



**Oral History Interview with
Leslie Holness, M.D.
Branch Chief, Division of Blood Applications,
Office of Blood Research and Review,
Center for Biologics Evaluation and Research
1991 - 2013**

**FDA Oral History Program
Final Edited Transcript
January 29, 2013**

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Oral History Abstract

Dr. Leslie Holness served as Branch Chief for the Division of Blood Applications in the Office of Blood Research and Review, in the Center for Biologics Evaluation and Research for over twenty years. Dr. Holness brought with him years of experience in blood banks, including the New York Blood Center, before arriving as a medical officer at the FDA. Throughout his nearly 50 years of experience working with blood, he witnessed the vast transformation of the industry and scientific technology. His expertise was pivotal in regulating blood donation, collection, storage, and use.

Keywords

Blood, HIV, nucleic acid test, American Red Cross

Citation Instructions

This interview should be cited as follows:

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Interviewer Biography

John Swann, Ph.D. is an Historian at the U.S. Food and Drug Administration. He is a subject matter expert in the history of the FDA, with a specialization in the history of pharmaceutical and biologics regulation. He joined the FDA in 1989, after earning his doctorate in the History of Science and Pharmacy from the University of Wisconsin, Madison, and researching a centennial history of the University of Texas Medical Branch at Galveston. He is the author of *Academic Scientists and the Pharmaceutical Industry: Cooperative Research in Twentieth-Century America*, as well as numerous articles on this history of therapeutic products published in scholarly journals and edited compilations.

FDA Oral History Program Mission Statement

The principal goal of FDA's OHP is to supplement the textual record of the Agency's history to create a multi-dimensional record of the Agency's actions, policies, challenges, successes, and workplace culture. The OHP exists to preserve institutional memory, to facilitate scholarly and journalistic research, and to promote public awareness of the history of the FDA. Interview transcripts are made available for public research via the FDA website, and transcripts as well as audio recordings of the interviews are deposited in the archives of the National Library of Medicine. The collection includes interviews with former FDA employees, as well as members of industry, the academy and the legal and health professions with expertise in the history of food, drug and cosmetic law, policy, commerce and culture. These oral histories offer valuable first-person perspectives on the Agency's work and culture, and contribute otherwise undocumented information to the historical record.

Statement on Editing Practices

It is the policy of the FDA Oral History Program to edit transcripts as little as possible, to ensure that they reflect the interviewee's comments as accurately as possible. Minimal editing is employed to clarify mis-starts, mistakenly conveyed inaccurate information, archaic language, and insufficiently explained subject matter. FDA historians edit interview transcripts for copy and content errors. The interviewee is given the opportunity to review the transcript and suggest revisions to clarify or expand on interview comment, as well as to protect their privacy, sensitive investigative techniques, confidential agency information, or trade secrets.

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Interview Transcript

JS: This is an oral history. The date is January 29, 2013. We are here in Rockville, Maryland. This is an interview with Dr. Leslie Holness, the Branch Chief of the Division of Blood Applications in the office of Blood Research and Review, in the Center for Biologics Evaluation and Research. I'm John Swann. And we'll go ahead and get started.

Dr. Holness, first of all, thank you very much for taking out the time to spend with us to talk, a little bit at least, about your career and what you've done here at FDA and before, and we'll go ahead and get started with where you got started. You were, of course, born in New York and educated there, and so I'd certainly appreciate hearing more about your early life experience and what led you to an interest in science and medicine, and then we can get into your education.

LH: Well, it's hard to really say. I was born in New York and, growing up, I had a science teacher, basically, in the sixth grade who said do science. He said basically that the world needs scientists and to be a scientist, in my sixth grade education. And from then on, it sort of, I sort of gravitated toward science. But I had a few drawbacks in that I didn't have money to go to the, well, to do it straight. I had to go to work early in life, so what I did was I became a laboratory aide for the New York City Health Hospital Corporation, and I worked as a laboratory aide in a hospital and I became interested in blood banking at the time, and I worked as a blood banker in the laboratory.

JS: How old were you? When was this? Was this, you were still a student, a high school student?

LH: Yes. I was in high school at the time. I worked part time, and then after high school I worked full time, and then I worked full time in the blood bank when I went through the university at NYU.

So, after I went to NYU, after I finished NYU, I was the laboratory chief in a hospital laboratory. I was the chief of hematology and blood banking in a couple of different hospitals in New York, in Metropolitan Hospital in New York. And then I was at [unclear] Hospital, which is now closed. And there, I met some foreign physicians who went to medical school but not in the countries that they were from, so I became interested in being a doctor, basically, from being in a laboratory and meeting and then interacting with doctors and going to seminars and things. So I went to, I applied to various medical schools and I was accepted by the Medical School in Romania, actually in Bucharest.

JS: What's that?

LH: The Faculty of Medicine in Bucharest, in Romania. It's Carol Davila. It's a university. They have the medical school, they have pharmacy, they have a bunch of different things. So I went there. Of course I didn't know the Romanian language, and I spent . . .

JS: That must have been interesting.

LH: Right. I spent about six months learning the Romanian language, and after about six months I was able to enter the school. What they do is they give you six months of Romanian,

and then they give you an exam to see how well you know the language, and it's like sort of finishing high school in Romania.

JS: Did you have any foreign language experience before then?

LH: I had done Spanish and French, and it's a romance language. It's very close to -- actually, it's close to Portuguese and Italian more than Spanish and French. So I had had some training in foreign languages here, when I did undergraduate school at NYU.

So I knew enough Romanian to enter the med school. It was a seven-year program. So I did actually eight years, because I stayed on and then did some more work there at the university.

JS: Did you have an idea, as you were finishing up there, where your special interests rested?

LH: Not really. I hadn't, no, not really, because what had happened was I had just gone to medical school out of the blood bank, and I really wasn't interested in blood that much anymore. I mean, I didn't think of blood per se as my lifelong calling, as it later came out to be. So I finished the med school in Romania and did like a thesis and everything, although I did do the thesis in hematology. It was on sickle-cell disease, so I did stay in some of the hematology framework.

And I came back here and I did a residency in internal medicine; then I did pathology at Harlem Hospital. [unclear] hospital in pathology. It was very hard to get a residency. Basically, I'd sent out 50 applications; I only got like 12 opportunities for interviews, and finally through

internal -- actually, it's knowing some people who knew something [unclear] sort of a first year, and then a five-year residency in anatomic and clinical pathology, basically.

So, after that, I applied for, after going through that, I figured that blood, since I knew . . . What happened, well, when I was a resident, I also worked in the blood bank a little bit at St. Luke's in New York, and so it would seem to be natural. It was a natural to do a fellowship in blood banking, so a two-year fellowship at the New York Blood Center. But I only did one year, actually, and then I was recruited for this job.

JS: Was there, at Columbia, was there a blood center there?

LH: Yes. There was a blood bank. Harlem Hospital basically had a Columbia affiliation. We had to go back and forth to Columbia for training, etc., but we worked pretty much . . .

JS: But they had their own blood bank.

LH: Yes, they had their own. Columbia had their own blood bank and Harlem Hospital had their own blood bank, so Dr. Richards was the director, Helen Richards, who actually taught me quite a bit.

So, after that, I kind of, I saw an ad for a blood banker for this division. They put an ad in the New England Journal of Medicine.

JS: Do you mind if -- I just wanted to ask one question. I do want to hear about the move to FDA, absolutely. But I wanted to ask one thing about your experience at the New York Blood Center.

LH: Right.

JS: And you were there a year.

LH: I was there a year, yes.

JS: A year. This was 1990 to 1991.

LH: Right.

JS: And that's a pretty interesting time to be involved in blood banking in any way. There's obviously a lot going on across the country with issues with the American Red Cross. Now, is New York Blood Center, is there a connection between the New York Blood Center and ARC? It's not a regional blood center, the ARC, or is it?

LH: No. They were independent. ARC, I was teaching phlebotomy for ARC, frankly, while I was at the New York Blood Center, so they were in New York but they weren't . . . The New York Blood Center was not a client hospital. The New York Blood Center had 58 client hospitals, and they draw blood; they draw 2,200 units a day for 58 hospitals which are in New

York and New Jersey basically. So I was a fellow there basically, so we did fellowship things in the meantime. I also did some phlebotomy training for the phlebotomists at ARC. It's a little bit of overlapping where New York, the areas that New York Blood Center didn't cover, ARC covered in terms of supplying blood, components, platelets, [inaudible] and plasma and red cells.

