Dr. Lewellys Barker
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Interview with Dr. Lewellys Barker conducted in Rockville, Maryland.

Conducted by: Jessie Saul.

Saul: So today, basically I wanted to talk to you about your time at FDA and while you were with NIH.

Barker: When I started, it was NIH. It became FDA in 1972, and it was the Bureau of Biologics before it was the [Laboratory of] Biologics.

Saul: And then, moving into your time, the issues that I was talking about that you were, Dr. Klein told me that you were head of the Blood Division in the Bureau of Biologics. Is that correct?

Barker: Yes. It was blood and blood products, director of that division in1972 and 1973.

Saul: And what brought you to that position?

Barker: Well, the short answer is hepatitis. The longer answer is, I trained in internal medicine at Johns Hopkins and Bellevue Hospital in New York, and I came to NIH to the Division of Biologic Standards to work mainly with vaccines, viral and rickettsial vaccines.

Saul: For hepatitis?

Barker: No, originally rickettsial, and I worked a little bit on a variety of different kinds of vaccines: smallpox, flu, mostly viral vaccines. One of the areas that I got involved in there was hepatitis research. None of the hepatitis

viruses had been discovered when I came there in the early ‘60s. But in the late ‘60s, something called the Australia antigens found by an NIH group -- Harvey Alter and Barry Blumberg and that, as I’m sure you know, turned out to be the piece of the hepatitis B virus. We got very involved in that because it looked like, for the first time, there might be a specific test for what we thought was *the* hepatitis virus that caused post-transfusion hepatitis. And so we established a very active research program. We also, by the early ‘70s, were dealing with products from manufacturers for testing blood, donated blood plasma for known as hepatitis B. It went through several name changes back in the beginning.

Saul: What was the division of biologics? Were you doing research?

Barker: Yeah. Actually, there were several groups at NIH that were working in this field. The NIH Blood Bank had people working on blood-transfusion hepatitis. They did one of the very important studies, for example, on commercial blood-bank blood from paid donors, and they looked at other kinds of markers, things like that to try to figure out a way to test blood. The NIAID had a lab that’s really one of the outstanding labs in the world, the Blood Bank and the NIAID lab that have for many years been under the leadership of Harvey Alter and Bob Purcell, and were doing hepatitis research. And I also worked for a while with Ray Shulman who I think is in Arthritis and Metabolic Disease. He got interested because he was interested in hemophilia, and there was quite a bit of hepatitis in people with hemophilia. And also, the original antibody reagent actually, I think,

came from some of his patients with hemophilia .So there were at least four different groups on the campus, and we knew each other and at times we collaborated and published together. We also worked with people at CDC who were working on hepatitis. So there were a number of foci of hepatitis research in the different places, and eventually FDA and NIH and CDC. Actually, we got fairly well coordinated in some areas at the direction of the Department of Health and Human Services. I guess that's what it was called then, and specifically Ted Cooper, who was assistant secretary of health. There was a federal concerted effort on hepatitis, so we both worked together and worked separately on what we were doing.

Saul: I was curious about a mandate for the FDA to do research. I mean, it wasn't the FDA...

Barker: The Division of Biologic Standards, which is where I came to work in 1962, was part of NIH. It is actually -- you're a history person, so you'd be interested in this. If you go back through history, you'll find that it was the original seat of NIH. The laboratory, I think, was Kinyoun's lab something like that that…I can't remember the names of all the … But there was a succession of entities which dealt with what we now call biologics and dealt with vaccines and serums and antitoxins. And over a period of 50 years, that seed expanded. So it was really where the NIH began, and it was a research organization. Actually, the Division of Biologic Standards was a research and a regulatory organization. It was the only, I think, part of NIH that had what you would call regulatory

responsibilities and licensed biologics in the Public Health Service, the Public Health Service Act centennial celebration. Anyway, there's a lot of interesting history there if you get to the centennial celebration. So when I came there, I came after I took my medical residency, and a lot of people came to NIH to sort of get research experience. After they'd gone through some phase of their clinical training, it was considered a good place to go for research experience, so that's really what I came here for. But what happened in the Division of Biologic Standards -- subsequently the Bureau of Biologics and then CBER -- is lots of people, particularly in the '60s, I would say most people had what I would dual careers, research and in regulation. That is to say we had research labs where we did clinical research, but we also served as reviewers of the applications for the licenses from manufacturers. So that was what I was doing and just about everybody was doing in biologics under its various names that moved from NIH to FDA in 1972, all the various factors. I'm not sure what all the factors were. I know what some of them were. But anyway, things did move around occasionally in the federal government from one agency to another, but some things changed and a lot of things we maintained, as you know, Biologics stayed on the NIH campus, still is on the NIH campus, still has a really extensive laboratory and probably some clinical research activities as well as having a very large menu of regulatory responsibilities. Biologics was considered a good idea, for various reasons, to be for people with regulatory responsibility research because they were

considered later on a little bit more complicated in some respects than products, and it was thought that if you really understood what biologics were about through trying to work on them in a research lab, you'd better understand the products that were being submitted for licensure and control. You know, biologics was very involved with some of the viral vaccines, including invention of the rubella vaccine. Of course, the polio vaccine back in the early '50s -- that was really the central activity of blood and blood products. I guess it would come under biologics for a long time, but in a sense that was…I actually worked for both areas. I worked in the vaccine area and I worked in the blood and blood-products area. That's a long answer to your question.

Saul: In doing research. It wasn't doing product-oriented research.

Barker: Well, yeah. A lot of our research was on products. Most of them were not products that were invented here. They were by and large developed elsewhere and the research in many cases was what I would call relevant research; that is to say, research on tests for safety, for example. Going back to the beginnings of biologics, the Public Health service was passed over due to a safety-related issue of contamination preparation. So safety was always a big issue with biologics. The safety issues with biologics are quite different from the safety issues with drugs. They relate, for example, to contamination with infectious agents because biologics very commonly, at least historically, came out of either animal or human sources or cell cultures, which were sort available in test tubes. But there was always the

potential for drugs, on the other hand, or chemicals made in chemistry laboratories on a much larger scale, and they don't really have this issue of contamination with these agents, which is still an issue. The West Nile virus being studied is one of the agents and probably not too difficult to deal with, but challenging, and something like the variant CJD, the cause of, you know, related to bovine encephalopathy, the human counterpart disease. That's a very complicated issue for biologics, but it's another example of where there is concern about blood products. It's more difficult to deal with. Take the West Nile virus…an enormous progress quite recently on tests for West Nile. I mean its technology that can be brought to bear very rapidly. That's not the case where you have a virus that somebody can get going in your laboratory to work to develop a test for so that's the progress on West Nile virus. Then there is post-transfusion disease. I mean, post-transfusion transmissions and it probably won't affect things like the virus process is in place of blood products. But with all the single-donor products, it's a small problem and we don't know what the West Nile epidemic is going to do. But if it does something like the AIDS epidemic, it could grow, it could grow. But I would say with West Nile, they'll be able to cut it off at the pass.

Saul: Going back to 1953 when you got there, you were involved with vaccine research?

Barker: Specifically, epidemic typhus, another historical epidemic. It was fascinating. One of the things that was interesting about it is it's a little bit

esoteric. You can count the people in the field on your fingers, and I kind of like that. But I eventually got into other fields which were, frankly, somewhat more relevant. Hepatitis is a disease spread by mice in social disruption.

Saul: So, how did you get in?

Barker: Well, I was, I mean, it was one of the things that was going on, and other people working there were doing. We were given, not complete freedom. I mean, we were assigned to some areas, but then we were also allowed to work in other areas there. This is common in research settings. This struck me as an interesting area of sort of unsolved . . . I mean, rickettsia not viruses; they're sort of between viruses and bacteria. Rickettsial problems were really well understood. They were treatable by antibiotics. But, in any case, I was interested in virology and I worked with a handful of different viruses, and hepatitis was just one of the ones that I was attracted to because it was obviously important. A lot of hepatitis in clinical medicine, and we didn't have anything in the way of specific tests for it. Because by then, most of the common viruses had been identified in the laboratory with either cell culture or one way or another, people had gotten their hands on most of the important viruses causing human diseases. Hepatitis was out there. It was one of the last important diseases or disease, but we didn't have a virus, at least in the laboratory we didn't have a virus. So that was an interesting thing to work on.

Saul: What happened once you made the switch to hepatitis, or did you ever

fully switch?

Barker: Well, I can't say that I was ever pure. I always have a few different things going. I mean, I would say hepatitis became my major interest after the Australian... I was spending most of my time on hepatitis, but there were some other things. I was working with smallpox vaccine initially, similar period, but we essentially dropped that in the early '70s because we stopped using smallpox vaccine. But I was working on that from the standpoint of major concern for totally different reasons. But at the time it was a concern because we knew children…smallpox vaccine so early. What can we do about…? Can we come up with a safer version of the smallpox vaccine? Clinical trials were a particular interest. There weren't very many. Somehow I got into this field through diseases and smallpox vaccine, a relatively small area, which was that you get to know everybody, smallpox in the late '60s and early '70s has changed. It's come back.

Saul: So what were your areas?

