JAN BULT INTERVIEW
BAD BLOOD: June 1st, 2009

MN: So if you can tell us you're name and your role at the PPTA, give us the full name of the PPTA

JB: My name is Jan Bult. I'm the president of the so called Plasma Protein Therapeutics Association in brief, PPTA.

MN: What exactly is the role of the PPTA?

JB: The mission of PPTA is to ah. . . promote the availability of safe and effective therapies for patients in the entire world. And I'm very proud to see that we've made enormous progress. One of the reasons is that we work very closely with patients and patient organizations.

MN: You work with patients that need, you left out the plasma piece.

JB: You wanted me to do it again?

MN: Sure, so the role of the PPTA

JB: The role of the PPTA is to promote the availability of safe and effective therapies that are made from human plasma and we've made enormous progress. One of the reasons is that we worked together with patients that need these life saving therapies.

MN: Give us a sense of the size of the plasma industry both in sense of patients and in the size of the industry financially.

JB: The ah . . . patients, that's the most important part, according to statistics of the World Federation of Hemophilia there are about 400,000 patients in the world that eh, that require treatment. However, only 25% get any form of treatment. Um. . .the entire size of the industry is dependent on all the manufactures in the world and we only represent seven manufacturing therapies so I've rather focus on the patients. There's not only hemophilia there's also immune deficiency, patients that have no ability to fight infectious diseases that another important group those are the patients we deal with.

MN: But you don't have any sense of how big. . . people trying to understand how big or small of an industry plasma is within the greater scope of pharmaceuticals.

JB: We, we don't measure the industry in terms of dollars. We. . . we measure the size of the industry in terms of patients we're serving.

MN: And so describe the challenges/risks of dealing with a product in human plasma.

JB: The biggest challenge is to have a sufficient number of people that are willing to donor, ah. . . to act as a donor to donate the plasma. It's process that takes about two hours, two and a half

hours, on a regular basis and we need to make sure that we have healthy donors, that they are checked regularly, that there's a medical screening and that we have those donors coming back to supply the enormous amount of plasma that's needed to produce these life saving therapies.

MN: What is the inherent risk of having a blood based therapy?

JB: What you want to do is you want to have donors that are healthy and do not carry any infectious disease. Now, how do you check that? First of all, when a donor comes to a center you check that that individual has not been deferred in the past for, for that reason. Then, you check the individual medically, so you test the plasma. You do that not only once, you do that at least twice because we want to have committed donors. We're not interested in donor that only want to come once. And it is this management that takes an enormous amount of time but results in a very safe donor population, resulting in collecting of safe plasma that is used to produce the life saving therapies that these patients, patients need so desperately.

MN: Infectious disease are carried in blood so could we kinda state that simply then we'll work towards what the PPTA does to help mitigate those risks. Specifically, that is the key challenge of plasma based therapies is that blood has a high risk of carrying infectious diseases so can we talk about that specifically?

JB: The risk that you have when you collect plasma is you wanna make sure that you collect plasma from a healthy donor. We have not seen and transmission of any infection for over two decades, so you cannot say the products aren't safe. What you can say is that the systems have worked extremely well resulted, resulting in the fact that there have been no transmissions. Now, that doesn't mean that you can sit still. You wanna make products safer tomorrow than they are today. Therefore, you have a whole set of systems in place that goes from very stringent donor selection, testing of plasma, keeping the plasma, (manufacturing) technologies to ensure that and the fact that we haven't seen any transmission for over two decades is proof of that.

MN: Help us understand the member organization of the PPTA there's a very difficult risk analysis that has to go on when you're dealing with a product that does have a potential to transmit disease and whether or not to put it on the market. What's the challenge of that risk/benefit for your clients? How do they make those decisions.

