(CD/SF) Session #1
Interviewee: Barbara Chang October 25, 1990
Interviewer: Susan Resnik Glendale, CA

Q: Today is October 25th and I'm in Glendale with Barbara Chang. Barbara is the Regional Business Manager for the Americas for the Hyland Division of Baxter.

Barbara, we first met in 1979 and I would be very much interested in your sharing how you originally came to work at Hyland and the beginnings of your life with the hemophilia community.

CHANG: Susan, you have a good memory and that is the exact year that I started with Hyland and in fact I started in October of 1979. Previous to working at Hyland, I was with Becton Dickenson. I was a sales representative for Blood Bank Reagents and then moved on to be International Marketing Manager. Prior to that I was a blood bank technologist and a chief technologist in good old New Jersey (since we're both from the east coast).

Q: Right.

CHANG: When I came to Hyland, I knew lots of basic information about blood therapy and about blood coagulation, about blood types but very, very little about hemophilia. It is something that isn't or at least at that time was certainly not a household word. And, it was not even commonly known in my own profession which was laboratory diagnostics and laboratory hospital related work. I found out shortly after coming to Hyland that the hemophilia community was rather grouped together in what I soon learned was comprehensive care centers. So when one was familiar with a treatment center or even a locale where there are a lot of patients, there was a lot of basic information about hemophiliacs. But outside of that in the hospital world, in the laboratory world, it was not commonly known.

Q: So, as you embarked upon this new adventure what was the relationship between Hyland and the hemophilia community at that time? What were they funding?

CHANG: One of the most exciting projects I was asked to work with when I started in approximately 1980, was to assist with the National Hemophilia Foundation in a project that involved Susan and many other nurses. The project was to create an educational working manual to help educate those families that were involved in hemophilia. And I was, of course, impressed, and actually surprised that a manufacturer such as Hyland was so closely involved with trying to help meet the needs of the person with hemophilia and be concerned much, much more beyond just producing a product and having that product available. What is so unique about the manufacturers, I think this stands for all

of the manufacturers, is that it is a very special product we make and our interests go far beyond just "here is the product" and handing it over to the physician and then it is given to the patients. I find all of the manufacturers and the representatives of the companies, involved in many, many ways. There is a range of things: participating in summer camps, participating in normal type workshops that the families attend and trying to help the nurse coordinators.

I was very impressed with the interrelationship between the people involved in manufacturing and producing products and the patients whenever possible. An early impression noted the small amount of key people involved in treating hemophilia. The physicians became household words, if you will very, very soon and I think those people are still with us today treating hemophilia, that's of course physicians such as Dr. Hilgartner and Dr. Aledort.

It was interesting that there was a tight community with the orthopods, only a few of the dentists and social workers and the nurses and the nurse coordinators. I remember being impressed that Hyland chose to work closely with the nurses and the nurse coordinators because they had come, I believe, from a position where the nurse just does all the work and doesn't get much recognition. I saw through the efforts of the nursing committees and NHF, these nurses had recognition and rewards. They are such an important part of the whole picture. It was very rewarding to see that someone was taking care to look after these people, social workers too but I think not as much. I think it is true today that the nurse coordinator is still an extremely important part of the group. So it was nice and immediately evident that one did not stand alone, as just making a product, but there was more to it. There was service involved and a concern for how the patient was educated and then that grew into the whole aspect of home care, which I would be glad to comment on later.

Q: Well, I'd like go on to the early times before the HIV appeared on the scene and if you have a sense that the other pharmaceutical or excuse me biological companies, I'm so used to calling them pharmaceutical companies, were as involved early on as well with funding specific projects like we were. Were the others involved too?

CHANG: First, I'd like to comment on the terms. It is confusing and we at Hyland, as I believe the other companies similar to ours, don't typically use the term pharmaceutical company because one thinks of the more typical drug manufacturers and pill producers, if you will, as pharmaceutical producers while those of us involved with biologicals are rather unique in that we have the same source, at least today, for all of our products that of course being human blood plasma. It makes us unique, we answer to a different division at the Food and Drug Administration and we are different, thus I guess we don't

think of ourselves as the typical pharmaceutical manufacturer. So, it is probably our thinking and not the public thinking that gives us the different terminology.

The funding projects as I recall were offered to all of the companies, I think different people chose to support different aspects. I know there was a lot of support for the leading physicians, this allowed these physicians to spread the word, if you will, both in the United States, and internationally, about comprehensive care, and we really did a lot to help other countries. The primary country I would say that very early on started treating similarly, the same as the U.S., was Germany. I know it was in great part due to the exchange of the physicians. The United States doctors going to Germany and the German physicians coming to the U.S. observing, participating, watching and learning just how well the comprehensive care system did in the United States. Funding could have been either for travel or it could have been for the nursing committee. I think Hyland was real proud to be part of the Patient/Family Model which I am sure still stands today on many shelves and I think is referenced still.

Q: When you think of the hemophilia community do you think of a community and to you, is it an international community, or national?

CHANG: Definitely. I would say since I travel internationally, it always surprises me that one of the first questions anybody asks is, well how many patients are there in a given country, or how many patients do you think exist in Mexico or whatever. I always say this is a hereditary disease or disorder and the answer to that question is directly proportioned to the population. This does vary we know and of course we know there are some other reasons that there's new findings in hemophilia but still it is basically the same as the population. Unfortunately, every country is not able to treat hemophilia. There are plenty of examples where-in a given population such as in China with billions of people, the numbers counted for hemophilia are still less than a thousand. One tends to think that there is a lesser population there, but that's just not true.