JS: Okay. This is an interesting time to be involved in blood banking, I guess wherever you're doing it, because there's a lot going on. There are issues with some blood centers around the country. There's the whole issue of ARC is working very closely with the FDA in trying to follow up an agreement that was developed between FDA and ARC in the late '80s, I guess.

LH: Yes, because they were out of control. I mean, basically, ARC had a lot of problems. They still do. And so rather than being shut down by FDA, they went into the agreement, this agreement, this compliance agreement with FDA that they would, FDA would look at all their SOPs, their standard operating procedures, and sign off on all their standard operating procedures until they got to a point where they were in compliance. There were a lot of complaints. There was a complaint in the Philadelphia Enquirer about them being or not being, having some shoddy procedures and not being able to trace . . .

JS: Particularly in the Washington area, right?

LH: Yes, and the Baltimore and Philadelphia group too. They weren't able to follow units that were collected back to the donor and very kind of dangerous, if you will, problems. And I don't know whether it was a whistleblower at ARC, but usually FDA is slow to act on adverse

events per se... in the sense that usually the deviations have to be pretty much egregious for us to come in like gangbusters and seize things and shut them down, stop their operating procedures. We will give them warning letters or these other letters, the lower-level letters, after inspections, but usually they won't get shut down. So [unclear] shut ARC down, and ARC draws over 50 percent of the nation's blood supply, I mean, shutting them down was a bit impractical per se. So the idea was to do the consent decree, what I'm trying to say, a consent decree in that the ARC agreed to continue, we agreed to let ARC continue operating, yet we look over all their SOPs and they become subject to a certain amount of inspections. And we've been, we're doing well up till now. It's just that they haven't gotten as well. But now they've done very well in the very recent . . . In the last two years they've gotten BioARC 2, which is sort of a computer tracing of all their units, and they have what's called [unclear], which is software that was developed by the French originally, but they're going to lay it on and have ISBT labeling, which is the new kind of labeling that all other blood, the latest labeling, which is supposed to be universal. In other words, units with ISBT labeling, units from the U.S. or units from Europe could be sort of interchangeable in terms of what you read on the label per se.

JS: There's been a long struggle, in other words.

LH: Right, yes. It's been quite a long struggle. But they're doing quite well, actually, considering.

JS: Well, I was curious. When you were at NYBC, if there was fallout coming -- I don't know how things were at the New York Blood Center when you were there, but certainly you

must have had a strong sense of what was going on in a lot of blood banking elsewhere around the country and that there's . . . And this is also, of course, this is after 1985, when obviously we were able to detect HIV . . .

LH: AIDS. That was a problem. The HIV, the first few times that HIV, when HIV reared its head and people were saying, "Well, it's in the blood," they didn't believe at first it was in the blood and blood products. The advisory committee said we need to study this a little bit more. However, it did turn out eventually.

And New York Blood Center was kind of more research oriented. They were doing cord bloods, which hadn't been done before; they were doing storing, collecting and storing of cord blood. They had some researchers there. They were doing the NAT testing, the nucleic acid testing, which hadn't been, which is now the standard in the industry but which hadn't been even done before. So they were developing all those at the New York center when I was there.

They didn't have that many regulatory problems per se, and they had a rare blood repository; they had a rare blood lab, and they had a rare blood repository that they would be able to furnish units, antibody-negative units, antigen-negative units for people who had rare antibodies. So if you had a rare antibody like [unclear] C and [unclear] B, we could supply you with the frozen unit that was [unclear] B negative or C negative so that it would be compatible with your [unclear] and we'd send it off to . . . So that was there. I mean, they weren't really concerned with so much with what was going on with the rest of the industry. It was sort of a research-oriented blood center, the New York Blood Center. I'm not sure how much was [unclear], but the people have changed over there. Al Kaplan was there. There were a lot of really good scientific people there.

JS: But it was also the, you know, where you were at the time, that you found out what FDA was interested in. I'm sorry to interrupt, but can you go ahead and proceed with what you started to talk about with your arrival at FDA?

LH: What happened was, I was in New York and I was kind of working. I had done the fellowship a little bit, and I was doing, I was sort of working also in a private lab, and the thing is that there are so many people in New York that there was work all over the place. I mean, you can just work yourself to death. So I said, if I don't get out of this, I'm just going to die of a heart attack. You know, it's crazy.

So I saw an ad in the New England Journal of Medicine for a medical officer for this division, which was called something else, LBB, the Laboratory of something or other. I forget. I should be able to get that name for you. Anyway, so I answered the ad basically, and I was interviewed and then, with some back-and-forth and haggling, I was interviewed in October, but I didn't get out until December.

JS: But this was a position essentially involved in blood banking applications?

LH: In the regulatory, right, in the regulatory end of blood banking, basically, to handle the regulatory end of blood banking. So I just sort of took the position and moved on it, stayed in the hotel for two weeks trying to figure out whether I liked the job or not.

JS: It was a very different approach to the field than you had been intimately involved in.

LH: Right, right.

JS: You were sort of at the other side of the . . .

LH: Right, I was hands-on in New York.

You know, blood banking is sort of an easy thing to do if you just do everything just like you're supposed to do. If you do everything according to the book, there's no problem with the regulatory, regulators or anything. And that's what we did basically. The easiest way is to just do it by the book the way it's supposed to be done, and that's what we did. But there are so many patients in New York and so much blood [unclear], so you just sort of, you know, you did things, you read the literature and you blood banked.

But here it's regulation. It's keeping, it's a control function. You keep track of what everybody else is doing, what the other blood banks are doing. You write policy, you write guidances, and you make sure that they adhere to the CFRs, the Code of Federal Regulations, which are [unclear] is set out as to what one does, how to run a blood bank, how to run a blood bank, how to treat donors, how to protect donor safety. There's a lot of stuff in there, there's a lot of offshoots of that that you have to kind of manage and take care of.

And then after that, I got into that for a while, I got into managerial, the managerial end. I was kind of recruited to the managerial end once I had stayed just as a medical officer in the blood bank in this division.

JS: How long was that before you moved into the management end of things? [unclear]?

LH: Right. Before I went, I was sort of looking at INDs and looking at and doing blood banking sort of from the regulatory end, you know. People would report to me about violative units. I did the mortality reports, I reviewed mortality reports, and I reviewed [unclear] action reports, and I looked at errors in manufacturing like temperature excursions. Blood has to be kept at [unclear] degrees for the life of the unit, 42 days for [unclear] units and 35 days for [unclear] units. So that's what I did until I was kind of recruited into management from there.

JS: How many medical officers were in the branch at this time, then?

LH: Well, there were two medical officers plus the, well, two medical officers, an assistant director, and a director basically. Now there's only one medical officer in this branch, and there's an assistant director who is also a physician. She is a medical officer already, but she's also assistant director and the director. So, basically, I advised them, when I leave, to hire another medical officer because they need one, so, because there's a lot of stuff, there's a lot of stuff here. On the surface it looks sort of, kind of bland; let's put it that way. But there's a lot of innuendos. There's the arm scrub that you use before you stick in the needle, you know, what kind of chemicals should be in it, how you scrub, whether it's done right. On inspections, they had to have it looked it and reviewed and see whether or not the standard operating procedures were followed. It's quite an intricate business in that sense.

JS: Right.

LH: And you have to do it for the whole country plus the Virgin Islands and all the U.S. territories, and the D.O.D. has blood banks.

JS: Okay. You've opened the way to another question, and that is what you just said. And that is, under the law, FDA has oversight over an enormous number of blood banks.

LH: Right, thousands.

JS: And I gather . . .

LH: And there are two groups. There's a registered group and a licensed group. The licensed group is if you send blood across the state lines, you have to be licensed. Right? If you just collect, if you just go in and collect blood like stuck within your state, you're registered, and there are like 3,000 and like 1,100 for the licensed group and more like over 3,000 for the registered group basically, so there are thousands and thousands of blood banks.