JB: If you manufacture a product that is made from human plasma you're regulated by a regulatory agency in the United States it's the FDA in Europe it's EMEA. Now other countries have other agencies. This industry is one of the most regulated industries in the entire world. So in order to put any product on the market you have to submit an enormous amount of technical data, you have to submit clinical data, that is reviewed by the regulatory agency. And it's only after reviewal of the agency that you receive the permission to put the products on the market. So, once the permission is granted, the product is safe and effective. The industry however, can do more than that. They have systems in place. They have standards in place to do more than what the regulatory requirements are. And the fact that we haven't seen any transmission in more than two decades is a proof of that.

MN: Did the PPTA come into being in 1992?

JB: Yeah, the association had a different name but the association activities started in the early, the early '90s.

MN: Was the mission somewhat defined by what happened in the hemophilia tragedy?

JB: The mission of the association is to promote the availability of safe and effective therapies for patients all over the world. And um. . . we have seen the tragedy that happened to the hemophilia community that's certainly, certainly an issue that's on their mind, but more importantly, we want to do a better job today than we did yesterday. And as a result of that we have safe and effective therapies that are used in the world, many diseases, many life thr. . . ah. . . saving therapies no transmission in more than two decades.

MN: In 1992 when the group was brought together and you were brought in was the task specifically to make the products safer than they had been yesterday as you say? Was that the goal in '92?

JB: The goal was to make products available to patients in the world. Safety ah. . . the World Federation of Hemophilia have had many meetings and what they've say today is safety is no longer the primary issue, it's a very important issue, we need to continue working on that but it's no longer the primary issue. And as I mentioned in, in other occasions the regulatory agencies um . . . the regulators industry, very very stringently and there, you can only put a product on the market when you meet all the requirements for safety and adequacy when that is met then a product can be on the market and it's safe.

MN: What was your goal at the time you came in to lead this organization. I need your help to bridge the gap between the story we tell in the film to where you are today so there's definitely no question that these products are safe and have been for twenty years. Help explain how you got there. Explain when you came to the organization in 1992 what was the challenge that lay before you. What did you think you needed to do?

JB: The association started in the early '90s. I personally got involved in the mid '90s um. . . to be the lead person for the organization and at the moment I saw the first standards in place that focused on the collection of plasma and the ah. . . activities in donor centers. Ah. . . from that moment on I was personally in the further development of additional standards to make the therapies better than they are today. And I'm very proud that these standards . . .

MN: You said you made the standards better than they are today but did you mean. . .

JB: Oh yeah, you're right. To make the products safer today than they were yesterday. Now, I'm very proud that all these standards are recognized by regulatory agencies, by patients all over the world.

MN: And so . . .

JB: I have to stop you for a second.

MN: Sure

(11:11)

MN: Ok, I know PPTA actually went above and beyond the regulatory guidelines that had been put in place by the FDA. . . what were the things that PPTA specifically addressed in a laundry list sort of way, what were they targeting to change?

JB: The association, PPTA, and it's predecessor focused on two very important part for the delivery of products. The first part is related to donor, the second part is related to therapy. If you look donor, there are a couple things that you wanna do. You wanna make sure that you collect plasma from a healthy donor. So you put standards in place that focus on donor education, donor deferral, make sure that nobody can be accept that has been deferred in the past, make sure you have double sets of testing and screening, medical screening so that you do everything you can to ensure the ah. . . collection of safe plasma. In addition to that you put in some um. . . standards in place that focus on manufacturing. You keep plasma in inventory for sixty days. You look at the kind of testing, the technology that can be used. You look at ah. . . you total donor profile eh. . . is there anything that you can do to ensure that you collect from low risk donor population. Those are a set of standards that we've been very active on and that has resulted in the fact that we haven't seen any transmission for over two decades.

MN: Just explain why you keep something for sixty days, why are you holding a product?

JB: The inventory hold standard says that once plasma is collected we keep it in inventory for sixty days for the eventual case that information becomes available after the collection that was not known. Now, I want to be a little more technical. When you get an infection, the natural situation is that the body reacts with so-called antibody. It takes some time before the antibody is built, you call that a window eh. . . period. So what you want to do is that, let's assume you become a donor today but you were infected yesterday, you don't know but you may get symptoms in three weeks from now. Well at that moment that it's known, and it gives us an opportunity to go back to your donations when you were asymptomatic and take it out of the process before it's being manufactured so it's a very effective mean to ah. . . work with post donation information.