Barker: Blood products. When I became the division director, do that, mainly because of the obvious sort of immediate importance of hepatitis testing and its application. It was not after we became part of FDA. He became head of the Bureau of Biologics. That was sometime in 1972. And he asked me if I was interested in moving from the Viral Division to the Blood Division, and I was a little bit because although I'd done some clinical training I consider myself an infectious disease person. But at that

particular moment, and, ironically, ever since, it seems like infectious diseases became sort of a centerpiece of blood and blood products. So I said sure and went to work with him. There was a lot going on and there were other areas of blood and blood products that needed general administrative responsibility, supporting the execution of various responsibilities, which included, at that time most of the inspections of blood bank. Not licensed because they weren't interstate commerce. But starting somewhere in the early to mid-'70s, the field of blood transfusion came under some degree of FDA regulation.

Saul: Hepatitis?

Barker: Yeah. Most transfusion hepatitis, one of the best early descriptions of that was in World War II in 1943. But what was known as serum hepatitis had been described much earlier and was known to be associated with various forms of therapy. It was a fascinating but with yellow fever vaccine human plasma, which actually came from students public health school, and the yellow fever vaccine caused a lot of hepatitis. It's a very interesting story. But certainly the hepatitis story goes back to the 19th century. And it actually was the vaccine for smallpox. Actually, it was in the early days of blood transfusion -- let's say the 1930s, pre-war days -- the greater concern with blood transfusion was syphilis. But a related concern was hepatitis. Hepatitis became more obvious and better documented when plasma was used in World War II for treating blood loss and injuries. So there were some people that took a lot of interest in a

clearly higher risk of blood collected from paid donors, particularly commercial blood banks compared with volunteer donor blood. That, among other things, socioeconomic risk factors as well as things like injection-drug use. We would have teams. We'd usually form review committees and I had the lead responsibility for some of the original test applications. And, again, even then there were a lot of diagnostic tests that I'm not sure if they came under any FDA scrutiny or Division of Diagnostics. But the test for hepatitis came under, originally, DBS, but shortly after that regulations, because they were going to be applied to blood and blood products, they were specific indications. The original tests had been designed for clinical applications on patients.

Barker: Abbott got the second one, test license. I can't recall for sure whether they had INDs for those tests or not. But in any case, there used to be, and still to some degree is, a fairly interactive process where we would see versions of tests as they were being developed, and we were responsible then. Biologics used to publish something called additional standards. They have kind of general standards in the *Code of Federal Regulations*, if you're familiar with those documents, things like this.

Saul: Oh, yes, I see.

Barker: And there are a lot of -- this is the one that has the biologics standards in it. And then there are these additional standards, and so we were responsible, I think we wrote some additional standards -- they may still be in here for all I know -- for hepatitis tests. And, in fact, there were

rules and regulations, internal, which I don't totally recall, but I know FDA wanted the standards to be published before licensing. I don't think that's necessarily the case anymore. I think they've gotten away from that. So we had relative responsibilities. We actually met with the manufacturers. I inspected their facilities. We tested their products in our laboratories. We had research programs using their products. They had research programs, and we would compare data. So there were a lot of elements, if you will, to getting a product on the market that involved interaction between the manufacturer, the Division of Biologic Standards/Bureau of Biologics, regulatory agency, other researchers, including people on the NIH campus that we already talked about and people scattered around, the Red Cross and academic medical centers and so forth. And there would be -- I'm not sure how much, but we definitely had some meetings that would bear some resemblance to the workshop that you went to recently. With hepatitis, it was kind of interesting. The National Academy of Sciences, NAS-NRC, had kind of a longstanding interest in hepatitis that went back to the problems with pool plasma and World War II and post-World War II, and so I think -- I don't think, I know that some of the first meetings involving hepatitis testing were downtown at the National Academy. I think there was one in 1969. In fact, John Finlayson, if you were there at the beginning of the West Nile workshop, he referred to, I think, one of those very early meetings on hepatitis testing, you know, use of this new test. There is always quite a

spectrum of, well, it is a new test, is it a really good test, is it really going to be helpful or harmful or confusing, and initially there are a lot of unanswered questions about new tests. We went through that fairly well with the HIV test, although we managed to move fairly rapidly through the issues. But with hepatitis, there were issues: how meaningful is this test? And so we participated in various meetings. And essentially, as I said, I think the test was licensed in '71. The first articles were published strongly linked the Australia -- it had different names -- serum hepatitis, hepatitis-associated antigen, several different names coming from different sources. But it was pretty clearly linked with post-transfusion hepatitis in 1969, where two articles, one from Fred Prince in the New York Blood Center and another from Ricucci in Japan, which showed this strong linkage of blood that contained the antigen with serum hepatitis and recipients of that blood who would also develop the antigen. So that really raised the index of suspicion pretty high that this was an antigen associated with hepatitis virus, and so testing for the antigen would be a useful way to try to get rid of the blood units that showed it, it got rid of some of them; it would get not get rid of all of them. That's when we discovered what was first known as non-A/non-B hepatitis, which didn't bat an eye at the hepatitis B surface-antigen test because it was caused by a totally different virus, it turned out to be. The regulatory process has multiple components. And, as I say, back in the Division of Biologic Standards, in the early Bureau of Biologics days, we kind of did

everything, from developing standards, including laboratory standards as well as written standards. We had a little panel, for example, that tests had to -- manufacturers' tests had to be run against this panel, and they had to detect the positives and not detect the negatives in the panel. It was very primitive, the original panel. I think things are much better designed these days than they were then. But still, it's the same. This goes back to the beginnings of biologics. Biologic standards by and large originally were in vials, and they're used in tests, developed at the very beginning by Paul Ehrlich for tetanus and diphtheria antitoxin. Standard antitoxins and standard toxins. Well, the same principles -- some of them are still in place, you know, biologic tests. You have to get some standards. I mean, biologics, compared with drugs, are not very pure, and they're much more heterogeneous serums and things like that, which contain a lot of things besides the active ingredient, if you will, and you can't weigh and measure them in a chemistry lab the way you can drugs. So that's what biologic standards are all about. And so we made the standards and we did the tests and we reviewed the documentation and we inspected the manufacturers' facilities and processes and interacted with researchers. It was very interesting, actually. It was a lot of fun. I enjoyed it tremendously.

Saul: Did you interact with others, bring in external experts?

Barker: Yeah. That was, I mean, things like these National Academy meetings. There was a series of hepatitis meetings. I have all those books at home

somewhere, I think, starting in, literally starting in ‘69. Actually, I think one of the first conferences was San Francisco, and then there was one here downtown. We were always involved in basically planning and organizing these things. There would usually be NIH biologics, NIH research people, eventually FDA, CDC. Well, originally there was a short list of academic centers that were actively in the field. Now it’s probably an enormous list of people. The hepatitis field isn’t that big, I guess. HIV/AIDS field is everywhere. I do not think there’s any academic study in that field. In fact, as I said, going way back, the abiding philosophies in biologics was it was important to be part of the research community as well as exercising the various regulatory functions that was considered important to the part of the research community. So we published papers, did all the things that people in the research community do, as well as doing regulatory things.

Saul: Sure. Tell me about the relationship between the biologics community and people at NIH. You were on the same campus. Did you work with others?

Barker: Yeah. Actually, there was a time -- and I think it was before my time -- when the NIH Blood Bank -- I believe it was part of the Division of Biologic Standards; I don’t know if you’ve talked to Paul Schmidt yet.

Saul: Yes.

Barker: He would know about that. Paul’s a great historian. So, as I said, I think by the time I got involved, the NIH Blood Bank was part of the Clinical

Center and not part of the DBS. But still, there were pretty close ties. The people knew each other and they worked with each other. Well, you know what the NIH campus is like. It's not that big. Although people tend to be focused on what they're doing right in their own laboratory, it was not that difficult to either pick up the phone or walk over and visit one or another. I was a blood donor all my life, so I used to be in the NIH Blood Bank on a regular basis, and I pretty much knew the nurses better than some of the other people. But I knew Paul Highland and Harvey Alter from way back, and we had a pretty good, I think, collegial relationship. I still consider a lot of these people old friends, scientific friends and colleagues, although I've totally changed fields several times since then. I'm not in the blood field at all anymore, pretty far removed from it.

Saul: Can you talk about the process?

Barker: About what?

Saul: About being a blood donor.

Barker: Being O negative, they always wanted me to come over and donate blood. I did many times.

Saul: If we could talk about safety practices for a second, I've talked to people over at the Blood Bank -- Paul Schmidt, Paul Vaughn, to people who've been involved over there -- about the safety practices that were in use in the Blood Bank itself. And I was wondering, in the research that you guys were doing at the Division of Biologic Standards and the Bureau of Biologics, how -- what were those safety practices, especially when you

were dealing with hepatitis? What were the safety concerns, first of all? What were the goals of safety practices in general, and how did those change over time?

Barker: Well, let's see. Are you talking about lab safety?

Saul: Lab safety particularly, but also as it refers to you. There are two kinds of safety practices that I am interested in, one is in the laboratory itself, keeping lab techs and scientists safe and trying to ensure that hepatitis wouldn't be spread within the laboratory. The second one is practices designed to enhance the safety of recipients of products.