JS: Now, do we, under the law, I think, we're supposed to inspect these annually, or at least the licensed establishments?

LH: They all get inspected.

JS: They all get inspected annually.

LH: They don't get inspected annually. They should be. Well, in my opinion, they probably should be inspected annually, but they're sort of biannually, or if you get a clean inspection and if you have no problems, they won't come back for another two years.

JS: But here's what people might wonder, is, how on earth does this happen when you have the agency with, you know, we have a finite number of people here and a finite number of investigators in the field. I do want to talk a little bit about how you interact with them. But how is that possible to even get feet in the establishments once every year, once every two years, when you have thousands of establishments?

LH: Well, you have the districts, you have districts. You have Atlanta District, Florida District, and every month you have a cadre call. We have a cadre call where all the district gets together and they find out sort of what's new and what's going on in blood banking, and they can ask questions. Sometimes they ask questions beforehand. There's a woman who collects questions before the call and they feed them back to us, and we figure out what the answers are, and usually one of us will talk on the phone and give the answers. The network of district offices are all, I mean, one or two people are on the cadre call per month. That's basically our link to the districts basically. And that's something we do. But the districts are short-handed and that's why they can't inspect every year.

JS: Now, unlike some of the other products we regulate, for example, some levels of medical devices, we do these inspections of blood establishments ourselves, is that correct? We don't have any agreements with states to . . .

LH: No. We do them ourselves.

This branch, our branch does inspections of new, if you want a new license, a new BLA, or you start a new procedure, like you start apheresis, platelet collection, collecting with apheresis machines, then we go out and inspect before. You send us your SOPs [unclear] and then we go out and inspect before we license you for the products, basically. After that, the district takes over. But we do it ourselves. We don't, we have no sort of proxies to do . . . I think the AABB has some proxies that do inspections for them, because they have sort of an inspection program as well.

JS: The American Association of Blood Banks.

LH: Yes, Blood Banks. And we sort of interact with them. We review their standards and we accept their standards and there's a donor history questionnaire that they developed that we've reviewed and we've accepted and we put out a guidance that we accepted their donor history questionnaire, in other words, and answers all the questions that we think are important for the safety of the donor and for the safety of the recipient, of course. So there's some interaction there.

We have a twice-a-year meeting with AABB, where the AABB asks us questions that their blood bank, their client blood bank, their member blood banks, actually, will answer. They're not clients. I mean, it's just an association. It's an association of blood banks that pay dues to be members, but they don't really . . . The AABB is a -- what am I trying to say -- like a

group that lobbies, sort of their interest group. So we have a meeting with them. They have an annual meeting every year, which we usually send representatives to, and they have . . .

JS: You've actually been an official liaison to that group too.

LH: Yes. They have committees that we . . . I was on the Clinical Transfusion Medicine Committee. I was [unclear] Paul Metz now, who's joined the center. He's now the new, will be the new committee member. And I was also on the [unclear] task force, which is the Transfusion Associated [unclear], which we actually brought to the attention of the blood bank for [unclear], the problem of transfusion-associated [unclear].

What happened was we had started to get a lot of, we looked at the fatality. From the CFR, you're supposed to report the fatalities related to blood transfusion or collection to the FDA. We looked at those and we started getting, we looked at a lot of them in which there was, the recipient would have like lung contusion. He would get a transfusion and his lungs would fill up with fluid, and his heart was okay. We didn't know, basically. So finally we had to, we looked in the literature and found out that in 1951 they had this phenomenon, which is where the donor had antibodies. The donor's white cells had antibodies to the recipient. And so we kind of brought that to the attention of the, I presented that at several AABB conferences, that white cells in the donor reacted with the antibodies in the incoming plasma primarily, plasma products. This is primarily plasma products and platelet products. Platelets are transfused with a certain amount of plasma. Antibodies in that plasma, the white cells, would react with the donor's white cells and would cause lung congestion.

JS: And no way to tell this in advance.

LH: No, you really can't. There's no way to test in advance. You can find the antibodies, but some people interact with the antibodies and some people don't, so it's not cost-effective to try to test everybody for antibodies in the donor's plasma. So they called it transfusion-associated lung injury, TRALI, Transfusion Related Acute Lung Injury.

So we kind of brought it out, and so now there's a lot of, now there's a TRALI Task Force and the AABB has a TRALI Committee. We presented it to the Blood Products Advisory Committee. We also present to the Blood Products Advisory Committee quarterly meeting of scientists on that need, and discuss blood issues, blood issues that have, that are sort of plaguing the FDA per se, that the FDA hasn't really found an answer. And the FDA can take the committee's recommendations or not. Usually there's no more than one or two blood bankers on the committee; most of them are surgeons and different people from different areas of medicine, and so we kind of take their advice.

One of the more recent ones was blood pressuring folks. In Europe, they have sort of stopped doing blood pressures on blood donors. If you walk into the blood bank to donate blood, your blood pressure is probably okay. So the AABB wanted us to adopt that here, so we brought it to the Blood Products Advisory Committee, and the Blood Products Advisory Committee kind of said, "Well, if their blood pressure is low and it's normal, it's okay, but if it's very high, we don't think you should probably be donating blood, even though donation of blood brings your blood pressure down somewhat."

JS: Really?

LH: Yes.

And so we didn't drop it. In other words, all blood banks must take blood pressure of their donors. [unclear] blood pressure even [unclear] in some countries in Europe, you don't have to. Like in England, for instance, you don't have to. They don't take blood pressures unless they have a reason to, unless they feel [unclear]. And there are some other problems that are being worked on.

JS: You've already mentioned the Blood Products Advisory Committee, and over the years they've added more consumer representation on that committee. And where I wanted to go with that is to kind of ask, and have that lead into sort of a policy area.

You know, one of the things that we've done over the years in terms of a deferral policy is we looked at, the FDA has looked at certain areas, certain groups, that have posed a problem for collection strategies. Certainly from the period of the '80s and early '90s, there were Haitian, recent Haitian immigrants. And, of course, just one of many groups, Haitian immigrants, men who had sex with men; people, sort of a different framework, people who spent a certain amount of time in Europe, in certain European countries, with concerns with mad cow disease.

LH: Right, right.

JS: And I guess it's no coincidence that you found more consumer representation sort of in the wake of some of these decisions and reactions, which have been quite intense.

So I guess my question is, when one has to craft policy to make the blood supply safe, in other words, one has to come to good public health decisions, how would you square that over the years with the sort of our also political decisions too, if that's what you want to call it. It must be a challenge for policymakers to do that in the face of what many people would consider stigmatizing.

LH: Yes. It's kind of a corroboration to some extent, and the Blood Products Advisory Committee has a lot, their input is sort of important. And it comes to the Federal Register. Here's what we're going to do. Can you comment on it? And then we get comments back before it becomes law. That's the rulemaking end of it, in other words, before it goes in. Of course, we've been working on that new CFR for years now. But that's what we do. We do a public, a Federal Register notice, proposal, a federal proposal, and then it's finalized, and it's open for comment, the docket is open for comment for a certain period of time and then it's finalized, and then you have a time . . .

Also, people that comment are not the general public so much, but blood bank directors, and it's [unclear] some of the difficulty that they have administrating these things.

It's interesting, you talk about MSM. Our MSM policy now is that if you had MSM since 1977, you're deferred basically. Some countries have said, well, [unclear]. Some donors weren't even born then, at that point, so how are we going to do that? So they've changed the MSM policy.

We've had [unclear] because there's another oversight committee. There's this Committee for Blood Transfusion and . . . You know, Jerry Holmberg was in charge of it for a while. I don't know. Anyway, there's another committee that meets, I guess, twice a year or so.

JS: This is an advisory committee?

LH: Yes, sort of an advisory committee as well, but they can talk about cost. We don't, FDA can't talk about cost so much. We only talk about the science and whether or not the science makes sense to some extent.

JS: Right.