Did I answer your question?

Q: Well, yes. You said you do think of it as an international community. I think that what's been fascinating to me is the whole concept of community, of all these different segments or components working together and having some sort of a sense of identity. I don't know whether in your work, because you have been involved primarily with blood, whether you have been involved with any other chronic or genetic illnesses as to whether they consider themselves a community as much or whether you've

had any contact with any other illnesses. Have you?

CHANG: I've had a good general exposure to Immune Deficiency Disorders and there is not the same tight knit group as with hemophilia. There seems to be not only a need but a desire for camaraderie, for networking, for assistance, and yet it always surprises me when I meet a new family and today (as literally, as recently as two weeks ago), to find a mother saying, "When my son was born, as a surprise I found out about hemophilia, I asked dozens of people and nobody knew where to send me and just by luck, I ran into someone that told me there was a Hemophilia Chapter and then once I got to the Chapter I found out there was this huge network." But, it just means that our work isn't done. There is still a lot of people that need to know about the disorder. Once we do learn about it, the community is just unbelievably strong. There is a network amongst the families and I think there is a network amongst all the professionals as well. And, it is true also as you said, internationally.

Q: Yes.

CHANG: When I go and meet the Hemophilia Association of a given country, their questions, their problems, their situations are almost identical to the ones we have here; slightly colored by the situation in that area but the needs are all the same. There is a need to know what another person did in the same situation, the questions are usually from when they're young and usually involve school or can there be normal lifestyle. Can the child play as a normal person or do I have to keep him home and fondle and cuddle him, and then of course will he be able to work and be a normal, contributing citizen. Those questions are always the same.

Q: It is interesting in terms of the communication links when you say networking, et cetera. Apparently you distribute a magazine. How does that get distributed, who gets it?

CHANG: The particular magazine you were looking at is something produced by the Home Care Division, Caremark Therapeutic Services. Because they supply product to patients at home, they have a mailing list and send that out to all of the patients. It is of course sent to all physicians that are on their mailing list and all of the centers. You'll find when you go to any center today several different communiques from the companies who are trying to bring messages such as the experiences of families experience and to share or network and to have pen pals if you will. It is that simple.

Q: As you look over the historical period that you've been

involved with working with the hemophilia community and Hyland's involvement, you mentioned home care. What, if you think back from 1979 on, what were the changes organizationally that you experienced over time and if you can relate them to what happened with HIV when that pops up, I'd appreciate that.

CHANG: When we -- when I started, which again was 1979, home care was already being taught to patients. But I felt it was limited. It was only at certain centers where the older group had been well organized. The nurse coordinator was usually the key person in teaching the family members. The child would first be treated at home by a parent and then when they were able to cope, the child would learn how to self infuse. But this was still not widespread, so I saw from probably 1980 to '81 or '82, a much more broadened application of home care. It of course meant so much more freedom for the family and for the patient involved that I would think it made a major impact on the lifestyle of the entire family. Because these patients that I talked to personally would say, "You know you just can't imagine what it is like, here I am, it's 3 AM and I know my knee is hurting and it probably means I'm bleeding. I have to go wake up Mom and Dad, they have to take me to the E.R., I'm going to sit there for four hours and then eventually I'm going to get an infusion. And now I wake up, rub my eyes, go to the refrigerator, take out the product, self-infuse and that's it -- the end of the story." That also left the patient in a much better medical condition.

Unfortunately, it took some number of years to get this idea spread so that it was a safe procedure. Even though this is true in the United States, it was even more graphic for me when I introduced the concept of home care to Japan. Now I know you're writing the story about the United States primarily.

Q: That's okay.

CHANG: But the Japanese story was so interesting because in 1980, '81 and '82 they asked us to come and discuss home care. I was able to go with several physicians and several teams of people, I was actually going for over three months to Japan. We travelled all over the country and met with many treaters and many groups of people, every single time the same question came up. "But is it safe? What would happen if there was a reaction at home?" The people that I was travelling with, the Dr. Levines and the Dr. Abilgaards always had the same answer and the answer was consistently, "I have never experienced or none of my patients have ever experienced an adverse reaction at home other than very simple things that would happen like maybe an increased heart rate or something like that." Slow the infusion down and everything was fine. There was never an emergency need that was directly related to home care. What was unique in

Japan, at this same time period diabetics were not able to give injections of insulin at home.

Q: Really?

CHANG: The medical community in Japan was strictly hands-off, everything had to be in a medical facility, a doctor's office or whatever.

Q: That's very interesting about the diabetic.

CHANG: Right. What we did -- I would say as a good business decision, we joined with the diabetic society since they were much closer to changing the law to allow for self-injection. Diabetic needs were easier to explain to people in government and to people that had to pass the laws to allow self administration. We rode on their coattails, provided the same reasons they provided, talked to the same people they talked to and stated it is reasonable to give insulin and it is also reasonable to give Factor VIII. About a year later Factor VIII was introduced as a product to be administered at home.

Q: Was there any sense that you are aware of families feeling ashamed of having children with this condition?