Barker: Yeah. Well, I mean, our whole interest in hepatitis was related to your second. I mean, that's the area. As far as laboratory-acquired infections and laboratory safety concerns, that's another field that has changed dramatically in my lifetime. When I started working with rickettsial diseases that was a big concern with rickettsial diseases, because we used to do things. You're probably familiar with Waring blenders. We used to grind stuff up in Waring blenders, which are fantastic for producing aerosols, frankly, and you grind up a milkshake or whatever in a Waring blender and you open it up, you may not notice it, but there's a cloud of stuff that will come out of there. Well, that was a cloud of . . . We used to grind up eggs, actually, in Waring blenders. So I was trained very early on to do a number of things, nothing like what's done now. I mean, when I started in the lab, pipetting was all done by "mouth" pipetting. You will not find anybody in a lab these days going to do a container of something

with a pipette in their mouth. But that's the way we did it. And it's interesting. There were two different kinds of pipettes used in laboratories on the NIH campus, and they had a central supply. For all the infectious-disease labs, we had mouth pipettes, which had little cotton dealies in the top, and these would be in museums. Paul Schmidt would probably have some, but you won't find them in use. And then the chemistry people, they didn't use these cotton things on their pipettes because I used to be amazed . . .Dave Aronson can tell you about some of this because Dave Aronson was kind of a clotting, blood coagulation, more chemical than infectious-disease type person. And I used to go into his lab, and he'd be pipetting up this human serum with just glass pipettes. Everything was glass, incidentally. That was totally changed over to plastic during, while I was working in the lab. It was glass, and we would autoclave everything between uses. But it's pretty easy for accidents to occur. I don't know why all the coagulation people didn't get hepatitis or something from swallowing stuff accidentally through their glass pipettes, frankly. They probably didn't get it because, at least hep B doesn't transmit very easily by the oral route, because I know they must have occasionally swallowed a little bit of that stuff they were pipetting. But anyway, we were -- in the rickettsial lab, we were very concerned, and despite our concern and whatnot, we had several laboratory-acquired infections while I was there. As far as laboratory-acquired hepatitis infections, I really don't know. I don't recall any that we actually knew about. And we took a fair amount

of precautions. But the kind of thing that can cause laboratory-acquired infection was an accidental needle stick, obviously, or an accidental break in a glass test tube, glass test tubes were in. But everything, when I started, everything was glass, glass slides, glass test tubes. In fact, when I was giving blood transfusions to patients, we used glass bottles, which were pretty awful, actually. There were a lot of problems with glass bottles. But they got away from those. We totally switched over to plastic.

Saul: Was the switch to plastic, was that a result of a particular stimulus or a goal or . . .

Barker: Well, you'd have to talk to people from Baxter, but there were a lot of reasons for it, I think. I mean, glass bottles had rubber stoppers. There was a real problem with bacterial contamination, I would say, which is actually still a problem, interestingly enough, in platelets, but for different reasons. But these rubber-stopper glass bottles, I mean, they were -- I don't like to think about them anymore. Then we had rubber tubing with steel needles that you'd poke into the glass. And all of this stuff was reused, incidentally, so it would be sterilized, to the best of everybody's ability, by autoclaving. But one of the things that was known, actually, way, way back was that the hepatitis virus was a very stable virus, and if your autoclaving was somehow, for some reason inadequate, it was possible to still have the virus around. Anyway, I don't know. There were various stimuli to going to plastic. One of them was the desire to separate

plasma from red cells, which is now pretty routinely done in blood banks. You probably know that. And that's done very easily with plastic containers, which you put in a centrifuge, spin, and you just squeeze them. Before that, with the glass bottles, you could do it, but you had to go in with a needle and you increased the chances of contaminating the contents. It was -- things have improved a lot. In many areas, things have improved a lot. I mean, plastic containers made it possible to do all the manipulations of blood, separating it into components, plasma and platelet and red-cell components, without entering the container. It was all done in a "closed" system. And that was a big advance, frankly, the closed system for processing blood. So the contamination now, the opportunity for contamination comes when you stick the needle into the skin and you get a little skin plug, and no amount of cleaning up can totally assure that the skin plugs won't ever have any bacteria on them. So there is contamination--platelets particularly these days, and there are probably reasons why there isn't a lot more. Which relate to the leukocytes cleaning up things initially.

Saul: Safety practices?

Barker: Yeah, safety practices in general. Well, safety, as I've already said, the history of biologics, going to the absolute beginnings, the beginning of the 20th century, related to safety. And, you know, to get a biologic license, it had to be "safe, pure, and potent." That's what the PHS Act says. Safety, of course, is always a relative. I mean, we're a society that we like to be

risk-free 100 percent. There isn't anything that's risk-free. Driving a car isn't risk-free; walking across the street isn't risk-free, as we know; riding a bicycle, which I do, isn't risk-free; and transfusing blood is not risk-free. To this day, it's not risk-free. But the sort of, I don't know, gold standard for biologics was to make them ideally risk-free, but from a practical standpoint, as low-risk as possible. You know, you look at all the vaccines that are out there, and they have risks, but they're, generally speaking, quite low risks. We're worried about smallpox vaccine because it's riskier than measles vaccine. Measles vaccine is not risk-free. It produces some problems, mumps, rubella. Yellow fever vaccine has recently been causing some considerable problems. So all these things and flu vaccine. They're always evaluated in sort of a risk-benefit manner, and it is desirable for the benefits to vastly exceed the risks. That hasn't always been the case, but generally, for most biologics, I would say the benefits tended to vastly exceed the risks. You probably have come across this in various places, but with blood transfusion, hepatitis was a recognized risk in the '40s and '50s and '60s. But it was considered, you know, some people say we were tolerant or accepting or whatever, but I guess the benefit-to-risk ratio was considered favorable for patients who were exsanguinating. It was better to transfuse and maybe they'd get hepatitis, but to not transfuse them because then they wouldn't get it because they'd be dead. So the benefit-to-risk ratio is considered favorable even though it was clear that these were risky products, there

were things that were done about it. Donors were asked whether they had a history of hepatitis, for example, and other things that were evaluated like enzyme tests. Way back, they were evaluated. I was involved in some of that very early on, actually, when I was in clinical work and looking at enzyme tests as a way of trying to reduce the risk associated with blood transfusion. Well, enzyme tests were really discovered by a couple of people at Memorial Sloan-Kettering, put in the literature, Wroblewski and Ladue, in the mid-'50s, around '56 or '57. I actually did some little research projects, when I was a medical student, on enzyme tests, mainly for heart attacks, which is another application of the same enzyme tests. They were called SGOT and SGPT at the time. But the Blood Bank got involved with these tests for hepatitis, and I was looking at them for both heart attacks and people with clinical hepatitis, and they were quite useful and to this day are used to diagnose heart attacks and clinical hepatitis. They've stood the test of time. And they were evaluated but didn't actually, weren't considered that helpful for post-transfusion hepatitis. Another clinical center did one of those studies in the '60s. Bill Miller, who has been in blood banking all his life, is, I think, the author of a clinical study. Probably one of the reasons they didn't seem to work as well is a lot of carriers of hepatitis B had little or no enzyme elevations, and the same thing was true of hepatitis C, so it wasn't a real reliable, didn't seem to be a real reliable test in the early evaluations. But people were always trying to make blood safer. I mean, not always.

During my years, we always knew. I mean, I remember when we would give people blood transfusions, and we knew there was a risk that those people might come down with hepatitis in a few weeks or a few months. So I guess, generally speaking, blood transfusion was used somewhat conservatively. You didn't give it for ingrown toenails. You hoped people didn't give it for ingrown toenails. You gave it for people who were losing blood and it looked like they wouldn't do well unless they got a blood transfusion.

Saul: Sure. Going back to the in-lab practices, when you started in the late '60s, were there -- what kinds of procedures did people take ?

Barker: I started working in the early '60s, and that's when I was telling you we had these mouth pipettes, so I actually started in the '50s, when I was a medical student with mouth pipettes, and we didn't have any of these hoods, laminar flow hoods. Almost everything we used was reused; that is to say, the pipettes and the test tubes and the flasks were washed and autoclaved, and then they came back and we'd use them again. I remember the pipettes. We used to drop them into, I forget, some sort of smelly solution or formaldehyde or something, and then they'd go and get washed and autoclaved and come back with new little cotton things in them so we would hopefully not suck the contents into our mouth. It's amazing. But while I was there, I would say by the '70s we had devices so you were no longer doing this and we had laboratories somewhere between, I would say, the mid-'60s and the mid-'70s switched over almost

entirely from glass to plastic, plastic being disposable. You didn't reuse anything. We got away from mouth pipetting to pipetting with these devices, which are still used. There are a variety of devices now that are used for pipetting. And also, not just for protecting the workers, but also for protecting the materials we were working with. We got into using laminar flow hoods. I mean, cell cultures, which are what are sort of the major, one of the major tools of virology laboratories of cell cultures, there's always a risk of contaminating them, contaminating them with things that are in their mouth or things that are in the room air or whatever, and that messes up your experiment, so people didn't want their cell cultures to get contaminated. So a whole lot of technology has basically evolved and been developed for protecting both lab workers, OSHA -- OSHA didn't exist, I don't think, when I started working in the lab, but OSHA now exists and there are a lot of requirements, actually. You can't -- there's no way the kind of laboratory that I worked in in the early '60s would be allowed to, you know, it would be illegal and immoral and everything else to work in a lab the way people used to. And I think probably the way I worked in a lab in the early '60s was very advanced compared with 20 or 30 years earlier.

Saul: In terms of safety practices?