MN: Talk briefly about the changes in patient notification.

JB: Patient notification is a very important means and why is that? Ah . . . let's assume you are a parent. When you're child needs a therapy you wanna make sure that the therapy's safe. Sometimes it happens, you see it in the car industry, you see it in other industry, that for whatever technical reason the product has to be recalled. Now, you want to make sure that the product you have in your refrigerator is safe. So in the late '90s we developed together patient organizations, together with regulators, a system where each individual can register into a um . . . system and it allows you to obtain information in any manner you choose; letter, email, phone call, fax, it's also on the website to ensure that the product that is in your refrigerator is safe. It's a voluntary system but very well accepted both in United States and in Canada.

MN: In laymen's terms what did the industry do to make some of the products safer for the hemophiliac community?

JB: The hemophilia community is a very special community because they need Factor 8 products, there's more but let's use it as Factor 8, to save their lives. Now, the clinic situations for individuals are different, Now the industry has developed different manufacturing technologies for these patients. Some of them use therapies that are made from human plasma, some of them are using technologies where you use ah. . . bioengineering processes to develop the same proteins but with a different technology. The problem is not everybody can use, use that therapy so you need both. So what you need to do is you need to make sure that both therapy are safe, effective, and meet all the regulatory requirements and um . . . as I have been able to demonstrate in other . . . um . . . situations, the standards that we have place for both recombinant and plasma derived show that there's has been no transmission of infectious disease for over two decades.

MN: Is there a more lay way to describe recombinant. . . is it accurate to say sort of gene therapy has allowed us to make products that don't have . . .

JB: No I wouldn't say because that's something totally different. No you can't say that.

MN: Have you figured out a way to say it to a really lay audience?

JB: I would be very careful ah . . . because you go into an enormous amount of technicalities. And um . . . ah. . . I wouldn't do it.

MN: Ok

JB: Let's put it this way, I'm very uncomfortable to use other terms

MN: Ok, I don't want to make you use a term that would make you uncomfortable so let's just explain recombinant one more time, maybe if you say it a different way we'll have two choices of the way you say it. However you're comfortable just re-explain recombinant.

JB: Ok, Hemophilia patients they need clotting factors that they do not have for whatever reasons. In order to get those factor 8, those are the most commonly used, Factor 8 products you can manufacture them in two ways. You can used human plasma and um . . . further develop them to a factor 8 concentrate, or you can use products that are made with different biotechnology means where you don't use the plasma but you end up with the same protein. The problem is, there is not eh. . . any therapy that would be suitable for each individual patients. The clinical situations are different therefore, you need both therapies to make sure that the. . . the patient gets a therapy that he needs.

MN: Give me the lead in that says industry worked to pioneer these new therapies. You didn't say the piece about over time industry has worked with new technologies to develop factor 8 in a new way.

JB: Yeah but the problem is that you try to put me, some words in my mouth and I'm very uncomfortable

MN: No, what I'm trying to do is have people understand that technology has changed since the days where our film stops. What's changed in those twenty years in the way blood products are received?

JB: Ok. When I got involved with the association in the mid '90s um . . . at that moment the only therapy that was available for, for hemophilia patients were the therapies that were made from human plasma. The systems are in place today show that those products are very safe and effective. There has been no transmission for over two decades. In addition to the plasma derived therapies there is another technology developed where factor 8 is made without the use of human plasma. That serves another group of patients very well. You need both therapies. You cannot just have one therapy because the clinical situation is different from individual to individual. But if you take the two together, the development of different technologies as well as the other standards in place, to make the plasma derived safer today then it was yesterday it results in very safe therapies. Let me point out something else that's very important. Today, the biggest problem for a hemophilia patient is not safety. That was an issue that was in the past but is no longer today the issue. The issue today is having products.