CHANG: Absolutely. That varies from location to location and in some areas it's more notable. When I'm talking about Japan that was also true. They were extremely afraid that their neighbors, their friends, their acquaintances would know about hemophilia. It really went back, I think, to a psychological problem where there was so much guilt and the did not want anyone to know that hemophilia existed. They were truly covering up. I do not think this is true today, or at least it was not true for a while until HIV came about. I think we regressed right back again to say we'd better hide this. I must jump now to the advent of AIDS.

Q: Okay.

CHANG: What I experienced with being so close to so many hemophilia patients and persons in the community was a sense of wellbeing.
Q: Yes.

CHANG: A sense of at last we've got concentrate, we've got home care, we've got this licked, we are in charge, we're doing just fine.

Q: Right.

CHANG: It's A-okay and then we were hit with AIDS and that just sent everybody in a tailspin right back down again.

Q: When did you first get an inkling of this AIDS situation, do you remember how for you personally?

CHANG: I remember very well. It comes two ways, to me personally and to me as an employee at Hyland. What we were doing, Susan, was routine improvement of product. We as well as everybody else in this business constantly try to make the product better, purity is always a question with Factor VIII. We know there is a lot of impurity that comes along with the plasma because of the plasma pools we are using. A consistent problem that's always been here and is still here today is hepatitis. We were trying to come up with a methodology in producing Factor VIII where we could reduce the risk of Hepatitis B. At that time we had moved away from the procedures that we had, to what we called a heat treatment process. The heat treatment process was patterned after pasteurization of albumin. Albumin is another product in this industry that has been used for years and years and has never had the problem of dealing with a virus, such as hepatitis. We thought we would apply the same technology to the Factor VIII, we had done that and we were almost at the end of our trials. Because we could not do human trials, we had to use chimpanzees. We had given our product, produced by the heat treatment method to the chimps. Then you have a long waiting period because the incubation period for hepatitis is approximately 28 weeks. We were exactly in that waiting period when the stories came out from Dr. Gottlieb and Dr. Gallo and others about this "strange new virus." I remember reading about it in the paper, probably just as everybody else remembers it. One or two or three of us looked at each other and said, it sounds like a virus, it sounds just like hepatitis. The mode is similar and it was like, "Oh my God, what if the heat treatment process that we had just finished could kill that virus?"

Q: I mean you thought of that early on?

CHANG: Right away. First thing, like this could be a minor miracle. And it was true.
Q: Yes.

CHANG: We're fortunate. As bad as AIDS is, and HIV is, that this is something that can be killed relatively simply. In fact, much easier than the hepatitis virus.

Q: Really?

CHANG: As soon as we were able to convince those people to provide samples, in order to spike product, expose it to the heat treatment and then check it, the findings were negative, we knew that at least we could get rid of it (HIV virus). The technology was immediately shared with all the

companies. I mean immediately there was no such thing as, well, this is a company protected finding.

Q: So your company was the first?

CHANG: Yes, we were the first licensed company with the heat treatment product.

Q: Okay. Okay.

CHANG: And, --

Q: And this was called what?
CHANG: The name of our product was Hemofil and then we just tagged on the letter "T". Hemofil T implied that it was treated or heat treated.

Q: Okay. Was any anger expressed directly at the pharmaceutical companies? We know it has been experienced ny physicians.

CHANG: I personally didn't feel that. I think as a community the people were quite forgiving, but I remember going to the first funeral.

Q: How did you happen to go to this funeral? I mean was it someone you knew personally -- or ?

CHANG: Yes it was someone we knew personally. Again, because I think we are continuously supporting your suggestion that we're a tight knit community that we do meet with these families and the people especially the leaders either politically or locally in many, many ways. One gets to know the people, and in some cases the families. Here in Southern California there is a very, very large number of patients and with Dr. Dietrich being an early treater (more than 25 years) there are many patients in this area. I am a participant in a local Board of Directors for Southern California Hemophilia Foundation. I want to go on record to say that I think it is an admirable and good idea for the people that care for the community such as a Hemophilia Chapter to include manufacturers as part of their organization. Every group doesn't feel that commercial people belong on those chapter boards. But I've seen it work successfully in many, many areas. I think all of us are capable of wearing two hats, or more, and it would be very foolish to think that you were just there for the interest of your company. So all of us are there for many interests and all of us become close to the needs and the desires of the community. When we lose somebody it is a friend that is lost.

Q: Yes. Well this has always been very visible to me seeing this involvement over time and quite fascinating and

wondering whether in fact this does exist with other disease entities.

CHANG: It doesn't seem to. There are many diseases that have tried. I know of a few, but most disorders that I'm involved with are more acute and not chronic.

Q: Right.

CHANG: There doesn't seem to be the same feelings that come with maybe something common like diabetes. The fact of the female carrier and the family history, it's so unique to hemophilia.

Q: I've heard different people express things like well also, we all know who we are. There is a certain number of people; it's a small community of treaters, and patients as well.

CHANG: Definitely, definitely. The thing that brought it out recently with HIV, very surprisingly, was the public awareness that hemophilia was one of the high risk groups for AIDS. I think there was a lot of bad press that came along at that time which is very unfortunate with all of the stories of the children that couldn't go to school, etc.
The good news is since then, I find people much more open and willing in requesting to learn, well what is this hemophilia? And, is it okay if I have a student in my class? And is it okay for that student to play with the other children? At least they're asking questions and I think the minds are opening.