Barker: Yeah, safety practices. I mean, safety practices are a big deal in the laboratory now, and rightly so for a variety of reasons. There's still no such thing as complete guarantee at 100 percent because people can still

accidentally stick themselves or break containers and accidentally inoculate themselves and whatnot, but I think a lot of measures have been over the years put in place to minimize the risk to workers. I mean, we didn't have things like biosafety level 3 facilities. We used to work with primates a lot then, and, in fact, one of the big issues . . . There were two big issues with primates. One was they could have tuberculosis, and the other was they could have a herpes virus, which was lethal for people, simian herpes virus, and so, slowly but surely, the practices for working with monkeys were improved. The same thing with all laboratory animals, I mean, laboratory animals are like people. They're full of microbes. People are full of microbes, some of which could cause serious problems if you get yourself accidentally infected with something in your lab animals. And so you didn't want the workers to get sick because then they couldn't work. You didn't want the stuff you were working with to get contaminated, so without -- I'm not an expert on the subject, but there are manuals, books, procedures ad nauseam nowadays for protecting people and what they're working with from infectious agents in the laboratory, many, many more precautions than there used to be, and I think that's good. That's an advance.

Saul: Just a couple of specifics. Did you guys use gloves at all when you first started?

Barker: No. Gloving, I think, "universal precautions" -- I'm sure you've come across that term -- I think universal precautions didn't really get a strong

push until HIV/AIDS. Now, when I started the lab, the only time we used gloves, I would say originally, was when we'd be working with animals probably. Maybe we'd use gloves in some other settings. But there were a lot of times we didn't use gloves. I used to inoculate animals with a mixture of human serum from the vaccine clinical trial and epidemic typhus organisms, which was a highly infectious mixture. I used to inoculate mice into the tail vein, and I know that I didn't use gloves. It wasn't considered . . . I mean, actually, they were considered but they would make you clumsy. In fact, I think that transition to routine gloving was not an easy transition, because it is easier to manipulate things without gloves than it is with gloves. I remember dentists were very resistant to gloves, but they eventually became essentially required. I mean, I remember when that switch occurred. Now you go to the dentist and wear gloves. Twenty-five years ago, you go to the dentist, they didn't wear gloves. In most laboratories, unless you were dealing with some very caustic solution, which if it got on your hands would burn through your skin or something like that, by and large, gloving was not routine when I started research. Nurses in blood banks didn't use gloves for most of my years of being a blood donor, but eventually, starting in the '80s, I would say, is when gloving and to some degree wearing masks and wearing the caps and wearing gowns began. Precautions have come into play both in research and in clinical care. But as I said, it was HIV/AIDS that gave universal precautions a big impetus because early on it seemed like that

was the only thing that could be done, or people weren't sure, actually. You were taking care of patients, and AIDS patients in the early '80s were very, very sick people. But hepatitis also helped the impetus to universal precautions. There was resistance because of what I just said. They made it more difficult to do things. It is more difficult to do things in a BL3, and it is very difficult to do things in a biosafety level 4 facility. That's where you're in a spacesuit and you don't have just little rubber gloves. You know what it looks like. And they use those for very-high-risk sort of infectious agents. I've never worked in a BL4 facility. I learned how to do a lot of the things that are now done in the equivalent of BL3 facilities. I'm not even sure when that nomenclature arrived, but it's pretty common parlance now.

Saul: Sure. Is there anything -- I'm just trying to wrap up the FDA section of my questions. Is there anything else about the safety procedures, concerns, particular concerns of the FDA to improve the safety of product?

Barker: Products, products. Yeah. We really haven't been talking very much about products. We've been talking about laboratories, which are -- there's a relationship, obviously. But, I mean, I could talk all day or all week or all year if you want me to, about the safety of biologic products, but you probably know most things you need to know about the subject. I mean, there's a lot that can be said about it. There are issues, concerns, measures that have been taken over the years. Sometimes they worked,

sometimes they didn't work. I mean, I don't know whether this is the time to mention it, but one of the things we did that was a little different in the '70s, when I was director of the Blood Division at the Bureau of Biologics, was we kind of went after "blood from paid donors" by getting a regulation in place that blood had to be labeled as to whether it came from a volunteer or paid donor. That caused a fair amount of uproar, actually, an amazing amount of uproar. Well, maybe not an amazing amount of uproar, because it was very intrusive upon, on what I would call the commercial blood-bank industry. They felt that it was unfair and discriminatory, and it was discriminatory because once we got that rule passed, it made blood with the paid-donor label on it very undesirable to use from both the patient standpoint and the liability standpoint and so forth. So I think it helped push our blood supply of what I want to keep calling single-donor products, the whole blood and red cells and platelets and so forth, in the direction of being a totally volunteer, donor-based blood supply, which was a big -- that was a big emphasis in the 1970s. We knew that testing for hepatitis-B surface antigen, as we call it now, had been helpful but had not solved the problem. We knew there was still a fair amount of hepatitis, and some of it, we slowly but surely figured out, was due to something different. We called it non-A/non-B because we didn't have our hands on the virus or the specific marker until 1989 for what is known as hepatitis C. We were looking for other ways we could do something to improve safety, and one of the ways we kind of settled

on, it was national blood policy, to go to an all-volunteer-donor system starting in the early '70s. I think that is when the national blood policy began, '73 or something like that. And the FDA -- I remember talking to Harry Meyer about this, and he was very clear. He said, "Well, we ought to do something about all this paid-donor blood that's been incriminated, if you will, as high risk." And what we did about it is we got into labeling, labeling of blood, and I think that rule is still in place.

Saul: Paid blood was never, to my knowledge, officially outlawed.

Barker: That's right. That's correct.

Saul: And up to this day isn't officially outlawed.

Barker: That's right.

Saul: Because the national blood policy was never officially enacted.

Barker: Well, I'm not sure what you mean by enacted. In other words, the national blood policy -- I don't know if you've read any of these documents. Basically, it was a policy. It was a set of principles, one of which was, our blood supply should come from volunteer donors. So the policy was put into the *Federal Register* or wherever it's published. I actually have some of those documents gathering dust at home because every once in a while somebody asks me about it and I have to dredge them up to refresh my memory. But it was kind of an interesting policy. This was during the Nixon, which was a Republican administration, and the policy of the government, the lay policy was to have the private sector do the things that would achieve the goals. And it was an all-volunteer

supply that was adequate so that it was there whenever anybody needed blood, and it was -- I don't know; I can't remember whether it was supposed to be affordable and accessible and safe and clean and so forth and so on, available. So that policy really was in place, but the implementation of it at the direction of the HHS -- and it was Richardson who was secretary of HHS at the time -- was for the private sector to implement it, and that resulted in the formation of the American Blood Commission, which was a private-sector entity. And the federal government was supposed to be kind of helpful but not have the primary responsibility for implementation, so NHLBI -- are you working with NHLBI?

Saul: I am.

Barker: Well, NHLBI ended up being told, "You will contribute to the operating costs of the American Blood Commission, like it or not," and they probably didn't like it too much. But they were basically given the responsibility for paying for things like the National Blood Data System or whatever, various things. In other words, the ABC -- they weren't given a blank check and told, "You can spend as much money as you want and be reimbursed by NHLBI," but something a little bit like that. NIH was to support research. Well, NHLBI also supported research in blood safety and various other aspects, and NIAID, blood bank, and intramural programs, CDC. I'm not sure if CDC was given much of a role early on. They were called, but FDA was expected -- by then, by '73, we were part

of FDA -- we were all expected to do things, if we could, that would contribute, but not to have the lead responsibility or whatever. Well, we'd already been involved in licensing tests and making sure they were being done, and the extra step, which the Bureau of Biologics, the part that FDA took, was to put in place the labeling requirement. You know, it's an interesting situation. One of the fiercest opponents of labeling -- and I'm talking fierce -- was Howard Taswell, who was director of the blood bank at the Mayo Clinic. Mayo Clinic is in the middle of Minnesota. They had a long, long tradition -- not long, 10, 20, however many years -- of paying their blood donors $25 for the time and nuisance and pain and suffering, whatever, of being a volunteer blood donor.

Saul: They weren't volunteers?

Barker: Well, there's no question, they weren't volunteers.

Saul: They wanted to go.

Barker: They were demographically or however is the best way to describe them, sociologically, whatever, yeah, they were volunteer blood donors. They were the same as the volunteer blood donors who go into the Minneapolis War Memorial or the St. Paul Red Cross. They were solid citizens of Minnesota, nice, healthy people. They weren't the kind of people that we wanted to get out of the blood supply. The kind of people we wanted to get out of the blood supply were the people that went to the commercial blood bank on Baltimore Street, who, you know, basically it was clearly a socioeconomic thing. I mean, there were two kinds of paid blood donors:

there were Mayo Clinic paid blood donors who were the crème de la crème of healthy, solid citizens, etc.; and then there were the people who were addicted to drugs, who were living in homeless shelters, I mean, the marginalized people. Unfortunately, this is where infectious diseases tend to prosper, including things like hepatitis B because of the fact that there is injection-drug use. Also, hepatitis B is a sexually transmitted disease which is highly associated with promiscuity. So if you have a population that's sort of mixed up with prostitution, male-female, etc., etc., injection-drug use, and is economically down and out, they're not people you want donating the blood that you might end up receiving. So those were the people, and it was those operations that we were trying to literally squeeze out. That was really, I mean, the national blood policy . . .You know, a lot of this is not what it was about. I mean, the NIH did the study. They were buying their blood from this commercial blood bank in Baltimore. They compared the hepatitis rate in their cardiac surgery patients. Do you know that study?

Saul: Yes.