Let me give you an example; when I went to a meeting at the World Federation of Hemophilia a few years ago and I hear this nurse talking about a two year old boy in Cambodia. And this boy comes in crying, terrible pain because he has a bleed in his joint. The nurse said to the audience, "The only thing I can do is send the boy home, knowing that he was gonna die." Today, patients die because there is no therapy available.

I just came back from China last week. Every year, 500 patients in China die because there is no therapy available. That is the problem we need to work on today. And yes, we have worked very hard to product, to make the products very safe and they are very safe but the biggest problem today is make them available to all patients in the world and not to a selected group.

MN: The industry sort of went above and beyond the FDA standards can you talk about that for me?

JB: The industry felt it was very important to have systems in place that ensure the collection of safe plasma from committed donors. So two set of standards were put in place. One, focused on the collection of plasma and that has multiple components. You have a system where you wanna check that each individual that becomes a donor has not been deferred in the past. If that happened, you cannot accept a donor again.

MN: I'm trying to understand the role, the relationship between the FDA regulatory standards and the industry's own, the PPTA's standards that go above and beyond what the FDA requires. Is that correct.

JB: That is what I was answering.

MN: You don't have to go into the specific standards because you did it for us

JB: Ok. Then rephrase your question.

MN: Are the standards put in place by the PPTA above and beyond the FDA standards? And if so, why? What was the PPTA trying to do by creating this extra level?

JB: The therapies that are made from human plasma um . . . have to be safe and effective. The regulatory agents look at it very carefully, you have to submit ah. . .submit data and once the data approved you can put a product on the market. The industry has done more. We wanna make sure that the whole system is so robust that we can demonstrate on all levels that the products are safe and effective and therefore, we look at two, some different components. We look at additional criteria for donor ah. . . related issues like donor deferral, like testing, like donor qualification as well as some manufacturing standards inventory hold ah. . . the, the kind of technology that is being used, above the regulatory requirements.

The result of that is that we have not seen any transmission in the last two decades. Another point that regulatory agencies have recognized these standards are currently considering codifying these standards and put them into regulation because they have seen the value.

MN: Are the FDA standards enough as far as you're concerned . . . what would be the reasons for going above and beyond the regulatory standards in place?

JB: The regulatory standards in place both in the United States by FDA and, and Europe are robust and are very stringent and result in safe and effective therapies. That doesn't mean that industry cannot go further. And it's not because we question FDA, We support FDA. The FDA is doing a very good job. But we can do more to show our responsibility to our part and that's why we developed voluntary standards.

MN: The voluntary standards put in place make sense so intuitively, what do you think stood in the way of having that prior to the mid '90s? What factors went into how donors were recruited and why wasn't it as intuitive as it probably seems to you?

JB: Well standards are being developed based on a knowledge that's available at a certain time. And the when you take into account all the information that is available you try to think about what can we do better today than we did yesterday and standard development is part of that. It's not to criticize what happened in the past but I think doing nothing, that will be a legitimate cr. . . criticism and the fact that we have these standards recognized by regulators and patients all over the world is a demonstration of the effectiveness of our standards.

MN: What is it about the hemophilia community that has allowed industry to work with the community in pretty unique way in regards to products?

JB: The patients organizations whether it's hemophilia or primary immune deficiency or (?) or you name it, they all play a very important role. The most important factor is that any of the

therapies ah. . . are life saving. If that therapy cannot be ah. . . provided a hemophilia patient cannot lead a normal life, may die, same true for immune deficiency. Therefore, for us it's very important to deal with all hemophilia but all patients organizations to understand the specific needs of that population. We deal with hemophilia, we deal with immune deficiency and all the others that are mentioned as well. Ah. . .for me, every patient is unique and for me I need to listen to all patients.

MN: Did you find that post tragedy the hemophilia became a more of an advocacy group?

JB: When I meet with patients all over the world, when you meet patients um. . . or parents of patients that lost a child that's terrible. I have met patients. . . ah . . .parents that lost ah. . . patients as a result of the tragedy in the '80s with the hemophilia community. I spoke with patients that lost children because there was not therapy for the primary immune deficiency. Um . . . I spoke with parents that lost multiple childs. It. . .it's terrible. And if there is anything that I can do personally and work on that is to convince the policy makers the importance of the therapies we produce that are life saving and that any barrier that would make these products available to these patients should be removed. Unfortunately, sometimes there are political barriers. There are ah . . .all kind of barriers to trade. They should not play a role. When the technicalities are available ah. . . for safe and effective therapy that is what matters.

