we need to right now? Is there anything that we can do better as an agency when it comes to drug-safety issues?

JB: Well, I think it's been proposed before and it keeps coming back, that the Office of Drug Safety should be a separate group, not part of FDA. It should be outside, and so it would be completely independent as far as the post-marketing evaluation, because right now the people who approve the drugs, they're not going to, they're going to feel bad about condemning the drugs FDA approves. That just doesn't work right now.

JS: Do you have an opinion about the wisdom or lack of wisdom of situating that responsibility, not only outside the Center for Drugs, but outside of the FDA itself?

JB: Well, it depends how it's done, you know, the little details. But the point is, you have to have independence. We have no connection with the drug company and no connection with the group within FDA.

JS: With the approving officials.

Do you think it might be possible to do that, yet have the entity remain within the agency?

JB: Well, I don't know. That's a possible thing. It could be tried; it certainly could be tried. But I can see how the independent people would have no pressure from the colleagues at FDA.

JS: You've been here for quite a while, and I'm curious, looking back on things, on the relationship between those in the agency who approve the application, the INDs, NDAs, and those who are involved more in post-marketing surveillance, has there been historical tension between the two groups?

JB: There was some tension in the way that, when there were Advisory Committee meetings, they wouldn't allow the ODS group to testify.

JS: Which group is this?

JB: The Office of Drug Safety.

JS: Okay.

JB: Instead of somebody from Drug Safety, they have somebody else from the division who approved the drug to give a presentation and this type of thing. There was some disagreement there.

JS: Who would make that decision that ODS would not be present at the Advisory Committee meetings? Would that come from the Director's office or something?

JB: The director's office, sure.

JS: Okay.

JB: What I'm thinking is these are completely honest people, see. They think they are doing their best, so I'm not saying that anybody's a crook. No. Nobody's being paid off here. It's just that I personally think you work some of these officers, medical officers who have these drugs, they're working with them for six months. They practically live with the drug. And when they approve it, they feel that's the best they could do. But if something comes up later on, it's difficult to be completely unbiased, try to explain it in

another way.

So I see a little bit of tension there with the Office of Drug Safety. But I think FDA through the years, as it developed, has done its best. But not everything is a hundred percent.

But just like when you look at medical care as far as emergency care, it's outside FDA more or less, but you really have the blessing of these helicopter transports, which means that if you have an accident out somewhere in Hagerstown or somewhere, you can get the best medical care which is available. Before the establishment of a system, you had to wait an hour before somebody would show up, you know. They would take you to the local hospital, and the nurse might be on call. So she comes in and she says, "Well, this guy's in pretty bad shape. Better call for a doctor." So it takes hours before he gets there. That's the way it used to be.

Now you have -- I remember, you know, anybody can call a helicopter basically. My first helicopter case came from the western part of Maryland. He was in an accident and he had some blood on his face. The policeman called the helicopter. They brought him in. Turned out he had a broken tooth; that's all. But that's what happens when you let bystanders make the decision.

But, actually, this works very well in a serious injury. This guy didn't need this transport, but he got it anyway.

JS: Had a nice helicopter ride.

RT: Well since probably the days of George Larrick, we have had as Commissioners,

for the most part, medical doctors or veterinarians, someone trained in the medical discipline. And that's, I guess, indicative of the fact we seem to be trying to provide more safety and efficacy in the drug control.

JB: Yes.

RT: In earlier times, that was maybe balanced more with food and other products that we regulated.

JB: Yes, yes.

RT: Do you have any particular suggestions? I know you're still active, so we're not trying to put you on the spot. But if you have any particular suggestions -- and John's kind of alluded at that -- for any policy changes in regard to this whole area?

JB: Well, I think the real thing, and that would be that tremendous improvement could be achieved in drug testing if one drug would be tested against another to see which is better, because right now what we are saying is, "Well, this drug has efficacy, it works, but we never say that's better than this other thing, and that would be a real step forward, when we can do that and say, "This drug is definitely better than this."

RT: Do you think that the pharmaceutical industry would be opposed to that?

JB: I'm sure they're averse to this because all of these me-too drugs wouldn't be developed.

JS: You look back at the Kefauver hearings and the possibility came up, they weren't too happy about that possibility.

JB: No. That's not . . .

JS: But that's a good point. That's what people, that's what practitioners . . .

JB: Yes, and it's better than this other thing? Well, we don't know for sure. All the things we say, it works.

RT: Doctor, if there's any other areas you'd like to cover, we'd welcome doing that. If not, we can close.

JB: Well, we can get together maybe later on.

RT: That would be great.

JB: We can discuss some other points.

JS: Absolutely.

Thank you so much for all the time you've spent with us this afternoon.

JB: Well, I enjoyed it because you have been a very good audience. Not everybody wants to know about these things.

JS: We were concerned that this might, us on one side of the table and you on the other, create some sort of tribunal appearance with this long table here, but I'm glad you obviously felt comfortable with the settings.

JB: Oh, yes.

RT: That's one of the riches of this oral history program. You get some of that. It's not in the written material necessarily.

JB: No, that's right. I don't mind coming back, you know.

RT: Great. We certainly appreciate that you've shared such a wealth of experience you've had, from a refugee to a very important role in this agency.

JB: Well, I mean, really, what makes me going and keeps me working is that I can see how things are developing continuously in the field of medicine, what improvements are occurring, especially with these new imaging modalities we have.

I remember when I was just a fellow in training, that we used to inject air, and we

used to put a needle in the spinal canal and inject air so it would bubble up into the brain and it would serve as a contrast area.

RT: We've come a long way.

JB: Yes, we've come a long way, really.

RT: Doctor, we'll have this transcribed and we will be in further touch with you. Thank you very much.

JB: Well, I enjoyed it, and you were pretty nice. It's always good when somebody listens to you.

END OF INTERVIEW