Barker: John Walsh's study. Okay. So you know the study and you know it was just . . . And before that, J. Garrott Allen,; I'm not sure if he's alive or not. J. Garrott Allen was a surgeon from Chicago who became chief of surgery at Stanford, and his life's work was trying to get rid of blood from paid donors supplied by commercial blood banks. He did studies long before, many years before the NIH Clinical Center blood bank showing

that there was a much higher risk of hepatitis associated with paid-donor blood. So that's what it was all about and the national blood policy wanted to, rightly so, increase the safety, make blood totally safe because there are people in the volunteer-donor population who are infected with hepatitis and HIV and everything else, hep C/B, but fewer of them. So that's why we got into labeling. As I say, people like Howard Taswell, and there were a few other people, I don't even know if Howard's still alive. I haven't seen him for a long time. He was very intelligent, he was running a wonderful operation. Mayo Clinic is the crème de la crème of medical centers in the country or the world. He felt very bent out of shape by what we were going to force him to do. He either had to stop giving his donors $25, which he didn't want to do, or he had to put paid donor on the label of the blood collected at the Mayo Clinic Blood Bank. Well, both of these were extremely offensive, and you can understand why. Here's one of your wonderful operations. His blood was safer than probably volunteer blood collected in many parts of the country. And he used to say that. I mean, he would get up in meetings and he would say that with vigor, with real aggression. He would say that. So that was kind of an interesting episode. There were other people that thought it was kind of a blunt instrument, which it was in a sense. I mean, an even blunter instrument would be to make it illegal, but for various reasons, we didn't think we could make it illegal. And, actually, operations like Howard Taswell's at Mayo Clinic were reasons why we didn't feel we

Saul: Could?

Barker: I mean, we got enough hassle getting labeling into the, you know, it's in the rules. We got enough hassle to get that in there, too. To literally ban paid-donor blood, we didn't, for various reasons, think we could get away with that, frankly. And among other things was, this was a period, the sort of '70s, when a certain amount of what was considered an essential part of our medical whatever, was coming, and particularly some of the big metropolitan areas, from commercial blood banks using paid donors. And without being specific, I can tell you that there were some metropolitan areas where the biggest users of blood were surgeons and anesthesiologists, which are kind of a team, and they said, "Well, if you ban paid blood in city X, we'll have maybe a 10 or 15 or 20 percent shortfall," because paid blood was not the predominant, but it was an essential. If you wipe out 20 percent of the blood supply anywhere, any day, you can create a very bad situation. The blood supply in this country has always been kind of close. We've never had a big pillow out there. I mean, I remember in Canada -- I know they've had more trouble recently -- but they used to have a big excess of blood. They would over collect by maybe 20 or 30 percent, and they were an all-volunteer system, too, but it's a totally different country. Canada is not like this country. They don't have the kind of cities, for the most part, that we have with the kind of issues that we have and so forth. So in Canada, it wouldn't have been that big of a deal to ban 20 or 30 percent of their blood. In this country, it

would have been a very big deal. So we had to do things that would sort of compress, and, actually, New York did a very creative process, I think . You know what they did? They went to something called Euro blood.

Saul: Right.

Barker: They ended up importing, I think, 20 to 30 percent of their blood supply from volunteer donors in Europe, because New York was a shining example . . . Without Euro blood, which they've now had to get rid of because of bovine, BSE, CJD, but at least that was their lifeline, and I remember that. We licensed. While I was in FDA, we licensed those Red Cross blood centers in Switzerland, Germany, I can remember the Netherlands. I used to inspect them. It was kind of nice, actually, inspecting blood banks in Switzerland and Germany. But, at the same time, there was a lot of feeling that this country ought not to be dependent on collecting its blood from volunteer donors in Europe, where, incidentally, they were massively over collecting, collecting far more than they needed, so they were like Canada. They had all this extra blood. They were happy to sell it the U.S. and it was pretty good blood. It was better than the blood from commercial blood banks.

Saul: Now, was part of the emphasis to label, to do something about the paid blood, was it strictly from the studies that were done comparing paid blood donors to volunteer donors, or did it have something to do with the book that was written *Gift Relationship*?

Barker: The Titmuss book? No. I would say it was 99.9 percent the former. The

Titmuss book, we didn't feel was particularly relevant to us. You know, it was about the U.K., and he said those Americans are terrible. They pay their blood donors. But we did feel that we had a problem with regard to hepatitis. Titmuss was more -- I think his argument was less . . . I never read his book. It wasn't required reading for us. But my impression of his book, having never read it, was that it was more about altruism and philosophical, you know, taking-care-of-your-fellow-man type arguments than it was about hepatitis arguments. Our issue was all hepatitis.Now, the national blood policy had probably a role in the salt-and-pepper mixture of safety and altruism as reasons why we should have an all-volunteer donor supply, but at FDA we were concerned about safety. We were concerned about hepatitis. In fact, we made a giant compromise in that we did not require paid-donor labeling to go on the plasma.

Saul: Right. Why was that?

Barker: Well, very simple. It would have killed an industry which was considered vitally important. Now, Western Europe, Canada to some degree, to varying degrees took the position that blood and plasma all had to come from voluntary donors. At the same time, these countries were buying most of their anti-hemophilic factor and albumin from our commercial plasma and plasma-derivatives industry. So we viewed it as a little hypocritical, I guess. They kept pointing fingers at us: you've got this terrible industry. Meanwhile, that's where they were getting their product, because they didn't have enough product from voluntary . . . I mean, the

reason they had so much in the way of extra red cells in places like Switzerland and Germany is that they were collecting whole blood from volunteer donors to get relative, you know, to get what plasma they could for fractionation. But still, we knew in this country, because the Red Cross and the community blood centers that were doing the same thing, sending their plasma for fractionation, this was taking care of maybe 20 percent of our plasma-derivative needs. You didn't have to figure it out. It was made very clear to us if we told the plasma industry that they had to go to a totally volunteer donor-based approach to collecting their plasma, it . . .You know, maybe over a period of many years, it could be done. It hasn't been done. And I don't know whether it could be done or not. I mean, selling plasma, which is still practiced on a very large scale in this country, is a couple of hours. People that do it, they do it weekly or -- you're allowed to do it twice a week up to X number of times a year. It's a big hassle. We have a big hassle with Europe, with WHO and whatnot. But while we were having this hassle, they were happily using the products made by this industry, and so were we. Incidentally, there's never been -- I don't think there's ever been data generated on risks associated with pooled plasma products that discriminated between products from voluntary donors and products from paid donors equivalent to the data for single-donor products, and so we didn't really feel that we even had the basis. I mean, and there's actually a reason for that. You know, if you pool 10,000 units of plasma from Red Cross volunteer donors, no question

that you're going to have hepatitis C in the pool. And when it was a problem, it was going to have HIV and it was probably going to have some residual hepatitis B. So although quantitatively you might have less contamination, unfortunately, from a practical standpoint; it wasn't going to be easy to prove that product X from paid commercial donors' pooled plasma was anything like a high risk product from a big pool of volunteer donors than it was if you took single-donor products, where you got something like the NIH study and the Garrott Allen studies and whatnot. So there were a number of factors. But it was interesting. I mean, there were people that wanted us to label plasma, but we just felt that would be a meaningless exercise because in that case they would have put the label on all the plasma and just kept going merrily on their way. The plasma did not go to hospitals and into patients. The plasma went to factories and into huge pools and into pooled products. It's a huge industry. I don't know, probably still is, was when I knew it. I don't know that much about it anymore. I'm sure it's still a big industry.

Saul: So the argument is that the commercial plasma fractionators that made the argument to do that?

Barker: Well, actually, it goes back further than that. The national blood policy did not call for the plasma for further manufacturing part of our whatever you want to call it, blood and blood products in aggregate, did not call for it to be all-volunteer donor. If you look at the national blood policy, you'll see that the exception was made there. So that would have made it even

more difficult if we'd wanted to, and we didn't particularly want to. You know, on one side, the case we thought was absolutely ironclad; on the other side we thought the case might have to be made on more of an altruism basis, and FDA wasn't about that. That's not FDA's job, to make altruistic products. It's to allow on the market altruistic products. And that's why we didn't think Titmuss was terribly . . . And Titmuss] was important from the standpoint of volunteer donor blood is important from a safety standpoint, but that wasn't really what he argued, I don't think. Have you read his book?

Saul: I've read most of it.

Barker: Well, good. You're ahead of me.

Saul: Is there any paid whole blood collected in this country?

Barker: I have no idea. But I imagine it would be smidgeon at this point.

Saul: But it would be legal if people . . .

Barker: Oh, yeah. But paid donor on the label. That's what it says right here in the regulations. And to this day, I would, without having any facts, I would hunch that almost every unit of blood that's being transfused has volunteer donor on the label. But there may be some places where . . . I actually doubt . . .I mean, there's sort of the stigma, which was the whole purpose of the exercise in a sense, was to stigmatize, but there's also the liability. I mean, imagine what it would be like for a surgeon to look up and see paid donor on the blood that's going into, or somebody treating an ulcer or whatever bleeding patient, to look up and see that, you know. Go

out and make sure the insurance is in good shape. Really. And that's, for better or for worse, I don't happen to like that particular controlling feature on what happens in this country because I think it can distort things badly, but there's no question about it, when we passed this labeling law, I think things moved fairly rapidly to pretty close to 100 percent. I don't know what eventually Howard Taswell did at the Mayo Clinic, whether he just kept paying his donors and putting the label on or stopped paying them, but I suspect he probably stopped paying them.