MN: Plasma industry in particular has such stringent regulatory standards on them and safety standards on them that it really does have a more significant impact on this industry than maybe on other industries. Can you talk about that?

JB: Well, when ya, when ya talk about unique situation of this industry, um . . .unlike other pharmaceuticals that I used for a lot of patients. For example, hypertension, high blood pressure or depression, or diabetes you talk about hundreds of thousands or millions of patients. In the United States when you talk about hemophilia it's less than 20,000. When you talk about emphysema it's less than 5,000. When you talk about immune deficiency it's less than 50,000 the definition of an orphan drug in the United States says; "Any patient group than 200,000 will have special considerations." All our patients together don't even meet that definition. So as a result, of that their manufacturing cost for these therapies are relatively high because (entry?) numbers are relatively low. That is the main difference between our sector and ah. . . traditional pharmaceutical.

MN: The safety standards add another expense can you reference that at all?

JB: Yeah, the regulatory requirements for this industry are very stringent. And, and they're very intense as they should because they have to result in safe and effective therapies. Our voluntary standards are very robust and have um . . . given additions layers of comfort, comfort for regulators and patients. They cost money. They're very expensive. The manufacturer of a therapy between eh. . . donation and delivery of products is over seven month. Can take over a year so it's very capital intensive. So if you don't realize the relatively small number of patients that are being served, then you understand the relative cost is higher than what you see in traditional pharmaceutical. But at then end of the day when you think about it, it in terms of cost or cost of life, it's low. There's nothing more important than a life that's being saved.

MN: What's the impact on patients when um . . . without profit without worrying about the business concern what's the impact on patients?

JB: Well, in a free economy any industry that works has to work under economic acceptable circumstances. Um. . . a few years ago our industry um . . . had significant issues and were losing money. People were losing their job. So, what happened was an enormous improvement in efficiency without jeopardizing safety and quality so you can ensure that the supply of products to patients was continued. It's in the benefit of the patients that we have a healthy industry. That a healthy industry can collect the plasma can, can sell the products in a . . . in a economic acceptable fashion and has money to do research and development to develop newer therapies, new technologies that make it better tomorrow than it is today. And that is an important message for all. I know it's said by many people but again, we you are saving lives cost should not be the factor that limits saving a life.

MN: Also in the PPTA materials all of these safety standards describe a higher cost of obtaining these, do you think that was part of the problem in the '60s and '70s. That made it harder to get a safer donor pool or donor population. Was it the cost/benefit that was making it hard? Were there other challenges?

JB: I came into the industry in the mid '90s and I saw that there were standards in place and they needed to be further developed, I helped on that to ensure safe and effective therapies. I cannot talk about anything in the '60s. I wasn't even there. I was going to high school and I hardly had any idea what was going on in the world.

MN: But you were in the Netherlands at the time you were working in the '80s in plasma products?

JB: I have to think back, in the '80s I was working in the Netherlands you're right.

MN: Were you in plasma products or something totally different?

JB: I was also involved in plasma products.

MN: So it was swirling around at the time you were in plasma. . . these issues.

JB: When I heard about these issues for the first time um . . . I was working in the pharmaceutical industry heard it and I started to work for industry related to this sector in 1990 um. . . so I've seen it. I learned about it and knew that um. . . if I could play a role to make products safer today, tomorrow than they are today than I would do it. And here I am.

MN: What lessons do you think should be learned from what happened in the '80s? What lessons have you learned and implemented at PPTA and what enduring lessons should people keep in mind?

JB: In life, we have to learn that we have to do a better job today than we did yesterday. We have to learn from any issues that have happened in the past. We should not be ignorant. We should be careful. We should be open-minded. We should be willing to make improvements wherever we can. But there's one other lesson that we have to learn; and it is that if we look at hemophilia today 300,000 patients in the world have no therapy at all. Patients today die because there's no therapy.