LH: This other committee -- I can get you the name and send it to you. It's [unclear]. But in dealing with MSM, MSM was discussed. There was a workshop with CDC, and CDC said, "Well, we don't think you should change it," basically, whatever it is. So some blood banks, some of the European blood banks in Israel, I think, and some of the other blood banks have gone to a year. If you haven't had MSM sex in a year, you can donate. But we still stick to 1977, and it's causing us some problems in the sense that it probably should be changed, but we really don't know what to change it to. We can't change it without it being discriminatory. If you change it to a year, even so, if you're an MSM, I mean, okay, the Gay-Lesbian Alliance says, "Well, it's still discriminatory because you're making us wait a year." And MSM is no worse than a person who's had multiple sex partners. Obviously, you have a [unclear] HIV if you've had more than four sex partners in a year, even if they're heterosexual. If you have more than six, you have even a higher still chance of having HIV. So, the question is, why are you not asking people how many sex partners they've had in a year. So we're still wrestling with that to some extent, and it'll get resolved at some level, just probably not right away. But right now it's

a little . . . And we've had congressional inquiry. One of the congressmen says this is discriminatory. It's not based on science.

In 1985, when they, they didn't know, they knew that sperm was a very good nutrient for HIV virus, but that's all they knew, and that's what it's sort of based on, that sperm, HIV virus can live in sperm very well, so that sort of, to some extent, is where is sort of came from to some extent. And CDC had to sort of approve that, and when CDC, even though they don't make policy, we take a lot of advice from them because they're a research organization and they do a lot of immunology research, so we take their [unclear] research. So I'm not sure where we'll go. But this oversight committee I talk about, they said, "FDA, solve it. Come up with a solution." So that's where we are.

And we have product experts. We have the Division of Transfusion Transmitted Diseases. They look at the tests, they look at the incidence of disease. [unclear] Nakashi [sp.] is now in charge of it [unclear] and Robin Desquas [sp.] is there, and some other folks [unclear], and they have an HIV expert who's a lady named Helen -- I can't think of her name. Anyway, so, and it's their task to kind of resolve these problems, and they can't to some extent. So then it goes to the wider, then it goes to Jay Epstein, who's an office director, and then eventually to BPAC. So we discuss the BPAC time again.

We had the problem of tattooing. If you have a new tattoo in the last 12 months, you can't, you're deferred basically, and some people, in Canada, for instance, [unclear] six months, so they suggested six months. I said, "No, no." The idea is that the ink that they use is used for several different people, and since it's in contact with their blood supply, there's a danger of having hepatitis or HIV from being transmitted, so they have to use sterile pens and sterile inks.

JS: Is that industry regulated?

LH: Well, that's the thing. They're regulated by the states. The FDA doesn't regulate the tattoo industry. So we have collaborated to some extent because if it's a state-licensed tattoo parlor, we'll accept that as the fact that they, as evidence that they use sterile pens and sterile inks.

JS: So there would not be this deferral.

LH: In some states, and usually there's a list of states at each of the [unclear].

JS: Does one bring in some kind of certificate saying you got this tattoo at a licensed . . .

LH: Right. Basically either that, or you say where you got it, and then they'll know that that tattoo parlor is licensed at the blood center. But that's basically how it, pretty much how it goes.

JS: Right.

LH: But those non-sterile inks and non-sterile pens can transfer [unclear], so that's another thing.

So Canada has gone to six months now, so we tried to go six months, and no, no, so it's still a year.

JS: How does one, how does a regulator, when coming up with policies like this, is it possible to even take into account issues of shortages? And that, I guess, would be the equivalent of the risk-benefit test. Anyway, there are shortages, and are shortages, and there have been shortages certainly throughout the period we're talking about, throughout your tenure here.

LH: Sure.

JS: But there have always been shortages, it seems like, in the blood supply, especially now. But to what extent are those, can you connect those to these public health deferral policies?

LH: If we know that it's causing a shortage, then it's factored in to some extent, so we can't do that because it'll cause a shortage, I mean, to some extent.

JS: As you were saying before with, talking about the New York Blood Center, what do you do with these places supplying an enormous amount of blood and you can't reasonably expect the supply to [unclear] shut them down.

LH: Right, yes. You can't. It's the same thing with ARC. That's the reason for the consent decree for ARC. It's exactly. It was a compromise. We're compromising all the time, because if you shut the ARC down, there will be a shortage of blood. Fifty percent of the blood supply will be unlicensed, and that'll be a catastrophe. You'll have unregulated blood in the land in that

sense. Unlicensed for blood going across state lines is considered pretty much unregulated. It's taken into account.

Most of the decisions here are done by consensus. It's discussed and discussed and re-discussed, and if no consensus can be found, it goes to [unclear] and see what they say. And then if their answer . . . FDA is not obliged to do what they say; they're only obliged to kind of take their opinion into account. It's kind of a wider view, if you will. But it's a problem. There's a political side in that sense.

There was a shortage of IV IG, intravenous immunoglobulin, and there are interest groups. There's the Society of 10,000, which are all folks who are hemophiliacs who lack Factor 8 and Factor 9, and they use the stuff. They need it to stay alive basically. So they come to the Blood Banks Advisory Committee and they give their opinion and tell us basically that it'll harm them if there's a shortage, so it's all kind of taken into account. There's hemophiliacs and there are some other groups too.

There's this group, the thalassemics and the iron-deficient group and sickle-cell people, and basically they need blood literally to stay alive, so what you do affects them and they have, they can be, not so much sickle cell as [unclear], but the thalassemics have been more vocal in that. Sickle-cell [unclear] need to be more vocal [unclear] folks. For some reason they don't [unclear]. It should be more typing of the, you know, people should get more . . . If you have sickle-cell disease, you tend to form antibodies because you're getting transfused so much, so many times. Every time you have a crisis, you get transfused, and so you form antibodies. And so there are a number of antibodies are regularly formed. There's Kel, there's e, there's silano, there's c. What we should do, what blood banks should do is give them units that are further

typed. In other words, not just give them A, B and Rh typing, but typing further out and give antigen-negative blood so that they don't form antibodies so quickly.

The average life for a sickle-cell disease patient is 35-40 years. If we could give them units of blood that were more extensively typed, they would live a lot longer in that sense. And this is being done at university [unclear], but it's being done sort of experimentally, and it should be, you know, everybody should, it should be universal basically. But it just doesn't get going that fast.

JS: You mentioned other groups that have gotten involved, particularly the advisory committee meetings [unclear] . . .

LH: Kind of the AABB comes and gives testimony, the American Blood Centers.

JS: Well, I wanted to ask you, as Branch Director, have you had much in the way of public interaction, representing your division and the work of your division when it comes to the public, in whatever venue it might be, whether it's in the context of the advisory committee meeting or talking to the press or what have you? Do you have much or have you historically had much interaction there with the public?

LH: [unclear] the Blood Products Advisory Committee several times. I've presented on TRALI, I've presented on AIDS, AIDS questionnaire, but I haven't had that much. You know, once in a while . . . The thing is, when you take it out of context, if you get a press release, it's sort of taken out of context in a lot of cases: "No, I didn't say that."

But the Blood Products Advisory Committee, there's a transcript. Everything is done with a transcript of the Blood Products Advisory Committee, so you can present to them and it'll all be written down somewhere. Well, I wouldn't be involved, but there's going to be a presentation about source plasma [unclear].

Source plasma is the base, it's plasma collected for further manufacture, manufacturing into intravenous immune globulin, and there are several types of intravenous immune globulin. What you have is a source plasma donor. The donor comes in and they just draw plasma. They give him back the red cells and they pay him for this. So there's been an uptick in the number of people, donors that die like a day after, the same thing, the day after their source plasma donation; and these donors represent some heavier donors, they have high BMIs, they have several problems basically. So we have developed a [unclear], which is basically divided by weight. We have three weights. If you weigh in in any of those three weights, that's how much plasma they take from you. If you're light, they take a little bit; if you're middle, they take a little more; and if you're heavy, they take some more plasma from you, so we think that may have something to do with it, and it'll be discussed again. It was discussed in 2003, and nothing was really done.

What happened was -- and I presented that in 2003 -- there's a group called Westat, which is an epidemiologic group, and they came and they said, "Well, the biggest cause of donors dying is heart disease. [unclear].

JS: Hold the thought [unclear] ancient technology here. Okay, please continue.