Saul: Interesting.

Barker: You could find out.

Saul: Yes. I think I will.

Barker: Call the Mayo Clinic.

Saul: Is there any record kept of how many paid blood donors, if there are any?

Barker: It wasn't very good information. You know, one of the things about the national blood policy that, you know, when you say we want to have an all-volunteer blood supply, then the logical question is, well, how far do we have to go to get there, and where are we this year and next year. And so, for that purpose, NHLBI was charged with creating some sort of blood data-collecting system, which became very controversial. It was ADC was going to do it, NHLBI was going to pay for it. I remember -- I can't say just how that played out except that I remember it caused a certain amount of rancor here and there. But, in any case, the FDA, incidentally, does not traditionally have quantitative information on the products that it

regulates; that is to say, we don't know how many units of product X, Y, or Z somebody is selling. I shouldn't say we. FDA doesn't know. And, in fact, that's been kind of considered proprietary information. I mean, there are businesses that know how much market share different companies have for different products, so forth and so on. And then there are organizations which do keep track. Red Cross knows how many units of blood it collects and distributes to hospitals, and it publishes that every year. Actually, Medicare knows a lot because they have a lot of figures. But as far as figures, I mean, what FDA knew at the time that we imposed the labeling requirement, is we knew how many licensed commercial blood banks there were because we licensed them. And I don't know how many there were, but the thing is, the thing that made even that kind of a statistic a little confusing was we licensed all the plasma centers, which were using paid donors, and they were commercial, for-profit, private businesses, still are, and so we didn't really, we didn't have hard numbers at FDA, and it wasn't really our job to have the hard numbers. I don't know, it would be interesting. At NHLBI, George or someone like that . . .

Saul: George who?

Barker: George Chrousos [unclear]. He's still there. I worked with him. He was -- well, Barbara Alving, who's head of the Blood Division, she was in the Blood Division of FDA when I was there. I don't know if you've met Barbara Alving. Well, you ought to meet her. She's good. But they might be able to dredge up some information. But my guess is, I don't

think we had really good numbers. And, again, it varied. In New York, pretty much what they brought in from Europe was, which was a lot, several hundred thousand units a year of red cells, I think was largely being supplied by commercial blood banks using paid donors.

Saul: Using paid donors?

Barker: Yeah. But then you go to the Mayo Clinic, and I think 100 percent of their blood was actually volunteer, although the donors were paid. So there's a big variety around the country. The most use of paid donors I think was in the big metropolitan areas, where you have a lot of big medical centers and hospitals doing a lot of surgery, and you probably know what New York City is like and Baltimore, Washington, whatever. It's a lot tougher, frankly, to meet the blood needs of these areas where you have enormously greater blood usage, say, than you might have in, I don't know, Roanoke, Virginia, or more outlying rural areas where there isn't a huge amount of cancer surgery and cardiac surgery and all that stuff. So anyway, commercial blood was largely New York, Philadelphia, Baltimore, Washington, Chicago, St. Louis, Houston, Dallas, Los Angeles, San Francisco. That's where most of the problem was. My hunch is that in the mid-'70s, probably between 10 and 20 percent of their blood supply was commercial and is that today, pretty close to 0 percent of their blood supply is from paid donors. I think that happened fairly rapidly, actually. Although -- and we may get there or not; we're using a lot of time -- but this was an interesting backdrop issue in the '80s, when some new events

occurred, was the fact that the blood supply was always a little bit tenuous. I mean, to this day it is a little bit tenuous. I get the American Blood Center's -- which used to be CCDC, now ABC -- newsletter every week, and just a few months ago, the blood supply was very dicey. I can't remember why; I'm not sure why that was. But it's a big effort. I mean, I worked at the Red Cross for 12 or so years, and I remember what a big effort it was, because it is a day-in and day-out counting, knocking on doors, calling people up, getting people to show up and donate blood. It's no small undertaking. And we use -- I don't know what we use now, probably 10 or 12 million units a year. I think it's virtually all from volunteer donors, whereas the plasma I think is…Predominantly, 80 percent probably from paid plasmapheresis donors. The rest are from blood centers, the Red Cross, and community blood centers, volunteer donors. They collect whole blood, squeeze off the plasma and the platelets, the platelets go to people who need platelets, the plasma goes for further manufacturing and derivatives, and the red cells go in the patients who need red cells. That's the way it works.

Saul: The whole, the labeling issue and the paid versus unpaid and the question of safety versus supply is what I'm really interested in, especially right now.

Barker: Yes, well, as I say, the '70s, it was kind of an exciting and interesting decade in that respect, and it was, you know, we felt like we were making some progress. Then we had the '80s, which set us back a bit, to put it

mildly. Now things are better. I mean, now the technology is out there. As I say, nothing's 100 percent, zero risk, or whatever, but I think the risk of a common serious agent, specifically the hepatitis B, hepatitis C, and HIV transmission via blood and blood products, is very, very low, incredibly low compared to what they were. When I started, they were high.

Saul: If we could talk just a little bit about your time at the American Red Cross, when did you leave the FDA?

Barker: 1978, it was, I think, the middle of the year.

Saul: And why make the transition?

Barker: My interests… essentially were crude. It was hard leaving the FDA because I liked working there. I liked the people I was working with. It was interesting work, but things were a little bit quiet. I mean, we'd done about as much as we thought we could do with B. We didn't have a handle on non-A/non-B. We'd done the paid-donor labeling thing. I'd gotten to know, although I have always considered myself, as I said right at the outset, more of an infectious-disease -- I'd gotten to know the blood-transfusion people pretty well in the '70s, and they were interesting people and they were doing interesting things, and I'd learned a fair amount about the field, I guess. I inspected all kinds of places in both plasma manufacturing and plasmapheresis as well as blood centers and whatnot, so I just thought it sounded like an interesting change. But it was not -- it wasn't that I didn't like where I was. I loved where I was. But it looked

like it might be an interesting place to be, so I changed jobs. I've changed jobs several times.

Saul: And your title or your job description?

Barker: Well, let's see. I went through a series everywhere I went, through various titles and job descriptions. I think I started out as vice president for blood services, which was a new title that they created when they were recruiting for someone to succeed Tibor Greenwalt, who was sort of an icon and had been head of the Red Cross blood program for a number of years before he retired. So I was responsible for blood services, and then after a few years, they changed me to vice president for health services or something like that and somewhat broadened my responsibilities. I was responsible for all of the, what I guess I would call, health and safety programs, things like CPR and first aid. I was pretty interested in those things, things that were traditional Red Cross activities, in addition to blood. And then the last few years, I basically got back into fairly much blood. I don't recall the years completely, but for the last few years before I retired, I was -- I can't remember what the title was, senior vice president or something, and I think chief medical officer. Titles, you know, we kept reorganizing and seeing what the government does. The Red Cross is not the government, but it is a big organization. You know, one thing that is predictable about big organizations is they will reorganize and come up with new titles and things every so often.

Saul: Absolutely. When you got to the American Red Cross, were the safety

concerns there similar to the ones that you had been dealing with at FDA?

Barker: Safety for the products or safety for the workers or . . .

Saul: Both.

Barker: Yeah. Well, I mean, I think yes. The short answer is yes. I mean, there's a -- I don't know what to call it, but I would say things like this sort of cross-cutting. I mean, the government is not -- there isn't a big lull, but on one side of which are a whole bunch of issues that the government is concerned with and the other side are a whole bunch of other issues. I mean, the same concerns tend to be pervasive. In fact, the FDA -- Harry Meyer used to say FDA is at least as much a mirror on the rest of society, it's not really separate. Although it has this regulatory role, it can only regulate what is being produced by the industry that it is regulating. Interested in having good, safe products that work and so forth and so on, because businesses do not tend to succeed unless they have good products that people feel are safe and work. So there is an enormous commonality of interest, I would say. Although, you know, the relationship is not always collegial and friendly, but at least the interests are the same. I mean, Red Cross has been in a standoff with FDA for years and years, but that doesn't mean Red Cross isn't interested in the safety of its blood and blood products. It's very interested in the safety of its blood and blood products and the quality, as well as its workers and so forth. So I would say that on a sort of global scale, the interests are common interests, not separate interests. It's safety of workers and safety of products and quality

of products.

Saul: Quick question, deviating a little from what we're talking about. FDA only regulatory, to regulate the products that have been applied for licenses.

Barker: That's pretty much the case. I mean, there are some . . . I mean, when you talk about workers it is more of an OSHA responsibility than an FDA responsibility.

Saul: Right, but OSHA wasn't around.

Barker: No, but FDA -- I remember we used to occasionally get involved in worker issues, but it's like you said. It would be as they relate to products. You know, some of these issues were very hard to sort of figure out what to do about. For example, what, if anything, should FDA do about a nurse who's collecting blood and who has chronic hepatitis B? Should FDA do something about that? I'm not going to try and answer that today. You know, FDA's concern would, if there was a possibility that that nurse could contaminate the blood that she's collecting, well, the fact is, the way blood's collected, it would be pretty hard for a nurse to contaminate it even if she was infected. I mean, these issues have come up with surgeons and dentists and nurses. For some people, it has been career-ending. I mean, surgeons, there certainly have been well-documented situations because surgeons do tend to puncture their gloves from time to time when they're operating. A surgeon who is chronically infected with any of the agents that people can be chronically infected with can be a risk to the

patients. But as far as risk to products, these were not -- the personnel . . . I mean, there are regulations for personnel in here, but -- and I can't quote them, but basically they say they have to be adequately trained and competent and so forth. They aren't, they don't regulate their medical conditions.