Q: Do you get involved with educating school personnel and things like that?

CHANG: Oh yes. We get calls all the time. We have produced an old film called Joey.
Q: Oh, right.

CHANG: Many, many years ago. There have been different versions of that kind of tape since Joey. Schools will call us, especially if there are some students that are either attending or are going to attend the school. They'll call a company such as ours. Also the word is spread through some of the educators. It just takes one to learn and then it is spread by word of mouth. The public likes to have information from companies like ours, where we can just spend one hour and educate so many people as to what is hemophilia and what it is like and what can be done and what the hopes are.

Q: That's interesting.

CHANG: The more people that learn the better it will be.

Q: Yes. Well, with the evolution of these new products and you talked about starting in with this treatment. What else has been happening in terms of new technology.

CHANG: Very specifically the next advent after heat-treatment was to treat the product in two ways. One that we call solvent detergent and the other monoclonal antibody. These are just ways to have a more specific Factor VIII with less unwanted foreign protein, if I could kind of sum it up that way. We are kind of getting rid of the junk and have Factor VIII that doesn't have other things which cause adverse reactions in the patient. The less unwanted protein there the better for the patient. This product with monoclonal antibody is only half way to what we're trying to achieve. We're trying to move totally away from plasma source Factor VIII, from human plasma source to a, if you will, genetically engineered product. One that is totally controlled and does not start with blood plasma. The particular area where we have been doing our research is known as recombinant Factor VIII, from recombinant DNA technology. In order to produce a recombinant Factor VIII we had to have a monoclonal antibody. In other words, a single Factor VIII of pure identified, total entity Factor VIII. It was something like a starter to go to the recombinant. We produced monoclonal purified Factor VIII. Once we realized that was such an improvement over the, at that time, heat treated Factor VIII, we went ahead and produced that as an intermediate product. Monoclonal purified Factor VIII is used today.

Q: Now, what about this solvent detergent? Are they all used, or just the monoclonal?

CHANG: In our case, we combined both technologies, monoclonal antibody and solvent detergent and another called immunoaffinity chromatography.

Q: What is that?

CHANG: I mean we can just keep on going. It all boils down to the technology we use is an absorption of just the particular Factor VIII we want with the unwanted materials washed out. We happen to use columns and everything else is washed out. You adhere the antibody to a positively charged particle and you get rid of all the stuff that is unwanted. This is a great, great advancement in the scheme of things but we are also anxious to move on to the next step that will probably forget this one very quickly.

We are in the fortunate position of having worked with another company called Genetics Institute -- Susan, I remember at a World Federation of Hemophilia meeting in Costa Rica and either in 1982 or 1984, probably 1982, there were presentations given by two people, one was a Ph.D. from

this company called Genetics Institute and the other was a Ph.D. from another company called Genentech. Genentech was working on a product for the company Cutter Biological, and the representatives of these two companies were able to tell the audience that they had found the exact molecule for Factor VIII and were able to show it on a slide. I can only describe it to you as a series of chemical compounds in long strings like a railroad track and the string started at the top, left hand corner of the slide and went across and down and across and down. The complete slide was covered and when the other person showed his, they were exactly the same. It was incredible.

Q: That must have been quite an incredible moment.

CHANG: It was just wonderful. It was the start and it showed they each verified the others findings.

Q: That's terrific.

CHANG: That's when we knew we were on the road, that we would get to this finding. Now we are much closer, both companies, I think it's wonderful there is competition, that is probably helping the total community. One probably is very similar to the other. We are now in the phase that we're waiting for the federal government to approve. All the clinicals are done and the work is in and the files are in, and it is just a matter of time, one day soon this recombinant derived Factor VIII will be available.

Q: So in other words are there people now getting it in clinical trial?
CHANG: In clinical trial, yes.

Q: So that's pretty close then?

CHANG: Yes, yes it is.

Q: That's very exciting.

CHANG: We are excited.

Q: What kind of people get involved in the trials, I mean how are they chosen?

CHANG: The first phase trial one must do is very simple, to see if we can achieve hemostasis with the hemophilia patient. He has a bleed, you give a product and the bleed resolves. The first two people were pretty brave that were willing to try the product. They happened to be in North Carolina, it was published and it was in all the newspapers et cetera and everything was fine and they did well. So that's the phase one clinical trial. Then, we have to gather a lot more information, there has to be a lot of

exposure to greater numbers of persons over a greater period of time. Those experiments have been done and obviously look good. The next group that one looks at are the previously untreated patients and it is important because you are comparing these products to all the other blood plasma derived products. We all know there is exposure to viruses and hepatitis is one of them and mostly all patients have been exposed. So, if you really want to definitely know your product is pure, you want to take a patient that has never been exposed to any other product. In order to do that with hemophilia it is almost absolutely 100% required they be newborn babies because you can't find a hemophilia patient unless it is a very mild patient that has had no treatment. So that's the phase we're in now. With hemophilia, typically a newborn baby in the first two years doesn't bleed very often. So we have literally years to collect the data and years to find out if we have achieved what we set out to achieve and it is a safe product that also provides hemostasis.