LH: Donors die of heart disease or they've had heart disease. Most SOPs say if you've had heart disease but you're on no medication or on medication, except aspirin, you can still donate. In some cases the relation of the blood volume will cause them to have a heart attack, cause the donor to have a heart attack and die. But there's no way of knowing beforehand if this going to happen, and the donor is not getting paid, so there's sort of a risk-benefit in there anyway. So our premise is basically that we think that the heavier donors should not be donating as much plasma as they are because they may be heavy in weight, but they don't have as much blood volume as we think they have. The blood volume is pretty much, lean folks have more vascular tissue than fat folks. If you're fat, you have fat tissue, but fat tissue is not as well vascularized as if you're lean, you're lean and muscled. So we think that that may be a problem and it'll be presented [unclear] CBER Blood, I present it for CBER Blood, but since I won't be here after this month, it'll probably be presented by a doctor [unclear] BTAC, or there's also another medical officer, Ricardo Espinoza [unclear].

So the question is whether this nomogram or this schedule of how much plasma you take a person should be changed, and so that would be the discussion, whether we should change it. If it's causing people to die, of course we should change it, but the question is how to change it. It'll have to be changed in accordance with the body mass index or the donor's, not just the donor's weight alone, but the body mass index, height and weight and [unclear]. So then the question is how to do that, and there are formulas and different things, and so it probably can be done on computer fairly easily. So, anyway, that's a wrinkle. I mean, those kinds of problems are problems that we send to the advisory committee to kind of decide for us basically.

JS: And, of course, the ultimate decision about whether something becomes a change in actual regulation or rule rests with us.

LH: Right.

JS: We get advice from them.

LH: Right. And we write a guidance. We usually write a guidance. A guidance goes out to all blood centers and all registered and licensed blood banks, and the guidance just says, the guidance will have a background, here's a problem and here's what we did about it, presented it to the Blood Bank Advisory Committee, they said XYZ, we think they're right, and here are the changes that you must effect immediately or within six months or whenever, whenever we think this is feasible. We've done that with tests for Chagas disease, tests for West Nile disease, tests for other things, hep C, hep B.

JS: Well, how many tests are the centers now conducting on the collected blood? It's a lot more than eight, it sounds like.

LH: Well, yes. You have to do one test on each. The test on Chagas disease should be done on each donor once now, and West Nile, it's seasonal; it's seasonal for West Nile. It's about 10; really, it's about 10 tests basically. And everybody gets NAT; everybody gets a NAT test in addition to any of the serological tests. You know, there are two types of tests. NAT is the nucleic acid test.

JS: What does that cover, then? The NAT test would detect . . .

LH: It would detect HIV, HCV, HBV, okay, the [unclear] serological test, the West Nile is in that test basically, but basically HIV, HBV, HCV are all done, have that test in addition to serological tests.

JS: Well, this is sort of genetic fingerprinting. Do you think it saved places like ARC money over . . . I mean, they were in trouble for quite a while, I mean, in part because they're running all these 12, 13 labs across the country and conducting all these tests now. Has this sort of simplification, not that you're speaking for ARC, but would you imagine that it's something that would have saved them a little expense?

LH: Well, we're not supposed to deal, really, with expense, but I would think so, if they consolidate those into a few. There's a lab up there up the street here. But I imagine it's saving them some money, yes.

The nucleic acid test is more accurate and more, I mean, you have to . . .

JS: It's a better test.

LH: It's a better test than a serologic test in most cases. You know, in cases of HIV and HCV, HBV, they're better tests. They're more advanced, they're better. They detect a lower detection of . . . They can pick up tests that the serologic tests miss, basically. See, it depends on how

many copies per mL, how many copies of virus per mL is in your blood, whether or not the test picks it up or not. And the NAT test will pick up a hundred copies per mL. There are NAT tests that will pick up 40 copies per mL, which is very, very early in infection. And that's what you need because the viral tests may not pick up. That's why your window period, which is the period -- there's the period in which you get infected and then the period in which the test shows up, and the NAT tests have shortened that period to 12 days where it used to be months. In the case of HCV, it was six months. It could be as long as six months before the serologic tests showed up, and we just had to deal with it before the NAT test came along and we can narrow that window period. And that's really the advantage of having NAT testing, basically, so that the window period is really shorter, a matter of days before you, between the time you get infected and the time that your test shows positive. Because if you donate blood in that window period, the test is negative, the blood goes out, and then somebody gets disease.

JS: And then the center has to stir around and start contacting people and explaining.

LH: Right, yes. And they have to try to recall any units that may still be out there. And that's another whole adverse-event problem. If there's still something that they haven't done much about is bacteria in the components. You have bacteria in platelets because platelets are kept at room temperature for five days, basically. Even though blood is refrigerated, it can get contaminated if the donor has bacteria in his bloodstream.

Luckily, most donors don't feel well enough if they have bacteria in their bloodstream when they donate. However, if it's a low enough amount of bacteria, it'll get into the unit; it'll get into the blood.

Now, for platelets and for -- we don't have a good test for red cells, but we have a good test for platelets and plasma called [unclear]. It's sort of almost a computerized test, basically, where there's cultures done. One is at day three, and then later there are . . . Actually, there's no new culture done, but at the last Blood Bank Advisory Committee, it was discussed whether a new culture should be done at day five. Most of the time the recipient is infected between day three and day five, and so the idea as to whether or not we should do a second, not culture, but there's a rapid test that can be done. But the question is, then again, you run into expense because the rapid test is a little bit expensive. But it'll save lives, though, basically. So if you test from day three and it's negative, then you're pretty sure that the platelets you transmit are going to be sterile. However, if there's a low level of contamination and the tests don't pick it up, and that grows between day three and day five, it'll infect the recipient.

JS: Blood products aren't heated, I mean, right? You can't do that.

LH: No, you can't heat blood products. But platelets are kept at room temperature. They're kept at ambient temperature and agitated so that the platelets stay, because you'll kill the platelets if you make them cold. So that's a big problem.

JS: It's a big problem, and one you take up. You've been chair of the Fatality Review Committee here at FDA for some time.

LH: Right.

JS: And I gather from what you've said, then, that many of those problems that we face when it comes to fatalities actually relate to bacterial contamination?

LH: Yes, right. We have 70 to 100 or so fatalities reported to FDA per year. When consider there are like 16 million components transfused, it's a low number. However, hospitals and many of the things will filter the fatalities through risk assessment before they come to us, and we kind of trust them. We have to trust them to some extent to tell us what happened, in other words, how the patient died. So if they, for instance, if they over-transfuse the patient, the patient [unclear] what's called transfusion associated circulatory overload. [unclear] they transfuse the patient to the point where he has a heart attack and dies, basically.

Now, it's pretty much the hospital's fault because they didn't regulate the inputs and outputs thoroughly. In some cases you can't. In a lot of cases, you have to regulate what you put into a patient in terms of what comes out in terms of urine and, well, urine primarily. So you can't over-transfuse a patient. So if that happens and it goes to risk assessment, risk assessment says, well, let's say the patient died of some underlying disease rather than transfusion-associated circulatory overload, that's just an illustration. That doesn't happen a lot. Most of the hospitals are fairly honest and do a pretty good job of reporting the fatalities.

[unclear] come to compliance. They're sort of the repositories. The cases are sent to us. We have five medical officers who meet once a month at the Fatality Review Committee. I was the chair; now it's going to be Celene [sp.], who's in [unclear] now. And we review those and we discuss them. We get together and each of us reviews three or four at a time, and we get together and discuss it and try to figure out whether this is actually what happened or whether it's feasible, whether it's medically, you know, whether they acted with medical responsibility,

or whether the problem is with the product. We're primarily interested in the products, whether there was a problem with the product, whether it was incorrectly stored, whether it was incorrectly cross-matched, whether it was used in an improper way.

And you talk about heated, whether, you know, there are blood warmers. There are people who can't get cold blood and they have to have the blood warmed. It has to be at body temperature, which is 98.6; otherwise they'll have a reaction. So, in some cases the blood may be placed in a blood warmer. There are blood warmers that are on the market, commercial blood warmers. They may have set too high. Sometimes, once in a while they stick blood in the microwave, and the cells are all lysed and it destroys the patient's kidneys. I mean, there are all kinds of problems that crop up.