Saul: Right.

Barker: Well, I mean, this is what we're talking about when it comes to transmissible diseases. There is no regulation that says people infected with HIV, hepatitis B or C can't work in blood or blood-product and vaccine jobs, manufacturing jobs. There isn't anything like that. There are just regulations saying people have to be trained, competent, qualified, those kind of things. But, as I say, there were -- this is not a subject, or this is a subject that has received attention in the past, and sometimes has been fairly controversial, but I don't think OSHA disallows the kind of hypothetical nurse that I just described from working, and I doubt if they would do that.

Saul: So OSHA would regulate working conditions.

Barker: OSHA I think is . . . I don't know that much about OSHA. You probably know more than I do, but, among other things, it's there to protect the workers, make sure that conditions for the workers are okay, as best can be, they can be.

Saul: And the universal safety precautions are sort of an industry standard? I am sort of trying to place them.

Barker: I think those must be OSHA, probably spoken to in OSHA regulations. I don't think these are noted in FDA regulations, and I don't even know that much about how OSHA. I guess they do inspections. I know they do some inspections and that kind of thing, but I don't know a lot about OSHA. It seems like there is OSHA and there's still part of CDC, NIOSH, which would be more of surveillance. That's a whole field that I have some familiarity and experience with, but I have more experience with the product field than I do the OSHA approach.

Saul: Sure, that is something that I hadn't thought about looking at for this particular project, but it might be.

Barker: You can look at it, obviously. I would view it as a little bit peripheral to what you are doing, but it's interesting. Become an expert on OSHA.

Saul: Sure. Once AIDS was on the scene and once it was realized that it was at least a potential concern, particularly for the blood supply, how did that change the safety concerns? You were at the American Red Cross by that point. Obviously, you were still trying to produce safe, effective, pure, potent products. Were there -- what were the biggest changes?

Barker: Oh, man. I don't know. The biggest changes. Well, I mean, the AIDS epidemic obviously has had enormous effects on all kinds of, not just the Red Cross or the blood supply or the FDA, and it's had enormous effects on society, understandably. It has continued to be a terrible epidemic, much worse in some other countries, but still big. We still have a lot of AIDS in this country, will continue to for the lifetime of my children and

grandchildren. I think AIDS is a permanent part of the landscape now, and a difficult part. It is a terrible disease. Fortunately, we can treat it fairly well now, but we are not sure how long the treatment is going to work because of drug resistance. Anyway, getting to your question, I don't know. How did it affect the Red Cross? Did it affect the blood field or blood and blood products?

Saul: Or even ideas about safety concerns?

Barker: Well, I would say we felt like we made some fairly good progress, and Harvey Alter has documented some of this with hepatitis in the '70s, first with testing, then with paid-donor labeling, and we felt like we obviously hadn't eliminated the problem and we knew there was still all this non-A/non-B. We weren't sure how serious that was, but we knew it was there. And then in the early '80s, the first half of the '80s, we found ourselves confronting a new risk, literally a new disease that was a terrible disease and was, slowly but surely it became clear that it was spread, among other things, by blood and blood products. And I think one of the things that . . . I mean, this was -- I can tell you, this was a very scary, uncomfortable time because one of the things that made an incredible difference and was incredibly fortunate, frankly, is that in the spring of 1984, the Gallo lab at NIH pretty well nailed down the agent, called HTLV-3 originally. There had actually been hints of retroviral etiology from the French a little earlier, but it was, I mean, it was just about a little less than two years because it was mid-'82 that the first three

hemophiliacs, people with hemophilia who developed this syndrome were reported, I think, in June, something like that.

Saul: I think it was March of ‘82, if I remember correctly.

Barker: No. It was May ‘82.

Saul: Was it May?

Barker: But you will find, I think, June.

Saul: Okay.

Barker: It appeared in MMWR (*Morbidity and Mortality Weekly Report).* Now, they may have known about it in CDC before it was published. But the first actual meeting, I don’t know where it was or who was there even -- I believe it was the end of June ‘82, because I was at an International Blood Transfusion Congress and I remember hearing about this meeting involving these three people with hemophilia, and maybe they had this syndrome. At the time was called KSOI syndrome, Kaposi’s sarcoma opportunistic infection syndrome. In the fall, in September, there was an infant that developed the syndrome in San Francisco following transfusions. By the end of ‘82, I know there was a meeting at FDA. I think it was December ‘82. It was one of the first meetings at FDA. I was at the Red Cross, obviously and one of the first meetings of the FDA Blood Advisory Committee, where this story was told and began to unfold, and then there was a meeting in January ‘83, which I didn’t get to, that was down at CDC, and then there was a whole string of events after that. You know, the story kept unfolding, I would say. You know, it was

interesting. Different people had different takes on this as it unfolded in terms of what was going on, was this a new agent, was this hemophiliacs who were exposed to all kinds of foreign protein -- what was it about? I would say the mid-‘82 to somewhere into ‘83 was a period when there were more, there was more confusion and uncertainty than there was clarity. By the end of ‘83 and early ‘84, when Jim Curran’s paper came out in the *New England Journal of Medicine* some 27 or so transfusion-associated AIDS cases, things were really starting to clarify. I think there was less and less doubt that this was a transmissible agent, it wasn’t hepatitis B virus, we didn’t know what it was. But the hepatitis B virus was suspected early on, and some people were sure it was some variant, new variant of hepatitis B virus, because the risk factors were similar, and there was the anti-core connection, which you may or may not know about. Anti-core is a test that we developed in my laboratory in the early ‘70s, actually, and looked at for hepatitis but didn’t think it was appropriate to use at the time. We already had hepatitis B surface antigen. In any case, there were similarities in connection with hepatitis B, so that was one of the suspects. There were quite a few suspects, but until the Gallo lab publication, I would say we really didn’t know. We knew we were dealing with a big problem, and in early ‘83 the Red Cross and other blood centers started taking steps to try to reduce the risk of blood transfusions transmitting this disease, and you’re probably familiar with some of those steps. I can’t remember, actually, some of the details, but

they included asking people about risk factors or getting them to try and exclude people with risk factors, specifically gay men. Injection-drug users were already excluded, or at least going quite a ways back. There had been measures in place to attempt to exclude injection-drug users. That didn't mean they couldn't sometimes get through, but they were not supposed to be donating blood, and so we basically took various steps to try to exclude gay men from being blood donors. We didn't have any specific tests and there were a lot of tests proposed and some were evaluated. Anti-core actually was evaluated and didn't look very good, but there were reasons why it didn't look good. CDC, Don Francis at CDC wanted that to be done, and it wasn't done. But, in any case, what happened was there were a few places that introduced anti-core testing back in '84. As soon as the Gallo lab information was published in *Science*, there was an enormous -- I don't know what to call it -- that was enormous relief because we could see that within a short time a specific test being available that would improve the safety of the blood supply. It didn't make it perfect, but it did make a huge difference. I mean, the antibody test still left room for some people to get through that had the virus in their blood. Before they made antibodies, detectable antibodies. But it made it possible to exclude the majority of people infected with the HIV virus. That test was approved in March of '85. I can remember that well because it was approved like -- I can't remember, it must have been on a Friday. By Saturday morning Red Cross had signed a contract to get

tests shipped to the blood centers, Red Cross and other blood center. It took a little while because Abbott got the first license for the antibody test, and you couldn't just throw a switch and have it in place in every blood center in the country the next day. But I think the blood industry, if I can call it that, moved about as rapidly as it was able to move into implementing testing. And by then, there were other things being done. I mean, we ended up doing a lot of things over the years, you know, look-backs eventually to try to find out about donations that were made before the test was available and somebody was found to have a positive test. And we got, I think, over time somewhat more stringent. I mean, I haven't donated blood for a year or so, but the last time I donated blood -- I think it may have been Christmas of last year, have you ever been a blood donor?

Saul: Yes, I am a blood donor.

Barker: Okay. So you get a pretty thorough grilling to be a blood donor these days. That is the consequence of going into more and more detail. I mean, I can tell you that a lot of the things that they ask me now -- and I've always been an NIH Blood Bank blood donor; I've always donated at Red Cross blood centers, too -- but I can tell you in the '60s, when I was a blood donor, they were just happy to see me. I can't remember if they asked. They may have asked a couple of questions, have you had malaria, hepatitis, or whatever? But it was not like the current screening that they do. All of that evolved starting somewhere in the '83-'84 period and

continuing ever since. And lots and lots of precautions: Have you lived in the United Kingdom? Have you traveled to Western Europe? Have you been anywhere, done anything? Just on and on and on. It's very, very detailed. Well, HIV was a terrible experience. It was a terrible experience for everyone -- patients, doctors, blood collectors and suppliers -- and it raised the threshold, if you will, of precautions, of product safety. At times I think they may be even excessive, but that's okay. I mean, we're able to pay for them. Well, I mean, I wouldn't say they're excessive, but I don't know. We've gotten into, we're there and I don't think we'll ever turn back on any of these things with testing. I have to say, blood is not my main field. I am more of a public health person. One of the things that happens is, if you keep putting more and more resources somewhere, you actually have less resources to put some other places. You know, we're doing a phenomenal job now as far as protecting the blood supply is concerned. I'm not sure that we're doing that good of a job with STDs or nutrition or a variety of areas. We are doing quite a good job with tuberculosis in this country. Most of the world has a huge problem with tuberculosis and, justifiably, is not doing anything like what we're doing with protecting the blood safety because it's not the same kind of priority. I mean, our priorities, I think, are not the world's priorities. So there are times when I think I'd like to see some of those resources going in directions that would benefit more people in more places, but politically, that's not the way things work.