Q: This is all very exciting and it seems to be emanating from manufacturers. Is the government involved in direct research? Is there anything that happens in any other setting beside your companies?

CHANG: I don't see the government involved in manufacturing procedures. I do know of the involvement of Child Maternal Health and things involving improvement in lifestyle and help for comprehensive care situations. I do know and must honestly say that one might consider the American Red Cross as a partially government funded organization. The American Red Cross has chosen to affiliate themselves with Hyland so we in fact receive the plasma from the Red Cross and produce Factor VIII for them. There is a lot of product available in the United States labeled as American Red Cross product which happens to be manufactured at Hyland. We have a longstanding contract with them.

Q: I see.

CHANG: Other than that there is very little direct funding from the government, and I think that is okay, scientifically, but what worries me much more and is much more concerning to the hemophilia community is a matter of reimbursement. The whole issue of reimbursement, which needs a lot of care and needs to be examined much more than it has been up until now. It is a very, very big issue.

Q: I hope to have some people speak to that issue. Are you interested in speaking a little bit about it?

CHANG: I definitely am. I have personally had staff at my company that report to me whose job it is to seek out

reimbursement. So we are totally involved everyday. We receive phone calls from patients and families who are not reimbursed for their product and seek help from us. We have major efforts in lobbying in Washington. We have major efforts with all the insurance companies. We try to give advise on State risk pools. We try to get involved with Medicare/Medicaid issues.

I don't think one can only suggest that price be controlled by the manufacturers as being the answer to having low cost care. I don't think one can expect to have continuous advancements and improved products and improved services if the only goal is to have lower price. It's just not possible in the world we live in. We, as a company with shareholders, want to have fair profit, we don't think that's unreasonable. We could easily say, "Fine, take the product as it is today, we'll work on better yields, we'll work on things that should make it cheaper." But instead we have never taken that attitude nor has I think anyone in this business taken that attitude. Instead it is we'll try our best to get lower prices but we're going to make all the scientific advances we can possibly make.

Q: In this kind of lobbying and all of these activities, do you work with NHF alone or how does it work?

CHANG: We have chosen to provide a very large grant to NHF for reimbursement and we therefore would hope they'll use the money wisely and can assist on a nationwide basis. But we think that is not enough on its own. We think there might be certain constraints National Hemophilia Foundation has to work with. Perhaps we have other avenues and other strengths because of our ties as a major manufacturer as part of the large corporation and we do have a voice in government. Also, we have our home care segment which has the service that they deliver product and ancillaries to the patient but they also handle all of the reimbursement issues for the patient.

Q: I wasn't aware of that.

CHANG: They work with the insurance company on an individual basis; they get approval prior to shipment; they then do all the billing on behalf of the patients, and this is a great service.

Q: Is this Eric's company?

CHANG: Yes.

Q: Okay tell me a little bit about how that started.

CHANG: Okay, back in the days when we thought we had the best product available and had enjoyed a good market segment, we looked again at the market and said what else

can we do? The pricing back in '83 and '84 was very, very low. There was absolutely no room to lower the price and we then turned to what can we do to improve service. We knew the patients had learned the technology and learned how to self administer, but they were still driving all kinds of distances to the center to pick up Factor product. We thought there must be a better way, and so we put together a service called Hyland Plus which was designed to receive a prescription from the physician, have it filled by a pharmacist so all the pharmaceutical laws were met; be able to deliver the product along with the ancillaries to the patient at whatever address he preferred. Here there were issues of confidentiality, some people preferred to have it sent to their office, some people preferred it at home. Whatever they desired. As much as possible we complied with their desires and we would send it to the home. Then, we would assist them with the reimbursement, and this was very well received because all of us absolutely hate insurance policies, rarely read them and don't know things that are important. And most of us, unfortunately don't have any idea what our lifetime maximum is, or if we're getting close to it or any of the issues involved and typically what happens is one never sees the problem until it's too late. And, whoops my insurance just lapsed, oh what can I can do now. When we got involved there was a requirement that the person would have to get out their policy and we would have to walk through with them and have to find specific details. This was, I think, a big service to the community. We never ever made medical decisions, although this was a fear. Doctors for a long time understood that when there was any medical problem they wanted the patient to call into the comprehensive care center. There was a big fear that if the product was delivered they wouldn't have to have that connection.

Q: Yes, that's what I was thinking about.

CHANG: That was overcome very quickly.

Q: Was it?

CHANG: Just by example. I mean, if the doctor still heard from the patient and all care was satisfactory, then home care service was acceptable.

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CHANG: My current thoughts on reimbursement is still an area that needs a lot of review and a lot of effort because we encounter on a daily basis people that are losing their insurance or they're in an area where there is nothing that can be provided to assist the patient or the family or both. It's extremely sad to hear a patient say, "Well, I'm HIV positive and my expected life span is short and so I'll just

take the less good product because it is all we can afford." That's a very sad thing to see in a state, in an area and a country such as ours where one shouldn't have to choose medical care based on price and believe me that exists today. That's not exaggerated at all. That has to be fixed. It is totally unfair to put this additional burden on the physicians to pick a product based on the cost of that product. That's just unheard of; that's where we are right now. It's a sad remark. There are some states, that are much better funded than others, and it always interested me that people never choose to move. People will stay in a state without coverage knowing that in their neighboring state they could receive the product.