But we try to determine the cause of death, and then we put like an FDA cause. We look at their cause and we look at the FDA cause and see pretty much if they match. And then we produce an annual summary, and it's on the web. I don't know if you . . .

JS: But what happens if they don't match?

LH: Well, what happens, if there's a suspicion, we send them a, we have them inspected. A field inspection will go out. In almost every case of bacterial contamination, the field goes out. The field goes out, and there's an inspection report, and based on the inspection report, you can send them either a warning letter or . . . There's a letter that's just before a warning letter. I can't think of it.

JS: Notice of inspection?

LH: Yes. Well, there's a Notice of Inspection 482 that's done, and then the 483 is the deviations, so whatever deviations . . .

JS: [unclear] warning letter.

LH: Right. So, the inspection looks at the manufacturing processes, and if they find deviations, they'll write them down. But that's basically as much as we do. We'll send them a warning letter, and they're obliged to change their process if we think their process had anything to do with the storage or the manufacturing or storage of the component.

JS: Using microwaves isn't something that we recommend.

LH: Yes, that's an extreme case basically. But there are blood warmers which will keep the temperature at body temperature, keep the blood at body temp. You thread through tubing and then the blood goes through this filter and then goes through the tubing before it gets into the body, and that tubing is kept, is warmed to body temperature so that the blood goes in a few drops at a time at body temperature. So that's supposed to happen, but sometimes it doesn't.

There are so many nuances. There's leukocyte reduction. Leukocyte reduction basically, you want to take the leukocytes, the donor's leukocytes out of the blood before they're transfused to the patient basically, because . . . Okay. In the literature, there's the problem of extraneous leukocytes, you know, leukocytes from the donor having a problem with the donor's immune system, reacting with the recipient's immune system, rather. So it causes immune

modulation. So the thinking is that if leukocytes are not there, if leukocytes from the donor are not there, it's a safer {unclear}. You know, Canada has adopted universal leukocyte reduction. Here in the States, doctors can order leukocyte-reduced blood if they want it, but usually, otherwise, they get the regular blood. It wasn't considered, well, [unclear] arguments about it, but it wasn't considered serious enough to do universal leukocyte reduction as they do in Canada. I mean, it all depends on who's in charge and how serious they think the problem is.

JS: So there are good arguments on either side.

LH: Right, there are good arguments on either side. What can I tell you? So that's another problem.

There was, there were so many things.

JS: Well, this might be a good opportunity to kind of reflect back on that, to look back a little bit, and over the past 20 years, more . . .

LH: Twenty-one years.

JS: Twenty-one years, yes. Kind of look back and think about what you believe are some of the sort of milestones in the way, since you've been here, the milestones in the way we've changed our approach to regulating blood banks or the way blood bank practices are conducted.

LH: Well, we've gotten a lot more, just in a general sense, we've gotten a lot more hands-on. When I came in '91, there were submissions here that were two years old that we still hadn't gotten to. Now, there's a policy group that keeps us on our toes, that makes sure that all submissions are met, that timelines are met, that . . . Most of our submissions go out before their due date. Submissions were left beyond their due date when I got here in '91 and nobody really did much about it, but now that's all changed, so that's just an overall kind of view of things here in the FDA.

JS: That's an internal group you're referring to, by the way, right, this policy group?

LH: There's a new, yes, sort of a QC group. They hired some folks and [unclear] in charge of it. I don't know if you know [unclear].

JS: No.

LH: So in terms of, within CBER, so that's kind of an oversight group. There's a monthly forum called a Reg Forum where you talk about any submissions that have problems, that for some reason are held up by problems. I mean, the submission, we review, and the way we work pretty much is they send us SOPs, whether it's both new BLAs and if they want to change their BLA in any way. There are sort of two different kinds. A new BLA is a brand-new blood bank that wants a license. They want to be licensed to sell their products across state lines. They send us all of their SOPs. We review them and we sign off on them, and then they get inspected, and then after their inspection, sort of off they go. If they want to change anything in their SOP, it's

a manufacturing change, and then they have to send it to us: we're changing this. We're now, before we deferred people who had cancer, now, after five years, if you had cancer and you're clear after five years, now we're allowing them to donate. What do you think about it?

JS: So they're not notifying, they're requesting.

LH: Yes, they're requesting approval, yes. They're requesting approval. If they don't get approval, then they can't change their SOPs. It's not notification.

A minor change can be notification. We have annual reports in which they're notification, so there is a category of minor changes that are notifying [unclear]: we're buying a new machine or we're buying a [unclear] plasma phoresis machine, replacing 4.1, we're going to 5.3 or something. It's a minor change, refining a centrifuge, that kind of thing. They send it to us and they put it in their annual report. We review also annual reports, and then we just, we said fine.

There are three types of things. There are CBEs, which is CBE, CBE30s, and annual, one-year review. CBE means, it's a notification; it's a minor thing, notification to us, we're doing this basically, and if we object, they have to stop. CBE30 is, we're going to do this, and you have 30 days to stop us. And an annual, they can't put anything within a year. It's a major change. The difference is basically that if they're doing things according to our guidances and our memoranda, then we can [unclear]. And they mention it: we're doing it in accordance with guidance number 66J7, which says you must do XYZ. So that's pretty much our oversight, you know, our kind of oversight scheme in a nutshell sort of. Well, that's the way we regulate. They ask us, can we change our SOPs, and we say yes or no.

There's also deviations. If a refrigerator breaks down and the temperature goes up from 1 to 6 degrees, which is where blood is stored, to 10 degrees, they ask us, we had a refrigerator break down, the temperature went to 10 degrees. Can we use the blood? And we decide. We talk about it and decide. We ask them how long was the blood . . . Because it's violative; now they have a violative product, a product that has violated FDA regs. So we ask them how long has it been violative, and if we decide it's not too much of a problem, then that's when some of your blood bank experience kicks in, and we tell them yes, you can use it or, no, you have to destroy it. And they comply. It's not a real major problem.

That's sort of nuts-and-bolts kind of. This is what we do every day. Every day we look at submissions, every day we look at SOPs, every day we're doing temperature excursions, experiences, answering questions, that kind of thing, and there's a lot of questions. There's always a lot of questions from the blood bank that come in.

JS: The regulations spell out explicitly what's expected in an application that you're going to review, right?

LH: Yes, sort of. We've just gone to electronic applications basically, which spells out more than it used to. It's esubmitter. I don't know if you've heard of that. It's an electronic application. It's sort of like Turbo Tax. You say, "I want to submit something," you go online and you put your information in, and you send it to us on disk basically. And the way it does this, there's this flip-down thing, "What do you want to submit? Is it a BLA, an extra submission," that kind of thing. You choose and do the thing. And also, we've incorporated guidances into it: you may want to look at this guidance if you're doing this; you may want to

look at this guidance or that guidance. That we developed. That's sort of a major one. Actually, that's a major step forward basically. Esubmitter submissions have grown faster than your regular paper submissions.

And then we have, we had a workshop two years ago where we tell everybody pretty much what's required in a submission for each kind of submission, for both blood, whole blood, and for plasma and source plasma. There's whole blood for transfusions, platelets for transfusions, [unclear] plasma transfusion, and then source plasma is for further manufacture. It's stored for 10 years and then sent to a fractionator, where [unclear] put it in a column and then cone fractionation, just like in fracking, just like the petroleum industry and you get different components. You get albumin, you get various factors all from different levels that go to different products. That's source plasma for further manufacturing, and that's a different, a whole sort of different ballgame than the whole blood for transfusion, platelets for transfusion, [unclear] for transfusion.

JS: I guess all the more important than checking the tracking unit by unit where things go. If you have a unit of blood that's eventually going to be dispersed to any number of plasma products, I guess you want to know where those products came from. Right?

LH: Sure, sure, especially if there are bugs in it. There's bacterial contamination; there's babesia, which is plasmodium kind of parasite, babesiosis. It's a parasite that's caused by deer ticks. And so if you walk in the woods and you get a deer tick, you don't feel anything because you're healthy sort of, but if you give blood and that blood is given to somebody who's immunosuppressed and in the hospital, it'll kill them fairly fast, multiply and kill them fairly fast,

basically. So what happens is, if you give your blood and it's made into components, you may have babesia in each component, so you may be giving it in different places, so you kind of have that problem. Well, [unclear] the same as HIV.