I would like to use my personal example last week. I went to China, and before I was able to enter the country I had to be checked three times for my temperature. I had to fill out paper work to make sure that nobody is going to enter China that has a suspected relationship to the flu. Now, I'm very grateful for authorities that ah. . . have these measures in place to prevent anything damaging happening to the population. Why is it then that there's no therapy available in China that 500 people die every single year, nobody's gonna do anything about it? That's wrong. So if I can change that, I will do it.

MN: Is there anything else that you wanna add that we didn't cover? Actually let's say very explicitly, you said it, are these products safe today?

JB: Oh yes, These products are very safe. Very safe and has resulted in a quality of life in hemophilia patients that we've never seen before. We see people ah. . . on motorcycles,, mountain climbing, ah. . . skydiving. That was something that was unheard of decades ago.

MN: So if you don't mind repeating that part of products being safe.

JB: All the therapies made from human plasma today are very safe, and have reached a level that we've never seen before.

MN: Is there anything else that you wanted to add that you think we didn't cover?

JB: Um. . . The one thing that is very important to me and I've said it several times is that we have to realize that there are many patients in the world that have no therapy at all. And it's a shame, it's a shame. There's no need today to have therapies not being available for political reasons.

MN: So why? Why isn't it available in China?

JB: Because they don't allow the import of these products.

MN: It's purely a nationalistic protection? They're afraid of (factor) products given what have happened?

JB: Well, that, that's part of it. It's. . .it's. . . it's no longer there . . .and . . . and why would you. . .

MN: Just say that for me in a full sentence because I think that will help include the part you want to include.

JB: Ok give me twenty seconds to formulate my thought and I'll do that and I can have my water.

Ok I'll . . . I'll give an answer and you can do with it what you want ok. But I'm going to do it in a very personal form. Ok? When I'm traveling in the world, sometimes I'm traveling with hemophilia patients. And when I see what they had to go through when they go through security on an airport to explain why they have medication that's a very painful and, and sometimes embarrassing process because the security agent don't understand. But if you realize that those patients are in a relative fortunate situation because they can travel and they have medication. There are so many patient that have nothing. Um. . . my wife went to the Philippines last year and there was a situation in a hospital there was one therapy available for hemophilia patient. And at that moment somebody came in with a motorcycle accident and there was another patient that had a bleeding, so who are you gonna give the therapy to? And decision was made to give it to the one with the motorcycle accident. The next day, the other patient died. And when you look at other countries, China where there are limitations about the availability of Factor 8 it's even in the media that patients are dying. I feel, that we have a responsibility to do everything we can to make ore products available and help to convince policy makers what the real priorities should be, and one of them is health care for their population and have them lead a normal life. When I see today patients in the western world, childs no joint problems at all leading a normal life, that's wonderful. I would like to see that in other parts of the world as well.

MN: Explain to me that there are some countries that have this instinctive response to what happened in the '80s but that these products are in fact safer so that's the regret. That's what's regrettable about this situation.

JB: It's unfortunate that some countries have national policies in place that only allow the use of local plasma for being the source material of their um . . of their therapies. And that limits the availabilities of therapies and this is happening in many countries of the world and that's something that should be reconsidered.

MN: I don't think most of our audience will understand the connection between what happened in the '80s and sort of why these countries are afraid today.

JB: When you have situations in countries where products are not available on the scale as they should be there are multiple reasons for that. If it's a technical, scientific reason that's one thing. If it's political, now why is it political? When you have countries that do not allow the import of products eh . . . because of what happened in the '80s that means they are standing still. They are not looking at technological developments, they are not looking at the safety records of the product today and that should be the reason why those restrictions should be lifted. If other countries look at the criteria for the collection and only use plasma collected in their own territory are not willing to import products of, of plasma that's collected in other countries another unnecessary limitation and the end result is patients are suffering. And that's unnecessary.