Q: Is that true? Because I thought that some do.

CHANG: Some states are much, much better funded than others.

Q: What are some of the states that are well funded?

CHANG: In California, there is a very unique funding system which is known as GHPP which comes from Genetically Handicapped Persons Program. This is a program that provides payment for the cost of Factor concentrates to the hemophilia patient. So, the vast majority of patients in California do not have any financial hardship. Where that certainly isn't true in other states. What we have done specifically as a company to address this issue is that we have people going out doing workshops, travelling around the country and the workshop is usually presented on a Saturday, usually together with a local chapter of NHF. The people are invited to come and we just discuss on a typically non commercial basis, what one should look for in their policy; things such as "Do you know that in the State of Virginia once a year there is an open enrollment with Blue Cross?" Things of that nature that are very, very important, but just are not commonly known. It is a hands-on workshop with the families and making suggestions and offers. It is not an end-all to all questions but it sure helps. That along with getting to the bigger problems I think are in the larger programs, the Medicare and the Medicaid. They just have to find ways to fund needed product for this disorder.

Q: Did the other manufacturing companies, do they do workshops like you? Do they do things like this? I don't know.

CHANG: Not to my knowledge. I think it is unique. I know that we started it and by the time someone listens to this tape there probably will be somebody else doing it. But as of now, no, we're unique.

Q: When did you start doing this?

CHANG: The lady who works for me has been doing workshops for three years. We offered it initially as part of the home care service and it has stayed ever since because there never seems to be an end to the need. Every state wants it or wants to have it again.

Q: Tell me about -- okay. Tell me again more about this home care service in terms of the evolution of it. It seems to be interesting.

CHANG: I think we were able to provide a great service to everyone. What I think was unexpected when we started, we knew we would help the patient and we knew we would help the family members but I think we also helped the treatment centers a great deal too. Because certainly that professional educator, nurse coordinator or whoever really didn't need the burden of counting the number of vials of Factor VIII that were handed or Factor IX, and keeping track of what was used. One thing that I forgot to mention, but is equally important to the service is we also have methods of keeping track of the product that is used. Only in the last two years have we gone to an electronic scanning device where the patients fill in a form to show what products they used, what lot number, when they used it, what kind of bleed they were treating and other pertinent information. We find now, compliance from these patients. I can't tell you the number of patients that I've talked to that will "'fess up" that they really didn't keep serious logs most of the time and usually when they went into their treatment center and knew that they were going to be asked, they would sit there with a pencil and fill in all the data like, oh yea, I infused on so and so and such and such date. So compliance has always been a problem.

Q: Right.

CHANG: This one little form that we've invented is just one way to help keep track. The other way we helped was from a delivery point of view. We knew how many Factor units we would send to each patient and when. And so we just ran computer reports that were sent to the physician. This report is a great tool when physicians apply for grants or whatever, to say here is the data, here is the number of patients, here is the exact number of Factor VIII units or 9 units, that they've received and here is the number of bleeds they treated and et cetera. So this is another little service that we're able to bundle together.

Q: Sounds like the role of technology has developed into vise a vie the computer and what has happened over time.

CHANG: Oh, definitely.

Q: There is another theme that I haven't really addressed that maybe should look at.

CHANG: Yes. It's definitely there. Whatever makes data retrievable and record keeping easier is going to help us as a community.

The other part of the home delivery, home treatment service that we added was to once again recognize the need for education. We felt that, as a reimbursement if you will, to the comprehensive care centers if in fact they were continuing the role of educating the patient and teaching the patient how to administer the product, that we as a company would recognize that and actually provide educational grants to those centers to continually educate the patients. Because if we look at other home care services in completely different arenas, such as the Baxter dialysis programs, it is usually the burden of the company providing the service to also do the education. So, one would normally include teaching the patient to self-administer or have the parent administer the product, as part of the service.

Q: I see.

CHANG: But we in no way felt that was our place to offer self-administration training because it was already being done, and being done so well. We have many instances where we provided and continued to provide educational grants to the centers; you keep up the education, we'll supply the product.

Q: I see, that's interesting.

CHANG: I can't tell you how many times people have resisted self-administration. I have personally taught people to learn to self-administer. When one reaches a new physician or a new area or in a new country and the doctor looks at you and says, "But my dear this is intravenous, you couldn't possibly have a patient -- how could anybody ever stick themselves?" I mean, I'm sure that question will be asked forever, and I always say, the first one is the hardest but it can be done. It's heartwarming to see these little, little children.

Q: How young?

CHANG: I, with Eric Delson, taught a five year old, and he was beautiful. No problem. I think the mother was much more nervous than her child.

Q: That's really interesting.

CHANG: We find that the childrens' typical comment is,

"It hurt much less than I thought it would hurt. I am able to do it to myself better than someone else doing it to me." Because it is very simple, once you learn exactly your anatomy and your own body, and your vein in particular, and you know where you're going to go with the needle. You can do it with your eyes shut, after some practice.

Q: Yes. That's really remarkable.

CHANG: I have a list of things in front of me and I would --

Q: Okay.