HIV is pretty much eradicated. There's a very, very low HIV transmission now because the tests are so good, and the lab tests are very good in our experience.

JS: What seems to be today the biggest concern with things [unclear] transmitted?

LH: Bacteria, because the tests for bacteria aren't that specific, aren't that good. If you transfuse platelets that are late in their shelf life, three to five days, they could transmit bacterial contamination. It's a major problem.

JS: Do you see autologous blood donations are, in the '90s and forward, I guess, became more and more popular, but is it not exactly practical if you have an accident or if you're not near where your blood is or you need it right away if it's frozen or other problems? But have we seen an uptick or a decrease in the amount of units that are autologously donated in the recent past?

LH: Well, most autologous units are donated for elective surgery. So if you know you're going to have surgery, the doctor will tell you go have some autologous units, one or two autologous units drawn, and that's fine. Autologous units for emergencies are impractical. You really can't do it because blood really doesn't last that long. And if you freeze it, freezing is special. You can freeze blood, but it takes a long time to be deglyced. You know, you freeze it

with glycerin. Glycerin needs to protect the cells in the frozen state, and then it has to be defrosted and the glycerin washed off before you can transfuse it, and so you can't freeze enough to be significant if you're in an emergency, if you have a lot of blood loss. If you're in a traffic accident and you have a lot of blood loss, you can't defrost enough units fast enough to save a patient's life, basically. But if you have elective surgery, autologous units is fine and is used, widely used.

JS: Still the case.

LH: Yes. It's the best blood for you, your own. But it has to be planned. The surgery is planned and you have to be, of course, have a good hemoglobin and be in good shape. You can't have low hemoglobin and you can't donate blood for stuff.

JS: Right.

LH: I don't know [unclear].

JS: So, as you look back on things, have there been vast changes in the way the industry has changed over the years?

LH: Oh, yes.

JS: NAT testing is a good example, I guess. That's [unclear] since the time you've been on board here.

LH: Yes. And even bacterial testing of platelets has helped, apheresis, platelets, and even whole-blood platelets are tested to some extent. And it'll get better. I mean, it's getting better. So it's lowered the number of contaminated, bacterially contaminated platelet transfusions, but it hasn't eliminated them, but it lowered the number, having this testing between day one and three, basically. So, yes, so things are much better.

JS: Where does artificial blood stand? Is this like the Holy Grail? Is it feasible, artificial blood, today, or is there one on the horizon, if not?

LH: Well, it's on the horizon. I think it's been approved for dogs. I'm not sure. There are some problems with it. We don't really, I mean, it's not our group that looks at it, to tell you the truth. It's the Division of Hematology, Larry Landau's [sp.] group. It's not really our group. There are some problems with it. I'm not sure what remains, to tell you the truth. But it'll be, you know, to take a patient to the hospital, it's great because it's sort of a product that doesn't have to be refrigerated, put it on the shelf in the ambulance and then you can give it in the ambulance, and it'll take the patient to the hospital and then the patient can get his own blood in the hospital. That's where we are with it.

JS: [unclear].

LH: Yes. There's artificial blood. It's sort of a hemoglobin substitute, they call it.

JS: It's collected; it's manufactured from blood products.

LH: It's manufactured from expired red cells, basically, from blood components as a hemoglobin substitute. That's the theory, but they're still having some problems with it. That's why it's not [unclear]. It hasn't shown to be effective and not toxic. It's not non-toxic at the moment, basically. But they'll get there.

When I came here, I mean, when I started in blood banking -- not when I came here; when I came here was . . . When I started in blood banking in the 1950s, they were taking blood in glass bottles, basically. Blood was being collected in glass bottles. The shift to plastic bags was a huge advance. And I was a tech then. I was a tech [unclear]. The shift to plastic bags was a huge advance. NAT testing was a huge step forward in terms of infectious disease testing, and it's cut down the number of HIV, HBV, HCV cases. And HCV is bad; it's a bad disease. You get HCV, your liver slowly is destroyed. You can live fine, but you still have to take medicine the rest of your life and eventually you get liver cancer. It's not as quick and dirty as HIV, but it's still effective and it still does the same job. So, to get NAT testing on those things, that was a huge advance.

The sort of rediscovery of TRALI and how much damage it'll do was a major advance in the sense that now, if it's recognized early, it can be stopped. And in terms of, if a patient is experiencing TRALI, they can stop the transfusion and the patient immediately starts to get better. You give oxygen and fluids and the patient can be, even though you still have 10 to 15 percent . . . Of the number of people who get TRALI, 10 to 15 percent expire, but the rest of the

percentage live. And now, since we've sort of brought TRALI out into the light and there's a lot of research going on and it's now less than 10 percent. Now the number of TRALI reports is very low.

I can send you the link for the summary, our summary, because we didn't do that before I came, basically. We kind of [unclear] our summary. The committee, I came up with a committee, and then after the committee, the summary publication of the, the web publication of the [unclear].

JS: Well, that would be a nice addendum to this document.

LH: The summary report of fatality. And it has been quoted, so it's a good document. We've done a lot of work on it.

JS: [unclear] a representation of some of the work that's gone on.

LH: Right. Yes, the stuff [unclear]. And the germ contamination, they've made strides in it and they'll make more strides, but they've made strides, and it still happens but it's not as much as it happened in the past, before they had this [unclear] system, bacterial detection system, and they shed light on it. In our cases, when you shed light on a subject, then people start to do research and they come up with products that will resolve the problem.

There are still problems. There's a problem of iron in blood donors. When you take blood out of people, it lowers their iron.

JS: Right.

LH: So, some of those folks, their iron [unclear]. You can't take blood more often than every eight weeks, so if you take blood religiously every eight weeks, in a year you have low iron stores. Basically, you lower your iron stores basically, and so that's a problem that has to be discussed again.

JS: But you can give it more frequently, can you not, if you're giving it autologously, though, can you?

LH: No.

JS: No?

LH: No, you can't go more frequently for autologous. And according to the CFR, you can give more frequently if you're examined by a physician and he okays it, but you can't do that more than once or so, basically, and that's in special cases. But a regular blood donor would not be able to give blood more than once every eight weeks, and still, with that frequency, his iron stores are lower. And you can take iron-rich foods, you can do some other stuff, but somehow it's still . . . So we're trying to tackle that problem in that we might be able to, if we can either do interval, you know, extend the interval between blood donations or, well, you can't really take less blood, but schedule folks . . .

You know, there are tests that you can do on iron stores. There's ferritin tests, etc. So you can put a ferritin test. There's no quick ferritin, turnover ferritin test. What you can do is, once a donor has donated, you can take a ferritin test, and the next time he comes back, you can look at the ferritin test and see whether you can donate or not. That's not widely in blood banks now, but it probably will be in the next year or few years.

JS: And the computer database is such that pretty much anyone can send a donation of blood somewhere is going to find themselves in the database if you don't go back to the same blood center to donate?

LH: Yes. I mean, if you don't go back to the same blood center?

JS: In other words, if, I think one of the things that ARC wanted to do in the early '90s was to put together -- I might be wrong here -- but put together a system, a computerized system that would . . . I guess they must have had independent databases amongst their regions or something, and that . . .

LH: Yes, right, and they do talk to each other.

JS: Not that they're the only ones that collect blood. I realize they only do maybe half or less.

LH: Yes. You're in a database, and usually the database will send you a notice after eight weeks to come in and donate again if you want to. If you don't want to, you just ignore the notice. But, yes, that's one of the things that we try to put in the database.

JS: Okay.

LH: And some folks were resistant to it because they said, well, I don't want to be in a government, with our names on a government list or something, on a government supplies list. But we don't know anything about the government. The government doesn't get the ARC donor list in any sense of the word. But, yes, they've improved in the sense that there's databases now kind of are integrated; they talk to each other.

JS: And that's the way you can contact this person if they have an anemic issue or something, you could follow up.

LH: Right.

JS: I see.