Saul: And is that because, as a direct result of AIDS? I mean, it's interesting.

Barker: Well, even the AIDS virus is a good example. I mean, I don't know. To this day, if we're actually having 40,000 new HIV infections a year in this country, that's quite a lot, and maybe we're having five or 10 blood-related HIV infections a year. I don't know, one or two, a very small number anyway. In order to achieve the latter goal, which is wonderful, we're spending X amount of money. I have a feeling that if we were spending an equivalent amount, we wouldn't be having 40,000 new HIV infections a year, but we might not be able to afford to spend as much on prevention for various reasons. I mean, there is a limit. We don't have unlimited resources. So from the standpoint of, well, called the big public health picture for a moment, things are a little skewed, frankly.

Saul: Sure, absolutely.

Barker: They're spending an enormous amount of money to reduce to a very low level the risk of blood transfusion and relatively less money and therefore not reducing the equivalent, anything like equivalent of the risk in society getting this very serious infection. But that's getting a little philosophical, I realize, and I'm glad the blood supply is as safe as it is. I wish we could figure out how to reduce that 40,000 number to something much lower. That's a big number.

Saul: It is a big number.

Barker: And most of those people are eventually going to die of that infection. And it's going to be very expensive to treat those who have access to

treatment before they die. That's not good from a public health standpoint.

Saul: I'm probably more aligned with the public health perspective than many other perspectives.

Barker: There's a lot to do there, lots of need.

Saul: I went way over the time I told you I was going to.

Barker: Well, it's probably my fault. I talk a lot.

Saul: After AIDS, can you tell me anything more about the universal precautions? You said that they got their sort of kick-start with AIDS.

Barker: I think that's right. There were some precautions, to my sense. Well, one of the big concerns early on -- and I know you're not old enough to remember this, but you may have heard about it -- a big concern was taking care of AIDS patients.

Saul: Oh, I remember.

Barker: You remember it. Okay. Because we knew so little about it early on that people did not know whether the nurses would get it, the doctors would get it, the cleaning staff would get it, the secretaries would get it, the clerks… The CDC had a pretty good handle very early on on the epidemiology, and they were pretty sure that if you didn't stick yourself with a needle containing blood from a patient, or have sexual contact with a patient or basically get a blood transfusion from an infected person or get blood or a blood product from an infected person, it was safe. You know, they figured out very early that this did not spread like flu.

Universal precaution was the remedy, if you will, to this fear. I mean, to me, the essence of universal precautions is avoiding needle sticks. It's also wearing gloves and gowns, but the gloves and gowns and masks and caps are not what's protecting people from HIV, hepatitis B, or hepatitis C. And I gather -- I'm not really that close to it -- that we're a lot further along now. One of the precautions that I think was way up on the scale of importance, if you will, was the way syringes and needles got handled. I can tell you, we used to throw them into these autoclave things in the laboratory. Well, now you have these devices that you stick your syringe in and you chop it off and it falls into a container that nobody can put their hands into. I mean, that wasn't always the way needles and syringes were handled. You can imagine, in the days of glass syringes, stainless steel needles, people would take them apart, and they take everything apart. Occasionally the glass would break or they'd accidentally stick themselves with a stainless steel needle, because they were all reused. There are still parts of the world where this goes on. It doesn't go on in this country. I mean, everything is disposable, and we are more and more trying to get devices which make it almost impossible to stick yourself, with these sleeves that come out over the needle so that even if you wanted to, you couldn't stick yourself, a lot of needle-free delivery systems. That is one of the major objectives in the vaccine field, actually, is to be able to deliver vaccines without needles, and there are various ways you can do that. Obviously oral for some vaccines, this works very well for things

like live polio and whatnot. But there is a lot of work now on things like patches, the same kind of thing you use for nicotine. Patch technology is actually a very exciting field for delivering all kinds of things, and it will be a huge advantage. I mean, one of the big problems with vaccine distribution is that you do not just have to have a container with the vaccine in it; you have to have a needle and syringe, and you have to have a different one for every vaccinee. At least it is not considered good practice to use the same one over and over, for obvious reasons. There are a lot of advances that have been made under the aegis of better and better universal precautions. I mean, it started out just, don't worry about it, but don't stick yourself. And I viewed all the gowning and gloving and whatnot as reminders. I mean, I think in a way a lot of that was psychological. If you got sprayed in the face, you could have a problem, obviously, through mucus membranes and that sort of thing. And sometimes you can be pushing or pulling on syringes and something can come off and there's a splash, and that could be dangerous. Obviously, dentists may have that problem. They generate huge aerosols from their grinding away on people and that sort of stuff. You know, stuff's all flying around. I think they probably mostly wear glasses or masks or something. I think my dentist told me about something covering his eyes. Maybe he wears a mask on his face and his mouth so he won't inhale all the stuff that he's generating with his grinding equipment.B ut anyway, universal precautions. I think one of the big reasons for putting this much

emphasis on them. Oh, I'll tell you another area that was a big worry and actually was very hard to deal with, was CPR, because CPR involves mouth-to-mouth resuscitation. That was a big deal at Red Cross. You know, it was not just, well, do you do CPR on somebody . . . Let's say you're walking down the street and somebody collapses. Do you run over and do mouth-to-mouth resuscitation, because they might have AIDS, and how would you know? They could. But it was not just the person that falls down on the street. It was also the dummies that you practice on. Would you want to do a practice CPR on a dummy if you didn't know if the person before you was infected with AIDS or not? There was early-on concern that things like sputum, oral secretions might be able to transmit. And actually, as things unfolded over the years, although CDC took a very strong position that there are only this very short list of ways this virus can be transmitted, almost surely -- and this has, I think, turned up in some places -- sputum or oral secretions can transmit because occasionally you have blood in the mouth. Everybody knows that teeth and gums occasionally bleed so if there's any blood contamination mouth. But that's not a common way that this virus gets around, obviously, not common at all.

Saul: So it was an evolution of generally accepted standards of practice?

Barker: Yes, I mean, things have changed in the research lab, incidentally. Being in a virus research lab, one of your biggest concerns was that you didn't contaminate your viral cultures, and you also didn't want to get sick or

have your workers, your technicians, get sick. So I would say it was a combination of those, but more often than not, it wasn't worker risk, it was research materials, keeping the research materials clean, that drove a lot of the changes that occurred in the laboratory. I'm not sure about hospital laboratories, how they evolved, because I've never worked in a hospital laboratory after medical school. As far patient care is concerned and interaction with donors who aren't patients; they're healthy people but they can be carriers. I think it was HIV that really escalated this. I mean, there were a few dust-ups over dentists who didn't want to take care of people that had HIV, surgeons who didn't want to operate on people who had HIV. There was some justification, frankly, because , as I say, surgeons do get sick themselves, and I don't think the number is large, but there are surgeons that have developed this as an occupational risk. I mean, no amount of universal precautions can guarantee that a surgeon won't accidentally inoculate him- or herself in the process.I mean, think about working in emergency rooms. I don't know if you've ever been in an emergency room, but there's a lot of stuff flying around. People are flying around, blood's flying around, needles, syringes, machines. Stuff is all over the place, and universal precautions, one of the things about them is that they take a little time, and it takes longer to put on gloves and gowns and masks and caps than it does to not put them on. So emergency rooms are probably still coping with some hazard level related to just the nature of the beast. But anyway, I think everybody's probably pretty well

adapted to universal precautions. And, as I've already said, I think they're probably excessive in some respects, but I think that excess is, among other things, to keep top-of-mind awareness that there is risk associated with blood or bodily fluids or whatever you want to call it.

Saul: Right, sure.

Barker: And a lot of our stuff is disposable now. The plastics industry has certainly burgeoned as part of it.

Saul: Absolutely, I want to just officially thank you for all of your time.

Barker: Well, it's been a pleasure. I'm very interested in what you're doing.

Saul: Good, I'm glad, because some people aren't.

Barker: I think it's a nice undertaking.

Saul: I'll give you my card, so if you think of anything that you want to add later.

Barker: I should mention one person that's not on your list. There are a lot of people on your list. But a very interesting laboratory person who's not on your list is Roger Dodd, who's at the Red Cross right across the way. And Roger -- he's a wonderful guy. He's actually president of the AABB this year, which is quite unusual for a Red Cross person. He's a Ph.D., and I don't know if I have his phone number, but he's at the Red Cross lab. But I just zipped through your list, and it occurred to me I think you've got enough people.

Saul: Yes, for the moment anyway.

Barker: Roger would be an interesting person, because he's been there in the Red

Cross Transmissible Disease Department for this whole period that you're interested in. I think he started there in the '60s. He has done hepatitis and HIV and hepatitis B and hepatitis C, plus he's kind of a colorful character. Now that he's president of the AABB, he's probably running around the country a lot.

Saul: Probably.

Barker: He ought to stay in his office so that you can talk to him if you want to.

Saul: Right. Wonderful. Well, again, thank you so much. I really appreciate it.

Barker: You're welcome.

END OF INTERVIEW