CHANG: -- like to talk for a moment, really changing the subject, to talk about donors and the fact that as business stands today at least, we are very dependent on plasma donors to give us source material. What most of the companies needing donor plasma available have is unique donor centers and we for example have oh, in the vicinity of 25 or 30 centers. These are located all throughout the United States and I emphasize only in the United States. Many times people thought that plasma came from other sources, and typically, unwanted sources. But that is not true; they're all U.S. We typically are located in areas where we can have a lot of interaction with usually college students because of the time it takes. It used to take several hours. One would have to go into the donor center, be examined and believe me there are physical examinations. These are well run organizations, unlike the public belief. They then must donate a unit of blood, whole blood. It will be put into a centrifuge. The red cells and other cellular elements would go back to the donor and the plasma would be kept out. This is a procedure that would be repeated a second time and then the plasma is immediately frozen to preserve the Factor VIII and it would be kept frozen until it was delivered to the manufacturing facility. There is one little twist on this story which has occurred within the last year and a half, automation has been introduced to the centers. With this automation which is some kind of nice fancy equipment that automatically separates the blood as it is being taken, the patient is hooked up with tubing to the machine; as the blood is taken the red cells are given back and only the plasma is maintained. This does two things; it speeds up the whole procedure, now I understand it is less than an hour to give two units and it is much safer.

Q: Okay.

CHANG: So it is a much safer and faster procedure that's probably employed by most donor centers.

The good thing about the donor centers, is that these people typically are very often coming back to donate. Most donors are 40, 50, 60, 70 time repeat visitors if you

will, to the centers. If you interview these people, you'll find a great sense of doing something for humanity. We always inform these donors that this is a unique product, it's life giving, it will be a product that will be used by a patient and you will have an effect on their life. And that's a nice thing. Unfortunately there is a very bad aura and some public press about how bad it is to sell your blood. Well, frankly I -- we always say, we can't imagine anybody that would donate 4 hours of their time, every two weeks if they weren't getting a very small compensation. I'm talking five dollars, I mean 5, 6 or 7 dollars is the amount of money that the donors are paid. We feel that it is just a minimal compensation for their time. So, it is a safe procedure and it is not harmful for the donor and it is a blessed thing. We never want to have anybody come in nor any bad news spread that would negatively influence the donor. That same feeling goes on throughout the manufacturing facility.

Here at Hyland our facility is an old, old manufacturing area that was established in the 50's. That plant, that core is still there today. It has been expanded and doubled and tripled and quadrupled over the years of course, but you will find if you walk around, there are many people that have been here 20 years, 25 years whatever. The job looks quite menial but good feelings are there, you just know that they are so proud to be participating in making a product that is life giving.

Q: Could you talk a little bit about the beginnings of Hyland.

CHANG: Oh sure.

Q: I'm interested in that because I think that again, the innovativeness of what you've been describing in terms of interaction, the advocacy efforts, the counselling, the educational efforts. It's very interesting and I was just interested to hear a little bit about the background.

CHANG: When I came to Hyland, I as probably everybody else in the world said, why do they spell it that way. It's so funny, H-y-l-a-n-d, and of course it is because it's a family name. The founder of the company is named Dr. Clarence Hyland and he used to be Director of Clinical Laboratories at Children's Hospital in Los Angeles and was very interested in immune serum. He was working on the treatment of various things to help contagious diseases, such as measles. He realized that the source of his material was coming from human plasma and he started working on separating the various components of blood and one of the larger components, by far the largest component, is albumin. We were unfortunately very near to wartime and the need in 1943 was tremendous to have something that would provide volume for the loss of blood during the war. Albumen is

able to maintain life 'til one can have more proper and complete medical care. So that was how Dr. Hyland got started in having to have a big facility and making albumin. He put together a tremendous effort, using many and got all these volunteer ladies to package the albumin. He was then awarded something called the Army Navy E. Pennant Award by the government for extraordinary efforts in time of need. Aside from the albumin, he also knew that we could separate out and derive Factor VIII from the same source plasma. There was a physician named Dr. Murray Theilen, who came from North Carolina and he was himself a person with hemophilia. They were working on the first separation of Factor VIII product and Dr. Theilen knew right away that this product would be able to maintain hemostasis. I am told stories that he used the product on himself when he wasn't supposed to, in other words before clinicals or anything else were completed. He did have a very major bleeding event and it was told to me that the product saved his life. A very heartwarming kind of story.

Q: Was this during World War II or after?

CHANG: That was in 1966, so it was definitely afterwards.

Q: Okay.

CHANG: Unfortunately at the age of 39, Dr. Theilen succumbed to a pulmonary embolism, but because he was using Factor VIII, they found much to everyone's amazement that there was no hemorrhaging. It is unfortunate that he passed away but he certainly was proof that Factor VIII could help the hemophilia patient in almost all circumstances.

From the 60's we went on then to become a manufacturer of the first licensed Factor VIII product in the United States. It was a few years later that some of the other companies came along and as a matter of fact it was Cutter that had the first licensed Factor IX product. And then one year later our company also had a Factor IX. So, each of the other companies came along later in sequence and produced similar products each with their own uniqueness. We have been the only company to have remained totally 100% American, if you will. All the other companies are owned or associated with non U.S. based corporations.

We process in the vicinity of two million liters of plasma every year, there is a lot of plasma coming through and the technology has grown. If you walk through our facility you will see stainless steel tanks, floor to ceiling. There is a lot of refrigeration involved, a lot of cooling steps. So the rooms are frigid. They're wet and they're slippery. People are all gowned-up, of course, so as to not transmit any unwanted bacteria. Thus it is a very space-age view that one gets when walking through the facility.