LH: Right, right, right. And the hemoglobin test that they do in the blood bank is not really that accurate in terms of iron stores. In other words, your iron stores can go down and you can still pass the hemoglobin test to donate. So if you donate, [unclear] basically. There are other

tests, ferritin tests, that will give them more accurate detection of what your iron stores are, and they probably should be in blood banks, and they probably will be eventually.

Then there's giving iron. Some blood banks have, this is all controversial. You know, you lose a certain amount. They know how much iron you lose with each blood donation, so the idea is to give you an iron pill as you leave the blood bank and to take this pill, and it'll restore your iron. So some blood banks are for it, some blood banks are against it. It's still controversial because they think it's therapeutic, it's treating people who are basically normal and not really . . .

JS: It beats liver extract.

LH: Right. There's one blood bank that has an iron for women, because menstruating women basically are losing iron through their menses, so you give them iron and restore their iron, and so one blood bank has an iron-for-women program. The problem is, those programs need to be closely monitored to make sure the donor is taking the stuff, and that's sort of done by nurses basically [unclear] people dedicated to following up with the donor.

JS: So we believe, does FDA have an interest in this, right?

LH: Well . . .

JS: I mean, the donor is intimately affected by these sorts of issues.

LH: Right, right, yes, and then discussed back and forth. I mean, but those are kind of issues that kind of exist today that have started floating around and are still kind of being discussed. But back in the old days, they were basically testing and lowering the number of fatalities that occurred, now it's a little more kind of sophisticated, if you will. And preservation and storage, you know, storage conditions, keeping the proper storage conditions of the various components. That was, I mean, 20 years ago that was, those were the problems. But now it's become iron in donors, bacterial contamination, a little less [unclear] on the other infectious diseases. The 12-day window, they're closing. They're trying to close the 12-day window, so then it's a two-day window or a one- or two-day window. So, yes, they're also dealing with that.

And the [unclear] problem, of course. The [unclear] problem is sort of a large problem because it's a political problem as well basically. If you lower it to a year, what have you done? Have you increased risk any? It's hard to tell.

JS: Well, in the case where we did, I think we changed our policy in the early '90s with regard to Haitian immigrants.

LH: Right.

JS: And did we notice a change in . . . Honestly, did we notice a change in issues with the blood supply when that was instituted?

LH: Well, the problem is the Haitians don't donate blood.

JS: Oh, they don't.

LH: I mean, Haitians were very upset because they were being discriminated, and they marched in the streets and everything [unclear]. When it came down to it, you know, very few of them came to donate either before or after the flood, so it's hard to tell. There wasn't a real change when we dropped the Haitian immigrants.

And there probably won't be a real change in the tattoo thing. We got the tattoo business from 12 to six months. There probably won't be a real change because Canadian donors aren't much different than American donors, so there probably won't be real change if we drop the tattoo restriction.

And then there's also transgender people, which are making a lot of noise recently. We have said basically, [unclear] since 1977, you're deferred basically. Suppose you were a male and then you changed your gender to a female. You're now a female. [unclear] female. So now you're having sex with a male, so what do you do? Basically, can you donate blood or can't you? FDA has said [unclear], so we have said no. We said we're going by your genetic thing. If you're a male, if you're born a male, you can't donate even if you become a female basically. And the transgender folks are all up in arms, and they bother blood bank directors no end and say this is discriminatory and unfair, etc. I have no risk. Many of them say I have no risk, I have been with one partner or I've never had a partner, or they say different things. I mean, that's one of the problems. If you defer the whole class of people whether the promiscuous and the folks who never had sex ever in their lives, so the problem . . . So that's another sort of group. There's really no data. There's foreign data on transgender folks, but it's from Brazil and different places, Sao Paolo. And there's an American, CDC data, there's really no real data

which says that basically transgender folks are folks who are generally in a kind of, live a kind of low life and there may be different things. I mean, it's discriminatory sort of on its face, but it's the only data that's out there. So we have kind of stuck to the fact that maybe . . . Well, we've changed a little bit.

What have we done? The last AABB [unclear], we had decided to look at transgender individuals on a case-by-case basis. Those individuals who have never had sex -- I have it written down somewhere -- who have never had sex before they're 17, and after they changed to a woman, then they start to have sex. If they never had sex before the sex change, you can be treated as a woman. In other words, you don't have [unclear] the question basically. That's the latest wrinkle. Rather than just sweepingly, you're genetically a male, you can't do it, if you were genetically a male but you haven't had sex, and [unclear] have sex, you were sort of okay and we'll discuss it.

JS: So it's a policy that's in some flux.

LH: Yes, it's in a bit of flux, but it's a hard policy to keep up with.

JS: Clearly.

LH: And the ARC people are saying that we're being bombarded by these folks -- they're a small number of folks -- all the time. But what happens is it's discriminatory, and then when you say, okay, sure, you can do it, everybody goes away and nobody comes back and donates blood. And that happens all the time, and it's one of the things . . .

JS: And, in the meantime, there are the issues, the very real and concerning issues of shortages and what, how the shortages . . . How do you deal with that as an agency?

LH: Shortages [unclear] holidays and . . .

JS: It's seasonal?

LH: Yes, it's pretty much seasonal, and we don't really deal with them so much as an agency. Most blood banks will have a list of donors that they can call if there's a shortage. So they'll have folks of different types, in other words. If there's a shortage of A-positive, they'll have a list of A-positives they can call in and they'll come in and donate. It's not, it doesn't, I mean, it helps somewhat, but it's not foolproof. But there's never a really full supply of blood on the shelf at all times. It's pretty much seasonal. The 4th of July weekends, there's not that much blood; Labor Day weekends, there's not that much blood. Folks go to the beach and they don't [unclear]. And sometimes in disasters, like 9/11, [unclear].

JS: [unclear].

LH: [unclear]. In disasters, there's too much blood in some cases.

When 9/11 happened, the New York Blood Center called us up and said, "There are people around the block; there are lines of people around the block waiting to donate blood. What do we do?" basically. They fill up the refrigerators. Blood expires at 42 days; red cells are

gone and the platelets [unclear]. [unclear] you can keep for two years; you can freeze it and keep it for two years. But the red cells are gone in 42 days [unclear]. So we didn't really have anything to tell them except take their names and tell them we'll call you when we need you.

As it happened, there weren't that many survivors to 9/11. Folks were pretty much gone. So they had all this blood that they sort of didn't know what to do with, so they had a glut. And [unclear]. So they shipped some of it out to different places that had shortages. But that's what happens. If there's a disaster, there's a glut, folks. You know, the folks that are okay will come and donate blood, which is fine, which is good. That's a normal human reaction. But for a blood bank, it plays havoc with their supply, to keep inventories steady.

JS: So it's not a situation where they're actually discarding blood. It's just it's not used in that case and the survivors, then, you could send it to other blood centers.

LH: Yes.

JS: We could export it, I suppose.

LH: Yes. Well, we don't really export blood. They had an importing-blood program, but since mad cow, we don't import blood from Europe anymore. We export source plasma, but we don't import any components, any other components. Because we have, because of our, there's a lot of source plasma centers, we're becoming sort of the OPEC of source plasma. I mean, there are a lot of source plasma centers and a lot of source plasma donors, and it's exported to Europe because Europe has a lot of folks who are factor 11 deficient, factor 10 deficient. They make it

into derivatives, they call them, derivatives, you know, intravenous immune globulins. So we export but we don't import [unclear] anymore. We used to import; in the '50s, we imported. But after the mad cow, we don't import from them.

JS: Before that [unclear] less than 5 percent, wasn't it?

LH: Yes, less than 5 percent. Actually, the New York Blood Center was only, they imported red cells from Germany before they stopped. [unclear] from Germany and Austria [unclear].

Other questions?

JS: Well, we've covered a wide territory here, I think, some of the issues that are of great concern here as far as FDA is concerned, as far as public health is concerned.

So, once again, I very much appreciate your willingness to sit down here and talk about your experiences and especially in such a busy week for you. This is your last week here at FDA, and I'm sure you hopefully look back at your 21, 22 years here with some fondness and . . .

LH: [unclear] I'm sorry that I can't remember more than I do, but there are so many things that go on every day. And that's one of the good things about the job. You never know what you're going to need until new problems crop up every time.

JS: Right. Well, I want to thank you again very much.

[END OF INTERVIEW]

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