Q: Is that right here?

CHANG: It's right here in Glendale, like about a mile from where we are sitting. And it's continuously updated. Going again back to the 50's and prior, it was discovered that there was a product called cryoprecipitate.

Q: And that was Judith Graham Pool's discovery?

CHANG: Yes. Dr. Judith Graham Pool discovered if you took plasma and froze it and then started to thaw it, you could get Factor VIII. My personal description when I'm teaching anybody about this is, it's like orange juice. If you take orange juice and freeze it and then you start to thaw, it's pretty easy to pour off a lot of what looks like water.

Q: Yes.

CHANG: The real stuff is what remains as the last sort of globular junk and that contains the good stuff in this case, Factor VIII. So, it is not terribly difficult to produce cryo. What is more difficult is to be able to lyophilize it and get into a system where you can have stability and have a small vial which is easier to use.

Q: Does lyophilized product, Factor VIII come from cryo?

CHANG: Yes.

Q: So in other words it is just another step?

CHANG: That's right, that's right. It is very sad for me when travelling to go back to that side of things. To go to countries where cryoprecipitate is still used exclusively, because it brings along with it all the unwanted viruses. AIDS and HIV problems are associated with single donor cryo. I look at a country such as Mexico where in 1982 they were using approximately 50% concentrate and 50% cryo. They then experienced the unfortunate major disaster with the earthquake and when I visited Mexico in 1990, they were using 100% cryo and have a very, very, very large problem with AIDS. This is terrible.

Q: How devastating. Yes.

CHANG: It is just like going back to the dark ages. So that is part of our task. It is part of our job, it is part of what we must do, to help the other countries. When you become associated with the World Federation, you hear and exchange all these stories. In some countries like Thailand for example, they have done very, very well with improving conditions. They have a long way to go and they want to get a lot better, but they have worked on it. Then when you

look at Mexico and they're nowhere, it is very sad. We have to work with them and we will.

Q: It sounds like you have a job ahead.

CHANG: Yes. Well, specifically Mexico, they might be the host for the World Federation of Hemophilia in 1994, and that might help them a lot. In fact, what they say is they will make every effort to have better care by that time. So I hope that comes true.

Q: Are there any other topics that you would like to raise regarding your involvement?

CHANG: Well perhaps I should talk a little bit about the changing world of biological companies. By virtue of my suggestion one might think there will be a change in our role. I personally don't see it in the immediate future. I think we will forge ahead. I think we will produce the product as we know it and as we improve it along the line. I don't see any dramatic changes. I hope very frankly that financial conditions remain stable enough that people don't literally go out of business. That's always on the horizon. It's sad but true. There is no doubt that in this system, if someone is non-profitable they'll just focus someplace else and then will go away. That would be unheard of.

Q: Yes. With the genetic kinds of development in research going on since you -- the whole focus in your work emanates from human plasma, what would you see happening if in fact this arises?

CHANG: That's very interesting, we are on the forefront of calling ourselves a biotechnology company and we inside say to each other that it is our goal to put ourselves out of business and what we mean is put ourselves of business in terms of the plasma source material. We hope within and I'll even go as far as to say within five years, to at least be able to see the time when there will be no plasma whatsoever coming into this facility and no products derived from plasma. That is obviously very conceivable now with Factor VIII. With Factor IX it's a little bit further ahead and we would then have to look at albumin too. Because albumin is the back stay of -- I mean it's bread and butter for a company such as ours. There is all of these millions of liters of plasma that comes in to become thousands and thousands of liters of albumin. If we could make more, we would. We have not even come close to being able to meet the demand for the needs for albumin. Not to divert too much, but albumin could -- there could be much, much albumin used than is used today.

Q: What is albumin used for?

CHANG: It's basically a plasma expander. If you have for example, a tragic accident and cut off your arm, they pick you up in the ambulance, you need to have something to keep your circulatory system going and albumin can be used by everyone. It's not specific for types or anything else. It's a biologically comfortable thing to give to a person. So it's used in that area a great deal. Also it's used in shock, it's used in burns, again, a lot of fluid loss; in surgery and I am told could be used much, much more if it were available. The other solutions that are used, there are two terms crystalloid and colloid solutions and the others are chemical solutions and they seem to cause other problems because you now have imbalances of electrolytes and other things in the body. So if you had the best of all worlds, there would be much, much more albumin used. If it were available. So, I would predict here too, that within the foreseeable future, we will have recombinant derived albumin which will help a lot of people.

Q: That's fascinating.

CHANG: I would like to end this rambling story with thinking about hopes and future and expectations. As I know so many hemophilia families it's so rewarding to look, especially at the children, and to know there is a relatively safe product for them today. To know they will be cared for and cherished and grow. I think we have a terrible, immediate period to face where there will be, unfortunately, fewer hemophilia patients with us. People that we've known for many, many years. There are going to be a lot of deaths due to HIV, but there will be people that survive and there will be strong people that survive. There will be a lot of newborns and these children will do just fine. Everybody is with them. The hemophilia community is with them, the families are with them, and of course manufacturers are going to continue to do everything possible to help. There is hope. And we will overcome.

Q: Thank you very much.

*** END OF SESSION ***